THERAPEUTIC COMPOUNDS AND RELATED METHODS OF USE

RELATED APPLICATIONS

This application claims priority to U.S. Provisional Applications Serial Nos. 61/291,544, entitled "Therapeutic Compounds and Related Methods of Use" filed on December 31, 2009; 61/291,550, entitled "Therapeutic Compounds and Related Methods of Use" filed on December 31, 2009; and 61/291,554, entitled "Therapeutic Compounds and Related Methods of Use" filed on December 31, 2009, all of which are herein incorporated by reference in their entireties.

BACKGROUND OF INVENTION

Tyrosine phosphorylation of synaptic receptors and signaling molecules regulates synaptic activity. A number of protein tyrosine phosphatases specifically expressed within the brain have been identified, including STEP (for STriatal-Enriched tyrosine Phosphatase, also known as PTPN5). Recent evidence suggests that STEP plays an important role in synaptic plasticity, for review see (Braithwaite SP, et al., (2006), Trends Neurosci, 29 (8): 452; Baum ML, et al., (2010), Commun Integr Biol, 3 (5): 419). STEP is specifically expressed within neurons of the central nervous system. As its name indicates, the highest expression level is within the striatum. However, more recent work has found that it is expressed at lower levels in multiple brain regions including the neocortex, amygdala, hippocampus, and embryonic spinal cord.

Four groups of proteins that STEP regulates have been identified: the mitogen-activated protein kinases (MAPKs), the tyrosine kinase Fyn, the N-methyl-D-aspartate (NMDA) receptor complex (specifically the NR2B subunit) and AMPA receptors (specifically, GluR2, (Zhang Y, et al., (2008), J Neurosci, 28 (42): 10561)). Three additional new substrates for STEP have also been recently discovered; proline-rich tyrosine kinase 2 (Pyk2; Xu J, et al., (2010), Abstracts of the Society for Neuroscience Meetings) , the fragile X mental retardation protein (FMRP) (Goebel-Goody SM, et al., (2010), Abstracts of the Society for Neuroscience Meetings) and the cell-death mediator Bak (Fox JL, et al., (2010), EMBO J, 29 (22): 3853). Tyrosine

phosphorylation of one member of the MAPK family, the extracellular signal regulated kinase (ERK), is necessary for the expression and maintenance of synaptic plasticity in many brain regions, and disruption of the ERK pathway leads to a disruption of learning and memory. One of the functions of these src and Pyk2 kinases is to phosphorylate NMDA receptors, thereby modulating their channel conductance properties and facilitating their movement toward the surface of neuronal plasma membranes. Pyk2 and Fyn tyrosine kinases are activated by phosphorylation on tyrosine residues. NR2B phosphorylation on Tyrosine 1452 inhibits the receptor endocytosis. STEP acts as direct or indirect brake of NMDAR mediated signaling by either respectively dephosphorylating NR2B or its associated kinases, Pyk2 and Fyn. Activation of AMPA, NMDA receptors and MAPKs are required for the induction of several forms of long-term potentiation (LTP) and long-term depression (LTD). Hippocampal LTP is increased in transgenic mice model of Alzheimer lacking STEP (Zhang Y, et al., (2010), Proc Natl Acad Sci U S A, 107 (44): 19014). NR2B and AMPA receptor surface expression is increased in STEP KO mice. AMPA receptor endocytosis in group I metabotropic glutamate receptor I (mGluR) mediated LTD is mediated by a tyrosine phosphatase. AMPA receptor endocytosis induced by activation of group I mGLuR is blocked in STEP KO mice suggesting that STEP might also control mGluR mediated LTD.

Compounds that inhibit STEP activity should mimic the effects observed with the STEP KO and may be useful for treating conditions mediated by abnormal NMDA-receptor (NMDA-Rs) and/or MAP kinase pathway signaling. Both may mediate cognition, learning and memory, neurogenesis, and may also affect neuronal plasticity, pain perception, mood and anxiety, and neuroendocrine regulation.

Modulation of NMDA-Rs:

STEP decreases the tyrosine phosphorylation level of NMDA-Rs. Less phosphorylated NMDA-Rs have lower conductance states and thus will allow less current and fewer ions to pass. The NMDA-Rs will therefore be functionally less active (Alvestad RM, et al., (2003), J Biol Chem, 278 (13): 11020), which can lead to schizophrenic symptoms. Hypofunction of NMDA-Rs has been liked to

schizophrenia. For example, phencyclidine, ketamine, and other noncompetitive antagonists at NMDA-type glutamate receptors can exacerbate symptoms in patients (Lahti AC, et al., (1995), Neuropsychopharmacology, 13 (1): 9) and may produce a range of psychotic symptoms in volunteers that are similar to those of schizophrenic patients. NMDA-R hypofunction is also linked to psychosis and drug addiction (Javitt DC and Zukin SR, (1991), Am J Psychiatry, 148 (10): 1301). Chronic treatment of atypical antipsychotic clozapine and risperidone in mice result in significant increase of phosphorylation of ERK, NR2B and Pyk2 on tyrosine residues recognized by STEP (Carty NC, et al., (2010), Abstracts of the Society for Neuroscience Meetings). Treatment of these anti-psychotics also enhances cAMP and STEP phosphorylation. Since PKA mediated phosphorylation of STEP is know to inactivate STEP, these results suggest that STEP inhibition mediates the beneficial effect of antipsychotic drugs. Recent studies have linked abnormal NMDA-R activity and expression of STEP to the cognitive decline observed in Alzheimer's disease or transgenic mice expressing mutant APP (Tg2576 mice) (Snyder EM, et al., (2005), Nat Neurosci, 8 (8): 1051; Hynd MR, et al., (2004), J Neurochem, 90 (4): 913; Kurup P, et al., (2010), Channels (Austin), 4 (5)). More specifically, STEP KO mice are less susceptible to PCP-induced hyperlocomotion and PCP-induced cognitive deficits in the object recognition tasks (Carty NC, et al., (2010), Abstracts of the Society for Neuroscience Meetings). Compared to the Tg2576 mice expressing STEP, Tg2576 lacking STEP gene showed rescue in their deficits in hyppocampal LTP and in different behavioral cognitive tasks. Altogether, these results suggest that STEP inhibitors might represent a novel class of drugs that can treat both positive symptoms and cognitive deficit associated with schizophrenia.

Medications that modulate glutamatergic neurotransmission via NMDA-Rs may be also effective in treatment for mood and anxiety disorders. Administration of NMDA-R antagonists has anxiolytic effects in rodent models of anxiety (Falls WA, et al., (1992), J Neurosci, 12 (3): 854; Miserendino MJ, et al., (1990), Nature, 345 (6277): 716). NMDA-Rs antagonist like ketamine has been shown to be effective in drug-resistant unipolar depression (Machado-Vieira R, et al., (2009), Pharmacol Ther, 123 (2): 143).

Abnormal balance between the activity of NMDA receptors at synaptic (prosurvival linked to ERK activation) and extrasynaptic (proapoptotic linked to p38 activation) sites has been proposed in cellular and mouse model of Huntington Disease (HD) (Milnerwood AJ, et al., Neuron, 65 (2): 178). YAC128 mouse model (containing high number of glutamine repeat on huntingtin) of HD showed an increased activity of extrasynaptic NMDA receptors (NR2B subunit) and require p38 and caspase-6 cleavage activation. In YAC128 mice, NR2B synaptic expression is associated with high STEP expression and activity and a reduction in NR2B expression and phosphorylation (Gladding CM, et al., (2010), Abstracts of the Society for Neuroscience Meetings). Extrasynaptic NMDA receptors couple preferentially to excitotoxicity via calpain-mediated cleavage of STEP and activation of p38 (Xu J, et al., (2009), J Neurosci, 29 (29): 9330). Inhibiting STEP activity might therefore shift the balance toward the NMDA receptor/ERK synaptic prosurvival signaling pathway.

Modulation of ERK pathway:

STEP inhibition may translate into activation of ERK1/2 kinases, for example, in the central nervous system (CNS). Activation of the ERK pathway in the CNS can mediate neurotrophic pathways involved in cellular resilience. ERK signaling directly affects Bak phosphorylation through inhibition of STEP to promote cell survival (Fox JL, et al., (2010), EMBO J, 29 (22): 3853). BDNF and other neurotrophins can block apoptosis and increase cell survival of different type of CNS neurons *in vitro* and *in vivo* via stimulation of the ERK pathway. Mood stabilizers effective in bipolar disorder like valproate and lithium may be potent activators of ERK activity. This effect on ERK activation is believed to be responsible for the neurotrophic effects of mood stabilizers observed *in vitro* or in brains of treated patients with bipolar disorder, for review see (Engel SR, et al., (2009), Mol Psychiatry, 14 (4): 448; Chen G and Manji HK, (2006), Curr Opin Psychiatry, 19 (3): 313; Machado-Vieira R, et al., (2009), Bipolar Disord, 11 Suppl 2 92). *In vivo* disruption of STEP activity was shown to activate MAPK pathway, leading to significant rescue from neuronal cell death after pilocarpine-induced status epilepticus (Choi YS, et al., (2007), J Neurosci, 27 (11): 2999). Increasing cellular resilience could therefore limit or reduce neuronal

loss in several neurologic disorders. Recent work has suggested a positive role for STEP inhibition in fragile X syndrome (FXS). This disorder results from the mutation of fmr1 gene coding for the fragile X mental retardation protein (FMRP). STEP binds to FMRP and its expression is dysregulated in FXS. FMR KO mice model displayed audiogenic seizures. FMR KO mice lacking STEP gene show a significant reduction of these seizures (Goebel-Goody SM, et al., (2010), Abstracts of the Society for Neuroscience Meetings), suggesting that STEP modulators might be therapeutic approach for FXS.

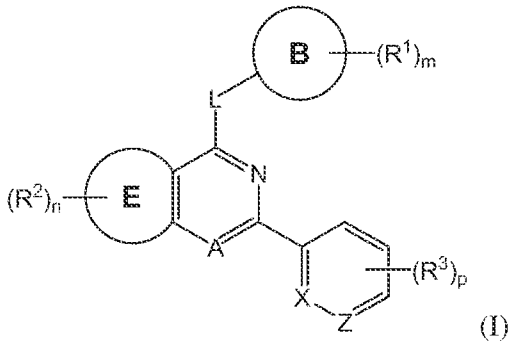
Various substituted heterocyclic compounds are disclosed in the art. For example, WO 02/062767 discloses quinazoline derivatives; WO 03/000188 discloses quinazolines and uses thereof; WO 2005/042501 discloses norepinephrine reuptake inhibitors for the treatment of central nervous system disorders; WO2006/058201 discloses heterocyclic and bicyclic compounds, compositions and methods; WO 2007/104560 discloses substituted 4-amino-quinazoline derivatives as regulators of metabotropic glutamate receptors and their use for producing drugs; WO 2007/133773 discloses CDKI pathway inhibitors; WO 2008/009078 discloses 4,6-DL- and 2,4,6-trisubstituted quinazoline derivatives useful for treating viral infections; WO 2009/000085 discloses quinoline and quinazoline derivatives useful as modulators of gated ion channels; US 2009/0143399 discloses protein kinase inhibitors; and Japan Publication Number 2007-084494A discloses substituted bicyclic compounds.

SUMMARY OF INVENTION

Described herein are compounds, pharmaceutical compositions containing the compounds, and methods of using the compounds to treat a disorder, e.g., schizophrenia or cognitive deficit, in a subject. The compounds disclosed herein include quinoline- and quinazoline-containing compounds that modulate (e.g., inhibit) the activity of STEP.

The present invention provides therapeutic compounds, pharmaceutical composition comprising said compounds, use of said compounds and method for treating or preventing a disorder as descrived in items 1 to 42 below.

Item 1. A compound of formula (I):



(I)

or a salt thereof,

wherein:

A is CR^4 or N;

B is aryl, cyclyl or a 5- or 6-membered heteroaryl;

m is 0, 1, 2, 3, 4 or 5;

E is aryl or a 5-membered heteroaryl;

n is 0, 1, 2, 3 or 4;

when E is aryl, n is 0, 1, 2, 3 or 4; and when E is a 5-membered heteroaryl, n is 0, 1, 2 or 3;

L is NR^5, S, O or a direct bond;

one of X and Z is N and the other is CH;

p is 0, 1, 2, 3 or 4;

each R^1, R^2 and R^3 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silyloxyalkynyl, silylalkoxy, silylalkoxyalkyl, –CN, oxo, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^6; wherein two R^1, together with the atoms to which they are attached, may form an optionally substituted cyclyl, heterocyclyl, aryl or heteroaryl ring;

R^4 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^cSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$, –OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$, each of which is optionally substituted with 1-3 R^6;

R^5 is hydrogen; or when m is not 0, R^5 and one R^1 may be taken together with the atoms to which they are attached to form an optionally substituted heteroaryl or heterocyclyl ring;

each R^6 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thioxo, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^cSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$,–OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$, each of which is optionally substituted with 1-3 R^7;

each R^7 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thioxo, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^cSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$, –OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$, each of which is optionally substituted with 1-3 R^9;

each R^9 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thioxo, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –

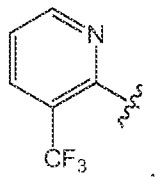
$NR^bR^{b'}$, $-OC(O)NR^bR^{b'}$, $-NR^cC(O)OR^{c'}$, $-SO_2NR^bR^{b'}$, $-NR^cSO_2R^{c'}$, $-NR^cC(Y)NR^bR^{b'}$, $-OR^d$, $-SR^{d'}$, $-C(Y)R^e$ or $-S(O)_qR^f$;

Y is O or S;

q is 1 or 2 and

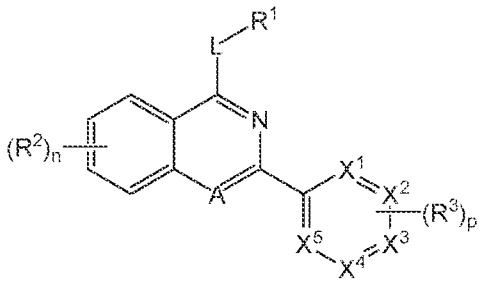
each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, acyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy or silylalkoxyalkyl;

wherein when B is phenyl, two R^1 are not taken together to form a pyrazole ring; and

when B is phenyl, R^2 is not 

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a compound of formula (II):



(II)

or a salt thereof,

wherein:

L is CR^4R^5, O, C(O), $NR^6C(O)$ or NR^7;

A is N;

each X^1, X^2, X^3, X^4 and X^5 is independently CH or N, provided that at least two of X^1, X^2, X^3, X^4 and X^5 are N;

n is 0, 1, 2, 3 or 4;

p is 0, 1, 2 or 3;

R^1 is C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl or heterocyclylalkyl, each of which is optionally substituted with 1-5 R^9; wherein R^1 or R^9 is optionally taken together with one of R^4, R^5, R^6 or R^7, and the atoms to which they are attached, to form a cyclyl, heterocyclyl, aryl or heteroaryl ring that is optionally substituted with 1-3 R^{10};

each R^2 and R^3 is independently hydrogen,C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^cSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$, –OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$; each of which is optionally substituted with 1-3 R^{11};

each R^4, R^5, R^6 and R^7 is independently hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^cSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$, –OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$;

each R^9, R^{10} and R^{11} is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thioxo, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^cSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$,–OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{12};

wherein, two R^9, two R^{10} or two R^{11} is optionally taken together with the atoms to which they are attached to form an optionally substituted cyclyl, heterocyclyl, aryl or heteroaryl ring;

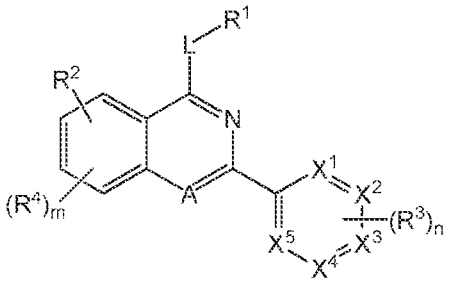
R^{12} is $-OR^d$;

Y is O or S;

q is 1 or 2 and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e, $R^{e'}$ and R^f is independently hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, acyl, cyclyl, heterocyclyl, aryl, heteroaryl, cyclylalkyl, heterocyclylalkyl, arylalkyl or heteroarylalkyl and

a compound of formula (III):



(III)

or a salt thereof,

wherein:

A is CH or N;

L is O, a direct bond or NR^6;

one of X^1, X^2, X^3, X^4 and X^5 is N and the others are CH;

m is 1, 2 or 3;

n is 1, 2, 3 or 4;

R^1 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, alkoxyalkyl, hydroxyalkyl, heteroaryl , heteroarylalkyl,arylalkyl, $-C(Y)R^e$, cyclyl ,cyclylalkyl or heterocyclyl, each of which is optionally substituted with 1-3 R^7;

R^2 is aryl or heteroaryl, each of which is optionally substituted with 1-5 R^9;

each R^3 or R^4 is independently hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, $-CN$, $-NO_2$, $-C(O)OR^a$, $-C(Y)NR^bR^{b'}$, $-NR^cC(Y)R^{c'}$, $-NR^bR^{b'}$, $-OC(O)NR^bR^{b'}$, $-NR^cC(O)OR^{c'}$, $-SO_2NR^bR^{b'}$, $-NR^cSO_2R^{c'}$, $-NR^cC(Y)NR^bR^{b'}$, $-OR^d$, $-SR^{d'}$, $-C(Y)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{10};

R^6 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, cyclyl or heterocyclyl, each of which is optionally substituted with 1-3 R^{11};

each R^7, R^9 and R^{10} is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thioxo, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^cSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$,–OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{12}; wherein two R^7, two R^9 or two R^{10} are optionally be taken together with the atoms to which they are attached to form an optionally substituted cyclyl, heterocyclyl, aryl or heteroaryl ring;

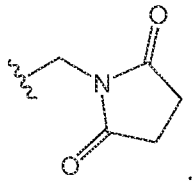
each R^{11} and R^{12} is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thioxo, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^cSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$,–OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$,each of which is optionally substituted with 1-3 R^{13};

R^{13} is independently C_1-C_8 alkyl, haloalkyl, halo, heterocyclyl, cyclyl,oxo or –$C(Y)NR^bR^{b'}$;

Y is independently O or S;

q is 1 or 2 ;and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, acyl, haloalkyl alkoxyalkyl, alkylaminoalkyl, dialkylaminoalkyl, cyclyl, heterocyclyl, aryl, heteroaryl, cyclylalkyl, heterocyclylalkyl, arylalkyl or heteroarylalkyl;

with proviso R^9 is not  .

Item 2. The compound according to item 1 represented by general formula(I) or a salt thereof,

wherein:

A is CR^4 or N;

B is aryl ,cyclyl or a 5- or 6-membered heteroaryl;

m is 0, 1, 2, 3, 4 or 5;

n is 0, 1, 2, 3 or 4;

E is aryl or a 5-membered heteroaryl;

when E is aryl, n is 0,1, 2, 3 or 4; and when E is a 5-membered heteroaryl, n is 0, 1, 2 or 3;

L is NR^5 ,S,O or a direct bond;

one of X and Z is N and the other is CH;

p is 0, 1, 2, 3 or 4;

each R^1, R^2 and R^3 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silyloxyalkynyl, silylalkoxy, silylalkoxyalkyl, –CN, oxo,–NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^eSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$, –OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$, each of which is optionally substituted with 1-3 R^6; wherein two R^1, together with the atoms to which they are attached, may form an optionally substituted cyclyl, heterocyclyl, aryl or heteroaryl ring;

R^4 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl,

alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^cSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$, –OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$, each of which is optionally substituted with 1-3 R^6;

R^5 is hydrogen; or when m is not 0, R^5 and one R^1 may be taken together with the atoms to which they are attached to form an optionally substituted heteroaryl or heterocyclyl ring;

each R^6 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thioxo, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^cSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$,–OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$, each of which is optionally substituted with 1-3 R^7;

each R^7 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thioxo, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^cSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$,–OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$,each of which is optionally substituted with 1-3 R^9;

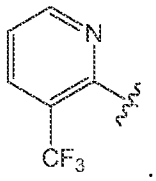
each R^9 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thioxo, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^cSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$,–OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$;

Y is O or S;

q is 1 or 2; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, acyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy or silylalkoxyalkyl;

wherein when B is phenyl, two R^1 are not taken together to form a pyrazole ring; and

when B is phenyl, R^2 is not 

.

Item 3. The compound according to item 2 represented by general formula (I) or a salt thereof,

wherein:

A is CH or N;

B is aryl, cyclyl or a 5- or 6-membered heteroaryl;

m is 0, 1, 2, 3 or 4;

E is aryl or a 5-membered heteroaryl;

n is 0, 1 or 2;

when E is aryl, n is 0, 1 or 2 and when E is a 5-membered heteroaryl, n is 0 or 1;

p is 0, 1 or 2;

each R^1, R^2 and R^3 is independently C_1-C_8 alkyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silyloxyalkynyl, –CN, oxo, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–SO_2NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^6; wherein two R^1, together with the atoms to which they are attached, may form an optionally substituted cyclyl, heterocyclyl, aryl or heteroaryl ring;

each R^6 is independently C_1-C_8 alkyl, heterocyclyl, heterocyclylalkyl, hydroxyalkyl, halo, haloalkyl, haloalkoxy, alkoxyalkyl, oxo, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OR^d$ or $–C(Y)R^e$, each of which is optionally substituted with 1-3 R^7;

each R^7 is oxo; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, acyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, haloalkyl, dialkylaminoalkyl, hydroxyalkyl or alkoxyalkyl.

Item 4. The compound according to item 3 represented by general formula (I) or a salt thereof,

wherein:

B or two R1 and B are taken together to form a group is phenyl, dihydroindenyl, dihydrobenzoxazinyl, dihydrobenzodioxinyl, chromenyl, tetrahydroquinoxalinyl, tetrahydroisoquinolinyl, tetrahydroquinolinyl, dihydroquinolinyl, quinolyl, isoquinolinyl, tetrahydroquinazolinyl, indolinyl, dihydrobenzothiazolyl, dihydrobenzimidazolyl, dihydrobenzoxazolyl, isoindolinyl, dihydroisobenzofuranyl, benzofuryl, benzothienyl, benzodioxolyl, indolyl, indazolyl, benzoimidazolyl, benzotriazolyl, benzisoxazolyl, benzoxazolyl, benzothiazolyl, benzoxadiazolyl, dihydrocyclopentathiophenyl, tetrahydrobenzothiophenyl, thienyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, thiadiazolyl, pyrrolyl or pyridyl;

E is phenyl, thienyl or pyrrolyl ;

when E is phenyl , n is 1 or 2; and when E is thienyl, n is 0 or 1;

each R^1, R^2 and R^3 is independently C_1-C_8 alkyl ,C_2-C_8 alkynyl, phenyl, thienyl, pyrrolyl, oxadiazolyl, pyridyl, benzodioxolyl, furyl, pyrimidinyl, oxazolyl, isoxazolyl, pyrazolyl, C_3-C_8 cycloalkyl, piperidyl, pyrrolidinyl, morpholinyl, dioxolanyl, phenylalkyl, thiomorpholinylalkyl, pyrrolidinylalkyl, morpholinylalkyl, piperidylalkyl, piperazinylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxyalkyl, silyloxyalkynyl, –CN, $–NO_2$, oxo, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, –

$SO_2NR^bR^{b'}$, $-OR^d$, $-SR^{d'}$, $-C(Y)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^6;

each R^6 is independently C_1-C_8 alkyl, tetrahydropyranyl, morpholinyl, thiomorpholinyl, morpholinylalkyl, dialkylaminoalkyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, oxo, –CN, $–NO_2$, $–C(O)OR^a$, $–NR^cC(Y)R^{c'}$, $–C(Y)NR^bR^{b'}$, $–NR^bR^{b'}$, alkoxyalkyl, $–OR^d$ or $–C(Y)R^e$; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 cycloalkyl, phenyl, pyridyl, dihydroindenyl, morpholinyl, tetrahydropyranyl, piperidyl, pyrrolidinyl, piperazinyl, thiomorpholinyl, phenylalkyl, thienylalkyl, furylalkyl, pyridylalkyl, tetrahydropyranylalkyl, dihydroindenylalkyl, tetrahydrofurylalkyl, hydroxyalkyl, thiazolylalkyl, pyrazolylalkyl, morpholinylalkyl, pyrrolidinylalkyl, dialkylaminoalkyl, piperidylalkyl, benzodioxolylalkyl, dihydrobenzodioxinylalkyl, benzothienylalkyl, C_3-C_8 cycloalkylalkyl, oxazolidinylalkyl, haloalkyl or alkoxyalkyl.

Item 5. The compound according to item 3 represented by general formula (I) or a salt thereof,

wherein:

B or two R1 and B are taken together to form a group is phenyl, dihydroindenyl, dihydrobenzoxazinyl, dihydrobenzodioxinyl, chromenyl, tetrahydroquinoxalinyl, tetrahydroisoquinolyl, tetrahydroquinolinyl, dihydroquinolyl, quinolyl, isoquinolyl, tetrahydroquinazolinyl, indolinyl, dihydrobenzothiazolyl, dihydrobenzimidazolyl, dihydrobenzoxazolyl, isoindolinyl, dihydroisobenzofuranyl, benzofuryl, benzothienyl, benzodioxolyl, indolyl, indazolyl, benzoimidazolyl, benzotriazolyl, benzisoxazolyl, benzoxazolyl, benzothiazolyl, benzoxadiazolyl, dihydrocyclopentathiophenyl, tetrahydrobenzothienyl, thienyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, thiadiazolyl, pyrrolyl or pyridyl;

E is phenyl, thienyl or pyrrolyl ;

when E is phenyl , n is 0, 1or 2; and when E is thienyl, n is 0 or 1;

each R^1, R^2 and R^3 is independently C_1-C_8 alkyl, C_2-C_8 alkynyl, phenyl, thienyl, pyrrolyl, oxazolyl, oxadiazolyl, pyridyl, benzodioxolyl, furyl, pyrimidinyl, isoxazolyl,

pyrazolyl, C_3-C_8 cycloalkyl, piperidyl, pyrrolidinyl, morpholinyl, dioxolanyl, phenylalkyl, thiomorpholinylalkyl, pyrrolidinylalkyl, morpholinylalkyl, piperidylalkyl, piperazinylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxyalkyl, silyloxyalkynyl, –CN, –NO_2, oxo, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$OC(O)NR^bR^{b'}$, –$SO_2NR^bR^{b'}$, –OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$, each of which is optionally substituted with 1-3 R^6;

each R^6 is independently C_1-C_8 alkyl, tetrahydropyranyl, morpholinyl, thiomorpholinyl, morpholinylalkyl, dialkylaminoalkyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, oxo, –CN, –NO_2, –$C(O)OR^a$, –$NR^cC(Y)R^{c'}$, –$C(Y)NR^bR^{b'}$, –$NR^bR^{b'}$, alkoxyalkyl, –OR^d or –$C(Y)R^e$, each of which is optionally substituted with 1-3 R^7;

R^7 is oxo; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 cycloalkyl, phenyl, pyridyl, dihydroindenyl, morpholinyl, tetrahydropyranyl, piperidyl, pyrrolidinyl, piperazinyl, thiomorpholinyl, phenylalkyl, thienylalkyl, furylalkyl, pyridylalkyl, tetrahydropyranylalkyl, dihydroindenylalkyl, tetrahydrofurylalkyl, hydroxyalkyl, thiazolylalkyl, pyrazolylalkyl, morpholinylalkyl, pyrrolidinylalkyl, dialkylaminoalkyl, piperidylalkyl, benzodioxolilalkyl, dihydrobenzodioxinylalkyl, benzothienylalkyl, C_3-C_8 cycloalkylalkyl, oxazolidinylalkyl, haloalkyl, or alkoxyalkyl.

Item 6. The compound according to item 5 represented by general formula (I) or a salt thereof,

wherein:

R^1 is C_1-C_8 alkyl, phenyl, thienyl, pyrrolyl, oxazolyl, C_3-C_8 cycloalkyl, dioxolanyl, phenylalkyl, halo, haloalkyl, haloalkoxy, alkoxyalkyl, –CN, oxo, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$SO_2NR^bR^{b'}$, –OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$, each of which is optionally substituted with 1-3 R^6;

R^2 is C_1-C_8 alkyl, C_2-C_8 alkynyl, phenyl, thienyl, pyridyl, benzodioxolyl, furyl, pyrimidinyl, isoxazolyl, pyrazolyl, C_3-C_8 cycloalkyl, pyrrolidinyl, morpholinyl , thiomorpholinylalkyl, pyrrolidinylalkyl, morpholinylalkyl, piperiridylalkyl,

piperazinylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxyalkyl, silyloxyalkynyl, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$,–$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –OR^d or –$C(Y)R^e$, each of which is optionally substituted with 1-3 R^6;

R^3 is C_1-C_8 alkyl, halo, haloalkyl, –$NR^bR^{b'}$ or –OR^d, each of which is optionally substituted with 1-3 R^6.

Item 7. The compound according to item 4 or 6 represented by general formula (I) or a salt thereof,

wherein:

R^1 is C_1-C_8 alkyl, phenyl, thienyl, pyrrolyl, oxazolyl, C_3-C_8 cycloalkyl, dioxolanyl, phenylalkyl, halo, haloalkyl, haloalkoxy, alkoxyalkyl, –CN, oxo, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$SO_2NR^bR^{b'}$, –OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$;

R^2 is C_1-C_8 alkyl, C_2-C_8 alkynyl, phenyl, thienyl, pyridyl, benzodioxolyl, furyl, pyrimidinyl, isoxazolyl, pyrazolyl, C_3-C_8 cycloalkyl, piperidinyl, pyrrolidinyl, morpholinyl, thiomorpholinylalkyl, pyrrolidinylalkyl, morpholinylalkyl, piperiridinylalkyl, piperazinylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxyalkyl, silyloxyalkynyl, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$,–$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –OR^d, –$C(Y)R^e$ or -$S(O)_qR^f$;

R^3 is C_1-C_8 alkyl, halo, haloalkyl, –$NR^bR^{b'}$ or –OR^d.

Item 8. The compound according to item 7 represented by general formula (I) or a salt thereof,

wherein:

B or two R1 and B are taken together to form a group is phenyl, dihydroindenyl, dihydrobenzoxazinyl, dihydrobenzodioxinyl, chromenyl, tetrahydroisoquinolyl, tetrahydroquinolinyl, dihydroquinolyl, quinolyl, tetrahydroquinazolinyl, indolinyl, dihydrobenzothiazolyl, dihydrobenzimidazolyl, dihydrobenzoxazolyl, isoindolinyl, benzofuryl, benzothienyl, benzodioxolyl, indolyl, indazolyl, benzoimidazolyl, benzotriazolyl, benzisoxazolyl, benzoxazolyl, benzothiazolyl, benzoxadiazolyl,

tetrahydrobenzothienyl, thienyl, thiazolyl, imidazolyl, pyrazolyl, thiadiazolyl or pyridyl;

m is 1, 2, 3 or 4;

R^1 is C_1-C_8 alkyl, halo, haloalkyl, haloalkoxy, alkoxyalkyl, –CN, oxo, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–SO_2NR^bR^{b'}$, $–OR^d$, or $-S(O)_qR^f$;

R^2 is C_1-C_8 alkyl, C_3-C_8 cycloalkyl, thiomorpholinylalkyl, pyrrolidinylalkyl, morpholinylalkyl, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxyalkyl, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$,$–NR^bR^{b'}$, $–OR^d$, $–C(Y)R^e$ or $-S(O)_qR^f$;

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 cycloalkyl, phenyl, dihydroindenyl, morpholinyl, tetrahydropyranyl, piperidyl, pyrrolidinyl, thiomorpholinyl, phenylalkyl, thienylalkyl, pyridylalkyl, tetrahydropyranylalkyl, dihydroindenylalkyl, tetrahydrofurylalkyl, hydroxyalkyl, morpholinylalkyl, pyrrolidinylalkyl, dialkylaminoalkyl, piperidylalkyl, benzodioxolilalkyl, dihydrobenzodioxinylalkyl, C_3-C_8 cycloalkylalkyl, haloalkyl or alkoxyalkyl.

Item 9. The compound according to item 1 represented by general formula (II) or a salt thereof,

wherein:

L is CR^4R^5, O, C(O), $NR^6C(O)$ or NR^7;

A is N;

each X^1, X^2, X^3, X^4 and X^5 is independently CH or N, provided that at least two of X^1, X^2, X^3, X^4 and X^5 are N;

n is 0, 1, 2, 3 or 4;

p is 0, 1, 2 or 3;

R^1 is C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl or heterocyclylalkyl, each of which is optionally substituted with 1-5 R^9; wherein R^1 or R^9 is optionally taken together with one of R^4, R^5, R^6 or R^7, and the atoms to which they are attached to

form a cyclyl, heterocyclyl, aryl or heteroaryl ring that is optionally substituted with 1-3 R^{10};

each R^2 and R^3 is independently hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{11};

each R^4, R^5, R^6 and R^7 is independently hydrogen , C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$,$–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$;

each R^9, R^{10} and R^{11} is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thioxo, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{12};wherein two R^8, two R^9, two R^{10} or two R^{11} is optionally taken together with the atoms to which they are attached to form an optionally substituted cyclyl, heterocyclyl, aryl or heteroaryl ring;

R^{12} is $–OR^d$;

Y is O or S;

q is 1 or 2; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e, $R^{e'}$ and R^f is independently hydrogen,

C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, acyl, cyclyl, heterocyclyl, aryl, heteroaryl, cyclylalkyl, heterocyclylalkyl, arylalkyl, or heteroarylalkyl.

Item 10. The compound according to item 9 represented by general formula (II) or a salt thereof,

L is NR^7;

n is 0, 1 or 2;

p is 0;

R^1 is C_1-C_8 alkyl, aryl or heteroaryl;

each R^2 and R^3 is independently hydrogen, C_1-C_8 alkyl, aryl, halo, heterocyclylalkyl, $-NR^cC(Y)R^c$, $-NR^bR^{b'}$ or $-OR^d$, each of which is optionally substituted with 1-3 R^{11};

R^7 is hydrogen; and

each R^9, R^{10} and R^{11} is independently C_1-C_8 alkyl, heterocyclyl, halo, haloalkyl, haloalkoxy, –CN, $-C(O)OR^a$, $-C(Y)NR^bR^{b'}$, $-OR^d$ or $-C(Y)R^e$;

Y is O;

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e, $R^{e'}$ and R^f is independently hydrogen, C_1-C_8 alkyl, cyclyl, heterocyclyl, aryl, or heteroaryl.

Item 11 .The compound according to item 10 represented by general formula (II) or a salt thereof,

wherein:

R^1 is C_1-C_8 alkyl, phenyl or benzodioxolyl;

each R^2 and R^3 is independently hydrogen, C_1-C_8 alkyl, phenyl, halo, morholinylalkyl, $-NR^cC(Y)R^c$, $-NR^bR^{b'}$or $-OR^d$;

R^9 is independently C_1-C_8 alkyl, morpholinyl, tetrahydropyranyl, halo, haloalkyl, haloalkoxy, –CN, $-C(O)OR^a$, $-C(Y)NR^bR^{b'}$, $-OR^d$ or $-C(Y)R^e$; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e, $R^{e'}$ and R^f is independently hydrogen, C_1-C_8 alkyl, C_3-C_8 cycloalkyl, tetrahydropyranyl, phenyl, or pyridyl.

Item 12. The compound according to item 10 represented by general formula (II) or a salt thereof,

wherein:

R^1 is C_1-C_8 alkyl, phenyl or benzodioxolyl;

each R^2 and R^3 is independently hydrogen, C_1-C_8 alkyl, phenyl, halo, morholinylalkyl, $-NR^cC(Y)R^c$, $-NR^bR^{b'}$ or $-OR^d$, each of which is optionally substituted with 1-3 R^{11};

each R^9, R^{10} and R^{11} is independently C_1-C_8 alkyl, morpholinyl, tetrahydropyranyl, halo, haloalkyl, haloalkoxy, –CN, $-C(O)OR^a$, $-C(Y)NR^bR^{b'}$, $-OR^d$ or $-C(Y)R^e$; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e, $R^{e'}$ and R^f is independently hydrogen, C_1-C_8 alkyl, C_3-C_8 cycloalkyl, tetrahydropyranyl, phenyl, or pyridyl.

Item 13. The compoundaccording to item 12 represented by general formula (II) or a salt thereof, wherein:

R^2 is C_1-C_8 alkyl, phenyl, halo, morholinylalkyl, $-NR^cC(Y)R^{c'}$, $-NR^bR^{b'}$ or $-OR^d$, each of which is optionally substituted with 1-3 R^{11};

R^3 is hydrogen;

R^9 is halo, haloalkoxy, –CN, $-C(O)OR^a$ or $-C(Y)NR^bR^{b'}$; and

R^{11} is C_1-C_8 alkyl, morpholinyl, tetrahydropyranyl, halo, –CN, $-OR^d$ or $-C(Y)R^e$;

Item 14. The compound according to item 11 or 13 represented by general formula (II) or a salt thereof, wherein:

R^2 is C_1-C_8 alkyl, phenyl, halo, morholinylalkyl, $-NR^cC(Y)R^{c'}$, $-NR^bR^{b'}$ or $-OR^d$;

R^3 is hydrogen; and

R^9 is halo, haloalkoxy, –CN, $-C(O)OR^a$ or $-C(Y)NR^bR^{b'}$.

Item 15. The compound according to item 1 represented by general formula (III) or a salt thereof,

wherein:

A is CH or N;

L is O, a direct bond or NH;

one of X^1, X^2, X^3, X^4 and X^5 is N and the others are CH;

m is 1, 2 or 3;

n is 1, 2, 3 or 4;

R^1 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, alkoxyalkyl, hydroxyalkyl, heteroaryl, heteroarylalkyl, arylalkyl, $-C(Y)R^e$, cyclyl, cyclylalkyl or heterocyclyl, each of which is optionally substituted with 1-3 R^7;

R^2 is aryl or heteroaryl, each of which is optionally substituted with 1-5 R^9;

each R^3 or R^4 is independently hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{10};

each R^7, R^9 and R^{10} is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thioxo, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{12}; wherein two R^7 or two R^9 are optionally be taken together with the atoms to which they are attached to form an optionally substituted cyclyl, heterocyclyl, aryl or heteroaryl ring;

R^{12} is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thioxo, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{13};

R^{13} is independently C_1-C_8 alkyl, haloalkyl, halo, heterocyclyl, cyclyl, oxo or –$C(Y)NR^bR^{b'}$;

Y is O or S;

q is 1 or 2; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, acyl, cyclyl, heterocyclyl, aryl, haloalkyl, alkoxyalkyl, alkylaminoalkyl, dialkylaminoalkyl, heteroaryl, cyclylalkyl, heterocyclylalkyl, arylalkyl or heteroarylalkyl..

Item 16. The compound according to item 15 represented by general formula (III) or a salt thereof,

wherein:

m is 1;

n is 1;

R^1 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, heteroaryl, heterocyclyl, arylalkyl, cyclylalkyl, heteroarylalkyl, alkoxyalkyl, hydroxyalkyl or –$C(O)R^e$, each of which is optionally substituted with 1-3 R^7;

R^2 is aryl, heteroaryl or benzofuryl, each of which is optionally substituted with 1-5 R^9;

each R^3 or R^4 is independently hydrogen, C_1-C_8 alkyl, halo, haloalkyl or –OR^d;

R^6 is hydrogen or C_1-C_8 alkyl;

each R^7 and R^9 is independently C_1-C_8 alkyl, aryl, heteroaryl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, alkoxyalkyl, oxo, –CN, –NO_2, –$C(O)OR^a$, –$C(O)NR^bR^{b'}$, –$NR^bR^{b'}$, –OR^d, –$C(O)R^e$ or -$S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{12};

R^{12} is independently C_1-C_8 alkyl, oxo, halo, haloalkyl, –CN, –$C(O)NR^bR^{b'}$ or –$C(O)R^e$ each of which is optionally substituted with 1-3 R^{13};

R^{13} is independently C_1-C_8 alkyl, halo or heterocyclyl; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, cyclyl, heterocyclyl, arylalkyl, alkoxyalkyl, heterocyclylalkyl, heteroarylalkyl, alkylaminoalkyl, dialkylaminoalkyl or phenyl.

Item 17. The compound according to Item 16 represented by general formula (III) or a salt thereof,

wherein:

R^1 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, alkoxyalkyl, hydroxyalkyl, imidazolyl, pyridylalkyl, phenylalkyl, oxazolylalkyl, thienylalkyl, thiazolidinyl isoindolyl, –C(O)R^e, dihydroindenyl, C_3-C_8 cycloalkyl, C_3-C_8 cycloalkylalkyl, piperidyl, morpholinyl, pyrrolidinyl, azetidinyl or piperazinyl, each of which is optionally substituted with 1-3 R^7;

R^2 is phenyl, naphthyl, benzofuryl, indazolyl, benzothienyl, pyridyl, pyrimidinyl, dihydrobenzodioxinyl, benzodioxolyl, benzoimidazolyl, isoxazolyl, pyrazolyl, indolinyl or benzoisoxazolyl, each of which is optionally substituted with 1-5 R^9;

each R^3 or R^4 is independently hydrogen, C_1-C_8 alkyl, halo, haloalkyl or –OR^d;

R^6 is hydrogen or C_1-C_8 alkyl;

each R^7 and R^9 is independently C_1-C_8 alkyl, phenyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, alkoxyalkyl, oxo, –CN, –NO_2, –C(O)OR^a, –C(O)$NR^bR^{b'}$,–$NR^bR^{b'}$,–OR^d, –C(O)R^e or -$S(O)_qR^f$; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, C_3-C_8 cycloalkyl, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, tetrahydropyranyl, phenylalkyl, alkoxyalkyl, morholinylalkyl, oxazolidinylalkyl, imidazolylalkyl, tetrahydropyranylalkyl, pyridylalkyl, pyrazolylalkyl, tetrazolylalkyl, thiazolylalkyl, pyrrolylalkyl, benzoxazolylalkyl, indazolylalkyl, dihydrobenzoxazinylalkyl, tetrahydrofurylalkyl, tetrahydrofuryl, alkylaminoalkyl, dialkylaminoalkyl or phenyl.

Item 18. The compound according to item 16 represented by general formula (III) or a salt thereof,

wherein:

R^1 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, alkoxyalkyl, hydroxyalkyl, imidazolyl, furylalkyl, pyridylalkyl, phenylalkyl, oxazolylalkyl, thienylalkyl, thiazolidinyl, isoindolyl, –C(O)R^e, dihydroindenyl, C_3-C_8 cycloalkyl,

C_3-C_8 cycloalkylalkyl, piperidyl, morpholinyl, pyrrolidinyl, azetidinyl or piperazinyl, each of which is optionally substituted with 1-3 R^7;

R^2 is phenyl, naphthyl, benzofuryl, indazolyl, benzothienyl, pyridyl, pyrimidinyl, dihydrobenzodioxinyl, benzodioxolyl, benzoimidazolyl, isoxazolyl, pyrazolyl, indolinyl or benzisoxazolyl, each of which is optionally substituted with 1-5 R^9;

each R^3 or R^4 is independently hydrogen, C_1-C_8 alkyl, halo, haloalkyl or $-OR^d$;

R^6 is hydrogen or C_1-C_8 alkyl;

each R^7 and R^9 is independently C_1-C_8 alkyl, phenyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, alkoxyalkyl, oxo, $-CN$, $-NO_2$, $-C(O)OR^a$, $-C(O)NR^bR^{b'}$, $-NR^bR^{b'}$, $-OR^d$, $-C(O)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{12};

R^{12} is independently C_1-C_8 alkyl, oxo, halo, haloalkyl, $-CN$, $-C(O)NR^bR^{b'}$ or $-C(O)R^e$, each of which is optionally substituted with 1-3 R^{13};

R^{13} is independently C_1-C_8 alkyl, halo or pyrrolidinyl; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, C_3-C_8 cycloalkyl, pyrrolidinyl, piperidyl, morpholinyl, piperazinyl, tetrahydropyranyl, phenylalkyl, alkoxyalkyl, morpholinylalkyl, oxazolidinylalkyl, imidazolylalkyl, tetrahydropyranylalkyl, pyridylalkyl, pyrazolylalkyl, tetrazolylalkyl, thiazolylalkyl, pyrrolylalkyl, benzoxazolylalkyl, indazolylalkyl, dihydrobenzoxazinylalkyl, tetrahydrofurylalkyl, tetrahydrofuryl, alkylaminoalkyl, dialkylaminoalkyl or phenyl.

Item 19. The compound according to item 18 represented by general formula (III) or a salt thereof,

wherein:

A is N;

R^3 is hydrogen, C_1-C_8 alkyl, halo, haloalkyl, or $-OR^d$;

R^4 is hydrogen, C_1-C_8 alkyl, halo, or $-OR^d$;

R^7 is C_1-C_8 alkyl, phenyl, halo, haloalkyl, oxo, $-C(O)OR^a$, $-C(O)NR^bR^{b'}$ or $-OR^d$ each of which is optionally substituted with 1-3 R^{12};

R^9 is C_1-C_8 alkyl, phenyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, alkoxyalkyl, $-CN$, $-NO_2$, $-C(O)NR^bR^{b'}$, $-C(O)OR^a$, $-NR^bR^{b'}$, $-OR^d$, $-C(O)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{12}; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, C_3-C_8 cycloalkyl, pyrrolidinyl, piperidyl, morpholinyl, piperazinyl, tetrahydropyranyl, phenylalkyl, alkoxyalkyl, morpholinylalkyl, oxazolidinylalkyl, imidazolylalkyl, tetrahydropyranylalkyl, pyridylalkyl, pyrazolylalkyl, tetrazolylalkyl, thiazolylalkyl, pyrrolylalkyl, benzoxazolylalkyl, indazolylalkyl, tetrahydrofurylalkyl, dihydrobenzoxazinylalkyl, tetrahydrofuryl, alkylaminoalkyl, dialkylaminoalkyl or phenyl.

Item 20. The compound according to item 17 or 19 represented by general formula (III) or a salt thereof,

wherein:

A is N;

R^3 is hydrogen, C_1-C_8 alkyl, halo, haloalkyl, or $-OR^d$;

R^4 is hydrogen, C_1-C_8 alkyl, halo, or $-OR^d$;

R^7 is C_1-C_8 alkyl, phenyl, halo, haloalkyl, oxo, $-C(O)OR^a$, $-C(O)NR^bR^{b'}$ or $-OR^d$;

R^9 is C_1-C_8 alkyl, phenyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, alkoxyalkyl, $-CN$, $-NO_2$, $-C(O)NR^bR^{b'}$, $-C(O)OR^a$, $-NR^bR^{b'}$, $-OR^d$, $-C(O)R^e$ or $-S(O)_qR^f$; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, C_3-C_8 cycloalkyl, pyrrolidinyl, piperidyl, morpholinyl, piperazinyl, tetrahydropyranyl, phenylalkyl, alkoxyalkyl, morpholinylalkyl, oxazolidinylalkyl, imidazolylalkyl, tetrahydropyranylalkyl, pyridylalkyl, pyrazolylalkyl, tetrazolylalkyl, thiazolylalkyl, pyrrolylalkyl, benzoxazolylalkyl, indazolylalkyl, tetrahydrofurylalkyl, tetrahydrofuryl, dihydrobenzoxazinylalkyl, alkylaminoalkyl, dialkylaminoalkyl or phenyl.

Item 21. The compound according to item 20 represented by general formula (III) or a salt thereof,

wherein:

R^1 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, alkoxyalkyl, hydroxyalkyl, imidazolyl, furylalkyl, pyridylalkyl, phenylalkyl, oxazolylalkyl, thienylalkyl, isoindolyl, $-C(O)R^e$, dihydroindenyl, C_3-C_8 cycloalkyl,

C_3-C_8 cycloalkylalkyl, piperidyl, morpholinyl, pyrrolidinyl, azetidinyl or piperazinyl, each of which is optionally substituted with 1-3 R^7;

R^2 is phenyl, which is optionally substituted with 1-5 R^9; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, pyrrolidinyl, morpholinyl, tetrahydropyranyl, alkoxyalkyl, morpholinylalkyl, tetrahydropyranylalkyl, pyridylalkyl, thiazolylalkyl, pyrrolylalkyl, tetrahydrofuryl, alkylaminoalkyl or phenyl.

Item 22. A pharmaceutical composition comprising the compound according to any one of items 1 to 21 or a salt thereof as an active ingredient and a pharmaceutically acceptable carrier.

Item 23. The pharmaceutical composition according to item 22 for preventing or treating central nervous system diseases.

Item 24. The pharmaceutical composition according to item 23 for treating or preventing central nervous system disorders selected from the group consisting of schizophrenia; refractory, intractable or chronic schizophrenia; emotional disturbance; psychotic disorder; mood disorder; bipolar I type disorder; bipolar II type disorder; depression; endogenous depression; major depression; melancholy and refractory depression; dysthymic disorder; cyclothymic disorder; panic attack; panic disorder; agoraphobia; social phobia; obsessive-compulsive disorder; post-traumatic stress disorder; generalized anxiety disorder; acute stress disorder; hysteria; somatization disorder; conversion disorder; pain disorder; hypochondriasis; factitious disorder; dissociative disorder; sexual dysfunction; sexual desire disorder; sexual arousal disorder; erectile dysfunction; anorexia nervosa; bulimia nervosa; sleep disorder; adjustment disorder; alcohol abuse; alcohol intoxication; drug addiction; stimulant intoxication; narcotism; anhedonia; iatrogenic anhedonia; anhedonia of a psychic or mental cause; anhedonia associated with depression; anhedonia associated with schizophrenia; delirium; cognitive impairment; cognitive impairment associated with Alzheimer's disease,

Parkinson's disease and other neurodegenerative diseases; cognitive impairment caused by Alzheimer's disease; Parkinson's disease and associated neurodegenerative diseases; cognitive impairment of schizophrenia; cognitive impairment caused by refractory, intractable or chronic schizophrenia; vomiting; motion sickness; obesity; migraine; pain (ache) ; mental retardation; autism disorder (autism); Tourette's disorder; tic disorder; attention-deficit/hyperactivity disorder; conduct disorder; and Down's syndrome.

Item 25. A process for producing a pharmaceutical composition comprising mixing a compound of the formula (I), (II), or (III) or a salt thereof according to any one of items 1 to 21 with a pharmaceutically acceptable carrier.

Item 26. Use of a compound of the formula (I), (II) or (III) or a salt thereof according to any one of items 1 to 21 as a drug.

Item 27. Use of the compound according to any one of items 1 to 21 represented by general formula(I), (II) or (III) or a salt thereof as a STEP inhibitor .

Item 28. A method of treating a disorder that would benefit by the modulation of STEP (e.g., by activation of inhibition of STEP) in a subject, the method comprising administering to a compound of formula (I), (II) or (III) or a salt thereof according to any one of items 1 to 21.

Item 29. The method of item 28, wherein the disorder is schizophrenia.

Item 30. The method of item 28, wherein the disorder is cognitive deficit.

Item 31. The method of item 28, wherein the compound of formula (I), (II), or (III) is administered in combination with an additional therapeutic agent.

Item 32.The method of item 28, wherein the additional therapeutic agent is an atypical antipsychotic.

Item 33. The method of item 28, wherein the additional therapeutic agent is selected from the group consisting of aripiprazole, clozapine, ziprasidone, risperidone, quetiapine, olanzapine, amisulpride, asenapine, iloperidone, melperone, paliperidone, perospirone, sertindole and sulpiride.

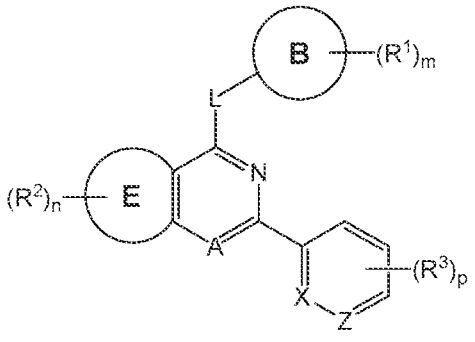
Item 34. The method of item 28, wherein the additional therapeutic agent is a typical antipsychotic.

Item 35. The method of item 28, wherein the additional therapeutic agent is selected from the group consisting of haloperidol, molindone, loxapine, thioridazine, molindone, thiothixene, pimozide, fluphenazine, trifluoperazine, mesoridazine, chlorprothixene, chlorpromazine, perphenazine, triflupromazine and zuclopenthixol.

Item 36. A kit comprising a composition comprising a compound of formula (I), (II), or (III) or a salt thereof according to any one of items 1 to 21 and an acceptable carrier.

Item 37. A kit comprising a pharmaceutical composition comprising a compound of formula (I), (II), or (III) or a salt thereof according to any one of items 1 to 21 and a pharmaceutically acceptable carrier.

Item 38. A compound of formula (IV):



(IV)

wherein:

A is CH, CR^4 or N;

B is aryl or a 5- or 6-membered heteroaryl;

m is 0, 1, 2, 3, 4 or 5;

E is aryl or a 5-membered heteroaryl;

when E is aryl, n is 1, 2, 3 or 4; and when E is a 5-membered heteroaryl, n is 0, 1, 2 or 3;

L is NR^5 or O;

one of X and Z is N and the other is CH;

p is 0, 1, 2, 3 or 4;

each R^1, R^2 and R^3 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$, each of which may be optionally substituted with 1-3 R^6; wherein two R^1, together with the atoms to which they are attached, may form an optionally substituted cyclyl, heterocyclyl, aryl or heteroaryl ring;

R^d is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, –

$SO_2NR^bR^{b'}$, $-NR^cSO_2R^{c'}$, $-NR^cC(Y)NR^bR^{b'}$, $-OR^d$, $-SR^{d'}$, $-C(Y)R^e$ or $-S(O)_qR^f$, each of which may be optionally substituted with 1-3 R^6;

R^5 is hydrogen; or when m is not 0, R^5 and 1 R^1 may be taken together with the atoms to which they are attached to form an optionally substituted heteroaryl or heterocyclyl ring;

each R^6 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thiono, –CN, $-NO_2$, $-C(O)OR^a$, $-C(Y)NR^bR^{b'}$, $-NR^cC(Y)R^{c'}$, $-NR^bR^{b'}$, $-OC(O)NR^bR^{b'}$, $-NR^cC(O)OR^{c'}$, $-SO_2NR^bR^{b'}$, $-NR^cSO_2R^{c'}$, $-NR^cC(Y)NR^bR^{b'}$, $-OR^d$, $-SR^{d'}$, $-C(Y)R^e$ or $-S(O)_qR^f$, each of which may be optionally substituted with 1-3 R^7;

each R^7 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thiono, –CN, $-NO_2$, $-C(O)OR^a$, $-C(Y)NR^bR^{b'}$, $-NR^cC(Y)R^{c'}$, $-NR^bR^{b'}$, $-OC(O)NR^bR^{b'}$, $-NR^cC(O)OR^{c'}$, $-SO_2NR^bR^{b'}$, $-NR^cSO_2R^{c'}$, $-NR^cC(Y)NR^bR^{b'}$, $-OR^d$, $-SR^{d'}$, $-C(Y)R^e$ or $-S(O)_qR^f$;

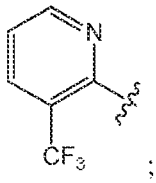
each Y is independently O or S;

q is 1 or 2; and

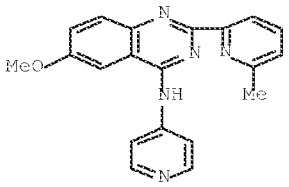
each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e, $R^{e'}$ and R^f is independently selected from hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, acyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy and silylalkoxyalkyl, each of which may be optionally substituted with 1-3 R^6, wherein R^b and $R^{b'}$, together with the atoms to which they are attached, may form an optionally substituted cyclyl or heterocyclyl ring;

or a pharmaceutically acceptable derivative or prodrug thereof,

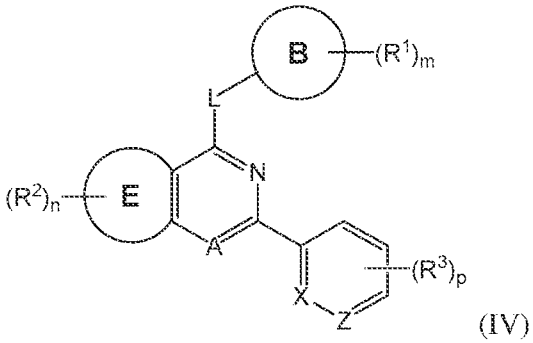
wherein when B is phenyl, two R^1 are not taken together to form a pyrazole ring;

when B is phenyl, R^2 is not  ;

and where in the compound is not:



Item 39. A compound of formula (IV) :



(IV)

wherein:

A is CH, CR^4 or N;

B is aryl or a 5-membered heteroaryl;

E is aryl or a 5-membered heteroaryl;

L is NR^5 or O;

one of X and Z is N and the other is CH;

m is 0, 1, 2, 3, 4 or 5;

n is 1, 2, 3 or 4;

p is 0, 1, 2, 3 or 4;

each R^1 and R^3 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl,

heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^cSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$,–OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$, each of which may be optionally substituted with 1-3 R^6; wherein two R^1, together with the atoms to which they are attached, may form an optionally substituted cyclyl, heterocyclyl, or aryl ring;

each R^2 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^cSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$,–OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$, each of which may be optionally substituted with 1-3 R^6; wherein two R^1, together with the carbons to which they are attached, may form an optionally substituted cyclyl, heterocyclyl, aryl or heteroaryl ring;

R^4 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^cSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$,–OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$, each of which may be optionally substituted with 1-3 R^6;

R^5 is hydrogen; or when m is not 0, R^5 and 1 R^1 may be taken together with the atoms to which they are attached to form an optionally substituted heteroaryl or heterocyclyl ring;

each R^6 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thiono, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –

$OC(O)NR^bR^{b'}$, $-NR^cC(O)OR^{c'}$, $-SO_2NR^bR^{b'}$, $-NR^cSO_2R^{c'}$, $-NR^cC(Y)NR^bR^{b'}$, $-OR^d$, $-SR^{d'}$, $-C(Y)R^e$ or $-S(O)_qR^f$, each of which may be optionally substituted with 1-3 R^7;

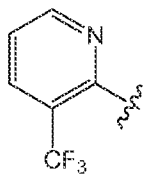
each R^7 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thiono, $-CN$, $-NO_2$, $-C(O)OR^a$, $-C(Y)NR^bR^{b'}$, $-NR^cC(Y)R^{c'}$, $-NR^bR^{b'}$, $-OC(O)NR^bR^{b'}$, $-NR^cC(O)OR^{c'}$, $-SO_2NR^bR^{b'}$, $-NR^cSO_2R^{c'}$, $-NR^cC(Y)NR^bR^{b'}$, $-OR^d$, $-SR^{d'}$, $-C(Y)R^e$ or $-S(O)_qR^f$;

Y is O or S;

q is 1 or 2; and

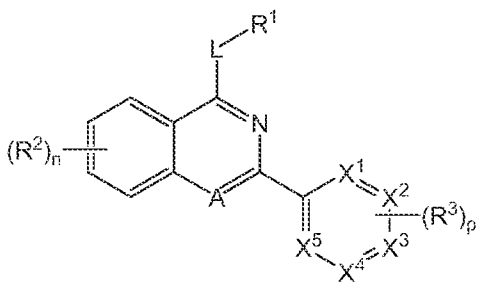
each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e, $R^{e'}$ and R^f is independently selected from hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, acyl, cyclyl, heterocyclyl, aryl, heteroaryl, cyclylalkyl, heterocyclylalkyl, aralkyl and heteroaralkyl, each of which may be optionally further substituted with 1-3 R^6, wherein R^b and $R^{b'}$, together with the atoms to which they are attached, may form an optionally substituted cyclyl or heterocyclyl ring;.

wherein when B is phenyl, two R^1 are not taken together to form a pyrazole ring; and

when B is phenyl, R^2 is not 

.

Item 40. A compound of formula (V) :



(V)

wherein:

L is CR^4R^5, O, C(O), $NR^6C(O)$, or NR^7;

A is CR^8, CH or N;

each X^1, X^2, X^3, X^4 and X^5 is independently CH or N, provided that at least two of X^1, X^2, X^3, X^4 and X^5 are N;

n is 0, 1, 2, 3 or 4;

p is 0, 1, 2 or 3;

R^1 is C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl or heterocyclylalkyl, each of which may be optionally substituted with 1-5 R^9; wherein R^1 or R^9 may optionally be taken together with one of R^4, R^5, R^6 or R^7, and the atoms to which they are attached, to form a cyclyl, heterocyclyl, aryl or heteroaryl ring that is optionally substituted with 1-3 R^{10};

each R^2 and R^3 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$,$–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$; each of which is optionally substituted with 1-3 R^{11};

each R^4, R^5, R^6 and R^7 is independently H, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl,–CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$,$–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$;

each R^8, R^9, R^{10} and R^{11} is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy,

silylalkoxyalkyl, oxo, thiono, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$, each of which may be optionally further substituted; wherein two R^8, two R^9, two R^{10} or two R^{11} may optionally be taken together with the atoms to which they are attached to form an optionally substituted cyclyl, heterocyclyl, aryl or heteroaryl ring;

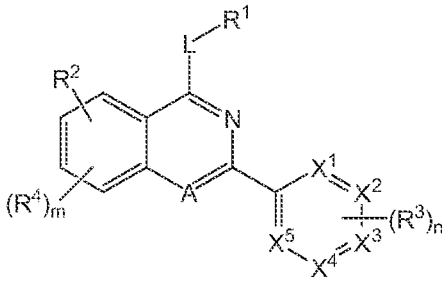
each Y is independently O or S;

q is 1 or 2; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e, $R^{e'}$ and R^f is independently selected from hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, acyl, cyclyl, heterocyclyl, aryl, heteroaryl, cyclylalkyl, heterocyclylalkyl, aralkyl and heteroaralkyl, each of which may be optionally substituted with 1-3 R^8,

or a pharmaceutically acceptable derivative or prodrug thereof.

Item 41. A compound of formula (VI):



(VI)

wherein:

A is CR^5, CH or N;

L is O or NR^6;

1, 2 or 3 of X^1, X^2, X^3, X^4 and X^5 are N and the others are CH;

m is 0, 1, 2 or 3;

n is 0, 1, 2, 3 or 4;

R^1 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, cyclyl or heterocyclyl, each of which is optionally substituted with 1-3 R^7; or when L is NR^6,

R^1 or R^7 may be taken together with R^6 and the atoms to which they are attached to form a heterocyclyl or heteroaryl ring that is optionally substituted with 1-3 R^8;

R^2 is aryl or heteroaryl, each of which is optionally substituted with 1-5 R^9;

each R^3, R^4 and R^5 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, $-NO_2$, $-C(O)OR^a$, $-C(Y)NR^bR^{b'}$, $-NR^cC(Y)R^{c'}$, $-NR^bR^{b'}$, $-OC(O)NR^bR^{b'}$, $-NR^cC(O)OR^{c'}$, $-SO_2NR^bR^{b'}$, $-NR^cSO_2R^{c'}$, $-NR^cC(Y)NR^bR^{b'}$,$-OR^d$, $-SR^{d'}$, $-C(Y)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{10};

R^6 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, cyclyl or heterocyclyl, each of which is optionally substituted with 1-3 R^{11};

each R^7, R^8, R^9 and R^{10} is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thiono, –CN, $-NO_2$, $-C(O)OR^a$, $-C(Y)NR^bR^{b'}$, $-NR^cC(Y)R^{c'}$, $-NR^bR^{b'}$, $-OC(O)NR^bR^{b'}$, $-NR^cC(O)OR^{c'}$, $-SO_2NR^bR^{b'}$, $-NR^cSO_2R^{c'}$, $-NR^cC(Y)NR^bR^{b'}$,$-OR^d$, $-SR^{d'}$, $-C(Y)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{12}; wherein two R^7, two R^8, two R^9 or two R^{10} may optionally be taken together with the atoms to which they are attached to form an optionally substituted cyclyl, heterocyclyl, aryl or heteroaryl ring;

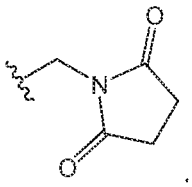
each R^{11} and R^{12} is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thiono, –CN, $-NO_2$, $-C(O)OR^a$, $-C(Y)NR^bR^{b'}$, $-NR^cC(Y)R^{c'}$, $-NR^bR^{b'}$, $-OC(O)NR^bR^{b'}$, $-NR^cC(O)OR^{c'}$, $-SO_2NR^bR^{b'}$, $-NR^cSO_2R^{c'}$, $-NR^cC(Y)NR^bR^{b'}$,$-OR^d$, $-SR^{d'}$, $-C(Y)R^e$ or $-S(O)_qR^f$;

each Y is independently O or S;

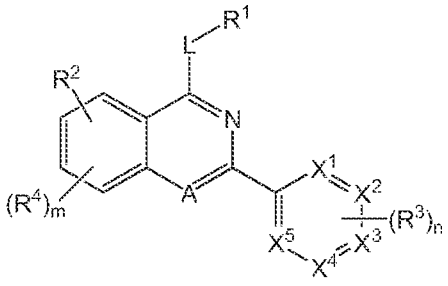
q is 1 or 2; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e, $R^{e'}$ and R^f is independently selected from hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, acyl, cyclyl, heterocyclyl, aryl, heteroaryl, cyclylalkyl, heterocyclylalkyl, aralkyl and heteroaralkyl, each of which may be optionally substituted with 1-3 R^7;

or a pharmaceutically acceptable derivative or prodrug thereof,

wherein when R^1 is cyclopropyl, R^9 is not: .

Item 42. A compound of formula (VI):



(VI)

wherein:

A is CR^5, CH or N;

L is O or NR^6;

1, 2 or 3 of X^1, X^2, X^3, X^4 and X^5 are N and the others are CH;

m is 0, 1, 2 or 3;

n is 0, 1, 2, 3 or 4;

R^1 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, cyclyl or heterocyclyl, each of which is optionally substituted with 1-3 R^7; or when L is NR^6, R^1 or R^7 may be taken together with R^6 and the atoms to which they are attached to form a heterocyclyl or heteroaryl ring that is optionally substituted with 1-3 R^8;

R^2 is aryl or heteroaryl, each of which is optionally substituted with 1-5 R^9;

each R^3, R^4 and R^5 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl,

heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{10};

R^6 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, cyclyl or heterocyclyl, each of which is optionally substituted with 1-3 R^{11};

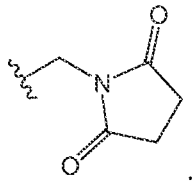
each R^7, R^8, R^9 and R^{10} is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thiono, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{12}; wherein two R^7, two R^8, two R^9 or two R^{10} may optionally be taken together with the atoms to which they are attached to form an optionally substituted cyclyl, heterocyclyl, aryl or heteroaryl ring;

each R^{11} and R^{12} is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thiono, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$;

each Y is independently O or S;

q is 1 or 2; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e, $R^{e'}$ and R^f is independently selected from hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, acyl, cyclyl, heterocyclyl, aryl, heteroaryl, cyclylalkyl, heterocyclylalkyl, aralkyl and heteroaralkyl, each of which may be optionally substituted with 1-3 R^7;

wherein R^9 is not:  .

Compounds of Formula (I)

The following aspects and embodiments relate to compounds of formula (I).

Item 2. The compound according to item 1 represented by general formula (I) or a salt thereof,

wherein:

A is CR^4 or N;

B is aryl, cyclyl or a 5- or 6-membered heteroaryl;

m is 0, 1, 2, 3, 4 or 5;

n is 0, 1, 2, 3 or 4;

E is aryl or a 5-membered heteroaryl;

when E is aryl, n is 0,1, 2, 3 or 4; and when E is a 5-membered heteroaryl, n is 0, 1, 2 or 3;

L is NR^5, S,O or a direct bond;

one of X and Z is N and the other is CH;

p is 0, 1, 2, 3 or 4;

each R^1, R^2 and R^3 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silyloxyalkynyl, silylalkoxy, silylalkoxyalkyl, –CN, oxo,–NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^cSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$, –OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$, each of which is optionally substituted with 1-3 R^6; wherein two R^1, together with the atoms to which they are attached, may form an optionally substituted cyclyl, heterocyclyl, aryl or heteroaryl ring;

R^4 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^cSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$, –OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$, each of which is optionally substituted with 1-3 R^6;

R^5 is hydrogen; or when m is not 0, R^5 and one R^1 may be taken together with the atoms to which they are attached to form an optionally substituted heteroaryl or heterocyclyl ring;

each R^6 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thioxo, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^cSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$,–OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$, each of which is optionally substituted with 1-3 R^7;

each R^7 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thioxo, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^cSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$,–OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$,each of which is optionally substituted with 1-3 R^9;

each R^9 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thioxo, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –

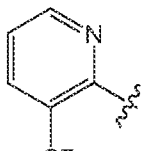
$NR^bR^{b'}$, $-OC(O)NR^bR^{b'}$, $-NR^cC(O)OR^{c'}$, $-SO_2NR^bR^{b'}$, $-NR^cSO_2R^{c'}$, $-NR^cC(Y)NR^bR^{b'}$, $-OR^d$, $-SR^{d'}$, $-C(Y)R^e$ or $-S(O)_qR^f$;

Y is O or S;

q is 1 or 2; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, acyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy or silylalkoxyalkyl;

wherein when B is phenyl, two R^1 are not taken together to form a pyrazole ring; and

when B is phenyl, R^2 is not 

.

Item 3. The compound according to item 2 represented by general formula (I) or a salt thereof,

wherein:

A is CH or N;

B is aryl, cyclyl or a 5- or 6-membered heteroaryl;

m is 0, 1, 2, 3 or 4;

E is aryl or a 5-membered heteroaryl;

n is 0, 1 or 2;

when E is aryl, n is 0, 1 or 2 and when E is a 5-membered heteroaryl, n is 0 or 1;

p is 0, 1 or 2;

each R^1, R^2 and R^3 is independently C_1-C_8 alkyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silyloxyalkynyl, –CN, oxo, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–SO_2NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$, each

of which is optionally substituted with 1-3 R^6; wherein two R^1, together with the atoms to which they are attached, may form an optionally substituted cyclyl, heterocyclyl, aryl or heteroaryl ring;

each R^6 is independently C_1-C_8 alkyl, heterocyclyl, heterocyclylalkyl, hydroxyalkyl, halo, haloalkyl, haloalkoxy, alkoxyalkyl, oxo, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OR^d$ or $–C(Y)R^e$, each of which is optionally substituted with 1-3 R^7;

each R^7 is oxo; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, acyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, haloalkyl, dialkylaminoalkyl, hydroxyalkyl or alkoxyalkyl.

Item 4. The compound according to item 3 represented by general formula (I) or a salt thereof,

wherein:

B or two R1 and B are taken together to form a group is phenyl, dihydroindenyl, dihydrobenzoxazinyl, dihydrobenzodioxinyl, chromenyl, tetrahydroquinoxalinyl, tetrahydroisoquinolinyl, tetrahydroquinolinyl, dihydroquinolinyl, quinolyl, isoquinolinyl, tetrahydroquinazolinyl, indolinyl, dihydrobenzothiazolyl, dihydrobenzimidazolyl, dihydrobenzoxazolyl, isoindolinyl, dihydroisobenzofuranyl, benzofuryl, benzothienyl, benzodioxolyl, indolyl, indazolyl, benzoimidazolyl, benzotriazolyl, benzisoxazolyl, benzoxazolyl, benzothiazolyl, benzoxadiazolyl, dihydrocyclopentathiophenyl, tetrahydrobenzothiophenyl, thienyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, thiadiazolyl, pyrrolyl or pyridyl;

E is phenyl, thienyl or pyrrolyl;

when E is phenyl , n is 1 or 2; and when E is thienyl, n is 0 or 1;

each R^1, R^2 and R^3 is independently C_1-C_8 alkyl ,C_2-C_8 alkynyl, phenyl, thienyl, pyrrolyl, oxadiazolyl, pyridyl, benzodioxolyl, furyl, pyrimidinyl, oxazolyl, isoxazolyl, pyrazolyl, C_3-C_8 cycloalkyl, piperidyl, pyrrolidinyl, morpholinyl, dioxolanyl, phenylalkyl, thiomorpholinylalkyl, pyrrolidinylalkyl, morpholinylalkyl, piperidylalkyl,

piperazinylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxyalkyl, silyloxyalkynyl, –CN, –NO_2, oxo, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$SO_2NR^bR^{b'}$, –OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$, each of which is optionally substituted with 1-3 R^6;

each R^6 is independently C_1-C_8 alkyl, tetrahydropyranyl, morpholinyl, thiomorpholinyl, morpholinylalkyl, dialkylaminoalkyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, oxo, –CN, –NO_2, –$C(O)OR^a$, –$NR^cC(Y)R^{c'}$, –$C(Y)NR^bR^{b'}$, –$NR^bR^{b'}$, alkoxyalkyl, –OR^d or –$C(Y)R^e$; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 cycloalkyl, phenyl, pyridyl, dihydroindenyl, morpholinyl, tetrahydropyranyl, piperidyl, pyrrolidinyl, piperazinyl, thiomorpholinyl, phenylalkyl, thienylalkyl, furylalkyl, pyridylalkyl, tetrahydropyranylalkyl, dihydroindenylalkyl, tetrahydrofurylalkyl, hydroxyalkyl, thiazolylalkyl, pyrazolylalkyl, morpholinylalkyl, pyrrolidinylalkyl, dialkylaminoalkyl, piperidylalkyl, benzodioxolylalkyl, dihydrobenzodioxinylalkyl, benzothienylalkyl, C_3-C_8 cycloalkylalkyl, oxazolidinylalkyl, haloalkyl, or alkoxyalkyl.

Item 5. The compound according to item 3 represented by general formula (I) or a salt thereof,

wherein:

B or two R1 and B are taken together to form a group is phenyl, dihydroindenyl, dihydrobenzoxazinyl, dihydrobenzodioxinyl, chromenyl, tetrahydroquinoxalinyl, tetrahydroisoquinolyl, tetrahydroquinolinyl, dihydroquinolyl, quinolyl, isoquinolyl, tetrahydroquinazolinyl, indolinyl, dihydrobenzothiazolyl, dihydrobenzimidazolyl, dihydrobenzoxazolyl, isoindolinyl, dihydroisobenzofuranyl, benzofuryl, benzothienyl, benzodioxolyl, indolyl, indazolyl, benzoimidazolyl, benzotriazolyl, benzisoxazolyl, benzoxazolyl, benzothiazolyl, benzoxadiazolyl, dihydrocyclopentathiophenyl, tetrahydrobenzothienyl, thienyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, thiadiazolyl, pyrrolyl or pyridyl;

E is phenyl, thienyl or pyrrolyl,;

when E is phenyl , n is 0, 1or 2; and when E is thienyl, n is 0 or 1;

each R^1, R^2 and R^3 is independently C_1-C_8 alkyl, C_2-C_8 alkynyl, phenyl, thienyl, pyrrolyl, oxazolyl, oxadiazolyl, pyridyl, benzodioxolyl, furyl, pyrimidinyl, isoxazolyl, pyrazolyl, C_3-C_8 cycloalkyl, piperidyl, pyrrolidinyl, morpholinyl, dioxolanyl, phenylalkyl, thiomorpholinylalkyl, pyrrolidinylalkyl, morpholinylalkyl, piperidylalkyl, piperazinylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxyalkyl, silyloxyalkynyl, –CN, –NO_2, oxo, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$OC(O)NR^bR^{b'}$, –$SO_2NR^bR^{b'}$, –OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$, each of which is optionally substituted with 1-3 R^6;

each R^6 is independently C_1-C_8 alkyl, tetrahydropyranyl, morpholinyl, thiomorpholinyl, morpholinylalkyl, dialkylaminoalkyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, oxo, –CN, –NO_2, –$C(O)OR^a$, –$NR^cC(Y)R^{c'}$, –$C(Y)NR^bR^{b'}$, –$NR^bR^{b'}$, alkoxyalkyl, –OR^d or –$C(Y)R^e$, each of which is optionally substituted with 1-3 R^7;

R^7 is oxo; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 cycloalkyl, phenyl, pyridyl, dihydroindenyl, morpholinyl, tetrahydropyranyl, piperidyl, pyrrolidinyl, piperazinyl, thiomorpholinyl, phenylalkyl, thienylalkyl, furylalkyl, pyridylalkyl, tetrahydropyranylalkyl, dihydroindenylalkyl, tetrahydrofurylalkyl, hydroxyalkyl, thiazolylalkyl, pyrazolylalkyl, morpholinylalkyl, pyrrolidinylalkyl, dialkylaminoalkyl, piperidylalkyl, benzodioxolilalkyl, dihydrobenzodioxinylalkyl, benzothienylalkyl, C_3-C_8 cycloalkylalkyl, oxazolidinylalkyl, haloalkyl, or alkoxyalkyl.

Item 6. The compound according to item 5 represented by general formula (I) or a salt thereof,

wherein:

R^1 is C_1-C_8 alkyl, phenyl, thienyl, pyrrolyl, oxazolyl, C_3-C_8 cycloalkyl, dioxolanyl, phenylalkyl, halo, haloalkyl, haloalkoxy, alkoxyalkyl, –CN, oxo, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$SO_2NR^bR^{b'}$, –OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$, each of which is optionally substituted with 1-3 R^6;

R^2 is C_1-C_8 alkyl, C_2-C_8 alkynyl, phenyl, thienyl, pyridyl, benzodioxolyl, furyl, pyrimidinyl, isoxazolyl, pyrazolyl, C_3-C_8 cycloalkyl, pyrrolidinyl, morpholinyl , thiomorpholinylalkyl, pyrrolidinylalkyl, morpholinylalkyl, piperiridylalkyl, piperazinylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxyalkyl, silyloxyalkynyl, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$,–$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –OR^d or –$C(Y)R^e$, each of which is optionally substituted with 1-3 R^6;

R^3 is C_1-C_8 alkyl, halo, haloalkyl, –$NR^bR^{b'}$ or –OR^d, each of which is optionally substituted with 1-3 R^6.

Item 7. The compound according to item 4 or 6 represented by general formula (I) or a salt thereof,

wherein:

R^1 is C_1-C_8 alkyl, phenyl, thienyl, pyrrolyl, oxazolyl, C_3-C_8 cycloalkyl, dioxolanyl, phenylalkyl, halo, haloalkyl, haloalkoxy, alkoxyalkyl, –CN, oxo, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$SO_2NR^bR^{b'}$, –OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$;

R^2 is C_1-C_8 alkyl, C_2-C_8 alkynyl, phenyl, thienyl, pyridyl, benzodioxolyl, furyl, pyrimidinyl, isoxazolyl, pyrazolyl, C_3-C_8 cycloalkyl, piperidinyl, pyrrolidinyl, morpholinyl, thiomorpholinylalkyl, pyrrolidinylalkyl, morpholinylalkyl, piperiridinylalkyl, piperazinylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxyalkyl, silyloxyalkynyl, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$,–$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –OR^d, –$C(Y)R^e$ or -$S(O)_qR^f$;

R^3 is C_1-C_8 alkyl, halo, haloalkyl ,–$NR^bR^{b'}$ or –OR^d.

Item 8. The compound according to item 7 represented by general formula (I) or a salt thereof,

wherein:

B or two R1 and B are taken together to form a group is phenyl, dihydroindenyl, dihydrobenzoxazinyl, dihydrobenzodioxinyl, chromenyl, tetrahydroisoquinolyl, tetrahydroquinolinyl, dihydroquinolyl, quinolyl, tetrahydroquinazolinyl, indolinyl,

dihydrobenzothiazolyl, dihydrobenzimidazolyl, dihydrobenzoxazolyl, isoindolinyl, benzofuryl, benzothienyl, benzodioxolyl, indolyl, indazolyl, benzoimidazolyl, benzotriazolyl, benzisoxazolyl, benzoxazolyl, benzothiazolyl, benzoxadiazolyl, tetrahydrobenzothienyl, thienyl, thiazolyl, imidazolyl, pyrazolyl, thiadiazolyl or pyridyl;

m is 1, 2, 3 or 4;

R^1 is C_1-C_8 alkyl, halo, haloalkyl, haloalkoxy, alkoxyalkyl, –CN, oxo, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–SO_2NR^bR^{b'}$, $–OR^d$, or $-S(O)_qR^f$;

R^2 is C_1-C_8 alkyl, C_3-C_8 cycloalkyl, thiomorpholinylalkyl, pyrrolidinylalkyl, morpholinylalkyl, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxyalkyl, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^bR^{b'}$, $–OR^d$, $–C(Y)R^e$ or $-S(O)_qR^f$;

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 cycloalkyl, phenyl, dihydroindenyl, morpholinyl, tetrahydropyranyl, piperidyl, pyrrolidinyl, thiomorpholinyl, phenylalkyl, thienylalkyl, pyridylalkyl, tetrahydropyranylalkyl, dihydroindenylalkyl, tetrahydrofurylalkyl, hydroxyalkyl, morpholinylalkyl, pyrrolidinylalkyl, dialkylaminoalkyl, piperidylalkyl, benzodioxolilalkyl, dihydrobenzodioxinylalkyl, C_3-C_8 cycloalkylalkyl, haloalkyl or alkoxyalkyl.

In some embodiments, A is N. In some embodiments, A is CH. In some embodiments, A is CR^4.

In some embodiments, B is aryl (e.g., phenyl).

In some embodiments, m is 0.

In some embodiments, m is 1. In some embodiments, m is 2. In some embodiments, m is 3.

In some embodiments, R^1 is in the ortho position. In some embodiments, R^1 is in the meta position. In some embodiments, R^1 is in the para position.

In some embodiments, R^1 is C_1-C_8 alkyl (e.g., methyl or tert-butyl). In some embodiments, R^1 is heteroaryl (e.g., oxazolyl, oxadiazolyl or quinazolinyl).

In some embodiments, R^1 is heteroaryl substituted with 1-3 R^6 (e.g., 1 R^6).

In some embodiments, R^1 is oxadiazolyl substituted with 1 R^6. some embodiments, R^6 is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, R^1 is heteroaryl substituted with 2 R^6. In some embodiments, R^1 is quinazolinyl substituted with 2 R^6. In some embodiments, one R^6 is halo (e.g., bromo) and the other is heteroaryl (e.g., pyridyl).

In some embodiments, m is 1 and R^1 is halo (e.g., fluoro, chloro or bromo). In some embodiments, m is 2 and each R^1 is halo (e.g., fluoro, chloro or bromo). In some embodiments, m is 3 and each R^1 is halo (e.g., fluoro, chloro or bromo). . In some embodiments, R^1 is haloalkyl (e.g., trifluoromethyl). In some embodiments, R^1 is haloalkoxy (e.g., difluoromethoxy or trifluoromethoxy).

In some embodiments, R^1 is haloalkoxy substituted with 1 R^6. In some embodiments, R^1 is $-O-CF_2-R^6$. In some embodiments, R^6 is $-C(Y)NR^bR^{b'}$. In some embodiments, Y is O, R^b is hydrogen and $R^{b'}$ is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^1 is $-O-CF_2-CH_2-R^6$. In some embodiments, R^6 is $-OR^d$. In some embodiments, R^d is hydrogen. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^6 is $-NR^bR^{b'}$. In some embodiments, R^b and $R^{b'}$ are each independently C_1-C_8 alkyl (e.g., R^b and $R^{b'}$ are both methyl). In some embodiments, R^6 is heterocyclyl (e.g., morpholino).

In some embodiments, R^1 is aminoalkyl. In some embodiments, R^1 is $-CH_2NH_2$. In some embodiments, R^1 is alkylaminoalkyl. In some embodiments, R^1 is $-CH_2NHCH_2CH_2CH_3$. In some embodiments, R^1 is dialkylaminoalkyl. In some embodiments, R^1 is $-CH_2N(CH(CH_3)_2)_2$.

In some embodiments, R^1 is hydroxyalkyl. In some embodiments, R^1 is $-CH_2OH$.

In some embodiments, R^1 is –CN.

In some embodiments, R^1 is $-NO_2$.

In some embodiments, R^1 is $-C(O)OR^a$. In some embodiments, R^a is hydrogen. In some embodiments, R^a is C_1-C_8 alkyl (e.g., methyl or ethyl).

In some embodiments, R^1 is $-NR^cC(Y)R^{c'}$. In some embodiments, one of R^c and $R^{c'}$ is hydrogen and the other is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, R^1 is $-OR^d$. In some embodiments, R^d is hydrogen. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl or ethyl).

In some embodiments, R^1 is $-SO_2NR^bR^{b'}$. In some embodiments, R^b and $R^{b'}$ are both hydrogen.

In some embodiments, R^1 is $-C(Y)R^e$. In some embodiments, Y is O. In some embodiments, R^e is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^e is heterocyclyl (e.g., pyrrolidinyl, piperidinyl or morpholino).

In some embodiments, R^1 is $-C(Y)NR^bR^{b'}$. In some embodiments, Y is S. In some embodiments, Y is O. In some embodiments, R^b and $R^{b'}$ are both hydrogen. In some embodiments, R^b is hydrogen. In some embodiments, R^b is hydrogen and $R^{b'}$ is aralkyl. In some embodiments, R^b is hydrogen and $R^{b'}$ is optionally substituted benzyl. In some embodiments, $R^{b'}$ is C_1-C_8 alkyl, e.g., methyl, ethyl, C_3 alkyl (e.g., n-propyl or isopropyl), C_4 alkyl (e.g., n-butyl, sec-butyl or tert-butyl), C_5 alkyl (e.g., n-pentyl, isopentyl or pentan-3-yl), C_6 alkyl (e.g., n-hexyl or 3,3-dimethylbutan-2-yl), or C_7 alkyl (e.g., n-heptyl or 2-heptyl).

In some embodiments, $R^{b'}$ is bicyclyl (e.g., indanyl). In some embodiments, $R^{b'}$ is heterocyclyl, e.g., a 6-membered heterocyclyl. In some embodiments, $R^{b'}$ is a 6-membered oxygen-containing heterocyclyl (e.g., tetrahydropyranyl). In some embodiments, $R^{b'}$ is a 6-membered nitrogen-containing heterocyclyl (e.g., piperidinyl).

In some embodiments, $R^{b'}$ is aralkyl. In some embodiments, the alkyl is a C_1-C_8 alkyl (e.g., C_1, C_2, C_3 or C_4 alkyl). In some embodiments, the alkyl is a straight-chain alkyl. In some embodiments, the alkyl is a branched alkyl. In some embodiments, the aryl is phenyl. In some embodiments, $R^{b'}$ is benzyl. In some embodiments, $R^{b'}$ is phenylethyl.

In some embodiments, $R^{b'}$ is heteroaralkyl. In some embodiments, the alkyl is a C_1-C_8 alkyl (e.g., C_1, C_2 or C_3 alkyl). In some embodiments, the alkyl is a straight-chain alkyl. In some embodiments, the alkyl is a branched alkyl. In some embodiments, the heteroaryl is pyridyl. In some embodiments, the heteroaryl is furanyl. In some embodiments, the heteroaryl is thiazolyl. In some embodiments, the heteroaryl is thienyl.

In some embodiments, $R^{b'}$ is cyclylalkyl. In some embodiments, the alkyl is a C_1-C_8 alkyl (e.g., C_1 alkyl). In some embodiments, the cyclyl group is cyclopropyl. In some embodiments, the cyclyl group is cyclopentyl. In some embodiments, the cyclyl group is a bicyclic group. In some embodiments, the bicyclic group is indanyl. In some embodiments, $R^{b'}$ is heterocyclylalkyl. In some embodiments, the alkyl is a C_1-C_8 alkyl (e.g., C_1 alkyl). In some embodiments, the heterocyclyl group is tetrahydropyranyl.

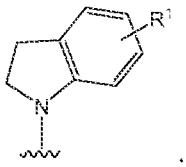
In some embodiments, $R^{b'}$ is haloalkyl (e.g., fluoroethyl, difluoroethyl, trifluoroethyl or trifluoropropyl).

In some embodiments, $R^{b'}$ is alkoxyalkyl. In some embodiments, the alkyl is a C_1-C_8 alkyl (e.g., C_1, C_2, C_3 or C_4 alkyl). In some embodiments, the alkyl is a straight-chain alkyl. In some embodiments, the alkyl is a branched alkyl. In some embodiments, the alkoxy is methoxy.

In some embodiments, R^b and $R^{b'}$ are each independently C_1-C_8 alkyl (e.g., R^b and $R^{b'}$ are both methyl, both ethyl, or both isopropyl).

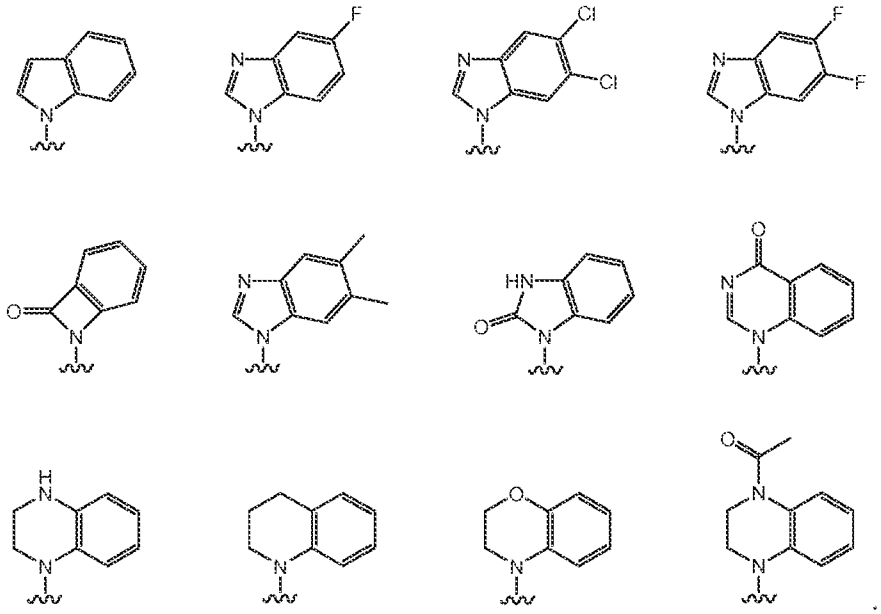
In some embodiments, two R^1 and B are taken together to form a bicyclic heteroaryl or heterocyclic ring.

In some embodiments, two R^1 and B are taken together to form



In some embodiments, R^1 is halo. In some embodiments, R^1 is at the 6, 7, or 8 position.

In some embodiments, two R^1 and B are taken together to form a group selected from:



In some embodiments, R^2 is aryl.

In some embodiments, each R^1 is independently C_1-C_8 alkyl (e.g., each R^1 is methyl). In some embodiments, each R^1 is independently halo (e.g., each R^1 is fluoro or each R^1 is chloro). In some embodiments, one R^1 is fluoro and the other is chloro. In some embodiments, one R^1 is chloro and the other is bromo.

In some embodiments, each R^1 is independently $-OR^d$. In some embodiments, each R^d is independently C_1-C_8 alkyl (e.g., each R^d is methyl).

In some embodiments, one R^1 is halo (e.g., chloro) and the other is C_1-C_8 alkyl (e.g., methyl). In some embodiments, one R^1 is halo (e.g., fluoro) and the other is heterocyclylalkyl (e.g.,–CH_2-heterocyclyl). In some embodiments, the heterocyclyl is morpholino. In some embodiments, the heterocyclyl is pyrrolidinyl. In some embodiments, the heterocyclyl is piperazinyl. In some embodiments, the piperazinyl is substituted with 1 R^6. In some embodiments, R^6 is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, one R^1 is halo (e.g., fluoro or chloro) and the other is haloalkyl (e.g., trifluoromethyl).

In some embodiments, one R^1 is halo (e.g., chloro) and the other is haloalkoxy (e.g., difluoromethoxy or trifluoromethoxy).

In some embodiments, one R^1 is halo (e.g., chloro) and the other is $-C(O)OR^a$. In some embodiments, R^a is hydrogen.

In some embodiments, one R^1 is halo (e.g., fluoro or chloro) and the other is –$C(Y)NR^bR^{b'}$. In some embodiments, Y is O. In some embodiments, R^b and $R^{b'}$ are both hydrogen. In some embodiments, one of R^b and $R^{b'}$ is hydrogen and the other is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, one R^1 is halo (e.g., chloro) and the other is –$NR^cC(Y)R^{c'}$. In some embodiments, Y is O. In some embodiments, R^c is hydrogen and $R^{c'}$ is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, one R^1 is halo (e.g., fluoro or chloro) and the other is –OR^d. In some embodiments, R^d is hydrogen. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, one R^1 is halo (e.g., fluoro or chloro) and the other is –CN.

In some embodiments, one R^1 is halo (e.g., chloro) and the other is –NO_2.

In some embodiments, one R^1 is –$C(O)OR^a$ and the other is –NO_2. In some embodiments, R^a is hydrogen.

In some embodiments, one R^1 is –$C(O)OR^a$ and the other is –OR^d. In some embodiments, each R^a and R^d is hydrogen.

In some embodiments, one R^1 is –$C(Y)NR^bR^{b'}$ and the other is haloalkyl (e.g., trifluoromethyl). In some embodiments, R^b and $R^{b'}$ are both hydrogen.

In some embodiments, one R^1 is –$C(Y)NR^bR^{b'}$ and the other is haloalkoxy (e.g., trifluoromethoxy). In some embodiments, R^b and $R^{b'}$ are both hydrogen.

In some embodiments, one R^1 is –$C(Y)NR^bR^{b'}$ and the other is –$S(O)_qR^f$. In some embodiments, R^b and $R^{b'}$ are both hydrogen. In some embodiments, R^f is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, one R^1 is –$C(Y)NR^bR^{b'}$ and the other is –CN. In some embodiments, R^b and $R^{b'}$ are both hydrogen.

In some embodiments, one R^1 is –OR^d and the other is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, one R^1 is –OR^d and the other is haloalkyl (e.g., trifluoromethyl). In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl).

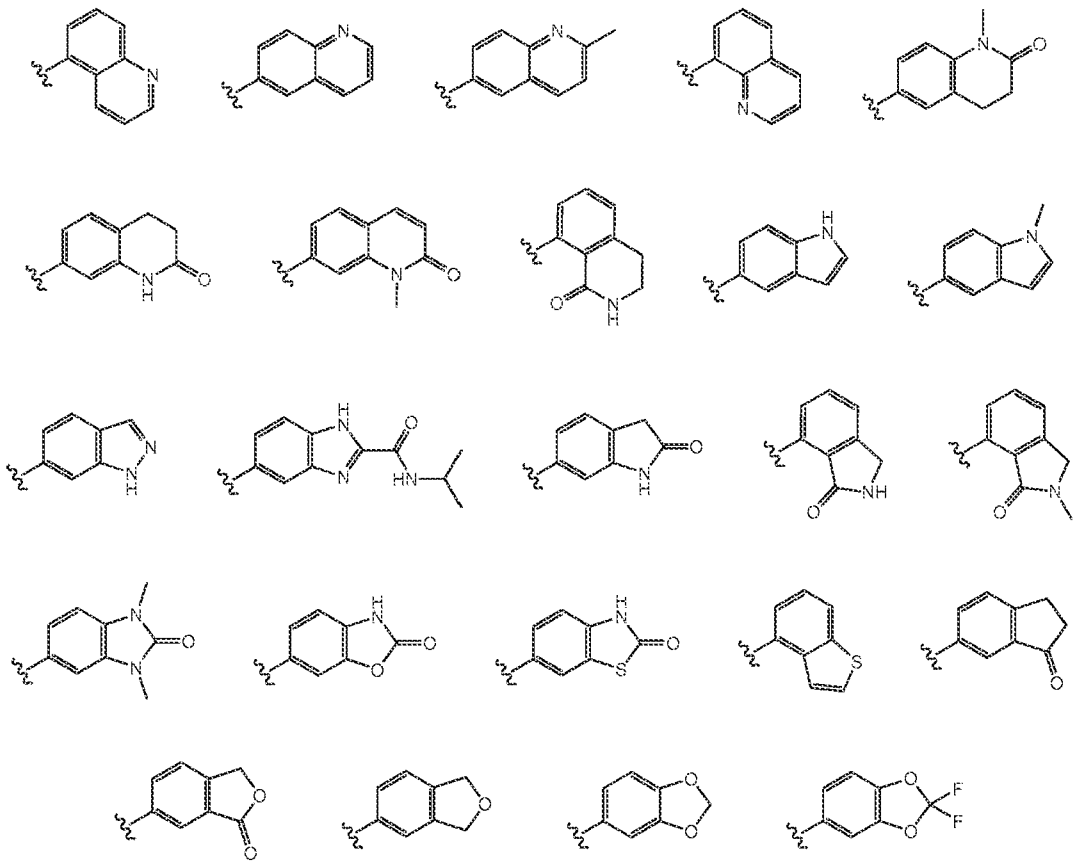
In some embodiments, one R^1 is $-OR^d$ and the other is $-C(O)OR^a$. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^a is hydrogen. In some embodiments, R^a is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, one R^1 is $-OR^d$ and the other is $-NR^cC(O)R^{c'}$. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^c is hydrogen and $R^{c'}$ is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, one R^1 is haloalkyl (e.g., trifluoromethyl) and the other is $-CN$.

In some embodiments, two R^1, together with the atoms to which they are attached, are taken together to form a cyclyl ring (e.g., a substituted cyclyl ring). In some embodiments, two R^1, together with the atoms to which they are attached, are taken together to form a heterocyclyl ring (e.g., a substituted heterocyclyl ring). In some embodiments, two R^1, together with the atoms to which they are attached, are taken together to form a heteroaryl ring (e.g., a substituted heteroaryl ring).

In some embodiments, two R^1 and ring B are taken together to form a group selected from:



In some embodiments, R^2 is aryl.

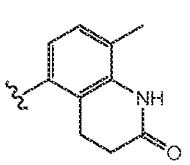
In some embodiments, each R^1 is independently halo (e.g., all three R^1 are fluoro or all three R^1 are chloro).

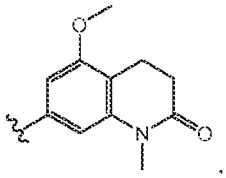
In some embodiments, two R^1 are independently halo (e.g., both are chloro) and the other is C_1-C_8 alkyl (e.g., methyl). In some embodiments, two R^1 are independently halo (e.g., both are chloro) and the other is heteroaryl (e.g., pyrrolyl). In some embodiments, two R^1 are independently halo (e.g., both are fluoro) and the other is $-C(Y)NR^bR^{b'}$ (e.g.,$-C(O)NH_2$). In some embodiments, two R^1 are independently C_1-C_8 alkyl (e.g., both are methyl) and the other is halo (e.g., chloro or bromo).

In some embodiments, one R^1 is C_1-C_8 alkyl (e.g., methyl), and two R^1, together with the atoms to which they are attached, are taken together to form a heterocyclyl ring.

In some embodiments, one R^1 is $-OR^d$, and two R^1, together with the atoms to which they are attached, are taken together to form a heterocyclyl ring. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, three R^1 and ring B are taken together to form a group selected from:



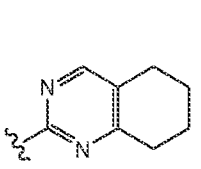


In some embodiments, B is a 6-membered heteroaryl.

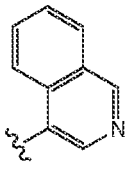
In some embodiments, B is pyridyl. In some embodiments, B is 3-pyridyl. In some embodiments, m is 2. In some embodiments, two R^1, together with the atoms to which they are attached, are taken together to form an aryl ring (e.g., a phenyl ring). In some embodiments, m is 3. In some embodiments, one R^1 is $-OR^d$, and two R^1, together with the atoms to which they are attached, are taken together to form an aryl ring (e.g., a phenyl ring). In some embodiments, R^d is hydrogen.

In some embodiments, B is pyrazolyl. In some embodiments, m is 2. In some embodiments, two R^1, together with the atoms to which they are attached, are taken together to form a cyclyl ring (e.g., a cyclohexyl ring).

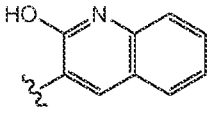
In some embodiments, B is selected from:



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and



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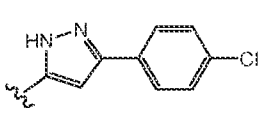
In some embodiments, B is a 5-membered heteroaryl (e.g., pyrazolyl).

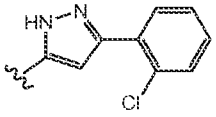
In some embodiments, m is 1.

In some embodiments, R^1 is aryl (e.g., phenyl).

In some embodiments, R^1 is phenyl substituted with 1 R^6.

In some embodiments, R^6 is halo (e.g., chloro). In some embodiments, R^1 is selected from:

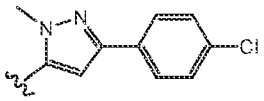


and


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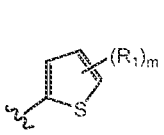
In some embodiments, m is 2.

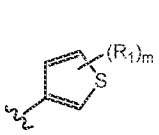
In some embodiments, one R^1 is C_1-C_8 alkyl (e.g., methyl) and the other is aryl (e.g., phenyl). In some embodiments, the aryl is phenyl substituted with 1 R^6. In some embodiments, R^6 is halo (e.g., chloro). In some embodiments, R^1 is:

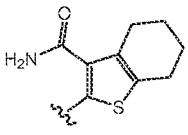


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In some embodiments, B is thienyl. In some embodiments, B is selected from:





and


.

In some embodiments, m is 1. In some embodiments, m is 2. In some embodiments m is 2 and two R^1, together with the atoms to which they are attached, form an optionally substituted cyclyl, heterocyclyl, aryl or heteroaryl ring

In some embodiments, R^1 is $-C(O)OR_a$. In some embodiments, R^a is C_1-C_8 alkyl (e.g., ethyl).

In some embodiments, R^1 is $-C(Y)NR^bR^{b'}$. In some embodiments, Y is O. In some embodiments, R^b and $R^{b'}$ are both hydrogen.

In some embodiments, m is 2.

In some embodiments, one R^1 is C_1-C_8 alkyl (e.g., methyl) and the other is $-C(Y)NR^bR^{b'}$. In some embodiments, Y is O. In some embodiments, R^b and $R^{b'}$ are both hydrogen.

In some embodiments, B is thiazolyl.

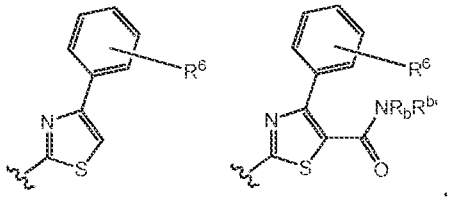
In some embodiments, m is 1.

In some embodiments, R^1 is aryl (e.g., phenyl).

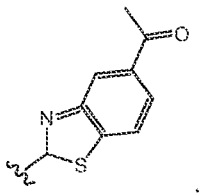
In some embodiments, m is 2.

In some embodiments, two R^1, together with the atoms to which they are attached, form an aryl ring. In some embodiments, the aryl ring is substituted with $-C(Y)R^e$. In some embodiments, Y is O. In some embodiments, R^e is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, B is:



In some embodiments, B is:



In some embodiments, E is aryl (e.g., phenyl).

In some embodiments, n is 1.

In some embodiments, R^2 is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, R^2 is C_1-C_8 alkyl substituted with 1-3 R^6. In some embodiments, R^2 is C_1 alkyl substituted with 1 R^6.

In some embodiments, R^6 is $-NR^bR^{b'}$. In some embodiments, R^b and $R^{b'}$ are each independently C_1-C_8 alkyl (e.g., R^b and $R^{b'}$ are both methyl, or R^b and $R^{b'}$ are both ethyl). In some embodiments, one of R^b and $R^{b'}$ is hydrogen and the other is haloalkyl (e.g., trifluoroethyl).

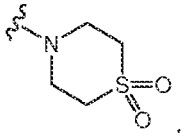
In some embodiments, R^6 is $-OR^d$. In some embodiments, R^d is cyclyl (e.g., cyclopentyl). In some embodiments, R^d is heterocyclylalkyl (e.g., $-CH_2$-tetrahydropyranyl).

In some embodiments, R^2 is C_2 alkyl substituted with 1 R^6.

In some embodiments, R^6 is $-C(Y)NR^bR^{b'}$. In some embodiments, Y is O. In some embodiments, R^b and $R^{b'}$ are both hydrogen. In some embodiments, R^b and $R^{b'}$ are each independently C_1-C_8 alkyl (e.g., R^b and $R^{b'}$ are both methyl). In some

embodiments, one of R^b and $R^{b'}$ is hydrogen and the other is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, R^6 is $-C(Y)R^e$. In some embodiments, Y is O. In some embodiments, R^e is heterocyclyl (e.g., morpholino or thiomorpholino). In some embodiments, R^e is thiomorpholino substituted with 2 R^7. In some embodiments, each R^7 is oxo. In some embodiments, R^e is:



In some embodiments, R^2 is C_3 alkyl substituted with 1 R^6.

In some embodiments, R^6 is $-C(Y)NR^bR^{b'}$. In some embodiments, Y is O. In some embodiments, R^b and $R^{b'}$ are both hydrogen. In some embodiments, R^b and $R^{b'}$ are each independently C_1-C_8 alkyl (e.g., R^b and $R^{b'}$ are both methyl). In some embodiments, one of R^b and $R^{b'}$ is hydrogen and the other is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, R^6 is $-NR^cC(Y)R^{c'}$. In some embodiments, Y is O. In some embodiments, R^c and $R^{c'}$ are each independently C_1-C_8 alkyl (e.g., R^c and $R^{c'}$ are both methyl).

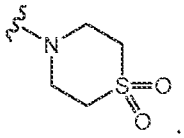
In some embodiments, R^6 is $-OR^d$. In some embodiments, R^d is hydrogen. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, R^6 is silyloxy (e.g., tert-butyldimethylsilyloxy).

In some embodiments, R^6 is $-C(Y)R^e$. In some embodiments, Y is O. In some embodiments, R^e is heterocyclyl (e.g., morpholino).

In some embodiments, R^2 is C_2-C_8 alkynyl. In some embodiments, R^2 is C_2-C_8 alkynyl substituted with 1 R^6 (e.g., C_3 alkynyl substituted with 1 R^6). In some embodiments, R^2 is $-C\equiv C-CH_2-R^6$. In some embodiments, R^6 is $-NR^bR^{b'}$. In some embodiments, R^b and $R^{b'}$ are each independently C_1-C_8 alkyl (e.g., R^b and $R^{b'}$ are both methyl). In some embodiments, R^6 is $-OR^d$. In some embodiments, R^d is hydrogen. In some embodiments, R^6 is silyloxy (e.g., tert-butyldimethylsilyloxy). In some embodiments, R^6 is heterocyclyl (e.g., morpholino or thiomorpholino). In some

embodiments, R^6 is thiomorpholino substituted with 2 R^7. In some embodiments, each R^7 is oxo. In some embodiments, R^6 is:



In some embodiments, R^2 is aryl (e.g., phenyl). In some embodiments, R^2 is unsubstituted phenyl.

In some embodiments, R^2 is phenyl substituted with 1 R^6.

In some embodiments, R^6 is heterocyclylalkyl (e.g., $-CH_2$-morpholino). In some embodiments, R^6 is haloalkyl (e.g., trifluoromethyl). In some embodiments, R^6 is –CN. In some embodiments, R^6 is $-OR^d$. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^6 is $-C(Y)R^e$. In some embodiments, Y is O. In some embodiments, R^e is heterocyclyl (e.g., morpholino).

In some embodiments, R^2 is phenyl substituted with 2 R^6.

In some embodiments, each R^6 is independently $-OR^d$. In some embodiments, each R^d is C_1-C_8 alkyl (e.g., methyl). In some embodiments, one R^6 is halo (e.g., fluoro) and the other is C_1-C_8 alkyl (e.g., methyl). In some embodiments, one R^6 is $-C(O)OR^a$ and the other is $-OR^d$. In some embodiments, R^a and R^d are each independently C_1-C_8 alkyl (e.g., R^a and R^d are both methyl).

In some embodiments, R^2 is heteroaryl.

In some embodiments, R^2 is isoxazolyl. In some embodiments, R^2 is isoxazolyl substituted with 2 R^6. In some embodiments, each R^6 is independently C_1-C_8 alkyl (e.g., R^6 is methyl).

In some embodiments, R^2 is pyrazolyl. In some embodiments, R^2 is pyrazolyl substituted with 1 R^6. In some embodiments, R^6 is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, R^2 is pyridyl. In some embodiments, R^2 is unsubstituted pyridyl. In some embodiments, R^2 is pyridyl substituted with 1 R^6. In some embodiments, R^6 is halo (e.g., fluoro). In some embodiments, R^6 is $-NR^bR^{b'}$. In some embodiments, R^b and $R^{b'}$ are each hydrogen. In some embodiments, R^6 is $-OR^d$. In some embodiments, R^d is hydrogen. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^6 is heterocyclyl (e.g., morpholino or

piperazinyl). In some embodiments, R^6 is piperazinyl substituted with 1 R^7. In some embodiments, R^7 is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, R^2 is pyrimidinyl.

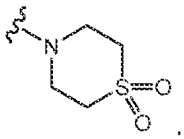
In some embodiments, R^2 is pyridazinyl.

In some embodiments, R^2 is cyclyl (e.g., cyclopropyl).

In some embodiments, R^2 is heterocyclyl (e.g., morpholino or pyrrolidinyl).

In some embodiments, R^2 is aralkyl (e.g., benzyl).

In some embodiments, R^2 is heterocyclylalkyl. In some embodiments, the alkyl is C_1 alkyl. In some embodiments, the alkyl is C_2 alkyl. In some embodiments, the alkyl is C_3 alkyl. In some embodiments, the heterocyclyl is piperidinyl. In some embodiments, the heterocyclyl is piperazinyl. In some embodiments, the heterocyclyl is piperazinyl substituted with 1 R^6. In some embodiments, R^6 is C_1-C_8 alkyl (e.g., methyl). In some embodiments, the heterocyclyl is pyrrolidinyl. In some embodiments, the heterocyclyl is morpholino. In some embodiments, the heterocyclyl is thiomorpholino. In some embodiments, the heterocyclyl is thiomorpholino substituted with 2 R^6. In some embodiments, each R^6 is oxo. In some embodiments, the heterocyclyl is:



In some embodiments, R^2 is halo (e.g., fluoro, chloro, bromo or iodo).

In some embodiments, R^2 is haloalkyl (e.g., trifluoromethyl).

In some embodiments, R^2 is haloalkoxy (e.g., trifluoromethoxy).

In some embodiments, R^2 is –CN.

In some embodiments, R^2 is $–NO_2$.

In some embodiments, R^2 is $–C(O)OR^a$. In some embodiments, R^a is hydrogen. In some embodiments, R^a is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, R^2 is $–C(Y)NR^bR^{b'}$. In some embodiments, Y is O. In some embodiments, R^b and $R^{b'}$ are each hydrogen. In some embodiments, R^b and $R^{b'}$ are each independently C_1-C_8 alkyl (e.g., R^b and $R^{b'}$ are both methyl). In some embodiments, one of R^b and $R^{b'}$ is hydrogen and the other is C_1-C_8 alkyl (e.g., methyl

or ethyl). In some embodiments, one of R^b and $R^{b'}$ is hydrogen and the other is heterocyclylalkyl (e.g., $-CH_2-CH_2$-morpholino). In some embodiments, one of R^b and $R^{b'}$ is hydrogen and the other is haloalkyl (e.g., trifluoroethyl).

In some embodiments, R^2 is $-NR^bR^{b'}$. In some embodiments, R^b and $R^{b'}$ are both hydrogen. In some embodiments, R^b and $R^{b'}$ are each independently C_1-C_8 alkyl (e.g., R^b and $R^{b'}$ are both methyl). In some embodiments, one of R^b and $R^{b'}$ is hydrogen and the other is C_1-C_8 alkyl (e.g., methyl). In some embodiments, one of R^b and $R^{b'}$ is hydrogen and the other is heterocyclyl (e.g., tetrahydropyranyl). In some embodiments, one of R^b and $R^{b'}$ is hydrogen and the other is heterocyclylalkyl. In some embodiments, the alkyl is C_1 alkyl. In some embodiments, the alkyl is C_2 alkyl. In some embodiments, the alkyl is C_3 alkyl. In some embodiments, the heterocyclyl is morpholino. In some embodiments, the heterocyclyl is pyrrolidinyl. In some embodiments, the heterocyclyl is tetrahydrofuranyl. In some embodiments, the heterocyclyl is tetrahydropyranyl. In some embodiments, one of R^b and $R^{b'}$ is hydrogen and the other is hydroxyalkyl. In some embodiments, the alkyl is C_2 alkyl. In some embodiments, one of R^b and $R^{b'}$ is hydrogen and the other is alkoxyalkyl. In some embodiments, the alkyl is C_2 alkyl. In some embodiments, the alkyl is C_3 alkyl. In some embodiments, the alkoxy is methoxy. In some embodiments, one of R^b and $R^{b'}$ is hydrogen and the other is $-C(Y)R^e$. In some embodiments, Y is O. In some embodiments, R^e is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^e is heterocyclyl. In some embodiments, R^e is tetrahydropyranyl.

In some embodiments, R^2 is $-OR^d$.

In some embodiments, R^d is hydrogen. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, R^d is ethyl. In some embodiments, R^d is C_3 alkyl (e.g., isopropyl or n-propyl). In some embodiments, R^d is optionally substituted heteroaralkyl. In some embodiments, R^d is optionally substituted pyrindinalkyl.

In some embodiments, R^d is n-propyl. In some embodiments, R^d is cyclyl (e.g., cyclopentyl).

In some embodiments, R^d is heteroaralkyl (e.g.,$-CH_2$-pyridyl).

In some embodiments, R^d is heterocyclylalkyl. In some embodiments, the alkyl is C_1 alkyl. In some embodiments, the alkyl is C_2 alkyl. In some embodiments, the alkyl is C_3 alkyl. In some embodiments, the alkyl is C_4 alkyl. In some embodiments, the heterocyclyl is morpholino. In some embodiments, the heterocyclyl is piperidyl. In some embodiments, the heterocyclyl is tetrahydrofuranyl. In some embodiments, R^d is cyclylalkyl (e.g.,$-CH_2$-cyclobutyl).

In some embodiments, R^d is alkoxyalkyl. In some embodiments, the alkyl is C_2 alkyl. In some embodiments, the alkyl is C_3 alkyl. In some embodiments, the alkoxy is methoxy.

In some embodiments, R^d is dialkylaminoalkyl. In some embodiments, the alkyl is C_2 alkyl. In some embodiments, the alkyl is C_3 alkyl. In some embodiments, the dialkylamino is dimethylamino.

In some embodiments, R^2 is $-C(Y)R^e$. In some embodiments, Y is O. In some embodiments, R^e is heterocyclyl. In some embodiments, R^e is piperidyl. In some embodiments, R^e is pyrrolidinyl. In some embodiments, R^e is piperazinyl. In some embodiments, R^e is morpholino. In some embodiments, R^e is thiomorpholino.

In some embodiments, n is 2.

In some embodiments, each R^2 is independently halo (e.g., each R^2 is chloro).

In some embodiments, each R^2 is independently $-OR^d$.

In some embodiments, each R^d is C_1-C_8 alkyl.

In some embodiments, each R^2 is methoxy. In some embodiments, one R^2 is methoxy and the other is ethoxy. In some embodiments, one R^2 is methoxy and the other is propoxy. In some embodiments, one R^2 is methoxy and the other is isopropoxy.

In some embodiments, one R^2 is methoxy and the other is ethoxy substituted with 1 R^6. In some embodiments, R^6 is $-NR^bR^{b'}$. In some embodiments, R^b and $R^{b'}$ are each independently C_1-C_8 alkyl (e.g., R^b and $R^{b'}$ are both methyl). In some embodiments, R^6 is $-OR^d$. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, one R^2 is methoxy and the other is propoxy substituted with 1 R^6. In some embodiments, R^6 is $-OR^d$. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, one R^2 is $-OR^d$ and the other is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl or ethyl).

In some embodiments, one R^2 is $-OR^d$ and the other is halo (e.g., chloro). In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, one R^2 is $-OR^d$ and the other is –CN. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, one R^2 is $-OR^d$ and the other is $-C(O)OR^a$. In some embodiments, R^d and R^a are both hydrogen.

In some embodiments, one R^2 is $-OR^d$ and the other is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, one R^2 is $-OR^d$ and the other is $-C(Y)R^e$. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl). In some embodiments, Y is O. In some embodiments, R^e is heterocyclyl (e.g., morpholino).

In some embodiments, one R^2 is halo (e.g., chloro or bromo) and the other is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, one R^2 is C_1-C_8 alkyl (e.g., methyl) and the other is -CN.

In some embodiments, one R^2 is C_1-C_8 alkyl (e.g., methyl) and the other is heteroaryl (e.g., pyridyl). In some embodiments, the pyridyl is substituted with 1 R^6. In some embodiments, R^6 is $-OR^d$. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, one R^2 is C_1-C_8 alkyl (e.g., methyl) and the other is heterocyclylalkyl (e.g., $-CH_2$-morpholino).

In some embodiments, p is 0.

In some embodiments, p is 1.

In some embodiments, R^3 is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^3 is halo (e.g., chloro). In some embodiments, R^3 is haloalkyl (e.g., trifluoromethyl). In some embodiments, R^3 is oxo.

In some embodiments, R^3 is $-OR^d$. In some embodiments, R^d is hydrogen. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, R^3 is $-NR^bR^{b'}$. In some embodiments, R^b and $R^{b'}$ are both hydrogen. In some embodiments, one of R^b and $R^{b'}$ is hydrogen and the other is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, R^3 is heterocyclyl (e.g., piperazinyl). In some embodiments, R^3 is piperazinyl substituted with 1 R^6. In some embodiments, R^6 is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, E is a 5-membered heteroaryl ring.

In some embodiments, E is a thiophene ring.

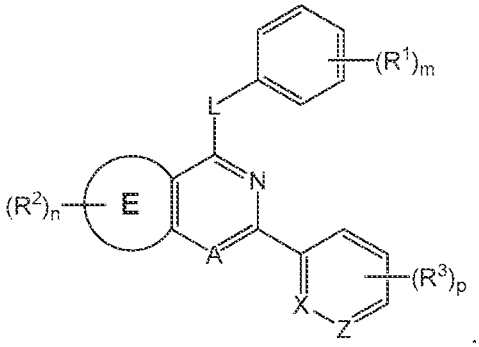
In some embodiments, E is a pyrrole ring.

In some embodiments, n is 1. In some embodiments, R^2 is C_1-C_8 alkyl (e.g., methyl). In some embodiments, E is an N-methylpyrrole ring.

In some embodiments, L is NR^5. In some embodiments, R^5 is hydrogen.

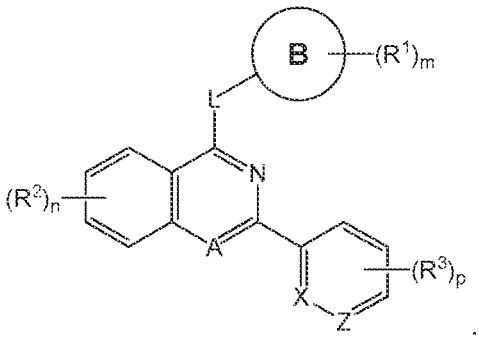
In some embodiments, L is O.

In some embodiments, the compound is:

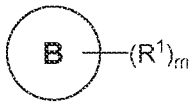
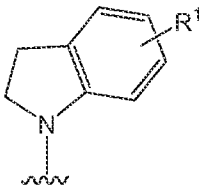


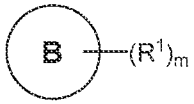
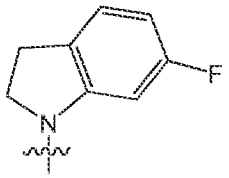
In some embodiments, R^2 is C_1-C_4 alkoxy. In some embodiments, R^2 is halo. In some embodiments, R^1 is $-C(Y)NR^bR^{b'}$.

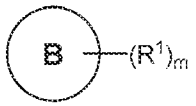
In some embodiments, the compound is:

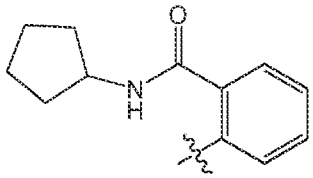
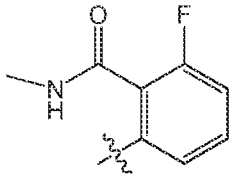
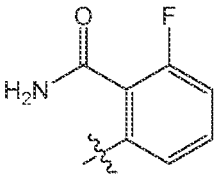


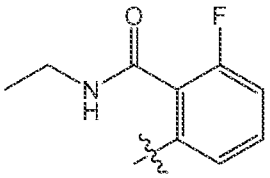
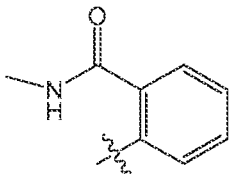
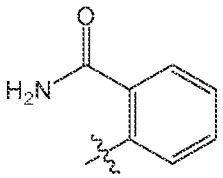
In some embodiments, R^2 is C_1-C_4 alkoxy. In some embodiments, R^2 is halo. In some embodiments, R^1 is $-C(Y)NR^bR^{b'}$.

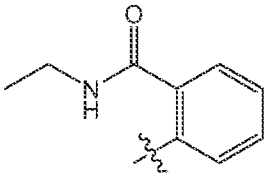
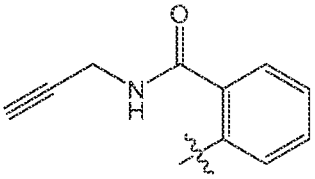
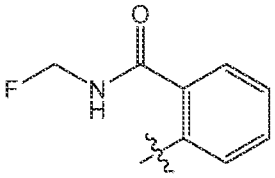
In some embodiments,  is .

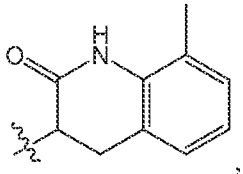
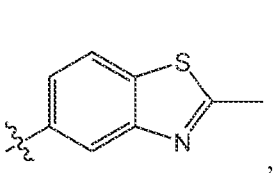
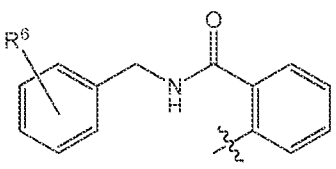
In some embodiments,  is .

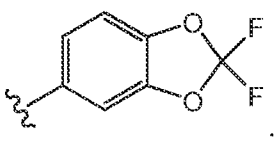
In some embodiments, L is NH, and  is selected from

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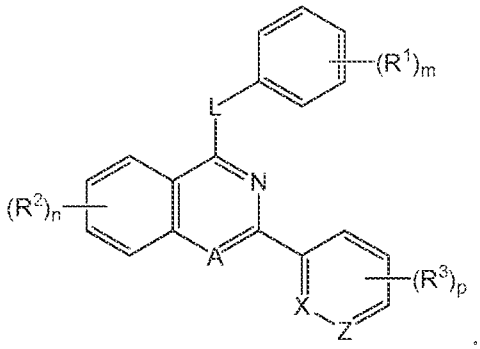
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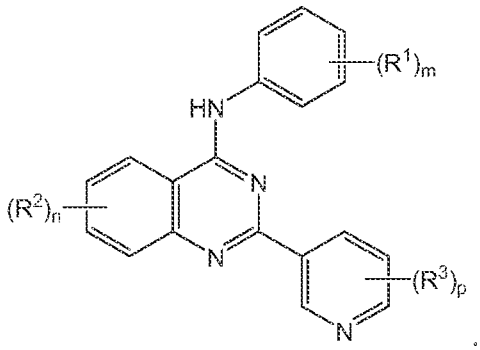
In some embodiments R^6 is halo.

In some embodiments, the compound is:



In some embodiments, R^1 is $-C(Y)NR^bR^{b'}$. In some embodiments, R^1 is halo. In some embodiments, R^2 is C_1-C_4 alkoxy. In some embodiments, R^2 is halo. In some embodiments, m is 2 and two R^1 are 3,4-dichloro; 3,4-difluoro, 3,5- dichloro; 3,5-difluoro; 3-chloro,4-fluoro; or 3-chloro,5-fluoro. In some embodiments, R^2 is $-C(O)NR^bR^{b'}$ and R^3 is H. In some embodiments, R^b and $R^{b'}$ are H. In some embodiments, R^b and $R^{b'}$ are independently C_1-C_4 alkyl or halo-substituted C_1-C_4 alkyl. In some embodiments, R^b is methyl and $R^{b'}$ is trifluoroethyl. In some embodiments, R^1 is C_1-C_4 alkoxy or halo-substituted C_1-C_4 alkoxy. In some embodiments, n and p are zero.

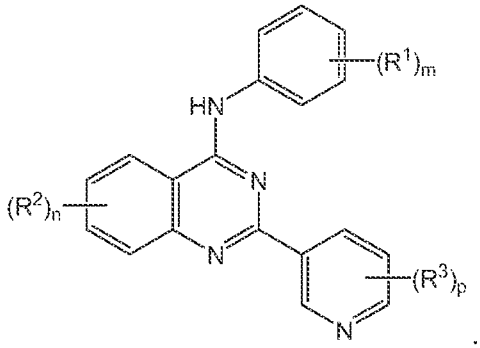
In some embodiments, the compound is:



In some embodiments, R^1 is $-C(Y)NR^bR^{b'}$. In some embodiments, R^1 is halo. In some embodiments, R^2 is C_1-C_4 alkoxy. In some embodiments, R^2 is halo. In some embodiments, m is 2 and two R^1 are 3,4-dichloro; 3,4-difluoro, 3,5- dichloro; 3,5-difluoro; 3-chloro,4-fluoro; or 3-chloro,5-fluoro. In some embodiments, R^2 is $-C(O)NR^bR^{b'}$ and R^3 is H. In some embodiments, R^b and $R^{b'}$ are H. In some

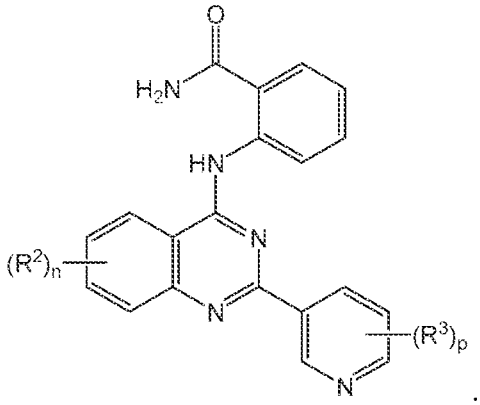
embodiments, R^b and $R^{b'}$ are independently C_1-C_4 alkyl or halo-substituted C_1-C_4 alkyl. In some embodiments, R^b is methyl and $R^{b'}$ is trifluoroethyl. In some embodiments, R^1 is C_1-C_4 alkoxy or halo-substituted C_1-C_4 alkoxy. In some embodiments, n and p are zero.

In some embodiments, the compound is:



In some embodiments, R^1 is $-C(Y)NR^bR^{b'}$. In some embodiments, R^1 is halo. In some embodiments, R^2 is C_1-C_4 alkoxy. In some embodiments, R^2 is halo. In some embodiments, m is 2 and two R^1 are 3,4-dichloro; 3,4-difluoro, 3,5- dichloro; 3,5-difluoro; 3-chloro,4-fluoro; or 3-chloro,5-fluoro. In some embodiments, R^2 is $-C(O)NR^bR^{b'}$ and R^3 is H. In some embodiments, R^b and $R^{b'}$ are H. In some embodiments, R^b and $R^{b'}$ are independently C_1-C_4 alkyl or halo-substituted C_1-C_4 alkyl. In some embodiments, R^b is methyl and $R^{b'}$ is trifluoroethyl. In some embodiments, R^1 is C_1-C_4 alkoxy or halo-substituted C_1-C_4 alkoxy. In some embodiments, n and p are zero.

In some embodiments, the compound is:



In some embodiments, R^1 is $-C(Y)NR^bR^{b'}$. In some embodiments, R^1 is halo. In some embodiments, R^2 is C_1-C_4 alkoxy. In some embodiments, R^2 is halo. In some embodiments, m is 2 and two R^1 are 3,4-dichloro; 3,4-difluoro, 3,5- dichloro; 3,5-difluoro; 3-chloro,4-fluoro; or 3-chloro,5-fluoro. In some embodiments, R^2 is $-C(O)NR^bR^{b'}$ and R^3 is H. In some embodiments, R^b and $R^{b'}$ are H. In some embodiments, R^b and $R^{b'}$ are independently C_1-C_4 alkyl or halo-substituted C_1-C_4 alkyl. In some embodiments, R^b is methyl and $R^{b'}$ is trifluoroethyl. In some embodiments, R^1 is C_1-C_4 alkoxy or halo-substituted C_1-C_4 alkoxy. In some embodiments, n and p are zero.

Compounds of Formula (II)

The following aspects and embodiments relate to compounds of formula (II).

Item 9. The compound according to item 1 represented by general formula (II) or a salt thereof,

wherein:

L is CR^4R^5, O, C(O), $NR^6C(O)$ or NR^7;

A is N;

each X^1, X^2, X^3, X^4 and X^5 is independently CH or N, provided that at least two of X^1, X^2, X^3, X^4 and X^5 are N;

n is 0, 1, 2, 3 or 4;

p is 0, 1, 2 or 3;

R^1 is C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl or heterocyclylalkyl, each of which is optionally substituted with 1-5 R^9; wherein R^1 or R^9 is optionally taken together with one of R^4, R^5, R^6 or R^7, and the atoms to which they are attached to form a cyclyl, heterocyclyl, aryl or heteroaryl ring that is optionally substituted with 1-3 R^{10};

each R^2 and R^3 is independently hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy,

silylalkoxyalkyl, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{11};

each R^4, R^5, R^6 and R^7 is independently hydrogen , C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$,$–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$;

each R^9, R^{10} and R^{11} is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thioxo, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{12};wherein two R^8, two R^9, two R^{10} or two R^{11} is optionally taken together with the atoms to which they are attached to form an optionally substituted cyclyl, heterocyclyl, aryl or heteroaryl ring;

R^{12} is $–OR^d$;

Y is O or S;

q is 1 or 2; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e, $R^{e'}$ and R^f is independently hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, acyl, cyclyl, heterocyclyl, aryl, heteroaryl, cyclylalkyl, heterocyclylalkyl, arylalkyl, or heteroarylalkyl.

Item 10. The compound according to item 9 represented by general formula (II) or a salt thereof,

L is NR^7;

n is 0, 1 or 2;

p is 0;

R^1 is C_1-C_8 alkyl, aryl or heteroaryl;

each R^2 and R^3 is independently hydrogen, C_1-C_8 alkyl, aryl, halo, heterocyclylalkyl, $-NR^cC(Y)R^c$, $-NR^bR^{b'}$ or $-OR^d$, each of which is optionally substituted with 1-3 R^{11};

R^7 is hydrogen; and

each R^9, R^{10} and R^{11} is independently C_1-C_8 alkyl, heterocyclyl, halo, haloalkyl, haloalkoxy, $-CN$, $-C(O)OR^a$, $-C(Y)NR^bR^{b'}$, $-OR^d$ or $-C(Y)R^e$;

Y is O;

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e, $R^{e'}$ and R^f is independently hydrogen, C_1-C_8 alkyl, cyclyl, heterocyclyl, aryl or heteroaryl.

Item 11 .The compound according to item 10 represented by general formula (II) or a salt thereof,

wherein:

R^1 is C_1-C_8 alkyl, phenyl or benzodioxolyl;

each R^2 and R^3 is independently hydrogen, C_1-C_8 alkyl, phenyl, halo, morholinylalkyl, $-NR^cC(Y)R^c$, $-NR^bR^{b'}$or $-OR^d$;

R^9 is independently C_1-C_8 alkyl, morpholinyl, tetrahydropyranyl, halo, haloalkyl, haloalkoxy, $-CN$, $-C(O)OR^a$, $-C(Y)NR^bR^{b'}$, $-OR^d$ or $-C(Y)R^e$; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e, $R^{e'}$ and R^f is independently hydrogen, C_1-C_8 alkyl, C_3-C_8 cycloalkyl, tetrahydropyranyl, phenyl or pyridyl.

Item 12. The compound according to item 10 represented by general formula (II) or a salt thereof,

wherein:

R^1 is C_1-C_8 alkyl, phenyl or benzodioxolyl;

each R^2 and R^3 is independently hydrogen, C_1-C_8 alkyl, phenyl, halo, morholinylalkyl, $-NR^cC(Y)R^c$, $-NR^bR^{b'}$or $-OR^d$, each of which is optionally substituted with 1-3 R^{11};

each R^9, R^{10} and R^{11} is independently C_1-C_8 alkyl, morpholinyl, tetrahydropyranyl, halo, haloalkyl, haloalkoxy, –CN, –C(O)OR^a, –C(Y)$NR^bR^{b'}$,–OR^d or –C(Y)R^e; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e, $R^{e'}$ and R^f is independently hydrogen, C_1-C_8 alkyl, C_3-C_8 cycloalkyl, tetrahydropyranyl, phenyl, or pyridyl.

Item 13. The compoundaccording to item 12 represented by general formula (II) or a salt thereof, wherein:

R^2 is C_1-C_8 alkyl, phenyl, halo, morholinylalkyl, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$ or –OR^d, each of which is optionally substituted with 1-3 R^{11};

R^3 is hydrogen;

R^9 is halo, haloalkoxy, –CN, –C(O)OR^a or –C(Y)$NR^bR^{b'}$; and

R^{11} is C_1-C_8 alkyl, morpholinyl, tetrahydropyranyl, halo, –CN, –OR^d or –C(Y)R^e;

Item 14. The compound according to item 11 or 13 represented by general formula (II) or a salt thereof, wherein:

R^2 is C_1-C_8 alkyl, phenyl, halo, morholinylalkyl, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$ or –OR^d;

R^3 is hydrogen; and

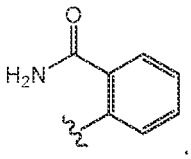
R^9 is halo, haloalkoxy, –CN, –C(O)OR^a or –C(Y)$NR^bR^{b'}$.

In some embodiments, A is CH. In some embodiments, A is N.

In some embodiments, L is NR^7. In some embodiments, R^7 is H.

In some embodiments, R^1 is aryl (e.g., phenyl).

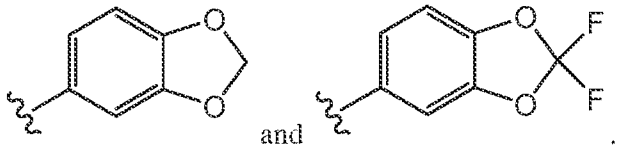
In some embodiments, R^1 is phenyl substituted with 1 R^9. In some embodiments, R^1 is phenyl substituted with 1 R^9 in the ortho position. In some embodiments, R^1 is phenyl substituted with 1 R^9 in the meta position. In some embodiments, R^9 is haloalkoxy (e.g., difluoromethoxy or trifluoromethoxy). In some embodiments, R^9 is –CN. In some embodiments, R^9 is –C(O)OR^a. In some embodiments, R^a is hydrogen. In some embodiments, R^9 is –C(Y)$NR^bR^{b'}$. In some embodiments, Y is O. In some embodiments, R^b and $R^{b'}$ are both hydrogen. In some embodiments, R^1 is:



In some embodiments, one of R^b and $R^{b'}$ is hydrogen and the other is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, R^1 is phenyl substituted with 2 R^9. In some embodiments, each R^9 is independently halo (e.g., each R^9 is fluoro or each R^9 is chloro). In some embodiments, one R^9 is fluoro and the other is chloro. In some embodiments, one R^9 is halo (e.g., chloro) and the other is haloalkoxy (e.g., difluoromethoxy or trifluoromethoxy).

In some embodiments, 2 R^9 are taken together with the atoms to which they are attached to form a heterocyclyl ring, e.g., a 5-membered heterocyclyl ring (e.g., a dioxole ring). In some embodiments, the dioxole ring is unsubstituted. In some embodiments, the dioxole ring is substituted. In some embodiments, the dioxole ring is substituted with two fluoro substituents. In some embodiments, R^1 is selected from:



and

In some embodiments, R^1 is aralkyl (e.g., benzyl). In some embodiments, R^1 is aralkyl substituted with 2 R^9 (e.g., benzyl substituted with 2 R^9). In some embodiments, 2 R^9 substituents are on the phenyl ring. In some embodiments, each R^9 is independently halo (e.g., each R^9 is chloro).

In some embodiments, R^1 is alkyl (e.g., methyl).

In some embodiments, n is 0.

In some embodiments, n is 1.

In some embodiments, R^2 is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^2 is C_1-C_8 alkyl substituted with 1 R^{11} (e.g., methyl substituted with 1 R^{11}). In some embodiments, R^{11} is heterocyclyl (e.g., morpholino).

In some embodiments, R^2 is aryl (e.g., phenyl). In some embodiments, R^2 is phenyl substituted with 1 R^{11}. In some embodiments, R^{11} is –CN. In some embodiments, R^{11} is $-OR^d$. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^{11} is halo.

In some embodiments, R^2 is halo (e.g., fluoro, chloro, bromo or iodo).

In some embodiments, R^2 is $-NR^cC(Y)R^{c'}$. In some embodiments, R^c is hydrogen. In some embodiments, Y is O. In some embodiments, $R^{c'}$ is alkyl (e.g., methyl). In some embodiments, $R^{c'}$ is aryl (e.g., phenyl). In some embodiments, $R^{c'}$ is phenyl substituted with 1 R^8. In some embodiments, R^8 is $-OR^d$. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, $R^{c'}$ is heteroaryl. In some embodiments, $R^{c'}$ is furanyl. In some embodiments, $R^{c'}$ is pyridyl. In some embodiments, $R^{c'}$ is pyridyl substituted with 1 R^8. In some embodiments, R^8 is $-OR^d$. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, $R^{c'}$ is cyclyl (e.g., cyclohexyl). In some embodiments, $R^{c'}$ is cyclohexyl substituted with 1 R^8. In some embodiments, R^8 is $-OR^d$. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, $R^{c'}$ is heterocyclyl (e.g., tetrahydropyranyl).

In some embodiments, R^2 is $-NR^bR^{b'}$. In some embodiments, R^b and $R^{b'}$ are both hydrogen. In some embodiments, R^b and $R^{b'}$ are each independently C_1-C_8 alkyl (e.g., R^b and $R^{b'}$ are both methyl).

In some embodiments, R^2 is $-OR^d$. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl or ethyl). In some embodiments, R^d is ethyl substituted with 1 R^8. In some embodiments, R^8 is $-OR^d$. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^2 is $-OCH_2CH_2OCH_3$. In some embodiments, R^2 is $-OCH_2CH_2OCH_2CH_2CH_3$. In some embodiments, R^2 is $-OCH_2CH_2OCH_2CH_2OCH_3$.

In some embodiments, n is 2.

In some embodiments, one R^2 is C_1-C_8 alkyl (e.g., methyl) and the other is halo (e.g., chloro).

In some embodiments, one R^2 is $-OR^d$ and the other is halo (e.g., chloro). In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl).

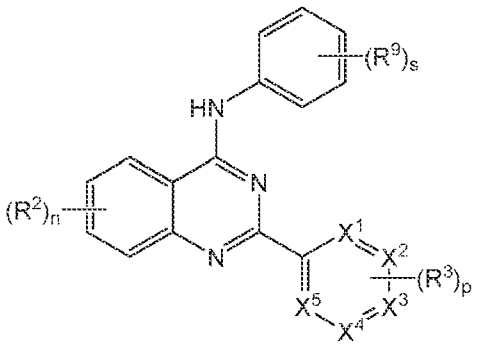
In some embodiments, X^1 and X^4 are N and X^2, X^3 and X^5 are CH.

In some embodiments, X^1 and X^3 are N and X^2, X^4 and X^5 are CH.

In some embodiments, X^2 and X^3 are N and X^1, X^4 and X^5 are CH.

In some embodiments, X^2 and X^4 are N and X^1, X^3 and X^5 are CH.

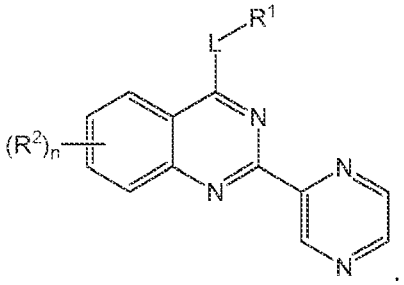
In some embodiments, the compound is:



wherein s is 0, 1, 2, 3 or 4.

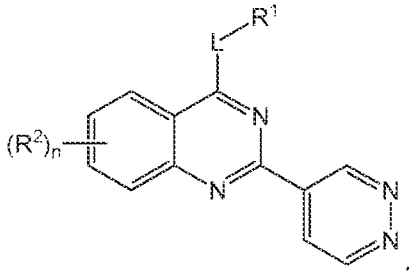
In some embodiments, R^9 is -C(O)NH_2, C_1-C_4 alkoxy, or substituted C_1-C_4 alkoxy. In some embodiments, R^9 is halo.

In some embodiments, the compound is:



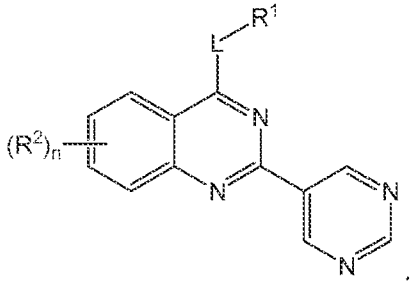
In some embodiments, R_1 is selected from methyl, cyclohexyl, t-butyl, and pyridinyl. In some embodiments, R_1 is heteroaralkyl (e.g.,–CH_2-pyridyl). In some embodiments, LR^1 is $NH(CH_3)$.

In some embodiments, the compound is:



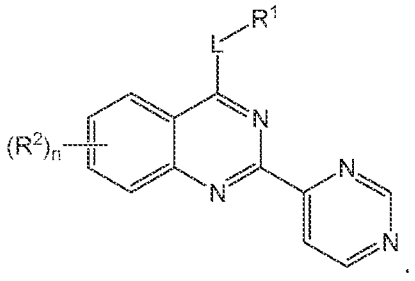
In some embodiments, R_1 is selected from methyl, cyclohexyl, t-butyl, and pyridinyl. In some embodiments, R_1 is heteroaralkyl (e.g.,–CH_2-pyridyl). In some embodiments, LR^1 is $NH(CH_3)$.

In some embodiments, the compound is:



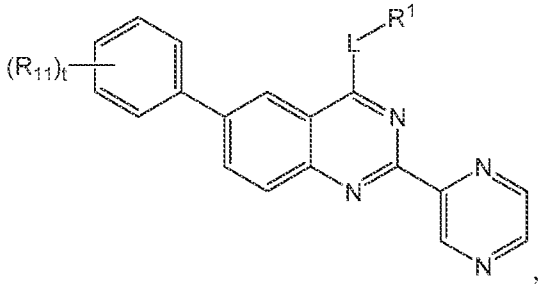
In some embodiments, R_1 is selected from methyl, cyclohexyl, t-butyl, and pyridinyl. In some embodiments, R_1 is heteroaralkyl (e.g.,–CH_2-pyridyl). In some embodiments, LR^1 is $NH(CH_3)$.

In some embodiments, the compound is:



In some embodiments, R_1 is selected from methyl, cyclohexyl, t-butyl, and pyridinyl. In some embodiments, R_1 is heteroaralkyl (e.g.,–CH_2-pyridyl). In some embodiments, LR^1 is $NH(CH_3)$.

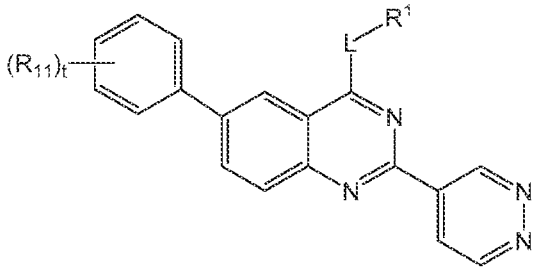
In some embodiments, the compound is:



, wherein t is 1-3.

In some embodiments, R_1 is selected from methyl, cyclohexyl, t-butyl, and pyridinyl. In some embodiments, R_1 is heteroaralkyl (e.g.,–CH_2-pyridyl). In some embodiments, LR^1 is $NH(CH_3)$. In some embodiments, R^{11} is independently halo, nitrile, C_1-C_4 alkoxy, -$C(O)NH_2$, hydroxy, or C_1-C_4 hydroxyalkyl. In some embodiments, R^{11} is fluoro. In some embodiments, R^{11} is methoxy, ethoxy, or methoxyethoxy ether. In some embodiments, R^{11} is $–OCH_2CH_2OCH_3$. In some embodiments, R^{11} is $– OCH_2CH_2OCH_2CH_2CH_3$. In some embodiments, R^{11} is $– OCH_2CH_2OCH_2CH_2OCH_3$.

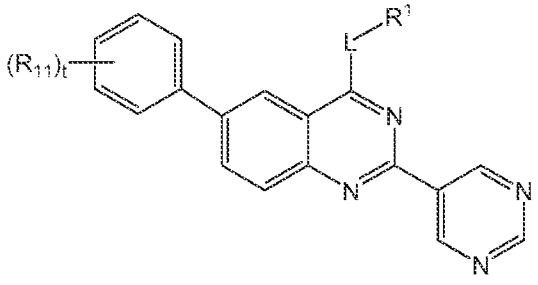
In some embodiments, the compound is:



, wherein t is 1-3.

In some embodiments, R_1 is selected from methyl, cyclohexyl, t-butyl, and pyridinyl. In some embodiments, LR^1 is $NH(CH_3)$. In some embodiments, R^{11} is independently halo, nitrile, C_1-C_4 alkoxy, -$C(O)NH_2$, hydroxy, or C_1-C_4 hydroxyalkyl. In some embodiments, R^{11} is fluoro. In some embodiments, R^{11} is methoxy, ethoxy, or methoxyethoxy ether. In some embodiments, R^{11} is $–OCH_2CH_2OCH_3$. In some embodiments, R^{11} is $– OCH_2CH_2OCH_2CH_2CH_3$. In some embodiments, R^{11} is $– OCH_2CH_2OCH_2CH_2OCH_3$.

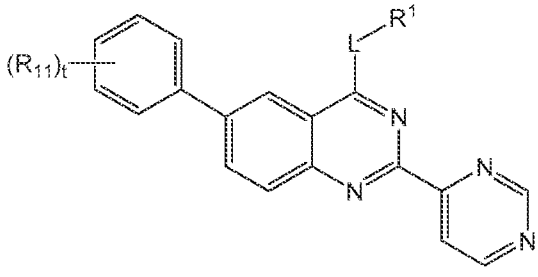
In some embodiments, the compound is:



, wherein t is 1-3.

In some embodiments, R_1 is selected from methyl, cyclohexyl, t-butyl, and pyridinyl. In some embodiments, LR^1 is $NH(CH_3)$. In some embodiments, R^{11} is independently halo, nitrile, C_1-C_4 alkoxy, $-C(O)NH_2$, hydroxy, or C_1-C_4 hydroxyalkyl. In some embodiments, R^{11} is fluoro. In some embodiments, R^{11} is methoxy, ethoxy, or methoxyethoxy ether. In some embodiments, R^{11} is $-OCH_2CH_2OCH_3$. In some embodiments, R^{11} is $-OCH_2CH_2OCH_2CH_2CH_3$. In some embodiments, R^{11} is $-OCH_2CH_2OCH_2CH_2OCH_3$.

In some embodiments, the compound is:



, wherein t is 1-3.

In some embodiments, R_1 is selected from methyl, cyclohexyl, t-butyl, and pyridinyl. In some embodiments, LR^1 is $NH(CH_3)$. In some embodiments, R^{11} is independently halo, nitrile, C_1-C_4 alkoxy, $-C(O)NH_2$, hydroxy, or C_1-C_4 hydroxyalkyl. In some embodiments, R^{11} is fluoro. In some embodiments, R^{11} is methoxy, ethoxy, or methoxyethoxy ether. In some embodiments, R^{11} is $-OCH_2CH_2OCH_3$. In some embodiments, R^{11} is $-OCH_2CH_2OCH_2CH_2CH_3$. In some embodiments, R^{11} is $-OCH_2CH_2OCH_2CH_2OCH_3$.

Compounds of Formula (III)

The following aspects and embodiments relate to compounds of formula (III).

item 15. The compound according to item 1 represented by general formula (III) or a salt thereof,

wherein:

A is CH or N;

L is O, a direct bond or NH;

one of X^1, X^2, X^3, X^4 and X^5 is N and the others are CH;

m is 1, 2 or 3;

n is 1, 2, 3 or 4;

R^1 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, alkoxyalkyl, hydroxyalkyl, heteroaryl, heteroarylalkyl, arylalkyl, –C(Y)R^e, cyclyl, cyclylalkyl or heterocyclyl, each of which is optionally substituted with 1-3 R^7;

R^2 is aryl or heteroaryl, each of which is optionally substituted with 1-5 R^9;

each R^3 or R^4 is independently hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, –NO_2, –C(O)OR^a, –C(Y)$NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^cSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$, –OR^d, –$SR^{d'}$, –C(Y)R^e or -$S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{10};

each R^7, R^9 and R^{10} is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thioxo, –CN, –NO_2, –C(O)OR^a, –C(Y)$NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^cSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$,–OR^d, –$SR^{d'}$, –C(Y)R^e or -$S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{12}; wherein two R^7 or two R^9 are optionally be taken together with the atoms to which they are attached to form an optionally substituted cyclyl, heterocyclyl, aryl or heteroaryl ring;

R^{12} is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo,

haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thioxo, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^cSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$,–OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{13};

R^{13} is independently C_1-C_8 alkyl, haloalkyl, halo, heterocyclyl, cyclyl, oxo or –$C(Y)NR^bR^{b'}$;

Y is O or S;

q is 1 or 2; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, acyl, cyclyl, heterocyclyl, aryl, haloalkyl, alkoxyalkyl, alkylaminoalkyl, dialkylaminoalkyl, heteroaryl, cyclylalkyl, heterocyclylalkyl, arylalkyl or heteroarylalkyl..

Item 16. The compound according to item 15 represented by general formula (III) or a salt thereof,

wherein:

m is 1;

n is 1;

R^1 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, heteroaryl, heterocyclyl, arylalkyl, cyclylalkyl, heteroarylalkyl, alkoxyalkyl, hydroxyalkyl or –$C(O)R^e$, each of which is optionally substituted with 1-3 R^7;

R^2 is aryl, heteroaryl or benzofuryl, each of which is optionally substituted with 1-5 R^9;

each R^3 or R^4 is independently hydrogen, C_1-C_8 alkyl, halo, haloalkyl or –OR^d;

R^6 is hydrogen or C_1-C_8 alkyl;

each R^7 and R^9 is independently C_1-C_8 alkyl, aryl, heteroaryl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, alkoxyalkyl, oxo, –CN, –NO_2, –$C(O)OR^a$, –$C(O)NR^bR^{b'}$, –$NR^bR^{b'}$, –OR^d, –$C(O)R^e$ or -$S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{12};

R^{12} is independently C_1-C_8 alkyl, oxo, halo, haloalkyl, –CN, –$C(O)NR^bR^{b'}$ or –$C(O)R^e$ each of which is optionally substituted with 1-3 R^{13};

R^{13} is independently C_1-C_8 alkyl, halo or heterocyclyl ; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, cyclyl, heterocyclyl, arylalkyl, alkoxyalkyl, heterocyclylalkyl, heteroarylalkyl, alkylaminoalkyl, dialkylaminoalkyl or phenyl.

Item 17. The compound according to Item 16 represented by general formula (III) or a salt thereof,

wherein:

R^1 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, alkoxyalkyl, hydroxyalkyl, imidazolyl, pyridylalkyl, phenylalkyl, oxazolylalkyl, thienylalkyl, thiazolidinyl isoindolyl, –$C(O)R^e$, dihydroindenyl, C_3-C_8 cycloalkyl, C_3-C_8 cycloalkylalkyl, piperidyl, morpholinyl, pyrrolidinyl, azetidinyl or piperazinyl, each of which is optionally substituted with 1-3 R^7;

R^2 is phenyl, naphthyl, benzofuryl, indazolyl, benzothienyl, pyridyl, pyrimidinyl, dihydrobenzodioxinyl, benzodioxolyl, benzoimidazolyl, isoxazolyl, pyrazolyl, indolinyl or benzoisoxazolyl, each of which is optionally substituted with 1-5 R^9;

each R^3 or R^4 is independently hydrogen, C_1-C_8 alkyl, halo, haloalkyl or –OR^d;

R^6 is hydrogen or C_1-C_8 alkyl;

each R^7 and R^9 is independently C_1-C_8 alkyl, phenyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, alkoxyalkyl, oxo, –CN, –NO_2, –$C(O)OR^a$, –$C(O)NR^bR^{b'}$,–$NR^bR^{b'}$,–OR^d, –$C(O)R^e$ or -$S(O)_qR^f$; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, C_3-C_8 cycloalkyl, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, tetrahydropyranyl, phenylalkyl, alkoxyalkyl, morholinylalkyl, oxazolidinylalkyl, imidazolylalkyl, tetrahydropyranylalkyl, pyridylalkyl, pyrazolylalkyl, tetrazolylalkyl, thiazolylalkyl, pyrrolylalkyl, benzoxazolylalkyl, indazolylalkyl, dihydrobenzoxazinylalkyl, tetrahydrofurylalkyl, tetrahydrofuryl, alkylaminoalkyl, dialkylaminoalkyl or phenyl.

Item 18. The compound according to item 16 represented by general formula (III) or a salt thereof,

wherein:

R^1 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, alkoxyalkyl, hydroxyalkyl, imidazolyl, furylalkyl, pyridylalkyl, phenylalkyl, oxazolylalkyl, thienylalkyl, thiazolidinyl, isoindolyl, $-C(O)R^e$, dihydroindenyl, C_3-C_8 cycloalkyl, C_3-C_8 cycloalkylalkyl, piperidyl, morpholinyl, pyrrolidinyl, azetidinyl or piperazinyl, each of which is optionally substituted with 1-3 R^7;

R^2 is phenyl, naphthyl, benzofuryl, indazolyl, benzothienyl, pyridyl, pyrimidinyl, dihydrobenzodioxinyl, benzodioxolyl, benzoimidazolyl, isoxazolyl, pyrazolyl, indolinyl or benzisoxazolyl, each of which is optionally substituted with 1-5 R^9;

each R^3 or R^4 is independently hydrogen, C_1-C_8 alkyl, halo, haloalkyl or $-OR^d$;

R^6 is hydrogen or C_1-C_8 alkyl;

each R^7 and R^9 is independently C_1-C_8 alkyl, phenyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, alkoxyalkyl, oxo, $-CN$, $-NO_2$, $-C(O)OR^a$, $-C(O)NR^bR^{b'}$, $-NR^bR^{b'}$, $-OR^d$, $-C(O)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{12};

R^{12} is independently C_1-C_8 alkyl, oxo, halo, haloalkyl, $-CN$, $-C(O)NR^bR^{b'}$ or $-C(O)R^e$, each of which is optionally substituted with 1-3 R^{13};

R^{13} is independently C_1-C_8 alkyl, halo or pyrrolidinyl; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, C_3-C_8 cycloalkyl, pyrrolidinyl, piperidyl, morpholinyl, piperazinyl, tetrahydropyranyl, phenylalkyl, alkoxyalkyl, morpholinylalkyl, oxazolidinylalkyl, imidazolylalkyl, tetrahydropyranylalkyl, pyridylalkyl, pyrazolylalkyl, tetrazolylalkyl, thiazolylalkyl, pyrrolylalkyl, benzoxazolylalkyl, indazolylalkyl, dihydrobenzoxazinylalkyl, tetrahydrofurylalkyl, tetrahydrofuryl, alkylaminoalkyl, dialkylaminoalkyl or phenyl.

Item 19. The compound according to item 18 represented by general formula (III) or a salt thereof,

wherein:

A is N;

R^3 is hydrogen, C_1-C_8 alkyl, halo, haloalkyl, or $-OR^d$;

R^4 is hydrogen, C_1-C_8 alkyl, halo, or $-OR^d$;

R^7 is C_1-C_8 alkyl, phenyl, halo, haloalkyl, oxo, $-C(O)OR^a$, $-C(O)NR^bR^{b'}$ or $-OR^d$ each of which is optionally substituted with 1-3 R^{12};

R^9 is C_1-C_8 alkyl, phenyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, alkoxyalkyl, $-CN$, $-NO_2$, $-C(O)NR^bR^{b'}$, $-C(O)OR^a$, $-NR^bR^{b'}$, $-OR^d$, $-C(O)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{12}; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, C_3-C_8 cycloalkyl, pyrrolidinyl, piperidyl, morpholinyl, piperazinyl, tetrahydropyranyl, phenylalkyl, alkoxyalkyl, morpholinylalkyl, oxazolidinylalkyl, imidazolylalkyl, tetrahydropyranylalkyl, pyridylalkyl, pyrazolylalkyl, tetrazolylalkyl, thiazolylalkyl, pyrrolylalkyl, benzoxazolylalkyl, indazolylalkyl, tetrahydrofurylalkyl, dihydrobenzoxazinylalkyl, tetrahydrofuryl, alkylaminoalkyl, dialkylaminoalkyl or phenyl;.

Item 20. The compound according to item 17 or 19 represented by general formula (III) or a salt thereof,

wherein:

A is N;

R^3 is hydrogen, C_1-C_8 alkyl, halo, haloalkyl, or $-OR^d$;

R^4 is hydrogen, C_1-C_8 alkyl, halo, or $-OR^d$;

R^7 is C_1-C_8 alkyl, phenyl, halo, haloalkyl, oxo, $-C(O)OR^a$, $-C(O)NR^bR^{b'}$ or $-OR^d$;

R^9 is C_1-C_8 alkyl, phenyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, alkoxyalkyl, $-CN$, $-NO_2$, $-C(O)NR^bR^{b'}$, $-C(O)OR^a$, $-NR^bR^{b'}$, $-OR^d$, $-C(O)R^e$ or $-S(O)_qR^f$; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, C_3-C_8 cycloalkyl, pyrrolidinyl, piperidyl, morpholinyl, piperazinyl, tetrahydropyranyl, phenylalkyl, alkoxyalkyl, morpholinylalkyl, oxazolidinylalkyl, imidazolylalkyl, tetrahydropyranylalkyl, pyridylalkyl, pyrazolylalkyl, tetrazolylalkyl, thiazolylalkyl, pyrrolylalkyl, benzoxazolylalkyl, indazolylalkyl, tetrahydrofurylalkyl, tetrahydrofuryl, dihydrobenzoxazinylalkyl, alkylaminoalkyl, dialkylaminoalkyl or phenyl.

Item 21. The compound according to item 20 represented by general formula (III) or a salt thereof,

wherein:

R^1 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, alkoxyalkyl, hydroxyalkyl, imidazolyl, furylalkyl, pyridylalkyl, phenylalkyl, oxazolylalkyl, thienylalkyl, isoindolyl, –C(O)R^e, dihydroindenyl, C_3-C_8 cycloalkyl, C_3-C_8 cycloalkylalkyl, piperidyl, morpholinyl, pyrrolidinyl, azetidinyl or piperazinyl, each of which is optionally substituted with 1-3 R^7;

R^2 is phenyl, which is optionally substituted with 1-5 R^9; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, pyrrolidinyl, morpholinyl, tetrahydropyranyl, alkoxyalkyl, morpholinylalkyl, tetrahydropyranylalkyl, pyridylalkyl, thiazolylalkyl, pyrrolylalkyl, tetrahydrofuryl, alkylaminoalkyl or phenyl.

In some embodiments, R^1 is C_1-C_8 alkyl, which is optionally substituted with 1-3 R^7; or when L is NR^6, R^1 and R^6 may be taken together with the atoms to which they are attached to form a heterocyclyl or heteroaryl ring that is optionally substituted with 1-3 R^8.

In some embodiments, A is CH. In some embodiments, A is N.

In some embodiments, L is NR^6. In some embodiments, R^6 is hydrogen.

In some embodiments, R^1 is C_1-C_8 alkyl, e.g., methyl, ethyl, C_3 alkyl (e.g., n-propyl or isopropyl), C_4 alkyl (e.g., n-butyl, isobutyl or tert-butyl), or C_5 alkyl (e.g., pentan-3-yl).

In some embodiments, R^1 is C_1-C_8 alkyl substituted with 1-3 R^7 (e.g., C_1-C_8 alkyl substituted with 1 R^7). In some embodiments, R^1 is methyl substituted with 1 R^7. In some embodiments, R^7 is cyclyl (e.g., cyclopropyl). In some embodiments, R^7 is aryl (e.g., phenyl).

In some embodiments, R^1 is ethyl substituted with 1 R^7. In some embodiments, R^7 is aryl (e.g., phenyl). In some embodiments, R^7 is –OR^d. In some embodiments, R^d is aryl (e.g., phenyl).

In some embodiments, R^1 is n-propyl substituted with 1 R^7. In some embodiments, R^7 is –OR^d. In some embodiments, R^d is C_1-C_8 alkyl (e.g., C_3 alkyl, e.g., n-propyl).

In some embodiments, R^1 is C_1-C_8 alkyl substituted with 3 R^7. In some embodiments, R^1 is ethyl substituted with 3 R^7. In some embodiments, each R^7 is independently halo (e.g., each R^7 is fluoro). In some embodiments, R^1 is 2,2,2-trifluoroethyl.

In some embodiments, R^1 is C_2-C_8 alkenyl, e.g., C_3 alkenyl (e.g., $-CH_2-CH=CH_2$).

In some embodiments, R^1 is C_2-C_8 alkynyl, e.g., C_3 alkynyl (e.g. $-CH_2-C\equiv CH$).

In some embodiments, R^1 is cyclyl (e.g., cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl). In some embodiments, the cyclyl group is a bicyclic group (e.g., indanyl).

In some embodiments, R^1 is heterocyclyl (e.g., piperidyl). In some embodiments, R^1 is piperidyl substituted with 1 R^7. In some embodiments, R^7 is $-C(Y)R^e$. In some embodiments, Y is O. In some embodiments, R^e is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^7 is $-OR^d$.

In some embodiments, R^6 is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, R^1 and R^6 are taken together with the atoms to which they are attached to form a heterocyclyl ring (e.g. a pyrrolidine ring).

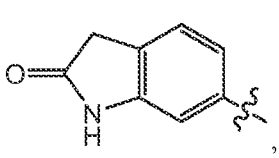
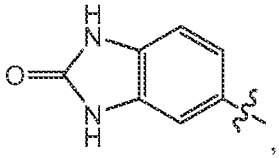
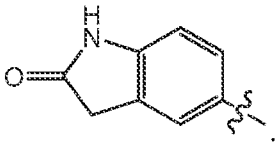
In some embodiments, R^1 and R^6 are taken together with the atoms to which they are attached to form a heteroaryl ring (e.g., an imidazole ring).

In some embodiments, L is O.

In some embodiments, R^1 is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, R^2 is aryl (e.g., phenyl). In some embodiments, R^2 is unsubstituted phenyl. In some embodiments, R^2 is phenyl substituted with 1-3 R^9. In some embodiments, R^2 is phenyl substituted with 1 R^9.

In some embodiments, R^2 is:


, 
, or 
.

In some embodiments, R^9 is halo (e.g., fluoro or chloro). In some embodiments, R^9 is –CN. In some embodiments, R^9 is $–NO_2$. In some embodiments, R^9 is haloalkoxy (e.g., trifluoroethoxy). In some embodiments, R^9 is $–NR^bR^{b'}$. In some embodiments, R^b and $R^{b'}$ are each independently C_1-C_8 alkyl (e.g., R^b and $R^{b'}$ are both methyl).

In some embodiments, R^9 is $–OR^d$. In some embodiments, R^9 is $–OCH_2CH_2OCH_3$. In some embodiments, R^9 is $–OCH_2CH_2OCH_2CH_2CH_3$. In some embodiments, R^9 is $–OCH_2CH_2OCH_2CH_2OCH_3$. In some embodiments, R^d is hydrogen. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^d is ethyl.

In some embodiments, R^9 is hydroxyalkyl (e.g.,$–CH_2OH$). In some embodiments, R^9 is alkoxyalkyl (e.g., $–CH_2$-O-CH_3). In some embodiments, R^9 is $–C(O)R^e$. In some embodiments, R^e is heterocyclyl (e.g., morpholino). In some embodiments, R^9 is $–S(O)_qR^f$. In some embodiments, q is 1. In some embodiments, R^f is C_1-C_8 alkyl (e.g., methyl.).

In some embodiments, R^2 is phenyl substituted with 2 R^9. In some embodiments, each R^9 is independently halo (e.g., each R^9 is fluoro). In some embodiments, each R^9 is independently $–OR^d$. In some embodiments, each R^d is independently C_1-C_8 alkyl (e.g., each R^d is methyl).

In some embodiments, R^2 is heteroaryl. In some embodiments, R^2 is a 6-membered heteroaryl. In some embodiments, R^2 is a 6-membered nitrogen-containing heteroaryl, e.g., pyridyl. In some embodiments, R^2 is unsubstituted pyridyl.

In some embodiments, R^2 is pyridyl substituted with 1 R^9. In some embodiments, R^9 is $-OR^d$. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, R^2 is a 5-membered heteroaryl. In some embodiments, R^2 is a 5-membered nitrogen-containing heteroaryl (e.g., pyrrolyl or oxazolyl).

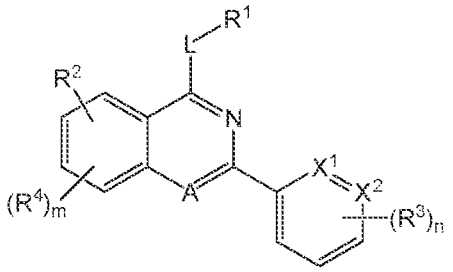
In some embodiments, m is 0.

In some embodiments, m is 1.

In some embodiments, R^4 is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^4 is $–OR^d$. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl). In some

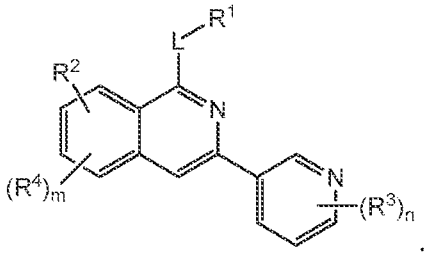
embodiments, R^4 is halo. In some embodiments, R^4 is methoxy. In some embodiments, R^d is C_1-C_8 alkyl.

In some embodiments, the compound has the following structure:



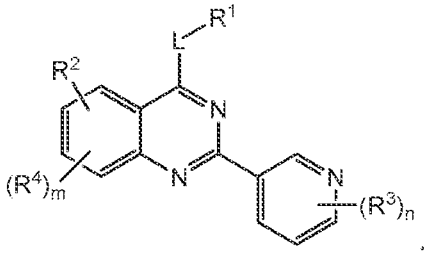
wherein one of X^1 and X^2 is N and the other is CH.

In some embodiments, X^1 is CH and X^2 is N. In some embodiments, X^1 is N and X^2 is CH. In some embodiments, the compound has the following structure:



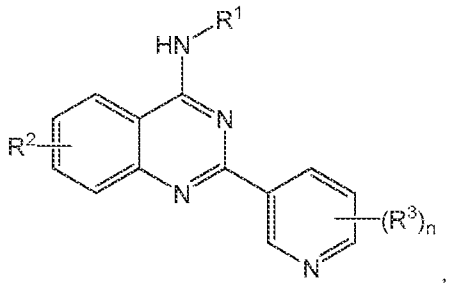
In some embodiments, R^2 is aryl. In some embodiments, R^2 is heteroaryl. In some embodiments, R^1 is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, the compound has the following structure:



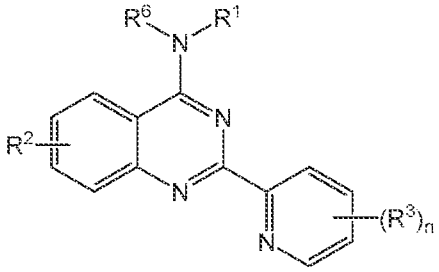
In some embodiments, R^2 is aryl. In some embodiments, R^2 is heteroaryl. In some embodiments, R^1 is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, the compound has the following structure:



In some embodiments, R^2 is aryl. In some embodiments, R^2 is heteroaryl. In some embodiments, R^1 is C_1-C_8 alkyl (e.g., methyl).

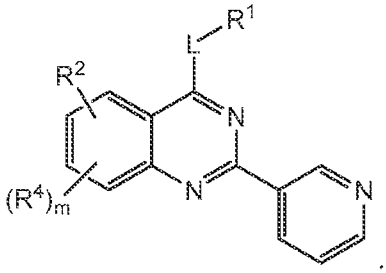
In some embodiments, the compound has the following structure:



wherein R^1 is C_1-C_8 alkyl, which is optionally substituted with 1-3 R^7.

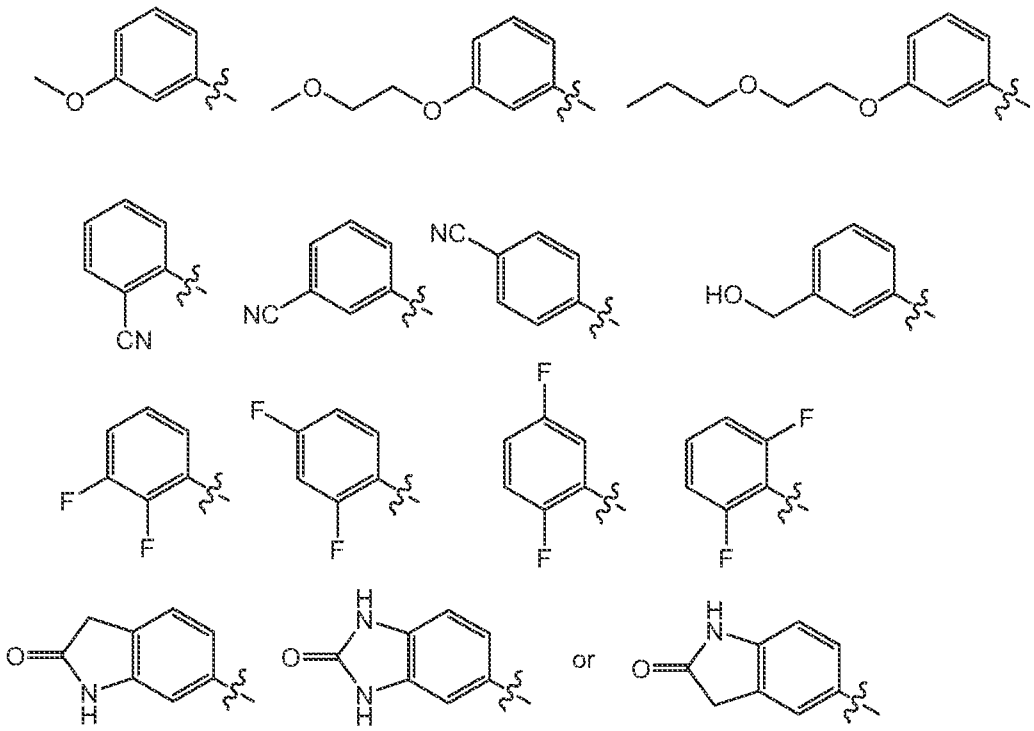
In some embodiments, R^2 is aryl. In some embodiments, R^2 is heteroaryl. In some embodiments, R^1 is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, the compound has the following structure:

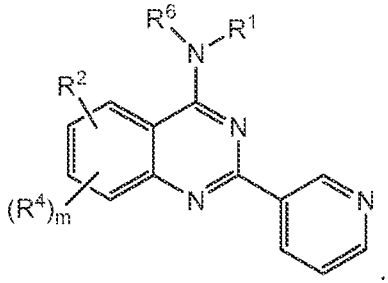


In some embodiments, R^2 is aryl. In some embodiments, R^2 is heteroaryl. In some embodiments, R^1 is C_1-C_8 alkyl (e.g., methyl).

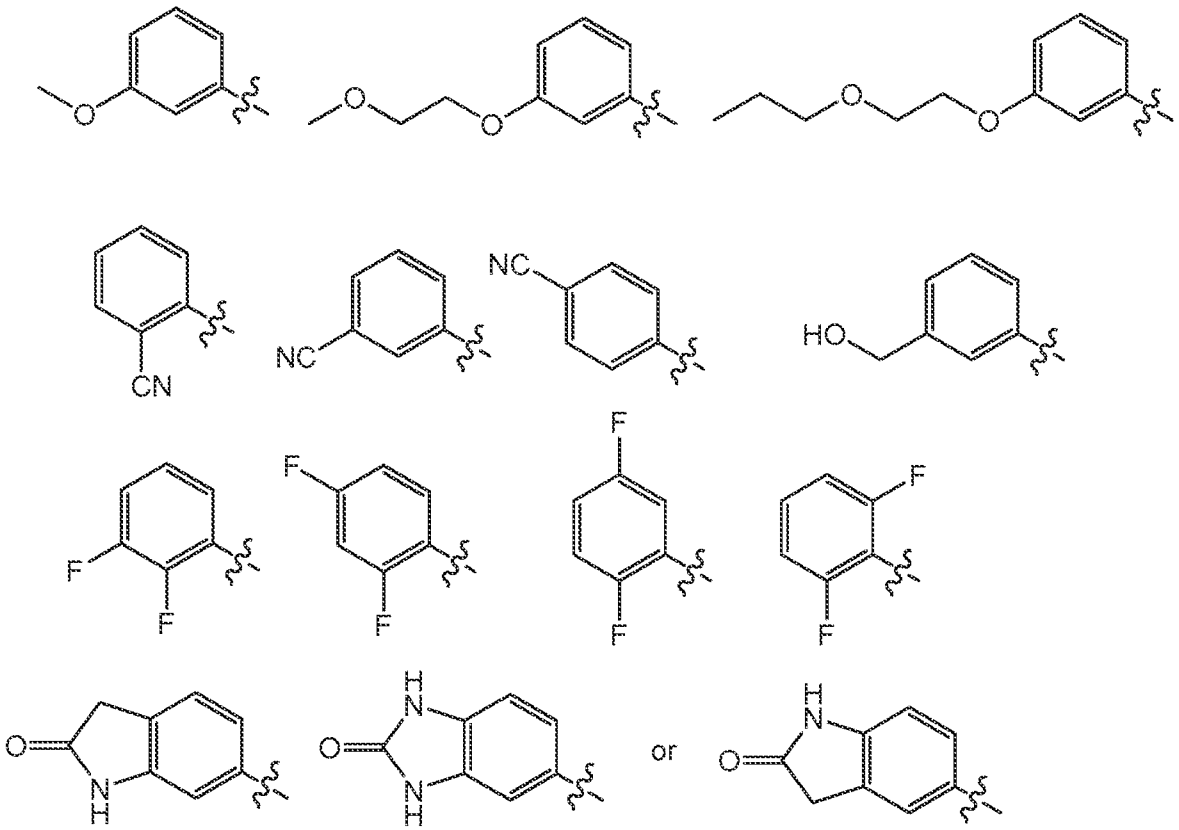
In some embodiments, R^2 is



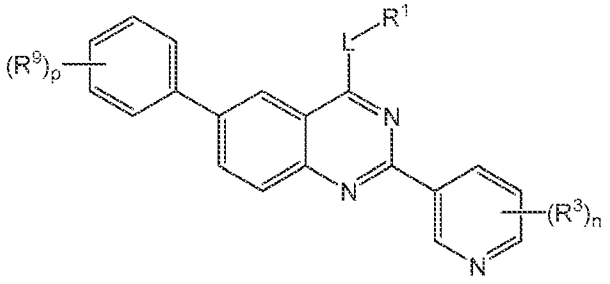
In some embodiments, the compound has the following structure:



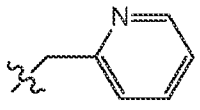
In some embodiments, R^2 is aryl. In some embodiments, R^2 is heteroaryl. In some embodiments R^1 is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^2 is



In some embodiments, the compound has the following structure:



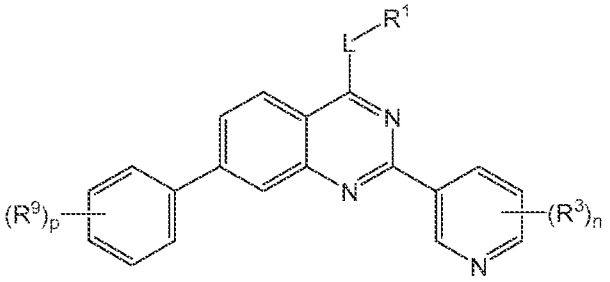
wherein p is 1, 2, 3, 4 or 5.

In some embodiments, L is NR^6. In some embodiments, L is O. In some embodiments, R^1 is hydrogen or C_1-C_8 alkyl. In some embodiments, R^1 is cyclyl or heterocyclyl. In some embodiments, R^1 is aralkyl or heteroaralkyl. In some embodiments, R^1 is methyl, cyclohexyl, t-butyl, or 

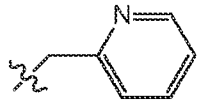
. In some embodiments, R^6 is hydrogen or C_1-C_8 alkyl.

In some embodiments, R^9 is C_1-C_8 alkyl, halo, -CN, or -OR^d. In some embodiments, R^3 is hydrogen.

In some embodiments, the compound has the following structure:



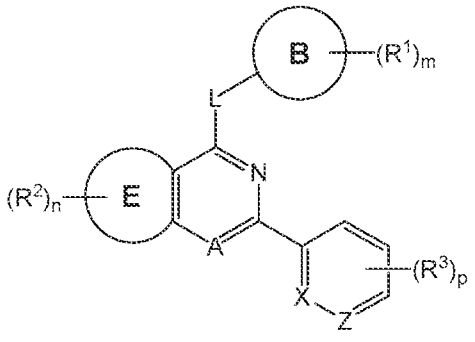
wherein p is 1, 2, 3, 4 or 5.

In some embodiments, L is NR^6. In some embodiments, L is O. In some embodiments, R^1 is hydrogen or C_1-C_8 alkyl. In some embodiments, R^1 is cyclyl or heterocyclyl. In some embodiments, R^1 is aralkyl or heteroaralkyl. In some embodiments, R^1 is methyl, cyclohexyl, t-butyl, or . In some embodiments, R^6 is hydrogen or C_1-C_8 alkyl. In some embodiments, R^9 is C_1-C_8 alkyl, halo, -CN, or -OR^d. In some embodiments, R^3 is hydrogen.

Compounds of Formula (IV)

The following aspects and embodiments relate to compounds of formula (IV), corresponding to formula (I) of U.S. Provisional Patent Application No. 61/291,544, entitled "Therapeutic Compounds and Related Methods of Use" filed on December 31, 2009, and incorporated herein by reference in its entirety.

Item 38. A compound of formula (IV):



(IV)

wherein:

A is CH, CR^4 or N;

B is aryl or a 5- or 6-membered heteroaryl;

m is 0, 1, 2, 3, 4 or 5;

E is aryl or a 5-membered heteroaryl;

when E is aryl, n is 1, 2, 3 or 4; and when E is a 5-membered heteroaryl, n is 0, 1, 2 or 3;

L is NR^5 or O;

one of X and Z is N and the other is CH;

p is 0, 1, 2, 3 or 4;

each R^1, R^2 and R^3 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$, each of which may be optionally substituted with 1-3 R^6; wherein two R^1, together with the atoms to which they are attached, may form an optionally substituted cyclyl, heterocyclyl, aryl or heteroaryl ring;

R^d is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, –

$SO_2NR^bR^{b'}$, $-NR^cSO_2R^{c'}$, $-NR^cC(Y)NR^bR^{b'}$, $-OR^d$, $-SR^{d'}$, $-C(Y)R^e$ or $-S(O)_qR^f$, each of which may be optionally substituted with 1-3 R^6;

R^5 is hydrogen; or when m is not 0, R^5 and 1 R^1 may be taken together with the atoms to which they are attached to form an optionally substituted heteroaryl or heterocyclyl ring;

each R^6 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thiono, $-CN$, $-NO_2$, $-C(O)OR^a$, $-C(Y)NR^bR^{b'}$, $-NR^cC(Y)R^{c'}$, $-NR^bR^{b'}$, $-OC(O)NR^bR^{b'}$, $-NR^cC(O)OR^{c'}$, $-SO_2NR^bR^{b'}$, $-NR^cSO_2R^{c'}$, $-NR^cC(Y)NR^bR^{b'}$, $-OR^d$, $-SR^{d'}$, $-C(Y)R^e$ or $-S(O)_qR^f$, each of which may be optionally substituted with 1-3 R^7;

each R^7 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thiono, $-CN$, $-NO_2$, $-C(O)OR^a$, $-C(Y)NR^bR^{b'}$, $-NR^cC(Y)R^{c'}$, $-NR^bR^{b'}$, $-OC(O)NR^bR^{b'}$, $-NR^cC(O)OR^{c'}$, $-SO_2NR^bR^{b'}$, $-NR^cSO_2R^{c'}$, $-NR^cC(Y)NR^bR^{b'}$, $-OR^d$, $-SR^{d'}$, $-C(Y)R^e$ or $-S(O)_qR^f$;

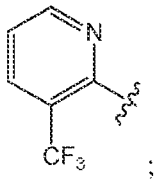
each Y is independently O or S;

q is 1 or 2; and

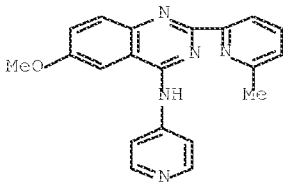
each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e, $R^{e'}$ and R^f is independently selected from hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, acyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy and silylalkoxyalkyl, each of which may be optionally substituted with 1-3 R^6, wherein R^b and $R^{b'}$, together with the atoms to which they are attached, may form an optionally substituted cyclyl or heterocyclyl ring;

or a pharmaceutically acceptable derivative or prodrug thereof,

wherein when B is phenyl, two R^1 are not taken together to form a pyrazole ring;

when B is phenyl, R^2 is not  ;

and where in the compound is not:



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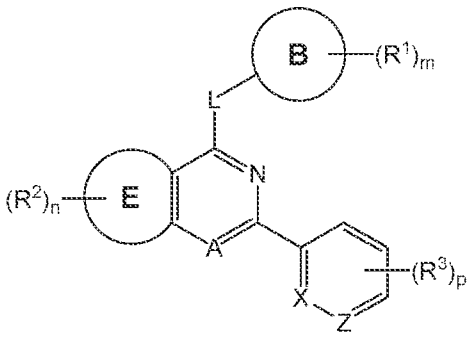
In some embodiments, when B is phenyl, R^2 is not a substituted pyridyl. In some embodiments, when B is phenyl and n = 1, R^2 is not a substituted pyridyl.

In some embodiments, when X is N, B is not 4-pyridyl.

In some embodiments, each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e, $R^{e'}$ and R^f is independently selected from hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, acyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy and silylalkoxyalkyl, each of which may be optionally substituted with 1-3 R^6.

In some embodiments, B is aryl.

Item 39. A compound of formula (IV):



(IV)

wherein:

A is CH, CR^4 or N;

B is aryl or a 5-membered heteroaryl;

m is 0, 1, 2, 3, 4 or 5;

E is aryl or a 5-membered heteroaryl;

when E is aryl, n is 1, 2, 3 or 4; and when E is a 5-membered heteroaryl, n is 0, 1, 2 or 3;

L is NR^5 or O;

one of X and Z is N and the other is CH;

p is 0, 1, 2, 3 or 4;

each R^1, R^2 and R^3 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$, each of which may be optionally substituted with 1-3 R^6; wherein two R^1, together with the atoms to which they are attached, may form an optionally substituted cyclyl, heterocyclyl, aryl or heteroaryl ring;

R^4 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$, each of which may be optionally substituted with 1-3 R^6;

R^5 is hydrogen; or when m is not 0, R^5 and 1 R^1 may be taken together with the atoms to which they are attached to form an optionally substituted heteroaryl or heterocyclyl ring;

each R^6 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl,

hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thiono, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$, each of which may be optionally substituted with 1-3 R^7;

each R^7 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thiono, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$;

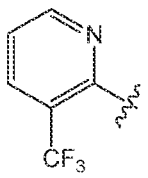
each Y is independently O or S;

q is 1 or 2; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e, $R^{e'}$ and R^f is independently selected from hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, acyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy and silylalkoxyalkyl, each of which may be optionally substituted with 1-3 R^6 wherein R^b and $R^{b'}$, together with the atoms to which they are attached, may form an optionally substituted cyclyl or heterocyclyl ring;

or a pharmaceutically acceptable derivative or prodrug thereof,

wherein when B is phenyl, two R^1 are not taken together to form a pyrazole ring; and

when B is phenyl, R^2 is not 

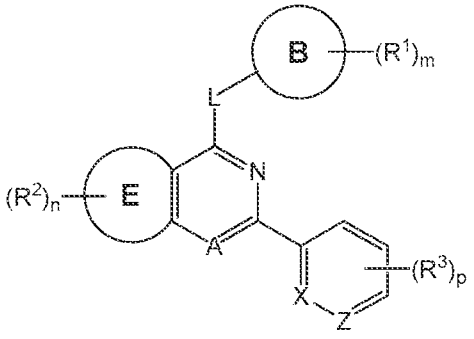
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In some embodiments, each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e, $R^{e'}$ and R^f is independently selected from hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, acyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl,

heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy and silylalkoxyalkyl, each of which may be optionally substituted with 1-3 R^6.

In some embodiments, when B is phenyl, R^2 is not a substituted pyridyl. In some embodiments, when when B is phenyl and n = 1, R^2 is not a substituted pyridyl.

In one aspect, the invention features a compound of formula (IV):



(IV)

wherein:

A is CH, CR^4 or N;

B is aryl or a 5-membered heteroaryl;

E is aryl or a 5-membered heteroaryl;

L is NR^5 or O;

one of X and Z is N and the other is CH;

m is 0, 1, 2, 3, 4 or 5;

n is 1, 2, 3 or 4;

p is 0, 1, 2, 3 or 4;

each R^1 and R^3 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$, each of which may be optionally substituted with 1-3 R^6; wherein two R^1, together with the atoms to which they are attached, may form an optionally substituted cyclyl, heterocyclyl, aryl or heteroaryl ring;

each R^2 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^cSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$,–OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$, each of which may be optionally substituted with 1-3 R^6; wherein two R^1, together with the carbons to which they are attached, may form an optionally substituted cyclyl, heterocyclyl, aryl or heteroaryl ring;

R^4 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^cSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$,–OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$, each of which may be optionally substituted with 1-3 R^6;

R^5 is hydrogen; or when m is not 0, R^5 and 1 R^1 may be taken together with the atoms to which they are attached to form an optionally substituted heteroaryl or heterocyclyl ring;

each R^6 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thiono, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^cSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$,–OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$, each of which may be optionally substituted with 1-3 R^7;

each R^7 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thiono, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –

$OC(O)NR^bR^{b'}$, $-NR^cC(O)OR^{c'}$, $-SO_2NR^bR^{b'}$, $-NR^cSO_2R^{c'}$, $-NR^cC(Y)NR^bR^{b'}$, $-OR^d$, $-SR^{d'}$, $-C(Y)R^e$ or $-S(O)_qR^f$;

Y is O or S;

q is 1 or 2; and

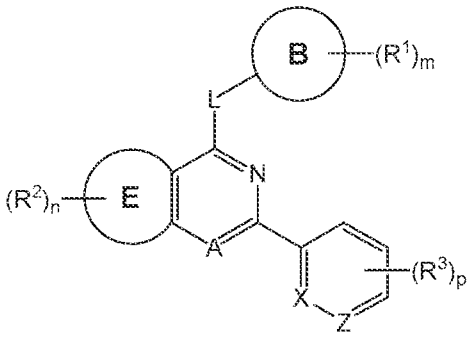
each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e, $R^{e'}$ and R^f is independently selected from hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, acyl, cyclyl, heterocyclyl, aryl, heteroaryl, cyclylalkyl, heterocyclylalkyl, aralkyl and heteroaralkyl, each of which may be optionally further substituted with 1-3 R^6 wherein R^b and $R^{b'}$, together with the atoms to which they are attached, may form an optionally substituted cyclyl or heterocyclyl ring;

or a pharmaceutically acceptable derivative or prodrug thereof,

wherein when B is phenyl, two R^1 are not taken together to form a pyrazole ring.

In some embodiments, each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e, $R^{e'}$ and R^f is independently selected from hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, acyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy and silylalkoxyalkyl, each of which may be optionally substituted with 1-3 R^6.

In one aspect, the invention features a compound of formula (IV):



(IV)

wherein:

A is CH, CR^4 or N;

B is aryl or a 5-membered heteroaryl;

E is aryl or a 5-membered heteroaryl;

L is NR^5 or O;

one of X and Z is N and the other is CH;

m is 0, 1, 2, 3, 4 or 5;

n is 1, 2, 3 or 4;

p is 0, 1, 2, 3 or 4;

each R^1 and R^3 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$, each of which may be optionally substituted with 1-3 R^6; wherein two R^1, together with the atoms to which they are attached, may form an optionally substituted cyclyl, heterocyclyl, or aryl ring;

each R^2 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$, each of which may be optionally substituted with 1-3 R^6; wherein two R^1, together with the carbons to which they are attached, may form an optionally substituted cyclyl, heterocyclyl, aryl or heteroaryl ring;

R^4 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$, each of which may be optionally substituted with 1-3 R^6;

R^5 is hydrogen; or when m is not 0, R^5 and 1 R^1 may be taken together with the atoms to which they are attached to form an optionally substituted heteroaryl or heterocyclyl ring;

each R^6 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thiono, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^cSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$,–OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$, each of which may be optionally substituted with 1-3 R^7;

each R^7 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thiono, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^cSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$,–OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$;

Y is O or S;

q is 1 or 2; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e, $R^{e'}$ and R^f is independently selected from hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, acyl, cyclyl, heterocyclyl, aryl, heteroaryl, cyclylalkyl, heterocyclylalkyl, aralkyl and heteroaralkyl, each of which may be optionally further substituted with 1-3 R^6, wherein R^b and $R^{b'}$, together with the atoms to which they are attached, may form an optionally substituted cyclyl or heterocyclyl ring;.

In some embodiments, A is N. In some embodiments, A is CH. In some embodiments, A is CR^4.

In some embodiments, B is aryl (e.g., phenyl).

In some embodiments, m is 0.

In some embodiments, m is 1. In some embodiments, m is 2. In some embodiments, m is 3.

In some embodiments, R^1 is in the ortho position. In some embodiments, R^1 is in the meta position. In some embodiments, R^1 is in the para position.

In some embodiments, R^1 is C_1-C_8 alkyl (e.g., methyl or tert-butyl). In some embodiments, R^1 is heteroaryl (e.g., oxazolyl, oxadiazolyl or quinazolinyl).

In some embodiments, R^1 is heteroaryl substituted with 1-3 R^6 (e.g., 1 R^6).

In some embodiments, R^1 is oxadiazolyl substituted with 1 R^6. some embodiments, R^6 is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, R^1 is heteroaryl substituted with 2 R^6. In some embodiments, R^1 is quinazolinyl substituted with 2 R^6. In some embodiments, one R^6 is halo (e.g., bromo) and the other is heteroaryl (e.g., pyridyl).

In some embodiments, m is 1 and R^1 is halo (e.g., fluoro, chloro or bromo). In some embodiments, m is 2 and each R^1 is halo (e.g., fluoro, chloro or bromo). In some embodiments, m is 3 and each R^1 is halo (e.g., fluoro, chloro or bromo). . In some embodiments, R^1 is haloalkyl (e.g., trifluoromethyl). In some embodiments, R^1 is haloalkoxy (e.g., difluoromethoxy or trifluoromethoxy).

In some embodiments, R^1 is haloalkoxy substituted with 1 R^6. In some embodiments, R^1 is $-O-CF_2-R^6$. In some embodiments, R^6 is $-C(Y)NR^bR^{b'}$. In some embodiments, Y is O, R^b is hydrogen and $R^{b'}$ is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^1 is $-O-CF_2-CH_2-R^6$. In some embodiments, R^6 is $-OR^d$. In some embodiments, R^d is hydrogen. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^6 is $-NR^bR^{b'}$. In some embodiments, R^b and $R^{b'}$ are each independently C_1-C_8 alkyl (e.g., R^b and $R^{b'}$ are both methyl). In some embodiments, R^6 is heterocyclyl (e.g., morpholino).

In some embodiments, R^1 is aminoalkyl. In some embodiments, R^1 is $-CH_2NH_2$. In some embodiments, R^1 is alkylaminoalkyl. In some embodiments, R^1 is $-CH_2NHCH_2CH_2CH_3$. In some embodiments, R^1 is dialkylaminoalkyl. In some embodiments, R^1 is $-CH_2N(CH(CH_3)_2)_2$.

In some embodiments, R^1 is hydroxyalkyl. In some embodiments, R^1 is $-CH_2OH$.

In some embodiments, R^1 is $-CN$.

In some embodiments, R^1 is $-NO_2$.

In some embodiments, R^1 is $-C(O)OR^a$. In some embodiments, R^a is hydrogen. In some embodiments, R^a is C_1-C_8 alkyl (e.g., methyl or ethyl).

In some embodiments, R^1 is $-NR^cC(Y)R^{c'}$. In some embodiments, one of R^c and $R^{c'}$ is hydrogen and the other is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, R^1 is $-OR^d$. In some embodiments, R^d is hydrogen. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl or ethyl).

In some embodiments, R^1 is $-SO_2NR^bR^{b'}$. In some embodiments, R^b and $R^{b'}$ are both hydrogen.

In some embodiments, R^1 is $-C(Y)R^e$. In some embodiments, Y is O. In some embodiments, R^e is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^e is heterocyclyl (e.g., pyrrolidinyl, piperidinyl or morpholino).

In some embodiments, R^1 is $-C(Y)NR^bR^{b'}$. In some embodiments, Y is S. In some embodiments, Y is O. In some embodiments, R^b and $R^{b'}$ are both hydrogen. In some embodiments, R^b is hydrogen. In some embodiments, R^b is hydrogen and $R^{b'}$ is aralkyl. In some embodiments, R^b is hydrogen and $R^{b'}$ is optionally substituted benzyl. In some embodiments, $R^{b'}$ is C_1-C_8 alkyl, e.g., methyl, ethyl, C_3 alkyl (e.g., n-propyl or isopropyl), C_4 alkyl (e.g., n-butyl, sec-butyl or tert-butyl), C_5 alkyl (e.g., n-pentyl, isopentyl or pentan-3-yl), C_6 alkyl (e.g., n-hexyl or 3,3-dimethylbutan-2-yl), or C_7 alkyl (e.g., n-heptyl or 2-heptyl).

In some embodiments, $R^{b'}$ is C_1-C_8 alkyl substituted with 1 R^6. In some embodiments, R^6 is $-OR^d$. In some embodiments, R^d is aryl (e.g., phenyl). In some embodiments, $R^{b'}$ is C_2-C_8 alkenyl, e.g., C_3 alkenyl (e.g., $-CH_2-CH=CH_2$). In some embodiments, $R^{b'}$ is C_2-C_8 alkynyl, e.g., C_3 alkenyl (e.g., $-CH_2-C\equiv CH$).

In some embodiments, $R^{b'}$ is aryl (e.g., phenyl). In some embodiments, $R^{b'}$ is aryl substituted with 1 R^6 (e.g., phenyl substituted with 1 R^6). In some embodiments, R^6 is haloalkyl (e.g., trifluoromethyl). In some embodiments, $R^{b'}$ is cyclyl (e.g., cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl or cycloheptyl). In some embodiments, $R^{b'}$ is cyclyl substituted with 1 R^6 (e.g., cyclopropyl substituted with 1 R^6 or cyclopentyl substituted with 1 R^6). In some embodiments, R^6 is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^6 is $-OR^d$. In some embodiments, R^d is aralkyl (e.g., benzyl).

In some embodiments, $R^{b'}$ is cyclohexyl substituted with 1 R^6. In some embodiments, R^6 is $-C(O)OR^a$. In some embodiments, R^a is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, $R^{b'}$ is bicyclyl (e.g., indanyl). In some embodiments, $R^{b'}$ is heterocyclyl, e.g., a 6-membered heterocyclyl. In some embodiments, $R^{b'}$ is a 6-membered oxygen-containing heterocyclyl (e.g., tetrahydropyranyl). In some embodiments, $R^{b'}$ is a 6-membered nitrogen-containing heterocyclyl (e.g., piperidinyl).

In some embodiments, $R^{b'}$ is heterocyclyl substituted with 1 R^6 (e.g., piperidinyl substituted with 1 R^6). In some embodiments, R^6 is $-C(O)OR^a$. In some embodiments, R^a is C_1-C_8 alkyl (e.g., ethyl). In some embodiments, R^6 is $-C(Y)R^e$. In some embodiments, Y is O. In some embodiments, R^e is C_1-C_8 alkyl (e.g., methyl or ethyl).

In some embodiments, $R^{b'}$ is aralkyl. In some embodiments, the alkyl is a C_1-C_8 alkyl (e.g., C_1, C_2, C_3 or C_4 alkyl). In some embodiments, the alkyl is a straight-chain alkyl. In some embodiments, the alkyl is a branched alkyl. In some embodiments, the aryl is phenyl. In some embodiments, $R^{b'}$ is benzyl. In some embodiments, $R^{b'}$ is phenylethyl. In some embodiments, the aryl is substituted with 1 R^6. In some embodiments, R^6 is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^6 is halo (e.g., fluoro or chloro). In some embodiments, R^6 is haloalkyl (e.g., trifluoromethyl). In some embodiments, R^6 is $-OR^d$. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl). In some embodiments, the aryl is substituted with 2 R^6. In some embodiments, each R^6 is independently $-OR^d$. In some embodiments, each R^d is independently C_1-C_8 alkyl (e.g., each R^d is methyl). In some embodiments, each R^6 is independently halo (e.g., each R^6 is fluoro).

In some embodiments, $R^{b'}$ is heteroaralkyl. In some embodiments, the alkyl is a C_1-C_8 alkyl (e.g., C_1, C_2 or C_3 alkyl). In some embodiments, the alkyl is a straight-chain alkyl. In some embodiments, the alkyl is a branched alkyl. In some embodiments, the heteroaryl is pyridyl. In some embodiments, the heteroaryl is furanyl. In some embodiments, the heteroaryl is thiazolyl. In some embodiments, the heteroaryl is thienyl. In some embodiments, the heteroaryl is substituted with 1 R^6.

In some embodiments, R^6 is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^6 is haloalkyl (e.g., trifluoromethyl).

In some embodiments, $R^{b'}$ is cyclylalkyl. In some embodiments, the alkyl is a C_1-C_8 alkyl (e.g., C_1 alkyl). In some embodiments, the cyclyl group is cyclopropyl. In some embodiments, the cyclyl group is cyclopentyl. In some embodiments, the cyclyl group is a bicyclic group. In some embodiments, the bicyclic group is indanyl. In some embodiments, $R^{b'}$ is cyclylalkyl substituted with 1 R^6. In some embodiments, R^6 is aryl (e.g., phenyl).

In some embodiments, $R^{b'}$ is heterocyclylalkyl. In some embodiments, the alkyl is a C_1-C_8 alkyl (e.g., C_1 alkyl). In some embodiments, the heterocyclyl group is tetrahydropyranyl.

In some embodiments, $R^{b'}$ is haloalkyl (e.g., fluoroethyl, difluoroethyl, trifluoroethyl or trifluoropropyl).

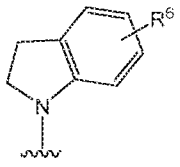
In some embodiments, $R^{b'}$ is alkoxyalkyl. In some embodiments, the alkyl is a C_1-C_8 alkyl (e.g., C_1, C_2, C_3 or C_4 alkyl). In some embodiments, the alkyl is a straight-chain alkyl. In some embodiments, the alkyl is a branched alkyl. In some embodiments, the alkoxy is methoxy.

In some embodiments, R^b and $R^{b'}$ are each independently C_1-C_8 alkyl (e.g., R^b and $R^{b'}$ are both methyl, both ethyl or both isopropyl).

In some embodiments, R^1 and R^5, together with the atoms to which they are attached, form a heteroaryl ring (e.g., a substituted heteroaryl ring). In some embodiments, R^1 and R^5, together with the atoms to which they are attached, form a heterocyclyl ring (e.g., a substituted heterocyclyl ring).

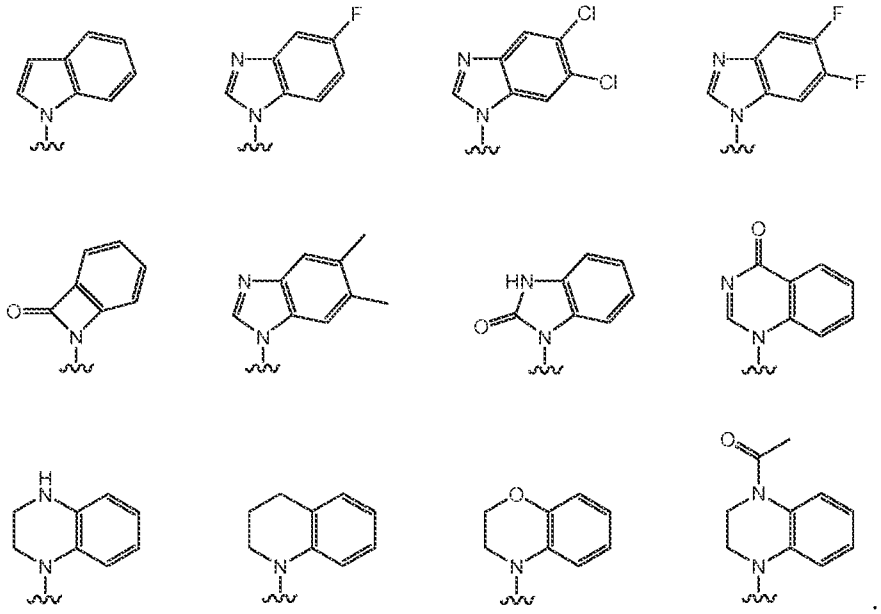
In some embodiments, R^1, R^5, B and L are taken together to form a bicyclic heteroaryl or heterocyclic ring.

In some embodiments, R^1, R^5, B and L are taken together to form



. In some embodiments, R^6 is halo. In some embodiments, R^6 is at the 6, 7, or 8 position.

In some embodiments, R^1, R^5, B and L are taken together to form a group selected from:



In some embodiments, R^2 is aryl.

In some embodiments, each R^1 is independently C_1-C_8 alkyl (e.g., each R^1 is methyl). In some embodiments, each R^1 is independently halo (e.g., each R^1 is fluoro or each R^1 is chloro). In some embodiments, one R^1 is fluoro and the other is chloro. In some embodiments, one R^1 is chloro and the other is bromo.

In some embodiments, each R^1 is independently -OR^d. In some embodiments, each R^d is independently C_1-C_8 alkyl (e.g., each R^d is methyl).

In some embodiments, one R^1 is halo (e.g., chloro) and the other is C_1-C_8 alkyl (e.g., methyl). In some embodiments, one R^1 is halo (e.g., fluoro) and the other is heterocyclylalkyl (e.g.,–CH_2-heterocyclyl). In some embodiments, the heterocyclyl is morpholino. In some embodiments, the heterocyclyl is pyrrolidinyl. In some embodiments, the heterocyclyl is piperazinyl. In some embodiments, the piperazinyl is substituted with 1 R^6. In some embodiments, R^6 is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, one R^1 is halo (e.g., fluoro or chloro) and the other is haloalkyl (e.g., trifluoromethyl).

In some embodiments, one R^1 is halo (e.g., chloro) and the other is haloalkoxy (e.g., difluoromethoxy or trifluoromethoxy).

In some embodiments, one R^1 is halo (e.g., chloro) and the other is $-C(O)OR^a$. In some embodiments, R^a is hydrogen.

In some embodiments, one R^1 is halo (e.g., fluoro or chloro) and the other is $-C(Y)NR^bR^{b'}$. In some embodiments, Y is O. In some embodiments, R^b and $R^{b'}$ are both hydrogen. In some embodiments, one of R^b and $R^{b'}$ is hydrogen and the other is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, one R^1 is halo (e.g., chloro) and the other is $-NR^cC(Y)R^{c'}$. In some embodiments, Y is O. In some embodiments, R^c is hydrogen and $R^{c'}$ is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, one R^1 is halo (e.g., fluoro or chloro) and the other is $-OR^d$. In some embodiments, R^d is hydrogen. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, one R^1 is halo (e.g., fluoro or chloro) and the other is –CN.

In some embodiments, one R^1 is halo (e.g., chloro) and the other is $-NO_2$.

In some embodiments, one R^1 is $-C(O)OR^a$ and the other is $-NO_2$. In some embodiments, R^a is hydrogen.

In some embodiments, one R^1 is $-C(O)OR^a$ and the other is $-OR^d$. In some embodiments, each R^a and R^d is hydrogen.

In some embodiments, one R^1 is $-C(Y)NR^bR^{b'}$ and the other is haloalkyl (e.g., trifluoromethyl). In some embodiments, R^b and $R^{b'}$ are both hydrogen.

In some embodiments, one R^1 is $-C(Y)NR^bR^{b'}$ and the other is haloalkoxy (e.g., trifluoromethoxy). In some embodiments, R^b and $R^{b'}$ are both hydrogen.

In some embodiments, one R^1 is $-C(Y)NR^bR^{b'}$ and the other is $-S(O)_qR^f$. In some embodiments, R^b and $R^{b'}$ are both hydrogen. In some embodiments, R^f is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, one R^1 is $-C(Y)NR^bR^{b'}$ and the other is –CN. In some embodiments, R^b and $R^{b'}$ are both hydrogen.

In some embodiments, one R^1 is $-OR^d$ and the other is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, one R^1 is $-OR^d$ and the other is haloalkyl (e.g., trifluoromethyl). In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl).

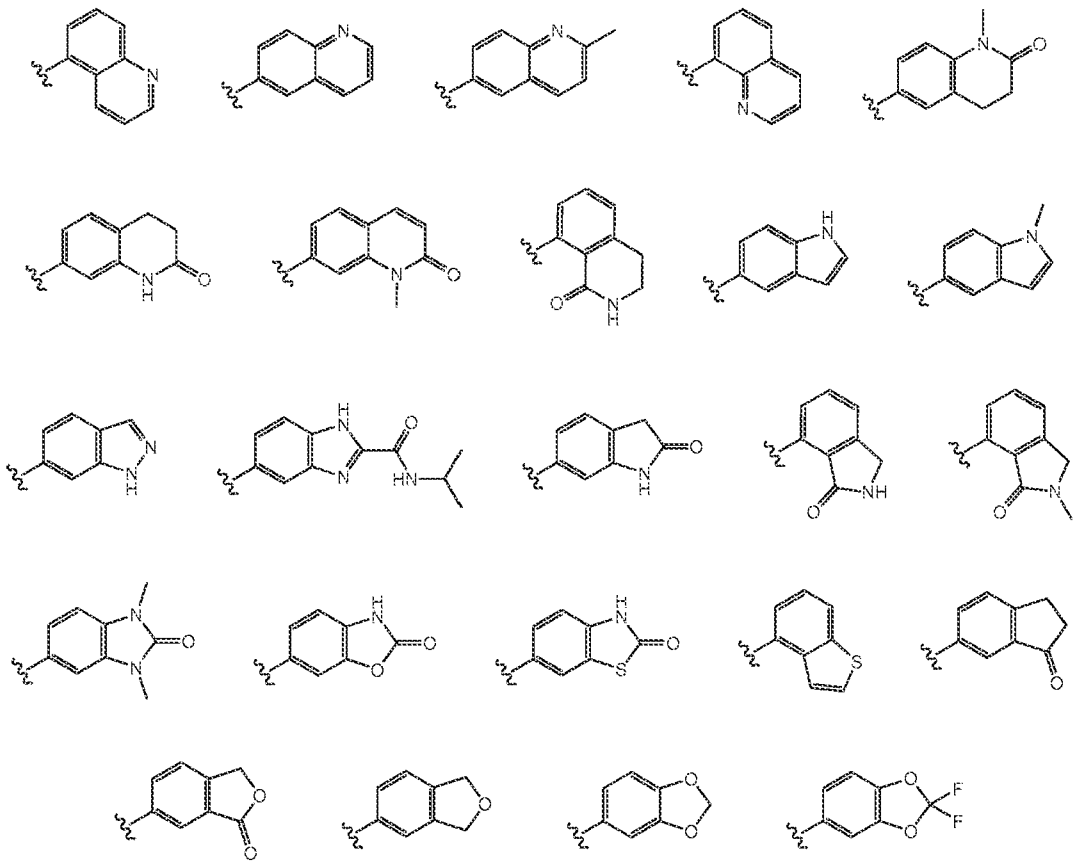
In some embodiments, one R^1 is $-OR^d$ and the other is $-C(O)OR^a$. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^a is hydrogen. In some embodiments, R^a is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, one R^1 is $-OR^d$ and the other is $-NR^cC(O)R^{c'}$. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^c is hydrogen and $R^{c'}$ is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, one R^1 is haloalkyl (e.g., trifluoromethyl) and the other is $-CN$.

In some embodiments, two R^1, together with the atoms to which they are attached, are taken together to form a cyclyl ring (e.g., a substituted cyclyl ring). In some embodiments, two R^1, together with the atoms to which they are attached, are taken together to form a heterocyclyl ring (e.g., a substituted heterocyclyl ring). In some embodiments, two R^1, together with the atoms to which they are attached, are taken together to form a heteroaryl ring (e.g., a substituted heteroaryl ring).

In some embodiments, two R^1 and ring B are taken together to form a group selected from:



In some embodiments, R^2 is aryl.

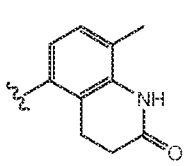
In some embodiments, each R^1 is independently halo (e.g., all three R^1 are fluoro or all three R^1 are chloro).

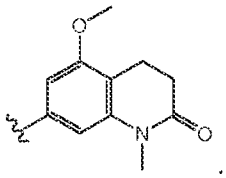
In some embodiments, two R^1 are independently halo (e.g., both are chloro) and the other is C_1-C_8 alkyl (e.g., methyl). In some embodiments, two R^1 are independently halo (e.g., both are chloro) and the other is heteroaryl (e.g., pyrrolyl). In some embodiments, two R^1 are independently halo (e.g., both are fluoro) and the other is $-C(Y)NR^bR^{b'}$ (e.g.,$-C(O)NH_2$). In some embodiments, two R^1 are independently C_1-C_8 alkyl (e.g., both are methyl) and the other is halo (e.g., chloro or bromo).

In some embodiments, one R^1 is C_1-C_8 alkyl (e.g., methyl), and two R^1, together with the atoms to which they are attached, are taken together to form a heterocyclyl ring.

In some embodiments, one R^1 is $-OR^d$, and two R^1, together with the atoms to which they are attached, are taken together to form a heterocyclyl ring. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, three R^1 and ring B are taken together to form a group selected from:



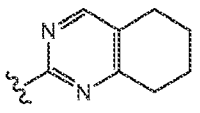


In some embodiments, B is a 6-membered heteroaryl.

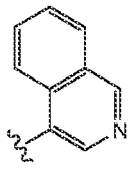
In some embodiments, B is pyridyl. In some embodiments, B is 3-pyridyl. In some embodiments, m is 2. In some embodiments, two R^1, together with the atoms to which they are attached, are taken together to form an aryl ring (e.g., a phenyl ring). In some embodiments, m is 3. In some embodiments, one R^1 is $-OR^d$, and two R^1, together with the atoms to which they are attached, are taken together to form an aryl ring (e.g., a phenyl ring). In some embodiments, R^d is hydrogen.

In some embodiments, B is pyrazolyl. In some embodiments, m is 2. In some embodiments, two R^1, together with the atoms to which they are attached, are taken together to form a cyclyl ring (e.g., a cyclohexyl ring).

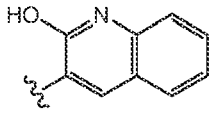
In some embodiments, B is selected from:



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and



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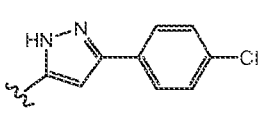
In some embodiments, B is a 5-membered heteroaryl (e.g., pyrazolyl).

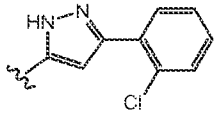
In some embodiments, m is 1.

In some embodiments, R^1 is aryl (e.g., phenyl).

In some embodiments, R^1 is phenyl substituted with 1 R^6.

In some embodiments, R^6 is halo (e.g., chloro). In some embodiments, R^1 is selected from:

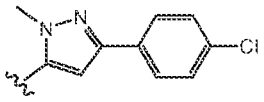


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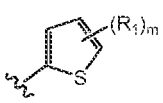
In some embodiments, m is 2.

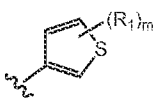
In some embodiments, one R^1 is C_1-C_8 alkyl (e.g., methyl) and the other is aryl (e.g., phenyl). In some embodiments, the aryl is phenyl substituted with 1 R^6. In some embodiments, R^6 is halo (e.g., chloro). In some embodiments, R^1 is:

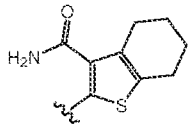


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In some embodiments, B is thienyl. In some embodiments, B is selected from:





and


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In some embodiments, m is 1. In some embodiments, m is 2. In some embodiments m is 2 and two R^1, together with the atoms to which they are attached, form an optionally substituted cyclyl, heterocyclyl, aryl or heteroaryl ring

In some embodiments, R^1 is $-C(O)OR_a$. In some embodiments, R^a is C_1-C_8 alkyl (e.g., ethyl).

In some embodiments, R^1 is $-C(Y)NR^bR^{b'}$. In some embodiments, Y is O. In some embodiments, R^b and $R^{b'}$ are both hydrogen.

In some embodiments, m is 2.

In some embodiments, one R^1 is C_1-C_8 alkyl (e.g., methyl) and the other is $-C(Y)NR^bR^{b'}$. In some embodiments, Y is O. In some embodiments, R^b and $R^{b'}$ are both hydrogen.

In some embodiments, B is thiazolyl.

In some embodiments, m is 1.

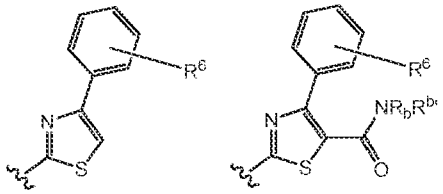
In some embodiments, R^1 is aryl (e.g., phenyl).

In some embodiments, m is 2.

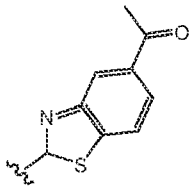
In some embodiments, two R^1, together with the atoms to which they are attached, form an aryl ring. In some embodiments, the aryl ring is substituted with –

$C(Y)R^e$. In some embodiments, Y is O. In some embodiments, R^e is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, B is:



In some embodiments, B is:



In some embodiments, E is aryl (e.g., phenyl).

In some embodiments, n is 1.

In some embodiments, R^2 is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, R^2 is C_1-C_8 alkyl substituted with 1-3 R^6. In some embodiments, R^2 is C_1 alkyl substituted with 1 R^6.

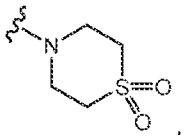
In some embodiments, R^6 is $-NR^bR^{b'}$. In some embodiments, R^b and $R^{b'}$ are each independently C_1-C_8 alkyl (e.g., R^b and $R^{b'}$ are both methyl, or R^b and $R^{b'}$ are both ethyl). In some embodiments, one of R^b and $R^{b'}$ is hydrogen and the other is haloalkyl (e.g., trifluoroethyl).

In some embodiments, R^6 is $-OR^d$. In some embodiments, R^d is cyclyl (e.g., cyclopentyl). In some embodiments, R^d is heterocyclylalkyl (e.g., $-CH_2$-tetrahydropyranyl).

In some embodiments, R^2 is C_2 alkyl substituted with 1 R^6.

In some embodiments, R^6 is $-C(Y)NR^bR^{b'}$. In some embodiments, Y is O. In some embodiments, R^b and $R^{b'}$ are both hydrogen. In some embodiments, R^b and $R^{b'}$ are each independently C_1-C_8 alkyl (e.g., R^b and $R^{b'}$ are both methyl). In some embodiments, one of R^b and $R^{b'}$ is hydrogen and the other is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, R^6 is $-C(Y)R^e$. In some embodiments, Y is O. In some embodiments, R^e is heterocyclyl (e.g., morpholino or thiomorpholino). In some embodiments, R^e is thiomorpholino substituted with 2 R^6. In some embodiments, each R^6 is oxo. In some embodiments, R^e is:



In some embodiments, R^2 is C_3 alkyl substituted with 1 R^6.

In some embodiments, R^6 is $-C(Y)NR^bR^{b'}$. In some embodiments, Y is O. In some embodiments, R^b and $R^{b'}$ are both hydrogen. In some embodiments, R^b and $R^{b'}$ are each independently C_1-C_8 alkyl (e.g., R^b and $R^{b'}$ are both methyl). In some embodiments, one of R^b and $R^{b'}$ is hydrogen and the other is C_1-C_8 alkyl (e.g., methyl).

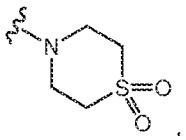
In some embodiments, R^6 is $-NR^cC(Y)R^{c'}$. In some embodiments, Y is O. In some embodiments, R^c and $R^{c'}$ are each independently C_1-C_8 alkyl (e.g., R^c and $R^{c'}$ are both methyl).

In some embodiments, R^6 is $-OR^d$. In some embodiments, R^d is hydrogen. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, R^6 is silyloxy (e.g., tert-butyldimethylsilyloxy).

In some embodiments, R^6 is $-C(Y)R^e$. In some embodiments, Y is O. In some embodiments, R^e is heterocyclyl (e.g., morpholino).

In some embodiments, R^2 is C_2-C_8 alkynyl. In some embodiments, R^2 is C_2-C_8 alkynyl substituted with 1 R^6 (e.g., C_3 alkynyl substituted with 1 R^6). In some embodiments, R^2 is $-C\equiv C-CH_2-R^6$. In some embodiments, R^6 is $-NR^bR^{b'}$. In some embodiments, R^b and $R^{b'}$ are each independently C_1-C_8 alkyl (e.g., R^b and $R^{b'}$ are both methyl). In some embodiments, R^6 is $-OR^d$. In some embodiments, R^d is hydrogen. In some embodiments, R^6 is silyloxy (e.g., tert-butyldimethylsilyloxy). In some embodiments, R^6 is heterocyclyl (e.g., morpholino or thiomorpholino). In some embodiments, R^6 is thiomorpholino substituted with 2 R^7. In some embodiments, each R^7 is oxo. In some embodiments, R^6 is:



In some embodiments, R^2 is aryl (e.g., phenyl). In some embodiments, R^2 is unsubstituted phenyl.

In some embodiments, R^2 is phenyl substituted with 1 R^6.

In some embodiments, R^6 is heterocyclylalkyl (e.g., $-CH_2$-morpholino). In some embodiments, R^6 is haloalkyl (e.g., trifluoromethyl). In some embodiments, R^6 is –CN. In some embodiments, R^6 is $-OR^d$. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^6 is $-C(Y)R^e$. In some embodiments, Y is O. In some embodiments, R^e is heterocyclyl (e.g., morpholino).

In some embodiments, R^2 is phenyl substituted with 2 R^6.

In some embodiments, each R^6 is independently $-OR^d$. In some embodiments, each R^d is C_1-C_8 alkyl (e.g., methyl). In some embodiments, one R^6 is halo (e.g., fluoro) and the other is C_1-C_8 alkyl (e.g., methyl). In some embodiments, one R^6 is $-C(O)OR^a$ and the other is $-OR^d$. In some embodiments, R^a and R^d are each independently C_1-C_8 alkyl (e.g., R^a and R^d are both methyl).

In some embodiments, R^2 is heteroaryl.

In some embodiments, R^2 is isoxazolyl. In some embodiments, R^2 is isoxazolyl substituted with 2 R^6. In some embodiments, each R^6 is independently C_1-C_8 alkyl (e.g., R^6 is methyl).

In some embodiments, R^2 is pyrazolyl. In some embodiments, R^2 is pyrazolyl substituted with 1 R^6. In some embodiments, R^6 is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, R^2 is pyridyl. In some embodiments, R^2 is unsubstituted pyridyl. In some embodiments, R^2 is pyridyl substituted with 1 R^6. In some embodiments, R^6 is halo (e.g., fluoro). In some embodiments, R^6 is $-NR^bR^{b'}$. In some embodiments, R^b and $R^{b'}$ are each hydrogen. In some embodiments, R^6 is $-OR^d$. In some embodiments, R^d is hydrogen. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^6 is heterocyclyl (e.g., morpholino or piperazinyl). In some embodiments, R^6 is piperazinyl substituted with 1 R^7. In some embodiments, R^7 is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, R^2 is pyrimidinyl.

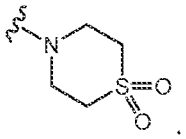
In some embodiments, R^2 is pyridazinyl.

In some embodiments, R^2 is cyclyl (e.g., cyclopropyl).

In some embodiments, R^2 is heterocyclyl (e.g., morpholino or pyrrolidinyl).

In some embodiments, R^2 is aralkyl (e.g., benzyl).

In some embodiments, R^2 is heterocyclylalkyl. In some embodiments, the alkyl is C_1 alkyl. In some embodiments, the alkyl is C_2 alkyl. In some embodiments, the alkyl is C_3 alkyl. In some embodiments, the heterocyclyl is piperidinyl. In some embodiments, the heterocyclyl is piperazinyl. In some embodiments, the heterocyclyl is piperazinyl substituted with 1 R^6. In some embodiments, R^6 is C_1-C_8 alkyl (e.g., methyl). In some embodiments, the heterocyclyl is pyrrolidinyl. In some embodiments, the heterocyclyl is morpholino. In some embodiments, the heterocyclyl is thiomorpholino. In some embodiments, the heterocyclyl is thiomorpholino substituted with 2 R^6. In some embodiments, each R^6 is oxo. In some embodiments, the heterocyclyl is:



In some embodiments, R^2 is halo (e.g., fluoro, chloro, bromo or iodo).

In some embodiments, R^2 is haloalkyl (e.g., trifluoromethyl).

In some embodiments, R^2 is haloalkoxy (e.g., trifluoromethoxy).

In some embodiments, R^2 is –CN.

In some embodiments, R^2 is $-NO_2$.

In some embodiments, R^2 is $-C(O)OR^a$. In some embodiments, R^a is hydrogen. In some embodiments, R^a is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, R^2 is $-C(Y)NR^bR^{b'}$. In some embodiments, Y is O. In some embodiments, R^b and $R^{b'}$ are each hydrogen. In some embodiments, R^b and $R^{b'}$ are each independently C_1-C_8 alkyl (e.g., R^b and $R^{b'}$ are both methyl). In some embodiments, one of R^b and $R^{b'}$ is hydrogen and the other is C_1-C_8 alkyl (e.g., methyl or ethyl). In some embodiments, the C_1-C_8 alkyl is ethyl substituted with 2 R^6.In some embodiments, each R^6 is independently $-OR^d$. In some embodiments, each R^d

is C_1-C_8 alkyl (e.g., each R^d is methyl). In some embodiments, one of R^b and $R^{b'}$ is hydrogen and the other is heterocyclylalkyl (e.g., $-CH_2$-CH_2-morpholino). In some embodiments, one of R^b and $R^{b'}$ is hydrogen and the other is haloalkyl (e.g., trifluoroethyl).

In some embodiments, R^2 is $-NR^bR^{b'}$. In some embodiments, R^b and $R^{b'}$ are both hydrogen. In some embodiments, R^b and $R^{b'}$ are each independently C_1-C_8 alkyl (e.g., R^b and $R^{b'}$ are both methyl). In some embodiments, one of R^b and $R^{b'}$ is hydrogen and the other is C_1-C_8 alkyl (e.g., methyl). In some embodiments, one of R^b and $R^{b'}$ is hydrogen and the other is heterocyclyl (e.g., tetrahydropyranyl). In some embodiments, one of R^b and $R^{b'}$ is hydrogen and the other is heterocyclylalkyl. In some embodiments, the alkyl is C_1 alkyl. In some embodiments, the alkyl is C_2 alkyl. In some embodiments, the alkyl is C_3 alkyl. In some embodiments, the heterocyclyl is morpholino. In some embodiments, the heterocyclyl is pyrrolidinyl. In some embodiments, the heterocyclyl is tetrahydrofuranyl. In some embodiments, the heterocyclyl is tetrahydropyranyl. In some embodiments, one of R^b and $R^{b'}$ is hydrogen and the other is hydroxyalkyl. In some embodiments, the alkyl is C_2 alkyl. In some embodiments, one of R^b and $R^{b'}$ is hydrogen and the other is alkoxyalkyl. In some embodiments, the alkyl is C_2 alkyl. In some embodiments, the alkyl is C_3 alkyl. In some embodiments, the alkoxy is methoxy. In some embodiments, one of R^b and $R^{b'}$ is hydrogen and the other is $-C(Y)R^e$. In some embodiments, Y is O. In some embodiments, R^e is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^e is heterocyclyl. In some embodiments, R^e is tetrahydropyranyl.

In some embodiments, R^2 is $-OR^d$.

In some embodiments, R^d is hydrogen. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^d is methyl substituted with 1 R^6. In some embodiments, R^6 is $-C(Y)R^e$. In some embodiments, Y is O. In some embodiments, R^e is heterocyclyl (e.g., morpholino). In some embodiments, R^6 is $-C(Y)NR^bR^{b'}$. In some embodiments, Y is O. In some embodiments, R^b and $R^{b'}$ are each independently C_1-C_8 alkyl (e.g., R^b and $R^{b'}$ are both methyl or R^b and $R^{b'}$ are both ethyl). In some embodiments, one of R^b and $R^{b'}$ is hydrogen and the other is C_1-C_8 alkyl (e.g., methyl or ethyl).

In some embodiments, R^d is ethyl. In some embodiments, R^d is C_3 alkyl (e.g., isopropyl or n-propyl). In some embodiments, R^d is optionally substituted heteroaralkyl. In some embodiments, R^d is optionally substituted pyrindinalkyl.

In some embodiments, R^d is n-propyl substituted with 1 R^6. In some embodiments, R^6 is $-NR^cC(Y)R^{c'}$. In some embodiments, Y is O. In some embodiments, R^c and $R^{c'}$ are each independently C_1-C_8 alkyl (e.g., R^c and $R^{c'}$ are both methyl). In some embodiments, R^d is cyclyl (e.g., cyclopentyl).

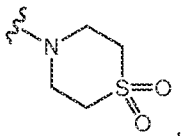
In some embodiments, R^d is heteroaralkyl (e.g.,$-CH_2$-pyridyl). In some embodiments, the pyridyl is substituted with 1 R^6. In some embodiments, R^6 is alkyl (e.g., methyl) or haloalkyl (e.g., CF_3). In some embodiments, R^6 is $-OR^d$. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, R^d is heterocyclylalkyl. In some embodiments, the alkyl is C_1 alkyl. In some embodiments, the alkyl is C_2 alkyl. In some embodiments, the alkyl is C_3 alkyl. In some embodiments, the alkyl is C_4 alkyl. In some embodiments, the heterocyclyl is morpholino. In some embodiments, the heterocyclyl is piperidinyl. In some embodiments, the heterocyclyl is tetrahydrofuranyl. In some embodiments, R^d is cyclylalkyl (e.g.,$-CH_2$-cyclobutyl).

In some embodiments, R^d is alkoxyalkyl. In some embodiments, the alkyl is C_2 alkyl. In some embodiments, the alkyl is C_3 alkyl. In some embodiments, the alkoxy is methoxy.

In some embodiments, R^d is dialkylaminoalkyl. In some embodiments, the alkyl is C_2 alkyl. In some embodiments, the alkyl is C_3 alkyl. In some embodiments, the dialkylamino is dimethylamino.

In some embodiments, R^2 is $-C(Y)R^e$. In some embodiments, Y is O. In some embodiments, R^e is heterocyclyl. In some embodiments, R^e is piperidinyl. In some embodiments, R^e is pyrrolidinyl. In some embodiments, R^e is piperazinyl. In some embodiments, R^e is piperazinyl substituted with 1 R^6. In some embodiments, R^6 is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^e is morpholino. In some embodiments, R^e is thiomorpholino. In some embodiments, R^e is thiomorpholino substituted with 2 R^6. In some embodiments, each R^6 is oxo. In some embodiments, R^e is:



In some embodiments, n is 2.

In some embodiments, each R^2 is independently halo (e.g., each R^2 is chloro).

In some embodiments, each R^2 is independently $-OR^d$.

In some embodiments, each R^d is C_1-C_8 alkyl.

In some embodiments, each R^2 is methoxy. In some embodiments, one R^2 is methoxy and the other is ethoxy. In some embodiments, one R^2 is methoxy and the other is propoxy. In some embodiments, one R^2 is methoxy and the other is isopropoxy.

In some embodiments, one R^2 is methoxy and the other is ethoxy substituted with 1 R^6. In some embodiments, R^6 is $-NR^bR^{b'}$. In some embodiments, R^b and $R^{b'}$ are each independently C_1-C_8 alkyl (e.g., R^b and $R^{b'}$ are both methyl). In some embodiments, R^6 is $-OR^d$. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, one R^2 is methoxy and the other is propoxy substituted with 1 R^6. In some embodiments, R^6 is $-OR^d$. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, one R^2 is $-OR^d$ and the other is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^d is C_1-C_8 alkyl (e.g, methyl or ethyl).

In some embodiments, one R^2 is $-OR^d$ and the other is halo (e.g., chloro). In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, one R^2 is $-OR^d$ and the other is –CN. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, one R^2 is $-OR^d$ and the other is $-C(O)OR^a$. In some embodiments, R^d and R^a are both hydrogen.

In some embodiments, one R^2 is $-OR^d$ and the other is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, one R^2 is $-OR^d$ and the other is $-C(Y)R^e$. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl). In some embodiments, Y is O. In some embodiments, R^e is heterocyclyl (e.g., morpholino).

In some embodiments, one R^2 is halo (e.g., chloro or bromo) and the other is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, one R^2 is C_1-C_8 alkyl (e.g., methyl) and the other is -CN.

In some embodiments, one R^2 is C_1-C_8 alkyl (e.g., methyl) and the other is heteroaryl (e.g., pyridyl). In some embodiments, the pyridyl is substituted with 1 R^6. In some embodiments, R^6 is $-OR^d$. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, one R^2 is C_1-C_8 alkyl (e.g., methyl) and the other is heterocyclylalkyl (e.g., $-CH_2$-morpholino).

In some embodiments, p is 0.

In some embodiments, p is 1.

In some embodiments, R^3 is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^3 is halo (e.g., chloro). In some embodiments, R^3 is haloalkyl (e.g., trifluoromethyl). In some embodiments, R^3 is oxo.

In some embodiments, R^3 is $-OR^d$. In some embodiments, R^d is hydrogen. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, R^3 is $-NR^bR^{b'}$. In some embodiments, R^b and $R^{b'}$ are both hydrogen. In some embodiments, one of R^b and $R^{b'}$ is hydrogen and the other is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, R^3 is heterocyclyl (e.g., piperazinyl). In some embodiments, R^3 is piperazinyl substituted with 1 R^6. In some embodiments, R^6 is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, E is a 5-membered heteroaryl ring.

In some embodiments, E is a thiophene ring.

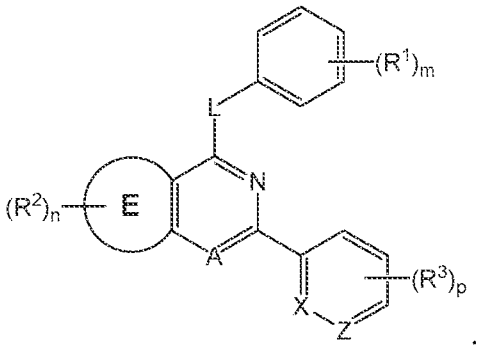
In some embodiments, E is a pyrrole ring.

In some embodiments, n is 1. In some embodiments, R^2 is C_1-C_8 alkyl (e.g., methyl). In some embodiments, E is an N-methylpyrrole ring.

In some embodiments, L is NR^5. In some embodiments, R^5 is hydrogen.

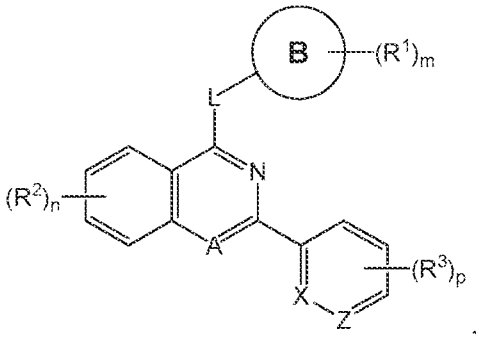
In some embodiments, L is O.

In some embodiments, the compound is:

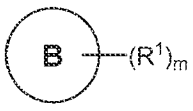
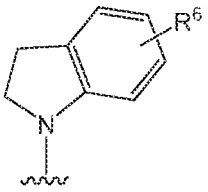
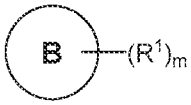
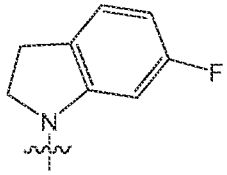
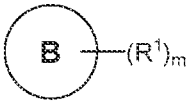


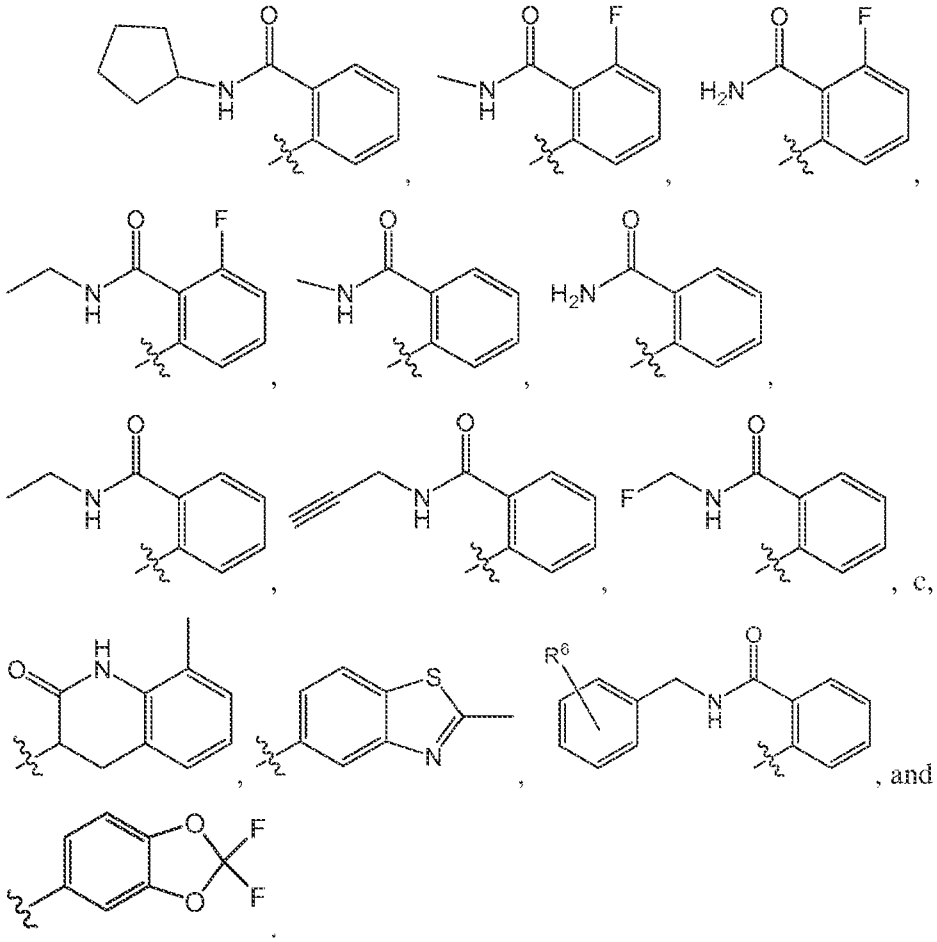
In some embodiments, R^2 is C_1-C_4 alkoxy. In some embodiments, R^2 is halo. In some embodiments, R^1 is $-C(Y)NR^bR^{b'}$.

In some embodiments, the compound is:



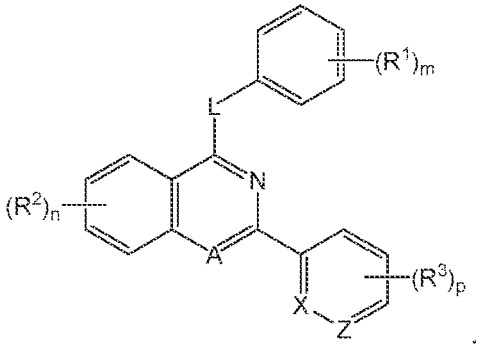
In some embodiments, R^2 is C_1-C_4 alkoxy. In some embodiments, R^2 is halo. In some embodiments, R^1 is $-C(Y)NR^bR^{b'}$.

In some embodiments, L and  are . In some embodiments, L and  are . In some embodiments, L is NH, and  is selected from



In some embodiments R^6 is halo. In some embodiments, R^b or $R^{b'}$ are disubstituted with R^6 (e.g., dichloro, 4-fluoro, 3-chloro, or difluoro).

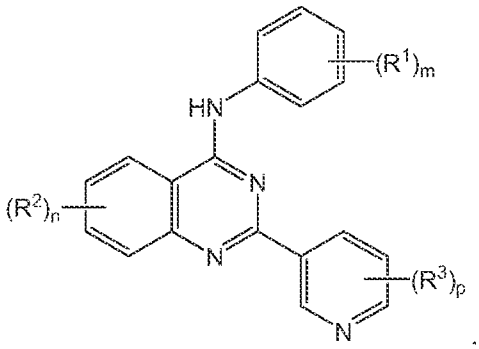
In some embodiments, the compound is:



In some embodiments, R^1 is $-C(Y)NR^bR^{b'}$. In some embodiments, R^1 is halo. In some embodiments, R^2 is C_1-C_4 alkoxy. In some embodiments, R^2 is halo. In some

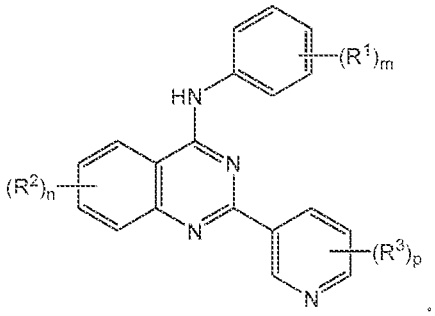
embodiments, m is 2 and two R^1 are 3,4-dichloro; 3,4-difluoro, 3,5- dichloro; 3,5-difluoro; 3-chloro,4-fluoro; or 3-chloro,5-fluoro. In some embodiments, R^2 is–$C(O)NR^bR^{b'}$ and R^3 is H. In some embodiments, R^b and $R^{b'}$ are H. In some embodiments, R^b and $R^{b'}$ are independently C_1-C_4 alkyl or halo-substituted C_1-C_4 alkyl. In some embodiments, R^b is methyl and $R^{b'}$ is trifluoroethyl. In some embodiments, R^1 is C_1-C_4 alkoxy or halo-substituted C_1-C_4 alkoxy. In some embodiments, n and p are zero.

In some embodiments, the compound is:



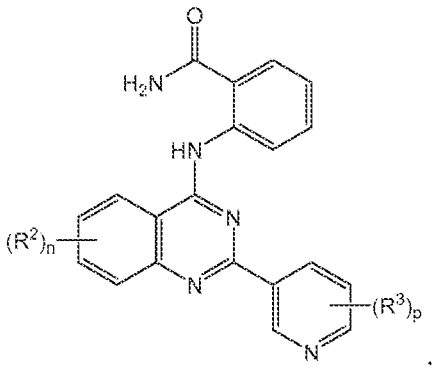
In some embodiments, R^1 is $–C(Y)NR^bR^{b'}$. In some embodiments, R^1 is halo. In some embodiments, R^2 is C_1-C_4 alkoxy. In some embodiments, R^2 is halo. In some embodiments, m is 2 and two R^1 are 3,4-dichloro; 3,4-difluoro, 3,5- dichloro; 3,5-difluoro; 3-chloro,4-fluoro; or 3-chloro,5-fluoro. In some embodiments, R^2 is–$C(O)NR^bR^{b'}$ and R^3 is H. In some embodiments, R^b and $R^{b'}$ are H. In some embodiments, R^b and $R^{b'}$ are independently C_1-C_4 alkyl or halo-substituted C_1-C_4 alkyl. In some embodiments, R^b is methyl and $R^{b'}$ is trifluoroethyl. In some embodiments, R^1 is C_1-C_4 alkoxy or halo-substituted C_1-C_4 alkoxy. In some embodiments, n and p are zero.

In some embodiments, the compound is:



In some embodiments, R^1 is $-C(Y)NR^bR^{b'}$. In some embodiments, R^1 is halo. In some embodiments, R^2 is C_1-C_4 alkoxy. In some embodiments, R^2 is halo. In some embodiments, m is 2 and two R^1 are 3,4-dichloro; 3,4-difluoro, 3,5- dichloro; 3,5-difluoro; 3-chloro,4-fluoro; or 3-chloro,5-fluoro. In some embodiments, R^2 is $-C(O)NR^bR^{b'}$ and R^3 is H. In some embodiments, R^b and $R^{b'}$ are H. In some embodiments, R^b and $R^{b'}$ are independently C_1-C_4 alkyl or halo-substituted C_1-C_4 alkyl. In some embodiments, R^b is methyl and $R^{b'}$ is trifluoroethyl. In some embodiments, R^1 is C_1-C_4 alkoxy or halo-substituted C_1-C_4 alkoxy. In some embodiments, n and p are zero.

In some embodiments, the compound is:



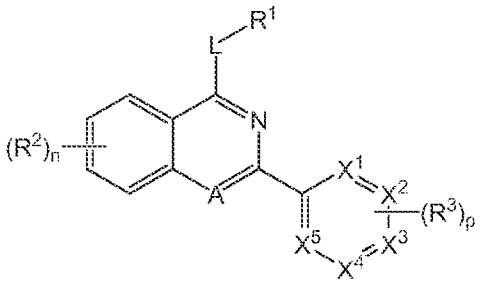
In some embodiments, R^1 is $-C(Y)NR^bR^{b'}$. In some embodiments, R^1 is halo. In some embodiments, R^2 is C_1-C_4 alkoxy. In some embodiments, R^2 is halo. In some embodiments, m is 2 and two R^1 are 3,4-dichloro; 3,4-difluoro, 3,5- dichloro; 3,5-difluoro; 3-chloro,4-fluoro; or 3-chloro,5-fluoro. In some embodiments, R^2 is $-C(O)NR^bR^{b'}$ and R^3 is H. In some embodiments, R^b and $R^{b'}$ are H. In some embodiments, R^b and $R^{b'}$ are independently C_1-C_4 alkyl or halo-substituted C_1-C_4 alkyl. In some embodiments, R^b is methyl and $R^{b'}$ is trifluoroethyl. In some

embodiments, R^1 is C_1-C_4 alkoxy or halo-substituted C_1-C_4 alkoxy. In some embodiments, n and p are zero.

Compounds of Formula (V)

The following aspects and embodiments relate to compounds of formula (V), corresponding to formula (I) of U.S. Provisional Patent Application No. 61/291,550, entitled "Therapeutic Compounds and Related Methods of Use" filed on December 31, 2009, and incorporated herein by reference in its entirety.

Item 40. A compound of formula (V):



(V)

wherein:

L is CR^4R^5, O, C(O), $NR^6C(O)$, or NR^7;

A is CR^8, CH or N;

each X^1, X^2, X^3, X^4 and X^5 is independently CH or N, provided that at least two of X^1, X^2, X^3, X^4 and X^5 are N;

n is 0, 1, 2, 3 or 4;

p is 0, 1, 2 or 3;

R^1 is C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl or heterocyclylalkyl, each of which may be optionally substituted with 1-5 R^9; wherein R^1 or R^9 may optionally be taken together with one of R^4, R^5, R^6 or R^7, and the atoms to which they are attached, to form a cyclyl, heterocyclyl, aryl or heteroaryl ring that is optionally substituted with 1-3 R^{10};

each R^2 and R^3 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl,

dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$,$–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$; each of which is optionally substituted with 1-3 R^{11};

each R^4, R^5, R^6 and R^7 is independently H, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl,–CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$,$–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$;

each R^8, R^9, R^{10} and R^{11} is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thiono, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$,$–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$, each of which may be optionally further substituted; wherein two R^8, two R^9, two R^{10} or two R^{11} may optionally be taken together with the atoms to which they are attached to form an optionally substituted cyclyl, heterocyclyl, aryl or heteroaryl ring;

each Y is independently O or S;

q is 1 or 2; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e, $R^{e'}$ and R^f is independently selected from hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, acyl, cyclyl, heterocyclyl, aryl, heteroaryl, cyclylalkyl, heterocyclylalkyl, aralkyl and heteroaralkyl, each of which may be optionally substituted with 1-3 R^8,

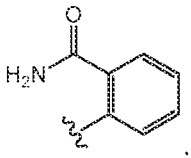
or a pharmaceutically acceptable derivative or prodrug thereof.

In some embodiments, A is CH. In some embodiments, A is N.

In some embodiments, L is NR^7. In some embodiments, R^7 is H.

In some embodiments, R^1 is aryl (e.g., phenyl).

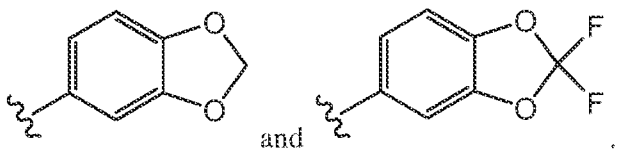
In some embodiments, R^1 is phenyl substituted with 1 R^9. In some embodiments, R^1 is phenyl substituted with 1 R^9 in the ortho position. In some embodiments, R^1 is phenyl substituted with 1 R^9 in the meta position. In some embodiments, R^9 is haloalkoxy (e.g., difluoromethoxy or trifluoromethoxy). In some embodiments, R^9 is –CN. In some embodiments, R^9 is $-C(O)OR^a$. In some embodiments, R^a is hydrogen. In some embodiments, R^9 is $-C(Y)NR^bR^{b'}$. In some embodiments, Y is O. In some embodiments, R^b and $R^{b'}$ are both hydrogen. In some embodiments, R^1 is:



In some embodiments, one of R^b and $R^{b'}$ is hydrogen and the other is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, R^1 is phenyl substituted with 2 R^9. In some embodiments, each R^9 is independently halo (e.g., each R^9 is fluoro or each R^9 is chloro). In some embodiments, one R^9 is fluoro and the other is chloro. In some embodiments, one R^9 is halo (e.g., chloro) and the other is haloalkoxy (e.g., difluoromethoxy or trifluoromethoxy).

In some embodiments, 2 R^9 are taken together with the atoms to which they are attached to form a heterocyclyl ring, e.g., a 5-membered heterocyclyl ring (e.g., a dioxole ring). In some embodiments, the dioxole ring is unsubstituted. In some embodiments, the dioxole ring is substituted. In some embodiments, the dioxole ring is substituted with two fluoro substituents. In some embodiments, R^1 is selected from:



In some embodiments, R^1 is aralkyl (e.g., benzyl). In some embodiments, R^1 is aralkyl substituted with 2 R^9 (e.g., benzyl substituted with 2 R^9). In some

embodiments, 2 R^9 substituents are on the phenyl ring. In some embodiments, each R^9 is independently halo (e.g., each R^9 is chloro).

In some embodiments, R^1 is alkyl (e.g., methyl).

In some embodiments, n is 0.

In some embodiments, n is 1.

In some embodiments, R^2 is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^2 is C_1-C_8 alkyl substituted with 1 R^{11} (e.g., methyl substituted with 1 R^{11}). In some embodiments, R^{11} is heterocyclyl (e.g., morpholino).

In some embodiments, R^2 is aryl (e.g., phenyl). In some embodiments, R^2 is phenyl substituted with 1 R^{11}. In some embodiments, R^{11} is –CN. In some embodiments, R^{11} is $-OR^d$. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^{11} is halo.

In some embodiments, R^2 is halo (e.g., fluoro, chloro, bromo or iodo).

In some embodiments, R^2 is $-NR^cC(Y)R^{c'}$. In some embodiments, R^c is hydrogen. In some embodiments, Y is O. In some embodiments, $R^{c'}$ is alkyl (e.g., methyl). In some embodiments, $R^{c'}$ is aryl (e.g., phenyl). In some embodiments, $R^{c'}$ is phenyl substituted with 1 R^8. In some embodiments, R^8 is $-OR^d$. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, $R^{c'}$ is heteroaryl. In some embodiments, $R^{c'}$ is furanyl. In some embodiments, $R^{c'}$ is pyridyl. In some embodiments, $R^{c'}$ is pyridyl substituted with 1 R^8. In some embodiments, R^8 is $-OR^d$. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, $R^{c'}$ is cyclyl (e.g., cyclohexyl). In some embodiments, $R^{c'}$ is cyclohexyl substituted with 1 R^8. In some embodiments, R^8 is $-OR^d$. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, $R^{c'}$ is heterocyclyl (e.g., tetrahydropyranyl).

In some embodiments, R^2 is $-NR^bR^{b'}$. In some embodiments, R^b and $R^{b'}$ are both hydrogen. In some embodiments, R^b and $R^{b'}$ are each independently C_1-C_8 alkyl (e.g., R^b and $R^{b'}$ are both methyl).

In some embodiments, R^2 is $-OR^d$. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl or ethyl). In some embodiments, R^d is ethyl substituted with 1 R^8. In

some embodiments, R^8 is $-OR^d$. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^2 is $-OCH_2CH_2OCH_3$. In some embodiments, R^2 is $-OCH_2CH_2OCH_2CH_2CH_3$. In some embodiments, R^2 is $-OCH_2CH_2OCH_2CH_2OCH_3$.

In some embodiments, n is 2.

In some embodiments, one R^2 is C_1-C_8 alkyl (e.g., methyl) and the other is halo (e.g., chloro).

In some embodiments, one R^2 is $-OR^d$ and the other is halo (e.g., chloro). In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl).

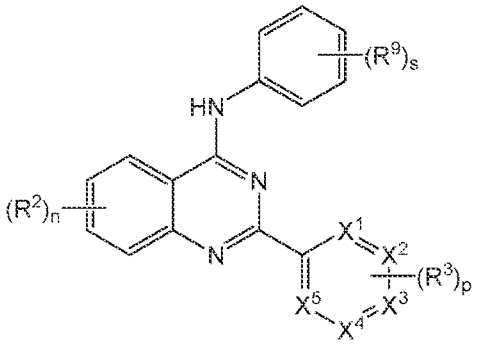
In some embodiments, X^1 and X^4 are N and X^2, X^3 and X^5 are CH.

In some embodiments, X^1 and X^3 are N and X^2, X^4 and X^5 are CH.

In some embodiments, X^2 and X^3 are N and X^1, X^4 and X^5 are CH.

In some embodiments, X^2 and X^4 are N and X^1, X^3 and X^5 are CH.

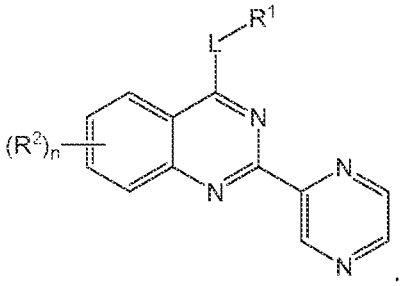
In some embodiments, the compound is:



wherein s is 0, 1, 2, 3 or 4.

In some embodiments, R^9 is $-C(O)NH_2$, C_1-C_4 alkoxy, or substituted C_1-C_4 alkoxy. In some embodiments, R^9 is halo.

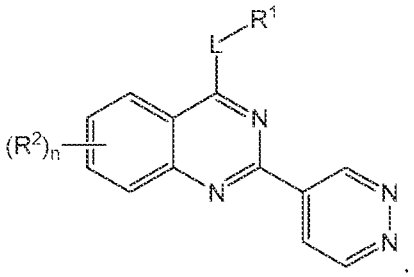
In some embodiments, the compound is:



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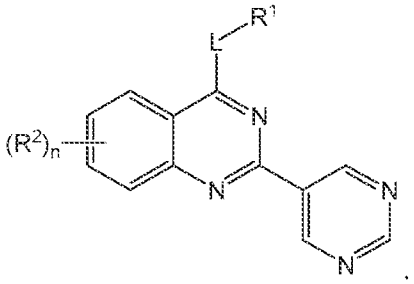
In some embodiments, R_1 is selected from methyl, cyclohexyl, t-butyl, and pyridinyl. In some embodiments, R_1 is heteroaralkyl (e.g.,–CH_2-pyridyl). In some embodiments, LR^1 is $NH(CH_3)$.

In some embodiments, the compound is:



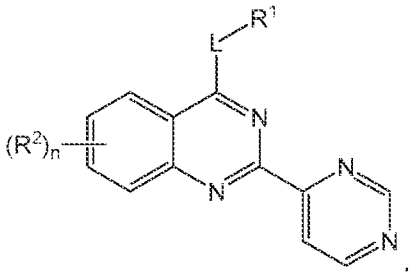
In some embodiments, R_1 is selected from methyl, cyclohexyl, t-butyl, and pyridinyl. In some embodiments, R_1 is heteroaralkyl (e.g.,–CH_2-pyridyl). In some embodiments, LR^1 is $NH(CH_3)$.

In some embodiments, the compound is:



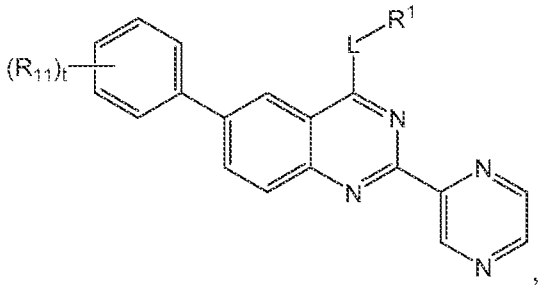
In some embodiments, R_1 is selected from methyl, cyclohexyl, t-butyl, and pyridinyl. In some embodiments, R_1 is heteroaralkyl (e.g.,–CH_2-pyridyl). In some embodiments, LR^1 is $NH(CH_3)$.

In some embodiments, the compound is:



In some embodiments, R_1 is selected from methyl, cyclohexyl, t-butyl, and pyridinyl. In some embodiments, R_1 is heteroaralkyl (e.g.,–CH_2-pyridyl). In some embodiments, LR^1 is $NH(CH_3)$.

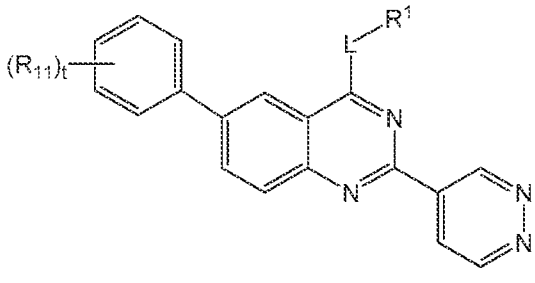
In some embodiments, the compound is:



, wherein t is 1-3.

In some embodiments, R_1 is selected from methyl, cyclohexyl, t-butyl, and pyridinyl. In some embodiments, R_1 is heteroaralkyl (e.g.,–CH_2-pyridyl). In some embodiments, LR^1 is $NH(CH_3)$. In some embodiments, R^{11} is independently halo, nitrile, C_1-C_4 alkoxy, -$C(O)NH_2$, hydroxy, or C_1-C_4 hydroxyalkyl. In some embodiments, R^{11} is fluoro. In some embodiments, R^{11} is methoxy, ethoxy, or methoxyethoxy ether. In some embodiments, R^{11} is $–OCH_2CH_2OCH_3$. In some embodiments, R^{11} is $–OCH_2CH_2OCH_2CH_2CH_3$. In some embodiments, R^{11} is $–OCH_2CH_2OCH_2CH_2OCH_3$.

In some embodiments, the compound is:

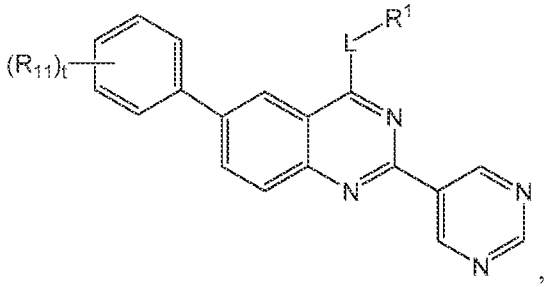


, wherein t is 1-3.

In some embodiments, R_1 is selected from methyl, cyclohexyl, t-butyl, and pyridinyl. In some embodiments, LR^1 is $NH(CH_3)$. In some embodiments, R^{11} is independently halo, nitrile, C_1-C_4 alkoxy, -$C(O)NH_2$, hydroxy, or C_1-C_4 hydroxyalkyl. In some embodiments, R^{11} is fluoro. In some embodiments, R^{11} is methoxy, ethoxy, or methoxyethoxy ether. In some embodiments, R^{11} is $–OCH_2CH_2OCH_3$. In some

embodiments, R^{11} is $-OCH_2CH_2OCH_2CH_2CH_3$. In some embodiments, R^{11} is $-OCH_2CH_2OCH_2CH_2OCH_3$.

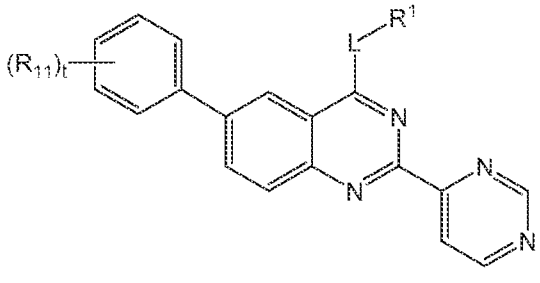
In some embodiments, the compound is:



, wherein t is 1-3.

In some embodiments, R_1 is selected from methyl, cyclohexyl, t-butyl, and pyridinyl. In some embodiments, LR^1 is $NH(CH_3)$. In some embodiments, R^{11} is independently halo, nitrile, C_1-C_4 alkoxy, $-C(O)NH_2$, hydroxy, or C_1-C_4 hydroxyalkyl. In some embodiments, R^{11} is fluoro. In some embodiments, R^{11} is methoxy, ethoxy, or methoxyethoxy ether. In some embodiments, R^{11} is $-OCH_2CH_2OCH_3$. In some embodiments, R^{11} is $-OCH_2CH_2OCH_2CH_2CH_3$. In some embodiments, R^{11} is $-OCH_2CH_2OCH_2CH_2OCH_3$.

In some embodiments, the compound is:



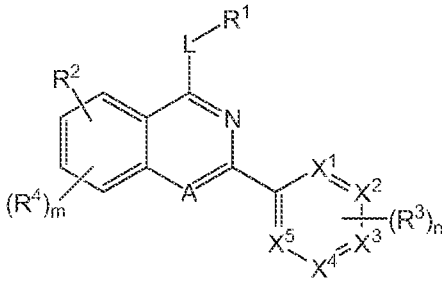
, wherein t is 1-3.

In some embodiments, R_1 is selected from methyl, cyclohexyl, t-butyl, and pyridinyl. In some embodiments, LR^1 is $NH(CH_3)$. In some embodiments, R^{11} is independently halo, nitrile, C_1-C_4 alkoxy, $-C(O)NH_2$, hydroxy, or C_1-C_4 hydroxyalkyl. In some embodiments, R^{11} is fluoro. In some embodiments, R^{11} is methoxy, ethoxy, or methoxyethoxy ether. In some embodiments, R^{11} is $-OCH_2CH_2OCH_3$. In some embodiments, R^{11} is $-OCH_2CH_2OCH_2CH_2CH_3$. In some embodiments, R^{11} is $-OCH_2CH_2OCH_2CH_2OCH_3$.

Compounds of Formula (VI)

The following aspects and embodiments relate to compounds of formula (VI) corresponding to formula (I) of U.S. Provisional Patent Application No. 61/291,554, entitled "Therapeutic Compounds and Related Methods of Use" filed on December 31, 2009, and incorporated herein by reference in its entirety.

Item41 . A compound of formula (VI):



(VI)

wherein:

A is CR^5, CH or N;

L is O or NR^6;

1, 2 or 3 of X^1, X^2, X^3, X^4 and X^5 are N and the others are CH;

m is 0, 1, 2 or 3;

n is 0, 1, 2, 3 or 4;

R^1 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, cyclyl or heterocyclyl, each of which is optionally substituted with 1-3 R^7; or when L is NR^6, R^1 or R^7 may be taken together with R^6 and the atoms to which they are attached to form a heterocyclyl or heteroaryl ring that is optionally substituted with 1-3 R^8;

R^2 is aryl or heteroaryl, each of which is optionally substituted with 1-5 R^9;

each R^3, R^4 and R^5 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{10};

R^6 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, cyclyl or heterocyclyl, each of which is optionally substituted with 1-3 R^{11};

each R^7, R^8, R^9 and R^{10} is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thiono, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^cSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$,–OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{12}; wherein two R^7, two R^8, two R^9 or two R^{10} may optionally be taken together with the atoms to which they are attached to form an optionally substituted cyclyl, heterocyclyl, aryl or heteroaryl ring;

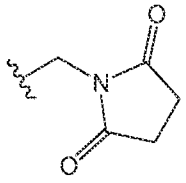
each R^{11} and R^{12} is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thiono, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^cSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$,–OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$;

each Y is independently O or S;

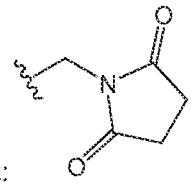
q is 1 or 2; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e, $R^{e'}$ and R^f is independently selected from hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, acyl, cyclyl, heterocyclyl, aryl, heteroaryl, cyclylalkyl, heterocyclylalkyl, aralkyl and heteroaralkyl, each of which may be optionally substituted with 1-3 R^7;

or a pharmaceutically acceptable derivative or prodrug thereof,

wherein when R^1 is cyclopropyl, R^9 is not: 

.

In some embodiments, R^9 is not:  .

In some embodiments, R^1 is C_1-C_8 alkyl, which is optionally substituted with 1-3 R^7; or when L is NR^6, R^1 and R^6 may be taken together with the atoms to which they are attached to form a heterocyclyl or heteroaryl ring that is optionally substituted with 1-3 R^8.

In some embodiments, A is CH. In some embodiments, A is N.

In some embodiments, L is NR^6. In some embodiments, R^6 is hydrogen.

In some embodiments, R^1 is C_1-C_8 alkyl, e.g., methyl, ethyl, C_3 alkyl (e.g., n-propyl or isopropyl), C_4 alkyl (e.g., n-butyl, isobutyl or tert-butyl), or C_5 alkyl (e.g., pentan-3-yl).

In some embodiments, R^1 is C_1-C_8 alkyl substituted with 1-3 R^7 (e.g., C_1-C_8 alkyl substituted with 1 R^7). In some embodiments, R^1 is methyl substituted with 1 R^7. In some embodiments, R^7 is cyclyl (e.g., cyclopropyl). In some embodiments, R^7 is aryl (e.g., phenyl).

In some embodiments, R^1 is ethyl substituted with 1 R^7. In some embodiments, R^7 is aryl (e.g., phenyl). In some embodiments, R^7 is $-OR^d$. In some embodiments, R^d is aryl (e.g., phenyl).

In some embodiments, R^1 is n-propyl substituted with 1 R^7. In some embodiments, R^7 is $-OR^d$. In some embodiments, R^d is C_1-C_8 alkyl (e.g., C_3 alkyl, e.g., n-propyl).

In some embodiments, R^1 is C_1-C_8 alkyl substituted with 3 R^7. In some embodiments, R^1 is ethyl substituted with 3 R^7. In some embodiments, each R^7 is independently halo (e.g., each R^7 is fluoro). In some embodiments, R^1 is 2,2,2-trifluoroethyl.

In some embodiments, R^1 is C_2-C_8 alkenyl, e.g., C_3 alkenyl (e.g., $-CH_2-CH=CH_2$).

In some embodiments, R^1 is C_2-C_8 alkynyl, e.g., C_3 alkynyl (e.g. $-CH_2-C\equiv CH$).

In some embodiments, R^1 is cyclyl (e.g., cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl). In some embodiments, the cyclyl group is a bicyclic group (e.g., indanyl).

In some embodiments, R^1 is heterocyclyl (e.g., piperidyl). In some embodiments, R^1 is piperidyl substituted with 1 R^7. In some embodiments, R^7 is $-C(Y)R^e$. In some embodiments, Y is O. In some embodiments, R^e is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^7 is $-OR^d$.

In some embodiments, R^6 is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, R^1 and R^6 are taken together with the atoms to which they are attached to form a heterocyclyl ring (e.g., a pyrrolidine ring).

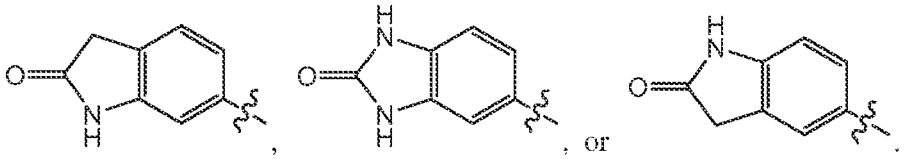
In some embodiments, R^1 and R^6 are taken together with the atoms to which they are attached to form a heteroaryl ring (e.g., an imidazole ring).

In some embodiments, L is O.

In some embodiments, R^1 is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, R^2 is aryl (e.g., phenyl). In some embodiments, R^2 is unsubstituted phenyl. In some embodiments, R^2 is phenyl substituted with 1-3 R^9. In some embodiments, R^2 is phenyl substituted with 1 R^9.

In some embodiments, R^2 is:



In some embodiments, R^9 is halo (e.g., fluoro or chloro). In some embodiments, R^9 is $-CN$. In some embodiments, R^9 is $-NO_2$. In some embodiments, R^9 is haloalkoxy (e.g., trifluoroethoxy). In some embodiments, R^9 is $-NR^bR^{b'}$. In some embodiments, R^b and $R^{b'}$ are each independently C_1-C_8 alkyl (e.g., R^b and $R^{b'}$ are both methyl).

In some embodiments, R^9 is $-OR^d$. In some embodiments, R^9 is $-OCH_2CH_2OCH_3$. In some embodiments, R^9 is $-OCH_2CH_2OCH_2CH_2CH_3$. In some embodiments, R^9 is $-OCH_2CH_2OCH_2CH_2OCH_3$. In some embodiments, R^d is hydrogen. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl). In some

embodiments, R^d is methyl substituted with 1 R^7. In some embodiments, R^7 is –$CYNR^bR^{b'}$. In some embodiments, Y is O and R^b and $R^{b'}$ are each independently C_1-C_8 alkyl (e.g., R^b and $R^{b'}$ are both methyl). In some embodiments, R^d is ethyl. In some embodiments, R^d is ethyl substituted with 1 R^7. In some embodiments, R^7 is –OR^d. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^7 is heterocyclyl (e.g., morpholino).

In some embodiments, R^9 is hydroxyalkyl (e.g.,–CH_2OH). In some embodiments, R^9 is alkoxyalkyl (e.g., –CH_2-O-CH_3). In some embodiments, R^9 is –$C(O)R^e$. In some embodiments, R^e is heterocyclyl (e.g., morpholino). In some embodiments, R^9 is –$S(O)_qR^f$. In some embodiments, q is 1. In some embodiments, R^f is C_1-C_8 alkyl (e.g., methyl.).

In some embodiments, R^2 is phenyl substituted with 2 R^9. In some embodiments, each R^9 is independently halo (e.g., each R^9 is fluoro). In some embodiments, each R^9 is independently –OR^d. In some embodiments, each R^d is independently C_1-C_8 alkyl (e.g., each R^d is methyl).

In some embodiments, R^2 is heteroaryl. In some embodiments, R^2 is a 6-membered heteroaryl. In some embodiments, R^2 is a 6-membered nitrogen-containing heteroaryl, e.g., pyridyl. In some embodiments, R^2 is unsubstituted pyridyl.

In some embodiments, R^2 is pyridyl substituted with 1 R^9. In some embodiments, R^9 is -OR^d. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl).

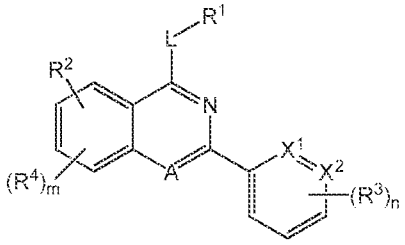
In some embodiments, R^2 is a 5-membered heteroaryl. In some embodiments, R^2 is a 5-membered nitrogen-containing heteroaryl (e.g., pyrrolyl or oxazolyl).

In some embodiments, m is 0.

In some embodiments, m is 1.

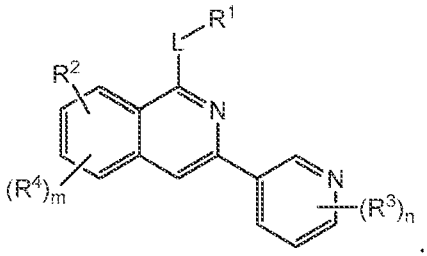
In some embodiments, R^4 is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^4 is –OR^d. In some embodiments, R^d is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^4 is halo. In some embodiments, R^4 is methoxy. In some embodiments, R^d is C_1-C_8 alkyl.

In some embodiments, the compound has the following structure:



wherein one of X^1 and X^2 is N and the other is CH.

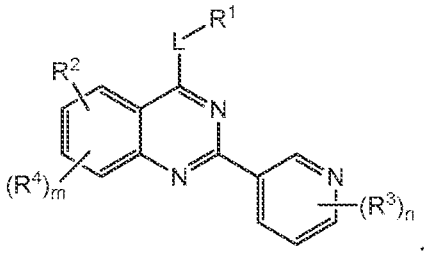
In some embodiments, X^1 is CH and X^2 is N. In some embodiments, X^1 is N and X^2 is CH. In some embodiments, the compound has the following structure:



.

In some embodiments, R^2 is aryl. In some embodiments, R^2 is heteroaryl. In some embodiments, R^1 is C_1-C_8 alkyl (e.g., methyl).

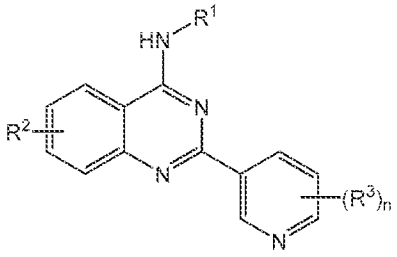
In some embodiments, the compound has the following structure:



.

In some embodiments, R^2 is aryl. In some embodiments, R^2 is heteroaryl. In some embodiments, R^1 is C_1-C_8 alkyl (e.g., methyl).

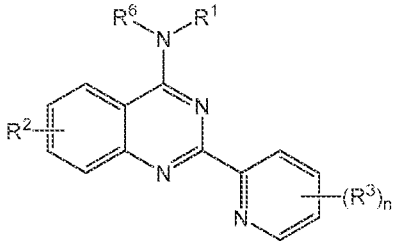
In some embodiments, the compound has the following structure:



.

In some embodiments, R^2 is aryl. In some embodiments, R^2 is heteroaryl. In some embodiments, R^1 is C_1-C_8 alkyl (e.g., methyl).

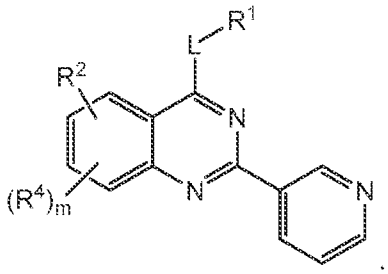
In some embodiments, the compound has the following structure:



wherein R^1 is C_1-C_8 alkyl, which is optionally substituted with 1-3 R^7.

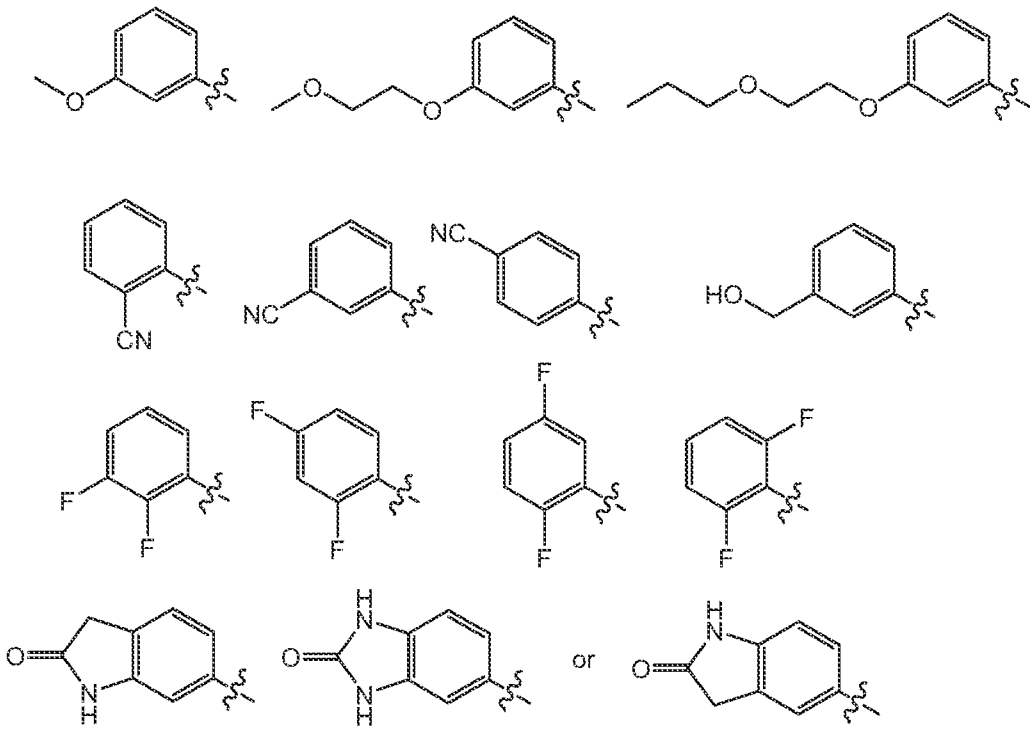
In some embodiments, R^2 is aryl. In some embodiments, R^2 is heteroaryl. In some embodiments, R^1 is C_1-C_8 alkyl (e.g., methyl).

In some embodiments, the compound has the following structure:

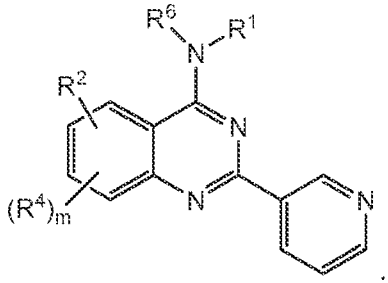


In some embodiments, R^2 is aryl. In some embodiments, R^2 is heteroaryl. In some embodiments, R^1 is C_1-C_8 alkyl (e.g., methyl).

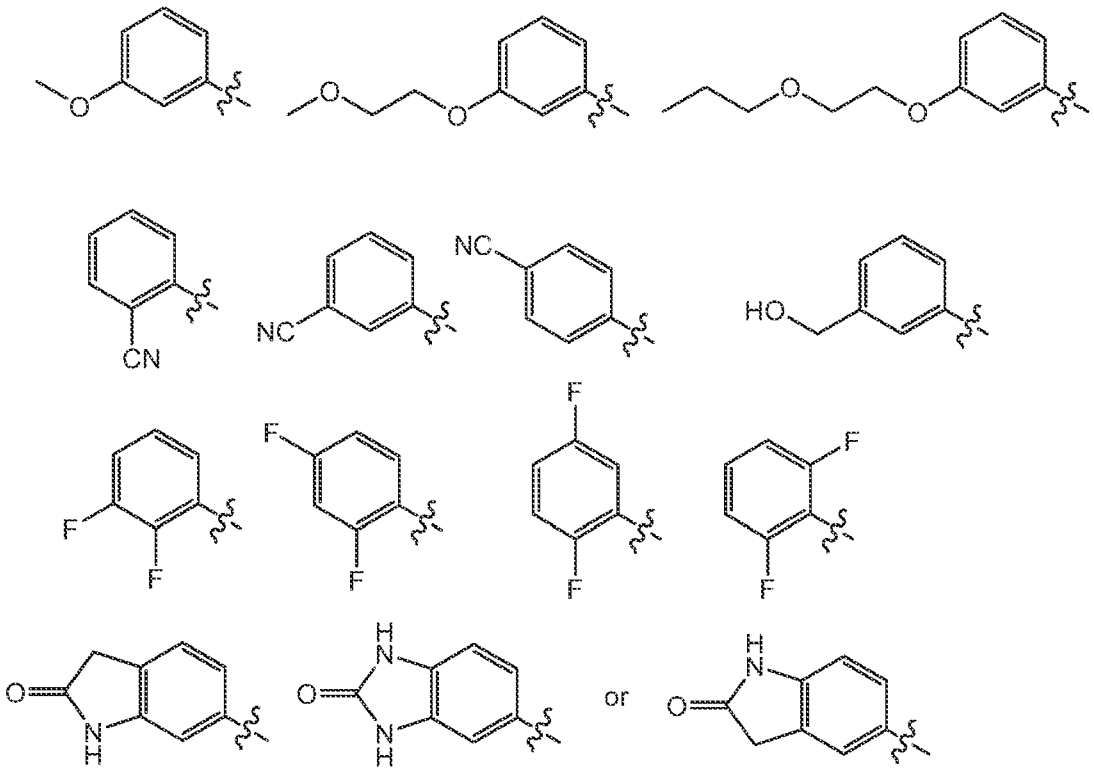
In some embodiments, R^2 is



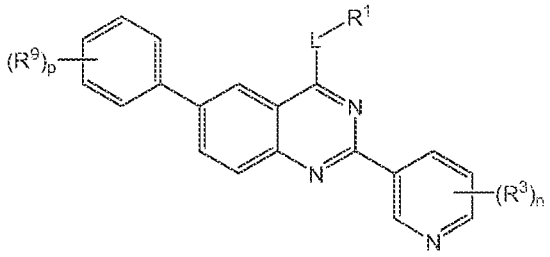
In some embodiments, the compound has the following structure:



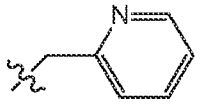
In some embodiments, R^2 is aryl. In some embodiments, R^2 is heteroaryl. In some embodiments R^1 is C_1-C_8 alkyl (e.g., methyl). In some embodiments, R^2 is



In some embodiments, the compound has the following structure:



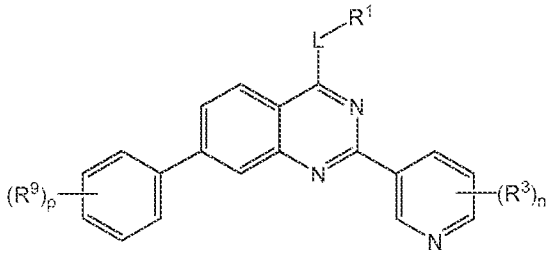
wherein p is 1, 2, 3, 4 or 5.

In some embodiments, L is NR^6. In some embodiments, L is O. In some embodiments, R^1 is hydrogen or C_1-C_8 alkyl. In some embodiments, R^1 is cyclyl or heterocyclyl. In some embodiments, R^1 is aralkyl or heteroaralkyl. In some embodiments, R^1 is methyl, cyclohexyl, t-butyl, or 

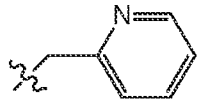
. In some embodiments, R^6 is hydrogen or C_1-C_8 alkyl.

In some embodiments, R^9 is C_1-C_8 alkyl, halo, -CN, or -OR^d. In some embodiments, R^3 is hydrogen.

In some embodiments, the compound has the following structure:



wherein p is 1, 2, 3, 4 or 5.

In some embodiments, L is NR^6. In some embodiments, L is O. In some embodiments, R^1 is hydrogen or C_1-C_8 alkyl. In some embodiments, R^1 is cyclyl or heterocyclyl. In some embodiments, R^1 is aralkyl or heteroaralkyl. In some embodiments, R^1 is methyl, cyclohexyl, t-butyl, or . In some embodiments, R^6 is hydrogen or C_1-C_8 alkyl. In some embodiments, R^9 is C_1-C_8 alkyl, halo, -CN, or -OR^d. In some embodiments, R^3 is hydrogen.

Aspects and Embodiments of Compounds of Formulas (I), (II), (III), (IV), (V), and (VI)

In one aspect, the invention features a composition comprising a compound of formula (I), (II), (III), (IV), (V), or (VI) and an acceptable carrier.

In one aspect, the invention features a pharmaceutical composition comprising a compound of formula (I), (II), (III), (IV), (V), or (VI) and a pharmaceutically acceptable carrier.

In one aspect, the invention features a kit comprising a composition comprising a compound of formula (I), (II), (III), (IV), (V), or (VI) and an acceptable carrier.

In one aspect, the invention features a kit comprising a pharmaceutical composition comprising a compound of formula (I), (II), (III), (IV), (V), or (VI) and a pharmaceutically acceptable carrier.

In one aspect, the invention features a dosage form comprising a composition comprising a compound of formula (I), (II), (III), (IV), (V), or (VI) and an acceptable carrier.

In one aspect, the invention features a dosage form comprising a pharmaceutical composition comprising a compound of formula (I), (II), (III), (IV), (V), or (VI) and a pharmaceutically acceptable carrier.

In one aspect, the invention features a method of treating a disorder that would benefit by the modulation of STEP (e.g., by activation or inhibition of STEP) in a subject, the method comprising administering to a subject in need thereof a compound of formula (I), (II), (III), (IV), (V), or (VI). In one aspect, the invention features a method of treating a disorder that would benefit by the inhibition of STEP, the method comprising administering to a subject in need thereof a compound of formula (I), (II), (III), (IV), (V), or (VI). In some embodiments, the disorder is selected from schizophrenia, schizoaffective disorder, bipolar disorder, manic-depressive disorder, psychosis, mood and anxiety disorders, mania, drug or substance addiction, cognition disorders, learning disabilities, learning and memory disorders, aging and neurologic disorders associated with or linked with cognitive impairments; mild cognitive impairments (MCI), Alzheimer's disease, Alzheimer-related cognition disorders, Huntington's disease, Parkinson's disease, CADASIL syndrome (cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy), amnesia, Wernicke-Korsakoff syndrome, Korsakoff syndrome, mild traumatic head injury (MBTI), traumatic head injury (TBI), fragile X syndrome, stroke, attention-deficit and hyperactivity disorder (ADHD), obsessive compulsive disorder (OCD), post-traumatic stress disorder (PTSD), loss of concentration, autism, cerebral palsy, encephalopathy, and narcolepsy. In some embodiments, the disorder affects learning and memory, neurogenesis, neuronal plasticity, pain perception, mood and anxiety, or neuroendocrine regulation. In some embodiments, the disorder is a cognitive deficit disorder. In some embodiments, the disorder involves pain perception or neuroendocrine regulation. In some embodiments, the disorder affects the central nervous system. In some embodiments the disorder is selected from the group consisting of schizophrenia; refractory, intractable or chronic schizophrenia;

emotional disturbance; psychotic disorder; mood disorder; bipolar I type disorder; bipolar II type disorder; depression; endogenous depression; major depression; melancholy and refractory depression; dysthymic disorder; cyclothymic disorder; panic attack; panic disorder; agoraphobia; social phobia; obsessive-compulsive disorder; post-traumatic stress disorder; generalized anxiety disorder; acute stress disorder; hysteria; somatization disorder; conversion disorder; pain disorder; hypochondriasis; factitious disorder; dissociative disorder; sexual dysfunction; sexual desire disorder; sexual arousal disorder; erectile dysfunction; anorexia nervosa; bulimia nervosa; sleep disorder; adjustment disorder; alcohol abuse; alcohol intoxication; drug addiction; stimulant intoxication; narcotism; anhedonia; iatrogenic anhedonia; anhedonia of a psychic or mental cause; anhedonia associated with depression; anhedonia associated with schizophrenia; delirium; cognitive impairment; cognitive impairment associated with Alzheimer's disease, Parkinson's disease and other neurodegenerative diseases; cognitive impairment caused by Alzheimer's disease; Parkinson's disease and associated neurodegenerative diseases; cognitive impairment of schizophrenia; cognitive impairment caused by refractory, intractable or chronic schizophrenia; vomiting; motion sickness; obesity; migraine; pain (ache) ; mental retardation; autism disorder (autism); Tourette's disorder; tic disorder; attention-deficit/hyperactivity disorder; conduct disorder; and Down's syndrome.

In one aspect, the invention features a method of treating a condition that would benefit by the modulation of STEP (e.g., by activation or inhibition of STEP) in a subject, the method comprising administering to a subject in need thereof a compound of formula (I), (II), (III), (IV), (V), or (VI). In some embodiments, the condition is selected from decreased neurogenesis, cell resilience, or neuronal plasticity due to normal aging, neurodegenerative disorders of the CNS; Alzheimer's disease, Huntington's disease, fragile X syndrome, amyotrophic lateral sclerosis/Lou Gehrig's disease, stroke, Parkinson's disease, parkinsonism, dementia, Pick disease, Corticobasal degeneration, Multiple system atrophy, Progressive supranuclear palsy, traumatic brain injury, head trauma, mild traumatic head injury (MBTI), traumatic head injury (TBI), encephalopathy, intoxication related to ethanol, alcoholism, fetal alcohol syndrome, drug addiction or drug abuse.

In some embodiments, a compound of formula (I), (II), (III), (IV), (V), or (VI) is administered in combination with an additional therapeutic agent. In some embodiments, the additional therapeutic agent is an atypical antipsychotic. In some embodiments, the additional therapeutic agent is selected from the group consisting of aripiprazole, clozapine, ziprasidone, risperidone, quetiapine, olanzapine, amisulpride, asenapine, iloperidone, melperone, paliperidone, perospirone, sertindole and sulpiride. In some embodiments, the additional therapeutic agent is a typical antipsychotic. In some embodiments, the additional therapeutic agent is selected from the group consisting of haloperidol, molindone, loxapine, thioridazine, molindone, thiothixene, pimozide, fluphenazine, trifluoperazine, mesoridazine, chlorprothixene, chlorpromazine, perphenazine, triflupromazine and zuclopenthixol.

DETAILED DESCRIPTION

A compound or composition described herein can be used, e.g., in a method of treating schizophrenia or cognitive deficit. Many of the compounds described herein modulate STEP activity and can be used, e.g., to reduce or inhibit STEP activity, e.g., in a subject.

Definitions

The term "acyl" refers to an alkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl, heterocyclylcarbonyl, or heteroarylcarbonyl substituent, any of which may be further substituted (e.g., by one or more substituents).

The term "alkenyl" refers to a straight or branched hydrocarbon chain containing 2-12 carbon atoms (unless otherwise noted) and having one or more double bonds. Examples of alkenyl groups include, but are not limited to, allyl, propenyl, 2-butenyl, 3-hexenyl and 3-octenyl groups. One of the double bond carbons may optionally be the point of attachment of the alkenyl substituent.

The term "alkenylene" refers to a divalent alkenyl, e.g. –CH=CH-, -CH_2-CH=CH-, and –CH=CH-CH_2-.

The term "alkynyl" refers to a straight or branched hydrocarbon chain containing 2-12 carbon atoms (unless otherwise noted) and characterized in having

one or more triple bonds. Examples of alkynyl groups include, but are not limited to, ethynyl, propargyl, and 3-hexynyl. One of the triple bond carbons may optionally be the point of attachment of the alkynyl substituent.

The term "alkynylene" refers to a divalent alkynyl, e.g. –CH≡CH-, -CH_2-CH≡CH-, and –CH≡CH-CH_2-.

The terms "alkoxyl" or "alkoxy" as used herein refers to an alkyl group, as defined below, having an oxygen radical attached thereto. Representative alkoxy groups include methoxy, ethoxy, propyloxy, tert-butoxy and the like. The term "alkoxyalkyl" refers to an alkyl in which one or more hydrogen atoms are replaced by an alkoxy group.

An "ether" is two hydrocarbons covalently linked by an oxygen.

The term "alkyl" refers to the radical of saturated aliphatic groups, including straight-chain alkyl groups, and branched-chain alkyl groups. In preferred embodiments, a straight chain or branched chain alkyl has 12 or fewer carbon atoms in its backbone (unless otherwise noted) e.g., from 1-12, 1-8, 1-6, or 1-4. Exemplary alkyl moieties include methyl, ethyl, propyl (e.g., n-propyl or isopropyl), butyl (e.g., n-butyl, isobutyl or t-butyl), pentyl (e.g., n-pentyl, isopentyl or pentan-3-yl), hexyl and hepty.

The term "alkylene" refers to a divalent alkyl, e.g., -CH_2-, -CH_2CH_2-, and -$CH_2CH_2CH_2$-.

The term "alkoxylene" refers to an alkylene wherein a CH_2 is substituted with an oxygen. For example, an aryl alkoxylene refers to a group with an alkylene attached to an aryl group through an oxygen, an optionally substituted heteroaryl alkoxylene refers to a group with an alkylene attached to an heteroaryl group through an oxygen.

The term "amino" refers to –NH_2.

The term "aminoalkyl" refers to an alkyl in which one or more hydrogen atoms are replaced by an amino group.

The terms "alkylamino" and "dialkylamino" refer to –NH(alkyl) and –N(alkyl)$_2$ radicals respectively.

The term "aralkylamino" or "arylalkylamino" refers to a –NH(aralkyl) radical. The term "alkylaminoalkyl" refers to a (alkyl)NH-alkyl- radical; the term "dialkylaminoalkyl" refers to an $(alkyl)_2N$-alkyl- radical.

The term "amido" refers to a –NHC(O)- or $C(O)NH_2$ substituent.

The term "aryl" refers to a 6-carbon monocyclic, 10-carbon bicyclic, or 14-carbon tricyclic aromatic ring system wherein 0, 1, 2, 3, or 4 atoms of each ring may be substituted by a substituent. Examples of aryl moieties include, but are not limited to, phenyl, naphthyl and the like. The term "arylalkyl" or "aralkyl" refers to alkyl substituted with an aryl. Exemplary aralkyls include but are not limited to benzyl, 1-phenylethyl, 2-phenylethyl, 3-phenylpropyl, 9-fluorenyl, benzhydryl, phenethyl, and trityl groups. The term "arylalkenyl" refers to an alkenyl substituted with an aryl. The term "arylalkynyl" refers to an alkynyl substituted with an aryl. Terms such as "arylC_2-C_6alkyl" are to be read as a further limitation on the size of the alkyl group. The term "arylalkoxy" refers to an alkoxy substituted with aryl. The term "arylenyl" refers to a divalent aryl (i.e., -Ar-).

The terms "cycloalkyl" or "cyclyl" as employed herein include saturated and partially unsaturated cyclic hydrocarbon groups having 3 to 12 carbons, preferably 3 to 8 carbons, and more preferably 3 to 6 carbons, wherein the cycloalkyl group may be optionally substituted. Exemplary cyclyl groups include, without limitation, cyclopropyl, cyclobutyl, cyclopentyl, cyclopentenyl, cyclohexyl, cyclohexenyl, cycloheptyl, and cyclooctyl. Cyclyl moieties also include both bridged and fused ring systems. Cyclyl groups also include those that are fused to additional ring systems, which may be saturated or unsaturated. A cyclyl group may thus be a bicyclic group in which one ring is saturated or partially unsaturated and the other is fully unsaturated (e.g., indanyl).

The term "cyclylalkyl" as used herein, refers to an alkyl group substituted with a cyclyl group. Cyclylalkyl includes groups in which more than one hydrogen atom of an alkyl group has been replaced by a cyclyl group.

The term "cycloalkylalkyl" as used herein, refers to an alkyl group substituted with a cycloalkyl group.

The term "halo" or "halogen" refers to any radical of fluorine, chlorine, bromine or iodine.

The term "haloalkyl" refers to an alkyl group that may have any number of hydrogens available on the group replaced with a halogen atom. Representative haloalkyl groups include but are not limited to: $-CH_2Cl$, $-CH_2ClCF_3$, $-CHBr_2$, $-CF_3$, $-CH_2F$, $-CHF_2$, and $-CH_2CF_3$. The term "fluoroalkyl" refers to an alkyl group that may have any number of hydrogens available on the group replaced with a fluorine atom. Representative fluoroalkyl groups include but are not limited to: $-CH_2F$, $-CH_2FCF_3$, $-CHF_2$ and $-CF_3$. The term "haloalkoxy" refers to an alkoxy group that may have any number of hydrogen atoms available on the alkyl group replaced with a halogen atom. Representative haloalkoxy groups include but are not limited to: $-OCH_2Cl$, $-OCH_2ClCF_3$, $-OCHBr_2$, $-OCHF_2$ or $-OCF_3$. The term "fluoroalkoxy" refers to an alkoxy group that may have any number of hydrogens available on the group replaced with a fluorine atom. Representative fluoroalkoxy groups include but are not limited to: $-OCH_2F$, $-OCH_2FCF_3$, $-OCHF_2$ or $-OCF_3$.

The term "heteroatom" as used herein means an atom of any element other than carbon or hydrogen. Preferred heteroatoms are nitrogen, oxygen, sulfur, phosphorus and silicon. A heteroatom may be present in any oxidation state (e.g., any oxidized form of nitrogen, sulfur, phosphorus or silicon) and any charged state (e.g., the quaternized form of any basic nitrogen), and includes a substitutable nitrogen of a heterocyclic ring, for example N (as in 3,4-dihydro-2*H*-pyrrolyl), NH (as in pyrrolidinyl) or NR^+ (as in N-substituted pyrrolidinyl).

The term "heteroaryl" refers to an aromatic 5-8 membered monocyclic, 8-12 membered bicyclic, or 11-14 membered tricyclic ring system having 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms selected from O, N, or S (e.g., carbon atoms and 1-3, 1-6, or 1-9 heteroatoms of N, O, or S if monocyclic, bicyclic, or tricyclic, respectively), wherein 0, 1, 2, 3, or 4 atoms of each ring may be substituted by a substituent. Examples of heteroaryl groups include pyridyl, furyl or furanyl, imidazolyl, benzimidazolyl, pyrimidinyl, thiophenyl or thienyl, quinolinyl, indolyl, thiazolyl, oxazolyl and the like. The term "heteroarylalkyl" or the term "heteroaralkyl" refers to an alkyl

substituted with a heteroaryl. The term "heteroarylalkenyl" refers to an alkenyl substituted with a heteroaryl. The term "heteroarylalkynyl" refers to an alkynyl substituted with a heteroaryl. The term "heteroarylalkoxy" refers to an alkoxy substituted with heteroaryl.

The term "heteroaryl" refers to a group having 5 to 14 ring atoms, preferably 5, 6, 9, or 10 ring atoms; having 6, 10, or 14 π electrons shared in a cyclic array; and having, in addition to carbon atoms, from one to five heteroatoms. A heteroaryl group may be mono-, bi-, tri-, or polycyclic, preferably mono-, bi-, or tricyclic, more preferably mono- or bicyclic. When a heteroaryl is substituted by a hydroxy group, it also includes its corresponding tautomer. The term "heteroaryl," as used herein, also includes groups in which a heteroaromatic ring is fused to one or more aryl rings. Nonlimiting examples of heteroaryl groups include thienyl, furanyl, pyrrolyl, imidazolyl, pyrazolyl, triazolyl, tetrazolyl, oxazolyl, isoxazolyl, oxadiazolyl, thiazolyl, isothiazolyl, thiadiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolizinyl, purinyl, naphthyridinyl, pteridinyl, indolyl, isoindolyl, benzothienyl, benzofuranyl, dibenzofuranyl, indazolyl, benzimidazolyl, benzthiazolyl, quinolyl, isoquinolyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, 4H-quinolizinyl, carbazolyl, acridinyl, phenazinyl, phenothiazinyl, phenoxazinyl, tetrahydroquinolinyl, tetrahydroisoquinolinyl, and pyrido[2,3-b]-1,4-oxazin-3(4H)-one. The term "heteroaryl" may be used interchangeably with the terms "heteroaryl ring", "heteroaryl group," or "heteroaromatic," any of which terms include rings that are optionally substituted. A ring nitrogen atom of a heteroaryl may be oxidized to form the corresponding N-oxide compound. A nonlimiting example of such a heteroaryl having an oxidized ring nitrogen atom is N-oxopyridyl.

The term "heteroarylalkyl" or "heteroaralkyl" refers to an alkyl group substituted by a heteroaryl. Heteroaralkyl includes groups in which more than one hydrogen atom has been replaced by a heteroaryl group.

As used herein, the terms "heterocycle," "heterocyclyl" and "heterocyclic ring" are used interchangeably and refer to a stable 3- to 8-membered monocyclic or 7-10-membered bicyclic heterocyclic moiety that is either saturated or partially unsaturated, and having, in addition to carbon atoms, one or more, preferably one to four,

heteroatoms, as defined above. When used in reference to a ring atom of a heterocycle, the term "nitrogen" includes a substituted nitrogen. As an example, in a saturated or partially unsaturated ring having 0-3 heteroatoms selected from oxygen, sulfur or nitrogen, the nitrogen may be N (as in 3,4-dihydro-2/y-pyrrolyl), NH (as in pyrrolidinyl), or NR^+ (as in N-substituted pyrrolidinyl). A heterocyclic ring can be attached to its pendant group at any heteroatom or carbon atom that results in a stable structure and any of the ring atoms can be optionally substituted. Examples of such saturated or partially unsaturated heterocyclic radicals include, without limitation, tetrahydrofuranyl, tetrahydropyranyl, tetrahydrothienyl, piperidinyl, decahydroquinolinyl, oxazolidinyl, piperazinyl, dioxanyl, dioxolanyl, diazepinyl, oxazepinyl, thiazepinyl, morpholinyl, and thiomorpholinyl. A heterocyclyl group may be mono-, bi-, tri-, or polycyclic, preferably mono-, bi-, or tricyclic, more preferably mono- or bicyclic. Additionally, a heterocyclic ring also includes groups in which the heterocyclyl ring is fused to one or more aryl, heteroaryl or cyclyl rings. A ring nitrogen atom of a heterocyclic ring also may be oxidized to form the corresponding N-hydroxy compound.

The term "heterocyclylalkyl" refers to an alkyl group substituted by a heterocyclyl. Heterocyclylalkyl includes groups in which more than one hydrogen atom has been replaced by a heterocyclyl group.

The terms "hetaralkyl" and "heteroaralkyl", as used herein, refers to an alkyl group substituted with a heteroaryl group. Examplary heteroaralkyl groups include but are not limited to methylpyridyl or methylpyrimidyl.

The term "heterocyclyl" or "heterocyclylalkyl" refers to a nonaromatic 5-8 membered monocyclic, 5-12 membered bicyclic, or 11-14 membered tricyclic ring system having 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms selected from O, N, or S (e.g., carbon atoms and 1-3, 1-6, or 1-9 heteroatoms of N, O, or S if monocyclic, bicyclic, or tricyclic, respectively), wherein 0, 1, 2 or 3 atoms of each ring may be substituted by a substituent. Examples of heterocyclyl groups include piperazinyl, pyrrolidinyl, dioxanyl, morpholinyl, tetrahydrofuranyl, and include both bridged and fused ring

systems. The term "heterocyclylalkyl" refers to an alkyl substituted with a heterocyclyl.

The term "heterocyclylalkyl", as used herein, refers to an alkyl group substituted with a heterocycle group.

The term "heteroalkyl," as used herein, refers to a saturate or unsaturated, straight or branched chain aliphatic group, wherein one or more of the carbon atoms in the chain are independently replaced by a heteroatom. Exemplary hetero atoms include O, S, and N.

In the case of aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl etc., groups described as optionally substituted, it is intended that either or both aryl, heteroaryl, cyclyl, heterocyclyl and alkyl moieties may be independently optionally substituted or unsubstituted.

The term "hydroxyalkyl" refers to an alkyl in which one or more hydrogen atoms are replaced by a hydroxy group.

The term "oxo" refers to an oxygen atom (=O), which forms a carbonyl when attached to carbon, an N-oxide when attached to nitrogen, and a sulfoxide or sulfone when attached to sulfur.

The term "thioalkyl" as used herein refers to an -S(alkyl) group, where the point of attachment is through the sulfur atom and the alkyl group is as defined above.

The term "thiono" or "thioxo" refers to a sulfur atom (=S), which forms a thioketone when attached to carbon.

The term "substituted" refers to moieties having substituents replacing a hydrogen on one or more carbons of the backbone. It will be understood that "substitution" or "substituted with" includes the implicit proviso that such substitution is in accordance with permitted valence of the substituted atom and the substituent, and that the substitution results in a stable compound, e.g., which does not spontaneously undergo transformation such as by rearrangement, cyclization, elimination, etc. As used herein, the term "substituted" is contemplated to include all permissible substituents of organic compounds. In a broad aspect, the permissible substituents include acyclic and cyclic, branched and unbranched, carbocyclic and heterocyclic, aromatic and non-aromatic substituents of organic compounds. The

permissible substituents can be one or more and the same or different for appropriate organic compounds. For purposes of this invention, the heteroatoms such as nitrogen may have hydrogen substituents and/or any permissible substituents of organic compounds described herein which satisfy the valences of the heteroatoms.

The term "substituent" refers to a group "substituted" on a moiety described herein. Any atom on any substituent can be substituted. Substituents can include any substituents described herein. Examplary substituents include, without limitation, alkyl (e.g., C1, C2, C3, C4, C5, C6, C7, C8, C9, C10, C11, C12 straight or branched chain alkyl), cycloalkyl, haloalkyl (e.g., perfluoroalkyl such as CF_3), aryl, heteroaryl, aralkyl, heteroaralkyl, heterocyclyl, alkenyl, alkynyl, cycloalkenyl, heterocycloalkenyl, alkoxy, haloalkoxy (e.g., perfluoroalkoxy such as OCF_3), halo, hydroxy, carboxy, carboxylate, cyano, nitro, amino, alkylamino, SO_3H, sulfate, phosphate, methylenedioxy (-O-CH_2-O- wherein oxygens are attached to vicinal atoms), ethylenedioxy, oxo, thioxo (e.g., C=S), imino (alkyl, aryl, aralkyl), $S(O)_n$alkyl (where n is 0-2), $S(O)_n$ aryl (where n is 0-2), $S(O)_n$ heteroaryl (where n is 0-2), $S(O)_n$ heterocyclyl (where n is 0-2), amine (mono-, di-, alkyl, cycloalkyl, aralkyl, heteroaralkyl, aryl, heteroaryl, and combinations thereof), ester (alkyl, aralkyl, heteroaralkyl, aryl, heteroaryl), amide (mono-, di-, alkyl, aralkyl, heteroaralkyl, aryl, heteroaryl, and combinations thereof), sulfonamide (mono-, di-, alkyl, aralkyl, heteroaralkyl, and combinations thereof). In one aspect, the substituents on a group are independently any one single, or any subset of the aforementioned substituents. In another aspect, a substituent may itself be substituted with any one of the above substituents.

As used herein, the phrase "optionally substituted" is used interchangeably with the phrase "substituted or unsubstituted." In general, the term "substituted", whether preceded by the term "optionally" or not, means that a hydrogen radical of the designated moiety is replaced with the radical of a specified substituent, provided that the substitution results in a stable or chemically feasible compound. The term "substitutable", when used in reference to a designated atom, means that attached to the atom is a hydrogen radical, which hydrogen atom can be replaced with the radical of a suitable substituent. Unless otherwise indicated, an "optionally substituted" group

may have a substituent at each substitutable position of the group, and when more than one position in any given structure may be substituted with more than one substituent selected from a specified group, the substituent may be either the same or different at every position. Combinations of substituents envisioned by this invention are preferably those that result in the formation of stable or chemically feasible compounds.

As used herein, the term "optionally substituted" means substituted or unsubstituted.

As used herein, the term "partially unsaturated" refers to a moiety that includes at least one double or triple bond between atoms. The term "partially unsaturated" encompasses rings, e.g., having one or more sites of unsaturation, but that are not completely unsaturated so as to be aryl or heteroaryl.

The term "chiral" refers to molecules which have the property of non-superimposability of the mirror image partner, while the term "achiral" refers to molecules which are superimposable on their mirror image partner. With respect to the nomenclature of a chiral center, terms "R" and "S" configuration are as defined by the IUPAC Recommendations. The term "enantiomers" refers to two stereoisomers of a compound which are non-superimposable mirror images of one another. An equimolar mixture of two enantiomers is called a "racemic mixture" or a "racemate." The term "isomers" or "stereoisomers" refers to compounds which have identical chemical constitution, but differ with regard to the arrangement of the atoms or groups in space. For example, isomers include *cis*– and *trans*–isomers, *E*– and *Z*–isomers, *R*– and *S*–enantiomers, diastereomers, (D)–isomers, (L)–isomers, racemic mixtures thereof, and other mixtures thereof. The term "diastereomers" refers to stereoisomers with two or more centers of dissymmetry and whose molecules are not mirror images of one another.

The term "administration" or "administering" includes routes of introducing the compounds, or a composition thereof, of the invention to a subject to perform their intended function. Examples of routes of administration that may be used include injection (subcutaneous, intravenous, parenterally, intraperitoneally, intrathecal), oral, inhalation, rectal and transdermal. The pharmaceutical compositions may be given by

forms suitable for each administration route. For example, these compositions are administered in tablets or capsule form, by injection, inhalation, eye lotion, ointment, suppository, etc. administration by injection, infusion or inhalation; topical by lotion or ointment; and rectal by suppositories. Oral administration is preferred. The injection can be bolus or can be continuous infusion. Depending on the route of administration, a compound described herein can be coated with or disposed in a selected material to protect it from natural conditions which may detrimentally affect its ability to perform its intended function. A compound or composition described herein can be administered alone, or in conjunction with either another agent as described above or with a pharmaceutically-acceptable carrier, or both. A compound or composition described herein can be administered prior to the administration of the other agent, simultaneously with the agent, or after the administration of the agent. Furthermore, a compound described herein can also be administered in a pro-drug form which is converted into its active metabolite, or more active metabolite *in vivo*.

The language "biological activities" of a compound described herein includes all activities elicited by a compound described herein in a responsive subject or cell. It includes genomic and non-genomic activities elicited by these compounds.

The terms "inhibit" and "inhibitor" as used herein means an agent that measurably slows or stops the production of STriatal-Enriched tyrosine Phosphatase (STEP), or decreases or inactivates STEP, or interferes with STEP-mediated biological pathways. Inhibitors of STEP include compounds of the invention, e.g., compounds of Formulas (I), (II), or (III). A compound can be evaluated to determine if it is an inhibitor by measuring either directly or indirectly the activity of STEP in the presence of the compound suspected to inhibit STEP. Exemplary methods of measure STEP inhibition are described in the EXAMPLES herein.

An "effective amount" or "an amount effective" refers to an amount of the compound or composition which is effective, upon single or multiple dose administrations to a subject and for periods of time necessary, in treating a cell, or curing, alleviating, relieving or improving a symptom of a disorder, e.g., a disorder described herein. An effective amount of a compound described herein may vary according to factors such as the disease state, age, and weight of the subject, and the

ability of a compound described herein to elicit a desired response in the subject. Dosage regimens may be adjusted to provide the optimum therapeutic response. An effective amount is also one in which any toxic or detrimental effects (e.g., side effects) of a compound described herein are outweighed by the therapeutically beneficial effects. The term "effective amount" includes an amount effective, at dosages and for periods of time necessary, to achieve the desired result, e.g., modulate or regulate protein tyrosine phosphatases, e.g., STEP, in a subject and/or treat a disorder described herein such as a protein tyrosine phosphatase related disorder. Exemplary disorders include those related to cognition, learning and memory, neurogenesis. An effective amount may also affect neuronal plasticity, pain perception, mood and anxiety, and neuroendocrine regulation.

An effective amount of a compound described herein may vary according to factors such as the disease state, age, and weight of the subject, and the ability of a compound described herein to elicit a desired response in the subject. Dosage regimens may be adjusted to provide the optimum therapeutic response. An effective amount is also one in which any toxic or detrimental effects (e.g., side effects) of a compound described herein are outweighed by the therapeutically beneficial effects.

A therapeutically effective amount of a compound described herein (i.e., an effective dosage) may range from about 0.001 to 50 mg/kg body weight, preferably about 0.01 to 40 mg/kg body weight, more preferably about 0.1 to 35 mg/kg body weight, still more preferably about 1 to 30 mg/kg, and even more preferably about 10 to 30 mg/kg. The skilled artisan will appreciate that certain factors may influence the dosage required to effectively treat a subject, including but not limited to the severity of the disease or disorder, previous treatments, the general health and/or age of the subject, and other diseases present. Moreover, treatment of a subject with a therapeutically effective amount of a compound described herein can include a single treatment or, preferably, can include a series of treatments. In one example, a subject is treated with a compound described herein in the range of between about 0.1 to 20 mg/kg body weight, one time per week for between about 1 to 10 weeks, preferably between 2 to 8 weeks, more preferably between about 3 to 7 weeks, and even more preferably for about 4, 5, or 6 weeks. It will also be appreciated that the effective

dosage of a compound described herein used for treatment may increase or decrease over the course of a particular treatment.

As used herein, an amount of a compound effective to prevent a disorder, or "a prophylactically effective amount" of the compound refers to an amount effective, upon single- or multiple-dose administration to the subject, in preventing or delaying the occurrence of the onset or recurrence of a disorder or a symptom of the disorder.

The language "improved biological properties" refers to any activity inherent in a compound described herein that enhances its effectiveness in vivo. In a preferred embodiment, this term refers to any qualitative or quantitative improved therapeutic property of a compound described herein, such as reduced off-target effects.

The term "modulate" refers to an increase or decrease, e.g., in the activity of an enzyme in response to exposure to a compound or composition described herein, e.g., the activation or inhibition of STEP, in at least a sub-population of cells in a subject such that a desired end result is achieved (e.g., a therapeutic result). In some embodiments, a compound as described herein inhibits a target described herein, e.g., STEP. In some embodiments, a compound as described herein is activates a target described herein, e.g., STEP.

As used herein, the term "subject" is intended to include human and non-human animals. Exemplary human subjects include a human patient having a disorder, e.g., a disorder described herein, or a normal subject. The term "non-human animals" includes all vertebrates, e.g., non-mammals (such as chickens, amphibians, reptiles) and mammals, such as non-human primates, domesticated and/or agriculturally useful animals, e.g., sheep, dog, cat, cow, pig, etc.

As used herein, the term "treat" or "treating" is defined as applying or administering a compound or composition, alone or in combination with a second compound or composition, to a subject, e.g., a patient, or applying or administering the compound or composition to an isolated tissue or cell, e.g., cell line, from a subject, e.g., a patient, who has a disorder (e.g., a disorder as described herein), a symptom of a disorder, or a predisposition toward a disorder, with the purpose to cure, heal, alleviate, relieve, alter, remedy, ameliorate, improve or affect the disorder, one or more symptoms of the disorder or the predisposition toward the disorder (e.g., to

prevent at least one symptom of the disorder or to delay onset of at least one symptom of the disorder).

The phrases "parenteral administration" and "administered parenterally" as used herein means modes of administration other than enteral and topical administration, usually by injection, and includes, without limitation, intravenous, intramuscular, intraarterial, intrathecal, intracapsular, intraorbital, intracardiac, intradermal, intraperitoneal, transtracheal, subcutaneous, subcuticular, intraarticular, subcapsular, subarachnoid, intraspinal and intrasternal injection and infusion.

The term "prodrug" or "pro-drug" includes compounds with moieties that can be metabolized *in vivo*. Generally, the prodrugs are metabolized *in vivo* by esterases or by other mechanisms to active drugs. Examples of prodrugs and their uses are well known in the art (See, *e.g.*, Berge *et al.* (1977) "Pharmaceutical Salts", *J. Pharm. Sci.* 66:1-19). The prodrugs can be prepared *in situ* during the final isolation and purification of the compounds, or by separately reacting the purified compound in its free acid form or hydroxyl with a suitable esterifying agent. Hydroxyl groups can be converted into esters *via* treatment with a carboxylic acid. Examples of prodrug moieties include substituted and unsubstituted, branch or unbranched lower alkyl ester moieties, (*e.g.*, propionoic acid esters), lower alkenyl esters, di-lower alkyl-amino lower-alkyl esters (*e.g.*, dimethylaminoethyl ester), acylamino lower alkyl esters (*e.g.*, acetyloxymethyl ester), acyloxy lower alkyl esters (*e.g.*, pivaloyloxymethyl ester), aryl esters (phenyl ester), aryl-lower alkyl esters (*e.g.*, benzyl ester), substituted (*e.g.*, with methyl, halo, or methoxy substituents) aryl and aryl-lower alkyl esters, amides, lower-alkyl amides, di-lower alkyl amides, and hydroxy amides. Preferred prodrug moieties are propionoic acid esters and acyl esters. Prodrugs which are converted to active forms through other mechanisms *in vivo* are also included.

The language "a prophylactically effective amount" of a compound refers to an amount of a compound described herein any formula herein or otherwise described herein which is effective, upon single or multiple dose administration to the patient, in preventing or treating a disease or condition.

The language "reduced off-target effects" is intended to include a reduction in any undesired side effect elicited by a compound described herein when administered

in vivo. In some embodiments, a compound described herein has little to no cardio and/or pulmonary toxicity (e.g., when administered to a subject). In some embodiments, a compound described herein has little to no hallucinogenic activity (e.g., when administered to a subject).

The term "selective" means a greater activity against a first target. In some embodiments a compound has a selectivity of at least 1.25-fold, at least 1.5 fold, at least 2-fold, at least 3-fold, at least 4-fold, at least 5-fold, at least 6-fold, at least 10-fold or at least 100-fold greater towards a first target relative to a second target. In some embodiments, a compound described herein, e.g., a compound of Formulas (I), (II), or (III) is selective toward STEP relative to one or more other protein tyrosine phosphatases.

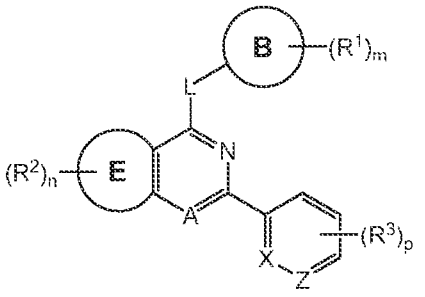
The term "subject" includes organisms which are capable of suffering from a serotonin-receptor-related disorder or who could otherwise benefit from the administration of a compound described herein of the invention, such as human and non-human animals. Preferred humans include human patients suffering from or prone to suffering from a serotonin-related disorder or associated state, as described herein. The term "non-human animals" of the invention includes all vertebrates, *e.g.*, mammals, *e.g.*, rodents, *e.g.*, mice, and non-mammals, such as non-human primates, *e.g.*, sheep, dog, cow, chickens, amphibians, reptiles, etc.

The phrases "systemic administration," "administered systemically", "peripheral administration" and "administered peripherally" as used herein mean the administration of a compound described herein(s), drug or other material, such that it enters the patient's system and, thus, is subject to metabolism and other like processes, for example, subcutaneous administration.

Compounds

The compounds described herein can be used for a variety of purposes, e.g., therapeutic purposes. Many of the compounds modulate STEP activity and can be used, for example to inhibit STEP, e.g., in a subject.

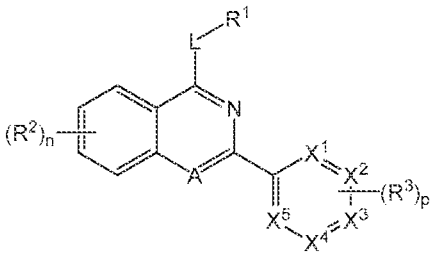
Exemplary compounds include a compound of formula (I):



(I)

wherein A, B, E, L, X, Z, R^1, R^2, R^3, m, n and p are as defined above in the section relating to compound of Formula (I). In preferred embodiments, L is NH, B is aryl (e.g., phenyl) that may be optionally substituted, E is aryl (e.g., phenyl), A is N, X is CH and Z is N.

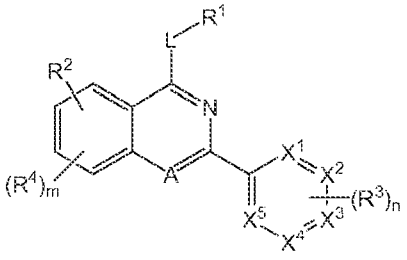
Exemplary compounds include a compound of formula (II):



(II)

wherein A, L, X^1, X^2, X^3, X^4, X^5, R^1, R^2, R^3, n and p are as defined above in the section relating to compound of Formula (II).

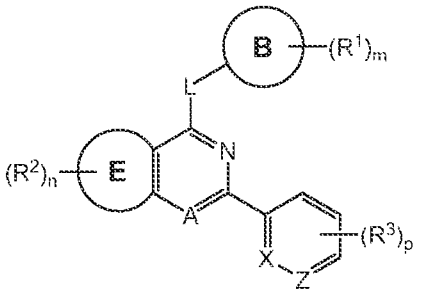
Exemplary compounds include a compound of formula (III):



(III)

wherein A, L, X^1, X^2, X^3, X^4, X^5, R^1, R^2, R^3, R^4, m, and n are as defined above in the section relating to compound of Formula (III).

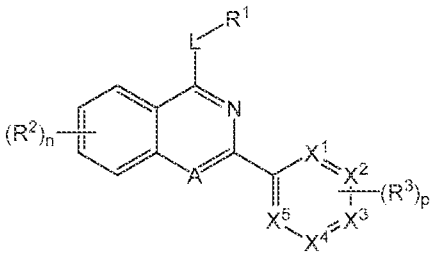
Exemplary compounds include a compound of formula (IV):



(IV)

wherein A, B, E, L, X, Z, R^1, R^2, R^3, m, n and p are as defined above in the section relating to compound of Formula (IV). In preferred embodiments, L is NH, B is aryl (e.g., phenyl) that may be optionally substituted, E is aryl (e.g., phenyl), A is N, X is CH and Z is N.

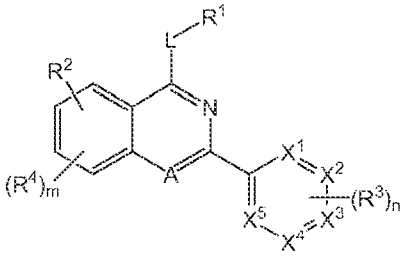
Exemplary compounds include a compound of formula (V):



(V)

wherein A, L, X^1, X^2, X^3, X^4, X^5, R^1, R^2, R^3, n and p are as defined above in the section relating to compound of Formula (V).

Exemplary compounds include a compound of formula (VI):



(VI)

wherein A, L, X^1, X^2, X^3, X^4, X^5, R^1, R^2, R^3, R^4, m, and n are as defined above in the section relating to compound of Formula (VI).

The present invention includes compounds that differ only in the presence of one or more isotopically enriched atoms. For example, compounds having the present structures except for the replacement of hydrogen by deuterium or tritium, the replacement of a carbon by a ^{13}C- or ^{14}C-enriched carbon, or the replacement of a

fluorine by a ^{19}F-enriched fluorine are within the scope of this invention. Such compounds are useful, for example, as analytical tools or probes in biological assays, or as bioactive agents.

In the compounds of the present invention, any atom not specifically designated as a particular isotope is meant to represent any stable isotope of that atom unless otherwise stated (e.g., hydrogen, ^{2}H or deuterium and ^{3}H or tritium). The formulas described herein may or may not indicate whether atoms at certain positions are isotopically enriched. When a structural formula is silent with respect to whether a particular position is isotopically enriched, it is to be understood that the isotopes at that particular position are present in natural abundance or, that the particular position is isotopically enriched with one or more naturally occuring stable isotopes. For example, the formula -CH_2- represents the following possible structures: –CH_2-, -CHD- or –CD_2-.

The variable "D" is defined as deuterium.

The terms "compound" or "compounds," when referring to a compound of this invention or a compound described herein, refers to a collection of molecules having an identical chemical structure, except that there may be isotopic variation among the constituent atoms of the molecules. Thus, it will be clear to those of skill in the art that a compound represented by a particular chemical structure containing indicated hydrogen atoms will contain lesser amounts of isotopologues having deuterium atoms at one or more of the designated hydrogen positions in that structure. Alternatively, a compound represented by a particular chemical structure containing indicated deuterium atoms will contain lesser amounts of isotopologues having hydrogen atoms at one or more of the designated deuterium positions in that structure. The relative amount of such isotopologues in a compound of this invention will depend on a number of factors including isotopic purity of deuterated reagents used to make the compound and the efficiency of incorporation of deuterium in the various synthetic steps used to prepare the compound. The relative amount of such isotopologues in total will be less than 55% of the compound. In other embodiments, the relative amount of such isotopologues in total will be less than 50%, less than 45%, less than

40%, less than 35%, less than 35%, less than 15%, less than 10%, less than 5%, less than 1%or less than 0.5% of the compound.

The term "isotopologue" refers to a species that differs from a specific compound of this invention only in the isotopic composition thereof. Isotopologues can differ in the level of isotopic enrichment at one or more positions and/or in the position(s) of isotopic enrichment.

The compounds of this invention may contain one or more asymmetric centers and thus occur as racemates and racemic mixtures, single enantiomers, individual diastereomers and diastereomeric mixtures. Described herein are enantiomerically enriched compounds (e.g., a compound resolved to an enantiomeric excess of 60%, 70%, 80%, 85%, 90%, 95%, 99% or greater). All such isomeric forms of these compounds are expressly included in the present invention. The compounds of this invention may also contain linkages (e.g., carbon-carbon bonds) or substituents that can restrict bond rotation, e.g. restriction resulting from the presence of a ring or double bond. Accordingly, all *cis/trans* and *E/Z* isomers are expressly included in the present invention. The compounds of this invention may also be represented in multiple tautomeric forms, in such instances, the invention expressly includes all tautomeric forms of the compounds described herein, even though only a single tautomeric form may be represented (e.g., alkylation of a ring system may result in alkylation at multiple sites, the invention expressly includes all such reaction products). All such isomeric forms of such compounds are expressly included in the present invention. All crystal forms of the compounds described herein are expressly included in the present invention.

Naturally occurring or synthetic isomers can be separated in several ways known in the art. Methods for separating a racemic mixture of two enantiomers include chromatography using a chiral stationary phase (see, *e.g.*, "Chiral Liquid Chromatography," W.J. Lough, Ed. Chapman and Hall, New York (1989)). Enantiomers can also be separated by classical resolution techniques. For example, formation of diastereomeric salts and fractional crystallization can be used to separate enantiomers. For the separation of enantiomers of carboxylic acids, the diastereomeric salts can be formed by addition of enantiomerically pure chiral bases

such as brucine, quinine, ephedrine, strychnine, and the like. Alternatively, diastereomeric esters can be formed with enantiomerically pure chiral alcohols such as menthol, followed by separation of the diastereomeric esters and hydrolysis to yield the free, enantiomerically enriched carboxylic acid. For separation of the optical isomers of amino compounds, addition of chiral carboxylic or sulfonic acids, such as camphorsulfonic acid, tartaric acid, mandelic acid, or lactic acid can result in formation of the diastereomeric salts. For example a compound can be resolved to an enantiomeric excess (e.g., 60%, 70%, 80%, 85%, 90%, 95%, 99% or greater) via formation of diasteromeric salts, e.g. with a chiral base, e.g., (+) or (-) α-methylbenzylamine, or via high performance liquid chromatography using a chiral column. In some embodiments a product is purified directly on a chiral column to provide enantiomerically enriched compound.

Combinations of substituents and variables envisioned by this invention are only those that result in the formation of stable compounds. The term "stable", as used herein, refers to compounds which possess stability sufficient to allow manufacture and which maintains the integrity of the compound for a sufficient period of time to be useful for the purposes detailed herein (e.g., therapeutic administration to a subject).

Compounds of formulas (I), (II), (III), (IV), (V), and (VI) are described herein, for example as provided in the summary above. Exemplary compounds are shown in Tables 1-30 in the Examples section.

Synthetic Methods

A compound described herein may be prepared via a variety of synthetic methods. Representative syntheses are shown in the Examples section.

As can be appreciated by the skilled artisan, further methods of synthesizing the compounds of the formulae herein will be evident to those of ordinary skill in the art. Additionally, the various synthetic steps may be performed in an alternate sequence or order to give the desired compounds. Synthetic chemistry transformations and protecting group methodologies (protection and deprotection) useful in synthesizing the compounds described herein are known in the art and

include, for example, those such as described in R. Larock, *Comprehensive Organic Transformations*, VCH Publishers (1989); T.W. Greene and P.G.M. Wuts, *Protective Groups in Organic Synthesis*, 2d. Ed., John Wiley and Sons (1991); L. Fieser and M. Fieser, *Fieser and Fieser's Reagents for Organic Synthesis*, John Wiley and Sons (1994); and L. Paquette, ed., *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons (1995), and subsequent editions thereof.

Additionally, the compounds disclosed herein can be prepared on a solid support. The term "solid support" refers a material to which a compound is attached to facilitate identification, isolation, purification, or chemical reaction selectivity of the compound. Such materials are known in the art and include, for example, beads, pellets, disks, fibers, gels, or particles such as cellulose beads, pore-glass beads, silica gels, polystyrene beads optionally cross-linked with divinylbenzene and optionally grafted with polyethylene glycol, poly-acrylamide beads, latex beads, dimethylacrylamide beads optionally cross-linked with N,N'-bis-acryloyl ethylene diamine, glass particles coated with hydrophobic polymer, and material having a rigid or semi-rigid surface. The solid supports optionally have functional groups such as amino, hydroxy, carboxy, or halo groups, (see, Obrecht, D. and Villalgrodo, J.M., *Solid-Supported Combinatorial and Parallel Synthesis of Small-Molecular-Weight Compound Libraries*, Pergamon-Elsevier Science Limited (1998)), and include those useful in techniques such as the "split and pool" or "parallel" synthesis techniques, solid-phase and solution-phase techniques, and encoding techniques (see, for example, Czarnik, A.W., *Curr. Opin. Chem. Bio.*, (1997) 1, 60).

A compound described herein may be modified by appending appropriate functionalities to enhance selective biological properties. Such modifications are known in the art and include those which increase biological penetration into a given biological compartment (e.g., brain, blood, lymphatic system, central nervous system), increase oral availability, increase solubility to allow administration by injection, alter metabolism and alter rate of excretion.

Included herein are pharmaceutically acceptable derivatives or prodrugs of the compounds described herein. A "pharmaceutically acceptable derivative or prodrug" means any pharmaceutically acceptable salt, ester, salt of an ester, or other

derivative of a compound of this invention (for example an imidate ester of an amide), which, upon administration to a recipient, is capable of providing (directly or indirectly) a compound described herein. Particularly favored derivatives and prodrugs are those that increase the bioavailability of the compounds of this invention when such compounds are administered to a mammal (e.g., by allowing an orally administered compound to be more readily absorbed into the blood) or which enhance delivery of the parent compound to a biological compartment (e.g., the brain or lymphatic system) relative to the parent species. In an exemplary embodiment, the prodrug is a derivative including a group that enhances aqueous solubility or active transport through the gut membrane is appended to the structure of formulae described herein. In another exemplary embodiment, the prodrug is suitable for treatment or prevention of those diseases and conditions that require the drug molecule to cross the blood brain barrier. In a preferred embodiment, the prodrug enters the brain, where it is converted into the active form of the drug molecule.

Pharmaceutically acceptable salts of the compounds of this invention include those derived from pharmaceutically acceptable inorganic and organic acids and bases. Examples of suitable acid salts include acetate, adipate, benzoate, benzenesulfonate, butyrate, citrate, digluconate, dodecylsulfate, formate, fumarate, glycolate, hemisulfate, heptanoate, hexanoate, hydrochloride, hydrobromide, hydroiodide, lactate, maleate, malonate, methanesulfonate, 2-naphthalenesulfonate, nicotinate, nitrate, palmoate, phosphate, picrate, pivalate, propionate, salicylate, succinate, sulfate, tartrate, tosylate and undecanoate. Salts derived from appropriate bases include alkali metal (e.g., sodium), alkaline earth metal (e.g., magnesium), ammonium and N-(alkyl)$_4^+$ salts. This invention also envisions the quaternization of any basic nitrogen-containing groups of the compounds disclosed herein. Water or oil-soluble or dispersible products may be obtained by such quaternization.

Evaluating Compounds

A variety of methods can be used to evaluate a compound for ability to modulate STEP activity. Evaluation methods include *in vitro* assays (e.g., enzyme-based assays), *in vitro* cell-based signaling assays, and *in vivo* methods (e.g., testing in

animal models). The evaluation methods can evaluate binding activity, phosphatase activity, or an activity downstream of STEP, such as the activity of ERK.

For example, a compound described herein may be evaluated using a fluorescence-based phosphatase assay. A phosphate-containing reagent may be used in the assay which, upon dephosphorylation by a phosphatase, generates a fluorescent product that may be detected using a fluorometer or fluorescence plate reader. Data may be expressed as percentage (%) inhibition of enzyme activity. For compounds showing enzymatic activation, data may be represented as percentage of inhibition but with negative values.

Compositions and routes of administration

The invention also provides a pharmaceutical composition, comprising an effective amount of a compound described herein (e.g., a compound capable of treating or preventing a condition as described herein, e.g., a compound of any formula herein or otherwise described herein) and a pharmaceutically acceptable carrier.

The compositions delineated herein include the compounds delineated herein (e.g., a compound described herein), as well as additional therapeutic agents if present, in amounts effective for achieving a modulation of disease or disease symptoms, including those described herein.

The term "pharmaceutically acceptable carrier or adjuvant" refers to a carrier or adjuvant that may be administered to a patient, together with a compound of this invention, and which does not destroy the pharmacological activity thereof and is nontoxic when administered in doses sufficient to deliver a therapeutic amount of the compound.

Pharmaceutically acceptable carriers, adjuvants and vehicles that may be used in the pharmaceutical compositions of this invention include, but are not limited to, ion exchangers, alumina, aluminum stearate, lecithin, self-emulsifying drug delivery systems (SEDDS) such as d-α-tocopherol polyethylene glycol 1000 succinate, surfactants used in pharmaceutical dosage forms such as Tweens or other similar polymeric delivery matrices, serum proteins, such as human serum albumin, buffer

substances such as phosphates, glycine, sorbic acid, potassium sorbate, partial glyceride mixtures of saturated vegetable fatty acids, water, salts or electrolytes, such as protamine sulfate, disodium hydrogen phosphate, potassium hydrogen phosphate, sodium chloride, zinc salts, colloidal silica, magnesium trisilicate, polyvinyl pyrrolidone, cellulose-based substances, polyethylene glycol, sodium carboxymethylcellulose, polyacrylates, waxes, polyethylene-polyoxypropylene-block polymers, polyethylene glycol and wool fat. Cyclodextrins such as α-, β-, and γ-cyclodextrin, or chemically modified derivatives such as hydroxyalkylcyclodextrins, including 2- and 3-hydroxypropyl-β-cyclodextrins, or other solubilized derivatives may also be advantageously used to enhance delivery of compounds of the formulae described herein.

The pharmaceutical compositions of this invention may be administered orally, parenterally, by inhalation spray, topically, rectally, nasally, buccally, vaginally or via an implanted reservoir, preferably by oral administration or administration by injection. The pharmaceutical compositions of this invention may contain any conventional non-toxic pharmaceutically-acceptable carriers, adjuvants or vehicles. In some cases, the pH of the formulation may be adjusted with pharmaceutically acceptable acids, bases or buffers to enhance the stability of the formulated compound or its delivery form. The term parenteral as used herein includes subcutaneous, intracutaneous, intravenous, intramuscular, intraarticular, intraarterial, intrasynovial, intrasternal, intrathecal, intralesional and intracranial injection or infusion techniques.

The pharmaceutical compositions may be in the form of a sterile injectable preparation, for example, as a sterile injectable aqueous or oleaginous suspension. This suspension may be formulated according to techniques known in the art using suitable dispersing or wetting agents (such as, for example, Tween 80) and suspending agents. The sterile injectable preparation may also be a sterile injectable solution or suspension in a non-toxic parenterally acceptable diluent or solvent, for example, as a solution in 1,3-butanediol. Among the acceptable vehicles and solvents that may be employed are mannitol, water, Ringer's solution and isotonic sodium chloride solution. In addition, sterile, fixed oils are conventionally employed as a

solvent or suspending medium. For this purpose, any bland fixed oil may be employed including synthetic mono- or diglycerides. Fatty acids, such as oleic acid and its glyceride derivatives are useful in the preparation of injectables, as are natural pharmaceutically-acceptable oils, such as olive oil or castor oil, especially in their polyoxyethylated versions. These oil solutions or suspensions may also contain a long-chain alcohol diluent or dispersant, or carboxymethyl cellulose or similar dispersing agents which are commonly used in the formulation of pharmaceutically acceptable dosage forms such as emulsions and or suspensions. Other commonly used surfactants such as Tweens or Spans and/or other similar emulsifying agents or bioavailability enhancers which are commonly used in the manufacture of pharmaceutically acceptable solid, liquid, or other dosage forms may also be used for the purposes of formulation.

The pharmaceutical compositions of this invention may be orally administered in any orally acceptable dosage form including, but not limited to, capsules, tablets, emulsions and aqueous suspensions, dispersions and solutions. In the case of tablets for oral use, carriers which are commonly used include lactose and corn starch. Lubricating agents, such as magnesium stearate, are also typically added. For oral administration in a capsule form, useful diluents include lactose and dried corn starch. When aqueous suspensions and/or emulsions are administered orally, the active ingredient may be suspended or dissolved in an oily phase is combined with emulsifying and/or suspending agents. If desired, certain sweetening and/or flavoring and/or coloring agents may be added.

The pharmaceutical compositions of this invention may also be administered in the form of suppositories for rectal administration. These compositions can be prepared by mixing a compound of this invention with a suitable non-irritating excipient which is solid at room temperature but liquid at the rectal temperature and therefore will melt in the rectum to release the active components. Such materials include, but are not limited to, cocoa butter, beeswax and polyethylene glycols.

Topical administration of the pharmaceutical compositions of this invention is useful when the desired treatment involves areas or organs readily accessible by topical application. For application topically to the skin, the pharmaceutical

composition should be formulated with a suitable ointment containing the active components suspended or dissolved in a carrier. Carriers for topical administration of the compounds of this invention include, but are not limited to, mineral oil, liquid petroleum, white petroleum, propylene glycol, polyoxyethylene polyoxypropylene compound, emulsifying wax and water. Alternatively, the pharmaceutical composition can be formulated with a suitable lotion or cream containing the active compound suspended or dissolved in a carrier with suitable emulsifying agents. Suitable carriers include, but are not limited to, mineral oil, sorbitan monostearate, polysorbate 60, cetyl esters wax, cetearyl alcohol, 2-octyldodecanol, benzyl alcohol and water. The pharmaceutical compositions of this invention may also be topically applied to the lower intestinal tract by rectal suppository formulation or in a suitable enema formulation. Topically-transdermal patches are also included in this invention.

The pharmaceutical compositions of this invention may be administered by nasal aerosol or inhalation. Such compositions are prepared according to techniques well-known in the art of pharmaceutical formulation and may be prepared as solutions in saline, employing benzyl alcohol or other suitable preservatives, absorption promoters to enhance bioavailability, fluorocarbons, and/or other solubilizing or dispersing agents known in the art.

When the compositions of this invention comprise a combination of a compound of the formulae described herein and one or more additional therapeutic agents, both the compound and the additional agent should be present at dosage levels of between about 1 to 100%, and more preferably between about 5 to 95% of the dosage normally administered in a monotherapy regimen. The additional agents may be administered separately, as part of a multiple dose regimen, from the compounds of this invention. Alternatively, those agents may be part of a single dosage form, mixed together with the compounds of this invention in a single composition.

The compounds described herein can, for example, be administered by injection, intravenously, intraarterially, subdermally, intraperitoneally, intramuscularly, or subcutaneously; or orally, buccally, nasally, transmucosally, topically, in an ophthalmic preparation, or by inhalation, with a dosage ranging from about 0.5 to about 100 mg/kg of body weight, alternatively dosages between 1 mg and

1000 mg/dose, every 4 to 120 hours, or according to the requirements of the particular drug. The methods herein contemplate administration of an effective amount of compound or compound composition to achieve the desired or stated effect. Typically, the pharmaceutical compositions of this invention will be administered from about 1 to about 6 times per day or alternatively, as a continuous infusion. Such administration can be used as a chronic or acute therapy. The amount of active ingredient that may be combined with the carrier materials to produce a single dosage form will vary depending upon the host treated and the particular mode of administration. A typical preparation will contain from about 5% to about 95% active compound (w/w). Alternatively, such preparations contain from about 20% to about 80% active compound.

Lower or higher doses than those recited above may be required. Specific dosage and treatment regimens for any particular patient will depend upon a variety of factors, including the activity of the specific compound employed, the age, body weight, general health status, sex, diet, time of administration, rate of excretion, drug combination, the severity and course of the disease, condition or symptoms, the patient's disposition to the disease, condition or symptoms, and the judgment of the treating physician.

Upon improvement of a patient's condition, a maintenance dose of a compound, composition or combination of this invention may be administered, if necessary. Subsequently, the dosage or frequency of administration, or both, may be reduced, as a function of the symptoms, to a level at which the improved condition is retained when the symptoms have been alleviated to the desired level. Patients may, however, require intermittent treatment on a long-term basis upon any recurrence of disease symptoms.

Methods of treatment

The compounds and compositions described herein can be administered to cells in culture, e.g. *in vitro* or *ex vivo*, or to a subject, e.g., *in vivo*, to treat, prevent, and/or diagnose a variety of disorders, including those described herein below.

The compounds and compositions described herein can be administered to a subject, for example using a method described herein, who is suffering from a disorder described herein, e.g., a disorder that would benefit from the modulation of STEP (e.g., activating or inhibiting STEP). The compounds and compositions described herein can be administered to a subject, for example using a method described herein, who is at risk for a disorder described herein, e.g., a disorder that would benefit from the modulation of STEP (e.g., activating or inhibiting STEP).

Inhibitors of STEP may increase phosphorylation of an NMDA-R. Thus, in some embodiments, a compound described herein, e.g., a compound that inhibits STEP, may be useful for treating a disorder in which increasing phosphorylation of an NMDA-R would be beneficial.

Inhibitors of STEP may activate an ERK1 or ERK2 kinase, for example, in the CNS. Thus, in some embodiments, a compound described herein, e.g., a compound that inhibits STEP, may be useful for treating a disorder in which activate an ERK1 or ERK2 kinase would be beneficial.

Compounds described herein may be useful in treating a variety of disorders, including disorders of the CNS. Exemplary disorders include schizophrenia, schizo-affective disorders, major depression, bipolar disorder, cognitive deficit, mild cognitive impairment (MCI), Alzheimer's disease (AD), attention-deficit/hyperactivity disorder (ADHD), dementia, generalized anxiety disorders, panic disorders, obsessive-compulsive disorders, phobias, post-traumatic stress syndrome, anorexia nervosa, drug addiction, ischemic stroke, head trauma or brain injury, Huntington's disease, Parkinson's disease, spinocerebellar degeneration, motor neuron diseases, epilepsy, neuropathic pain, chronic pain, neuropathies, autism and autistic disorders.

Compounds described herein may be useful for treating or preventing central nervous system disorders selected from the group consisting of schizophrenia; refractory, intractable or chronic schizophrenia; emotional disturbance; psychotic disorder; mood disorder; bipolar I type disorder; bipolar II type disorder; depression; endogenous depression; major depression; melancholy and refractory depression; dysthymic disorder; cyclothymic disorder; panic attack; panic disorder; agoraphobia; social phobia; obsessive-compulsive disorder; post-traumatic stress disorder;

generalized anxiety disorder; acute stress disorder; hysteria; somatization disorder; conversion disorder; pain disorder; hypochondriasis; factitious disorder; dissociative disorder; sexual dysfunction; sexual desire disorder; sexual arousal disorder; erectile dysfunction; anorexia nervosa; bulimia nervosa; sleep disorder; adjustment disorder; alcohol abuse; alcohol intoxication; drug addiction; stimulant intoxication; narcotism; anhedonia; iatrogenic anhedonia; anhedonia of a psychic or mental cause; anhedonia associated with depression; anhedonia associated with schizophrenia; delirium; cognitive impairment; cognitive impairment associated with Alzheimer's disease, Parkinson's disease and other neurodegenerative diseases; cognitive impairment caused by Alzheimer's disease; Parkinson's disease and associated neurodegenerative diseases; cognitive impairment of schizophrenia; cognitive impairment caused by refractory, intractable or chronic schizophrenia; vomiting; motion sickness; obesity; migraine; pain (ache) ; mental retardation; autism disorder (autism); Tourette's disorder; tic disorder; attention-deficit/hyperactivity disorder; conduct disorder; and Down's syndrome.

Compounds described herein may be useful for treating or preventing disorders selected from schizophrenia, schizoaffective disorder, bipolar disorder, manic-depressive disorder, psychosis, mood and anxiety disorders, mania, drug or substance addiction, cognition disorders, learning disabilities, learning and memory disorders, aging and neurologic disorders associated with or linked with cognitive impairments; mild cognitive impairments (MCI), Alzheimer's disease, Alzheimer-related cognition disorders, Huntington's disease, Parkinson's disease, CADASIL syndrome (cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy), amnesia, Wernicke-Korsakoff syndrome, Korsakoff syndrome, mild traumatic head injury (MBTI), traumatic head injury (TBI), fragile X syndrome, stroke, attention-deficit and hyperactivity disorder (ADHD), obsessive compulsive disorder (OCD), post-traumatic stress disorder (PTSD), loss of concentration, autism, cerebral palsy, encephalopathy, and narcolepsy. The disorder may affect learning and memory, neurogenesis, neuronal plasticity, pain perception, mood and anxiety, or neuroendocrine regulation. The disorder may be a cognitive deficit disorder. The disorder may involve pain perception or neuroendocrine regulation.

Schizophrenia

In some embodiments, a compound or composition described herein can be used in the treatment of schizophrenia. Schizophrenia is a psychiatric diagnosis that describes a mental disorder characterized by abnormalities in the perception or expression of reality. Distortions in perception may affect all five senses, including sight, hearing, taste, smell and touch, but most commonly manifests as auditory hallucinations, paranoid or bizarre delusions, or disorganized speech and thinking with significant social or occupational dysfunction. Onset of symptoms typically occurs in young adulthood, with approximately 0.4–0.6% of the population affected. Diagnosis is based on the patient's self-reported experiences and observed behavior.

The disorder is thought to mainly affect cognition, but it also usually contributes to chronic problems with behavior and emotion. People with schizophrenia are likely to have additional (comorbid) conditions, including major depression and anxiety disorders. Social problems, such as long-term unemployment, poverty and homelessness, are common. Furthermore, the average life expectancy of people with the disorder is 10 to 12 years less than those without, due to increased physical health problems and a higher suicide rate.

The Diagnostic and Statistical Manual of Mental Disorders (DSM) contains five sub-classifications of schizophrenia. These include Paranoid type (where delusions and hallucinations are present but thought disorder, disorganized behavior, and affective flattening are absent); Disorganized type (also known as hebephrenic schizophrenia, where thought disorder and flat affect are present together); Catatonic type (the subject may be almost immobile or exhibit agitated, purposeless movement; symptoms can include catatonic stupor and waxy flexibility); Undifferentiated type (psychotic symptoms are present but the criteria for paranoid, disorganized, or catatonic types have not been met); and Residual type (where positive symptoms are present at a low intensity only).

The International Statistical Classification of Diseases and Related Health Problems (10th Revision) defines two additional subtypes. These include Post-schizophrenic depression (a depressive episode arising in the aftermath of a schizophrenic illness where some low-level schizophrenic symptoms may still be

present); and Simple schizophrenia (insidious and progressive development of prominent negative symptoms with no history of psychotic episodes.)

An agent for the treatment of schizophrenia may improve so-called positive symptoms in the acute period of schizophrenia such as hallucinations, delusions, excitations and the like. An agent for treating schizophrenia may also improve so-called negative symptoms that are observed in the chronic period of schizophrenia such as apathy, emotional depression, hyposychosis and the like.

Schizoaffective Disorder

Schizoaffective disorder is a psychiatric diagnosis that describes a mental disorder characterized by recurring episodes of elevated or depressed mood, or simultaneously elevated and depressed mood that alternate or occur together with distortions in perception. The perceptual distortion component of the disorder, called psychosis, may affect all five senses, including sight, hearing, taste, smell and touch, but most commonly manifest as auditory hallucinations, paranoid or bizarre delusions, or disorganized speech and thinking with significant social and occupational dysfunction. The elevated, depressed or simultaneously elevated and depressed mood episode components of the disorder, called mood disorder, are broadly recognized as depressive and bipolar types of the illness; the division is based on whether the individual has ever had a manic, hypomanic or mixed episode. Onset of symptoms usually begins in early adulthood and is rarely diagnosed in childhood (prior to age 13). The lifetime prevalence of the disorder is uncertain (due to studies using varying diagnostic criteria), although it is generally agreed to be less than 1 percent, and possibly in the range of 0.5 to 0.8 percent. Diagnosis is based on the patient's self-reported experiences and observed behavior. No laboratory test for schizoaffective disorder currently exists. As a group, people with schizoaffective disorder have a more favorable prognosis than people with schizophrenia, but a worse prognosis than those with mood disorders.

The disorder is thought to mainly affect cognition and emotion, but it also usually contributes to ongoing problems with behavior and motivation. People with schizoaffective disorder are likely to have additional (comorbid) conditions, including anxiety disorders and substance abuse. Social problems, such as long-term

unemployment, poverty and homelessness, are common. Furthermore, the average life expectancy of people with the disorder is shorter than those without the disorder, due to increased physical health problems and a higher suicide rate.

Cognitive Deficit

Treatment using a compound or composition described herein may improve a cognitive deficit associated with a cognition-related disorder. Cognitive deficit is an inclusive term to describe any characteristic that acts as a barrier to cognitive performance. The term may describe deficits in global intellectual performance, such as mental retardation, it may describe specific deficits in cognitive abilities (learning disorders, dyslexia), or it may describe drug-induced cognitive/memory impairment, such as that seen with alcohol and the benzodiazepines. Cognitive deficits may be congenital or caused by environmental factors such as brain injuries, neurological disorders, or mental illness.

Exemplary cognition-related disorders (e.g., cognitive dysfunction) include, without limitation, mild cognitive impairment (MCI), dementia, delirium, amnestic disorder, Alzheimer's disease, Parkinson's disease and Huntington's disease; memory disorders including memory deficits associated with depression, senile dementia, dementia of Alzheimer's disease; cognitive deficits or cognitive dysfunction associated with neurological conditions including, for example, Parkinson's disease (PD), Huntington's disease (HD), Alzheimer's disease, depression, schizophrenia and other psychotic disorders such as paranoia and manic-depressive illness; cognitive dysfunction in schizophrenia; disorders of attention and learning such as attention deficit disorders (e.g., attention deficit hyperactivity disorder (ADHD)) and dyslexia; cognitive dysfunction associated with developmental disorders such as Down's syndrome and Fragile X syndrome; loss of executive function; loss of learned information; vascular dementia; schizophrenia; cognitive decline; a neurodegenerative disorder; and other dementias, for example, dementia due to HIV disease, head trauma, Parkinson's disease, Huntington's disease, Pick's disease, Creutzfeldt-Jakob disease, or due to multiple etiologies. Cognition-related disorders also include, without limitation, cognitive dysfunction associated with MCI and dementias such as Lewy Body, vascular, and post stroke dementias. Cognitive dysfunction associated

with surgical procedures, traumatic brain injury or stroke may also be treated in accordance with the embodiments described herein.

Major Depression

Major depression (also known as clinical depression, major depressive disorder, unipolar depression, or unipolar disorder) is a mental disorder characterized by a pervasive low mood, low self-esteem, and loss of interest or pleasure in normally enjoyable activities. Types of Major depressive disorder include, e.g., Atypical depression, Melancholic depression, Psychotic depression, Catatonic depression, Postpartum depression, and Seasonal affective disorder.

Bipolar Disorder

Bipolar disorder, also known as manic depressive disorder, manic depressive psychosis, manic depression or bipolar affective disorder, is a psychiatric diagnosis that describes a category of mood disorders defined by the presence of one or more episodes of abnormally elevated mood clinically referred to as mania or, if milder, hypomania. Individuals who experience manic episodes also commonly experience depressive episodes or symptoms, or mixed episodes in which features of both mania and depression are present at the same time. These episodes are usually separated by periods of "normal" mood, but in some individuals, depression and mania may rapidly alternate, known as rapid cycling. Extreme manic episodes can sometimes lead to psychotic symptoms such as delusions and hallucinations. The disorder has been subdivided into bipolar I, bipolar II, cyclothymia, and other types, based on the nature and severity of mood episodes experienced; the range is often described as the bipolar spectrum.

Anxiety Disorders

Anxiety disorder is a blanket term covering several different forms of abnormal and pathological fear and anxiety. Current psychiatric diagnostic criteria recognize a wide variety of anxiety disorders. Recent surveys have found that as many as 18% of Americans may be affected by one or more of them.

Generalized anxiety disorder is a common chronic disorder characterized by long-lasting anxiety that is not focused on any one object or situation. Those suffering from generalized anxiety experience non-specific persistent fear and worry and

become overly concerned with everyday matters. Generalized anxiety disorder is the most common anxiety disorder to affect older adults.

In panic disorder, a person suffers from brief attacks of intense terror and apprehension, often marked by trembling, shaking, confusion, dizziness, nausea, difficulty breathing. These panic attacks, defined by the APA as fear or discomfort that abruptly arises and peaks in less than ten minutes, can last for several hours and can be triggered by stress, fear, or even exercise; although the specific cause is not always apparent. In addition to recurrent unexpected panic attacks, a diagnosis of panic disorder also requires that said attacks have chronic consequences: either worry over the attacks' potential implications, persistent fear of future attacks, or significant changes in behavior related to the attacks. Accordingly, those suffering from panic disorder experience symptoms even outside of specific panic episodes. Often, normal changes in heartbeat are noticed by a panic sufferer, leading them to think something is wrong with their heart or they are about to have another panic attack. In some cases, a heightened awareness (hypervigilance) of body functioning occurs during panic attacks, wherein any perceived physiological change is interpreted as a possible life threatening illness (i.e. extreme hypochondriasis).

Obsessive compulsive disorder is a type of anxiety disorder primarily characterized by repetitive obsessions (distressing, persistent, and intrusive thoughts or images) and compulsions (urges to perform specific acts or rituals). The OCD thought pattern may be likened to superstitions insofar as it involves a belief in a causative relationship where, in reality, one does not exist. Often the process is entirely illogical; for example, the compulsion of walking in a certain pattern may be employed to alleviate the obsession of impending harm. And in many cases, the compulsion is entirely inexplicable, simply an urge to complete a ritual triggered by nervousness. In a minority of cases, sufferers of OCD may only experience obsessions, with no overt compulsions; a much smaller number of sufferers experience only compulsions.

The single largest category of anxiety disorders is that of Phobia, which includes all cases in which fear and anxiety is triggered by a specific stimulus or situation. Sufferers typically anticipate terrifying consequences from encountering the

object of their fear, which can be anything from an animal to a location to a bodily fluid.

Post-traumatic stress disorder or PTSD is an anxiety disorder which results from a traumatic experience. Post-traumatic stress can result from an extreme situation, such as combat, rape, hostage situations, or even serious accident. It can also result from long term (chronic) exposure to a severe stressor, for example soldiers who endure individual battles but cannot cope with continuous combat. Common symptoms include flashbacks, avoidant behaviors, and depression.

Combination therapies

In some embodiments, the subject is being treated with an additional therapeutic agent. Such additional agents include atypical antipsychotics such as aripiprazole, clozapine, ziprasidone, risperidone, quetiapine, olanzapine, amisulpride, asenapine, iloperidone, melperone, paliperidone, perospirone, sertindole and sulpiride; and typical antipsychotics such as haloperidol, molindone, loxapine, thioridazine, molindone, thiothixene, pimozide, fluphenazine, trifluoperazine, mesoridazine, chlorprothixene, chlorpromazine, perphenazine, triflupromazine and zuclopenthixol.

Clinical outcomes

In some embodiments, treatment with a compound or composition described herein, for example, using a method described herein, improves one or more clinical outcomes. For example, in some embodiments, treatment with a compound or composition described herein may improve cognitive function. Elements of cognitive function include memory, orientation, attention, reasoning, language and praxis.

In some embodiments, clinical outcomes may be assessed using known methods. One such method is the Brief Psychiatric Rating Scale (BPRS), a multi-item inventory of general psychopathology traditionally used to evaluate the effects of drug treatment in schizophrenia. The BPRS psychosis cluster (conceptual disorganization, hallucinatory behavior, suspiciousness, and unusual thought content) is considered a particularly useful subset for assessing actively psychotic schizophrenic patients.

In some embodiments, clinical outcomes may be assessed using the 7-point Clinical Global Impression (CGI) rating scale, a commonly used measure of symptom

severity, treatment response and the efficacy of treatments. The CGI reflects the impression of a skilled observer, fully familiar with the manifestations of schizophrenia, about the overall clinical state of the patient.

In some embodiments, clinical outcomes may be assessed using the 30-item Positive and Negative Symptoms Scale (PANSS). The name refers to the two types of symptoms in schizophrenia, as defined by the American Psychiatric Association: positive symptoms, which refer to an excess or distortion of normal functions (e.g. hallucinations and delusions), and negative symptoms, which represent a dimunition or loss of normal functions.

In some embodiments, clinical outcomes may be assessed using the Scale for Assessing Negative Symptoms (SANS). SANS assesses five symptom complexes to obtain clinical ratings of negative symptoms in patients with schizophrenia. They are: affective blunting; alogia (impoverished thinking); avolition/apathy; anhedonia/asociality; and disturbance of attention. Assessments are conducted on a six-point scale.

The invention is further illustrated by the following examples which are intended to illustrate but not limit the scope of the invention.

EXAMPLES

Abbreviations:

DCM: Dichloromethane
EA, EtOAc or AcOEt: Ethyl acetate
PE: Petroleum ether
DIPEA: Diisopropylethylamine
TEA: Triethylamine
rt: Room temperature
$SOCl_2$: Thionyl chloride
$POCl_3$: Phosphorous oxychloride
THF: Tetrahydrofuran
NaOAc: Sodium acetate
MeOH: Methanol
i-AmOH: Isoamyl alcohol

NaH: Sodium hydride
$NaBH_3CN$: Sodium cyanoborohydride
n-BuLi: *n*-Butyl lithium
LHMDS: Lithium bis(trimethylsilyl)amide
LDA: Lithium diisopropylamide
i-PrOH: Isopropyl alcohol
Na_2SO_4: Sodium sulfate
Mg_2SO_4: Magnesium sulfate
MeCN: Acetonitrile
NaOH: Sodium hydroxide
EtOH: Ethanol
CuI: Copper(I) iodide
$Pd(PPh_3)_2Cl_2$: trans-Dichlorobis(triphenylphosphine)palladium(II)
MsCl: Methanesulfonyl chloride
BINAM: [1,1'-Binaphthalene]-2,2'-diamine
Xphos: 2-Dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl
Sphos: 2-Dicyclohexylphosphino-2',6'-dimethoxybiphenyl
DavePhos: 2-(Dicyclohexylphosphino)-2'-(N,N-dimethylamino)biphenyl
Cs_2CO_3: Cesium carbonate
K_2CO_3: Potassium carbonate
Mwave or μW or mW: Microwave
t-BuOH: *tert*-Butanol
K_3PO_4: Potassium phosphate
$Pd(APhos)_2Cl_2$:Bis(di-tert-butyl(4-dimethylaminophenyl)phosphine)dichloro palladium(II)
$Pd(PPh_3)_4$: Tetrakis(triphenylphosphine)palladium (0)
$Pd(dppf)_2Cl_2$: Dichloro[1,1'-bis(diphenylphosphino)ferrocene]palladium(II)
PdOAc: Palladium(II) acetate
Pd_2dba_3: Tris(dibenzylideneacetone)dipalladium (0)
Pd-118: Dichloro[1,1'-bis(di-t-butylphosphino)ferrocene]palladium(II)
Xantphos: 9,9-Dimethyl-4,5-bis(diphenylphosphino)xanthene
BINAP: (±)-2,2'-Bis(diphenylphosphino)-1,1'-binaphthalene
EDCI: 1-Ethyl-3-(3-dimethylaminopropyl) carbodiimide
HOBt: Hydroxybenzotriazole
NH_4OH: Ammonium hydroxide
H_2O: Water
Pd/C: Palladium on carbon
DMF: *N*,*N*-Dimethylformamide
KOCN: Potassium cyanate
WSC-HCl or WSCDI: Water Soluble Carbodiimide hydrochloride
HATU: O-(7-Azabenzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate
HBTU: O-(Benzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate
Py-Brop: Bromotripyrrolidinophosphonium hexafluorophosphate
BOP: Benzotriazole-1-yl-oxy-tris-(dimethylamino)-phosphonium hexafluoro phosphate

DBU: diaza(1,3)bicyclo[5.4.0]undecene
DMSO: Dimethyl sulfoxide
LCMS: Liquid chromatography mass spectrometry
HPLC: High performance liquid chromatography
DMA: N,N-dimethylacetamide
h: hour
TLC: Thin layer chromatography
TFA: Trifluoroacetic acid
Et_3N: Triethylamine
DIPEA: N,N-Diisopropylethylamine
O.N: Overnight
TBSO: tert-Butyldimethylsilyloxy
DME: Dimethyl ether
NMP: 1-methyl-2-pyrrolidinone
PS-BEMP: 2-*tert*-Butylimino-2-diethylamino-1,3-dimethylperhydro-1,3,2-diazaphosphorine supported on Polystyrene
PBr_3 : Phosphorus tribromide
NaOtBu: Sodium tert-butoxide
KI : Potassium iodide
PPh_3 : Triphenylphosphine
NMM : *N*-Methylmorpholine
HCHO: Formaldehyde
PG: Protecting group
ISCO: Teledyne ISCO purification systems
BINAM: 1,1′-binaphthyl-2,2′-diamine.

General Experimental:

All exemplified target compounds are fully analyzed and characterized (TLC, LCMS, ^{1}H-NMR) prior to submission for biological evaluation. Thin-layer chromatography was carried out on native silica 254F plates. Visualization was accomplished with ultraviolet or phosphomolybdic acid. ^{1}H-NMR spectra were recorded on multiple NMR spectrometers, either on 400 MHz on a Avance III 400 Ultra shield-plus TM digital Spectrometer or on 300 MHz using a Varian Mercury 300Plus Spectrometer, designated by 400 MHz or 300 MHz, respectively. ^{1}H-NMR spectra were also recorded on a Bruker Spectrospin 300 MHz Spectrometer at 300.13 MHz in DMSO-d6 with TMS as an internal standard and will be designated as Bruker 300 Hz. NMR assignments are based on a combination of the ^{1}H, ^{13}C, ^{1}HCOSY, HMBC and HMQC spectra. Coupling constants are given in hertz (Hz). Anhydrous methylene chloride,

tetrahydrofuran, and dimethylformamide were obtained by distillation, and other materials are reagent grade.

LC-MS Methods are listed here:

Method A: Mobile phase: A = 0.1% TFA/H_2O, B = 0.01% TFA/MeCN; Gradient: B = 5%-95% in 1.5 min; Flow rate: 2.0 mL/min; Column: sunfire-C_{18}, 50 × 4.6 mm, 3.5 um;

Method B: Mobile phase: A = 10mM NH_4HCO_3/H_2O, B = MeCN; Gradient: B = 5%-95% in 1.5 min; Flow rate: 2.0 mL/min; Column: Xbridge-C_{18}, 50 × 4.6mm, 3.5 um;

Method C: Mobile phase: A = 10 mM ammonium formate/H_2O/4.9% MeCN, B = MeCN; Gradient: B = 5%-100% in 2.0 min; Flow rate: 2.5 mL/min; Column: Atlantis T3 3uM 4.6x30mm

Method D: Mobile phase: A = 0.1% formic acid/H_2O/4.9% MeCN, B = MeCN; Gradient: B = 5%-100% in 2.0 min; Flow rate: 2.5 mL/min; Column: Atlantis T3 3uM 4.6x30mm

Method E:: Mobile phase: A = 0.05% TFA/H_2O, B = 0.05% TFA/MeCN; Gradient: B = 5%-100% in 3.0 min; Flow rate: 0.8 mL/min; Column: CAPCELL PAK C18 (Shiseido, UG120, 3 mM, 2.0 mm I.D. x 50 mm).

Representative Conditions of PREP-HPLC are listed here:

PREP-HPLC Condition A (Basic Mobile Phase):

Instrument: Gilson 281

Mobile Phase: A = 0.01% NH_4HCO_3/H_2O, B = MeCN

Flow Rate: 40.0 mL/min

Column: AGT Venusil XBP C_{18}, 10.0 um, 30 mm× 100 mm

PREP-HPLC Condition B (Basic Mobile Phase):

Instrument: Gilson 281

Mobile Phase: A = NH_3-H_2O, 10 mmol/L, B = MeCN

Flow Rate: 40.0 mL/min

Column: Waters X-Bridge, 5.0 um, 30 mm × 150 mm

PREP-HPLC Condition C (Basic Mobile Phase):

Instrument: Gilson 281

Mobile Phase: A = 0.01% NH_4HCO_3/H_2O, B = MeCN

Flow Rate: 30.0 mL/min

Column: Shimadzu PRC-ODS, 10.0 um, 20 mm × 250 mm

Gradient: B = xx%-yy% 0.0 to 8.0 min

yy%-95% 8.0 to 8.2 min

95%-95% 8.2 to 11.0 min

The following table shows the relationship of representative value (xx%-yy%) of gradient and retention time on LC-MS of corresponding compound.

25%-30% 0.5-1.0 min

30%-50% 1.0-1.5 min

50%-70% 1.5-1.75 min

70%-90% 1.7-2.0 min

PREP-HPLC Condition D:

Instrument: Waters 600 pump, Waters 2996, Photodiode Array Detector, Waters Micromass ZQ, Gilson 215 Liquid Handler.

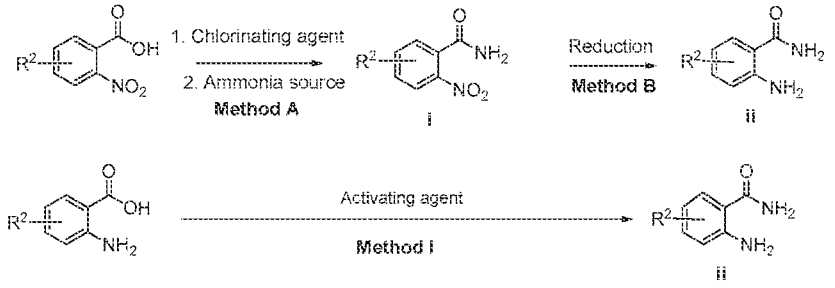
Mobile Phase: A = 0.05% TFA/H_2O, B = MeCN

Flow Rate: 36.0 mL/min

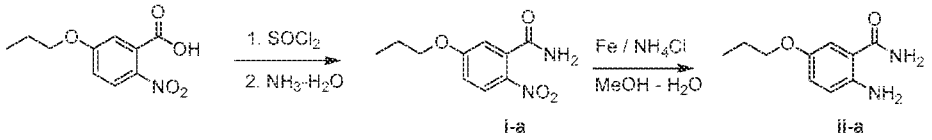
Column: Shiseido CAPCELL PAK C18, UG120, 5 uM, 20 mm I.D. x 50 mm

Gradient: B = 5%-100% 0.0 to 4.0 min

Scheme 1: General route for the synthesis of compounds with general formula ii



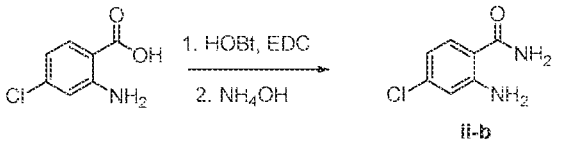
Scheme 2: Representative synthesis of compounds of formula ii (see Scheme 1)



Method A: 2-Nitro-5-propoxy-benzamide (i-a) A mixture of 2-nitro-5-propoxy-benzoic acid (1.97 g, 8.75 mmol) and DMF (0.1 mL) in $SOCl_2$ (20 mL) was stirred at 65 °C for 2 h. After the reaction was completed, the mixture was cooled to room temperature. $SOCl_2$ was removed *in vacuo* and the residue was dissolved in anhydrous CH_2Cl_2 (10 mL), which was added to NH_3-H_2O (28%) dropwise. After 1 h, the precipitate was collected and dried *in vacuo* to give 1.68 g of **i-a** as a yellow solid (85.2%). LCMS m/z = 208.1 (M-16), 225.1 (M+1) (Method B) (retention time = 1.88 min).

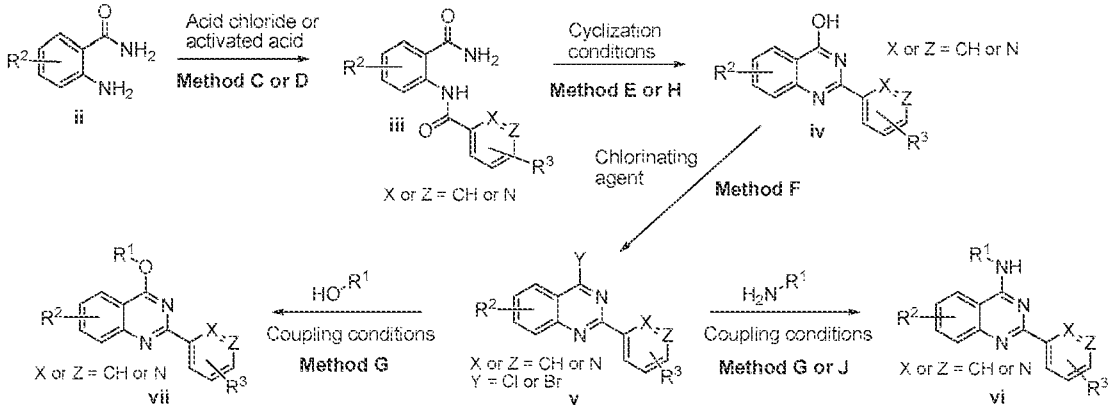
Method B: 2-Amino-5-propoxy-benzamide (ii-a) To a mixture of 2-nitro-5-propoxy-benzamide (1.20 g, 5.36 mmol) in MeOH-H_2O (v/v, 3:1, 60 mL) was added NH_4Cl (2.84 g, 53.6 mmol) and Fe (2.99 g, 53.6 mmol). The resulting mixture was stirred at 60 °C for 3 h. After the reaction was completed, the mixture was cooled to room temperature and the iron was filtered off. The filtrate was concentrated to 15 mL and the formed precipitate was collected and dried *in vacuo* to give 1.02 g of **ii-a** as a pale yellow solid (98%). LCMS m/z = 178.1 (M-16), 195.1 (M+1) (Method B) (retention time = 1.46 min).

Scheme 3: Representative synthesis of compounds of formula ii by Method I (see Scheme 1)



Method I : 2-Amino-4-chlorobenzamide (ii-b) To a mixture of 2-amino-4-chlorobenzoic acid (3.42 g, 20 mmol) in DMF (45 mL) was added HOBt (2.70 g, 20 mmol). After stirring for 10 min, EDC hydrogen chloride (3.82 g, 20 mmol) was added to the mixture. The resulted mixture was stirred at room temperature for 2 h. NH_4OH (28%, 5 mL) was added at 0 °C with vigorous stirring. After addition, the mixture was stirred at room temperature for another 2 h. The reaction mixture was added to water (200 mL) dropwise with stirring, then a precipitate formed. The precipitate was collected and dried *in vacuo* to give 2.98 g of **ii-b** as a grey solid (87.6% yield). LCMS m/z = 171.0 (M+1), 173.0 (M+3) (Method B) (retention time = 1.39 min). ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.27 (d, *J* = 9.6 Hz, 1H), 6.68 (d, *J* = 2.4 Hz, 1H), 6.60 (dd, *J* = 8.4, 2.0 Hz, 1H), 5.50 – 5.82 (m, 4H).

Scheme 4: General route for the synthesis of compounds with general formula vi and vii



Method F for Chlorinating Conditions

F1: $POCl_3$/N,N-dimethylbenzeneamine
F2: $SOCl_2$/DMF/80°C
F3: $SOCl_2$ (4-8 equiv.)/DMF/DCM/rt-40°C
F4: Phenylphosphinic dichloride/ 80-120°C
F5: $POCl_3/\Delta$
F6: $POCl_3$/Toluene/100 °C
F7: PBr_3/CH_2Cl_2/DMF/60°C

Method G for Coupling Conditions

G1: *i*-PrOH/85-100 °C
G2: THF/reflux
G3: *i*-AmOH/100-130 °C

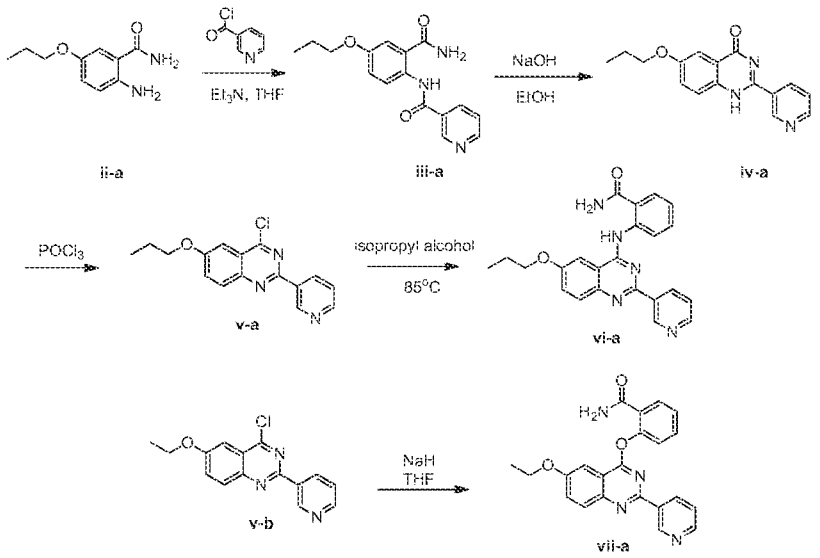
G4: MeOH/microwave/150 °C
G5: *i*-AmOH/ microwave/150 °C

G6: THF/Et_3N/reflux
G7: THF-H_2O/NaOAc/rt-60 °C
G8: NaH/THF
G9: *n*-BuLi/THF
G10: LHMDS/THF
G11: LDA/THF
G12: K_2CO_3/DMF/60 °C
G13: Cs_2CO_3/DMA/80 °C
G14: NaOtBu/DMF/Microwave/100 °C

Method J for Coupling Conditions

J1: $Pd(PPh_3)_4$/ *t*-BuOK/ Dioxane
J2: $Pd_2(dba)_3$/ Xantphos/ Cs_2CO_3/ Dioxane

Scheme 5: Representative synthesis of compounds of formula vi and vii (see Scheme 4)



Method C: N-(2-Carbamoyl-4-propoxy-phenyl)-nicotinamide (iii-a) To a solution of 2-amino-5-propoxy-benzamide (760 mg, 3.91 mmol) in THF (15 mL) and Et_3N (1 mL) was added nicotinoyl chloride (607 mg, 4.30 mmol) in anhydrous THF (15 mL) dropwise. The resulting mixture was stirred at room temperature for 3 h. After the reaction was completed, the volatiles were removed. The residue was washed with H_2O (10 mL). The pH was adjusted to approximately 5 by adding dilute HCl (2N in water). The resulting solid was collected and dried *in vacuo* to give 1.00 g of **iii-a** as a pale yellow solid (89.0%). LCMS m/z = 300.1 (M+1) (Method B) (retention time = 1.60 min).

Method D: 2-benzamido-5-methoxy-3-methylbenzamide (iii-b) A 50 mL round-bottom flask was charged with nicotinic acid (41 mg, 0.33 mmol, 1.0 eq.), 2-amino-5-methoxy-3-methylbenzamide (60 mg, 0.33 mmol, 1.0 eq.) and HBTU (190 mg, 0.50 mmol, 1.5 eq), which were suspended in 4 mL of DMF. DIPEA (86 mg, 0.66 mmol, 2.0 eq.) was added dropwise at room temperature and the reaction mixture was stirred overnight. The reaction mixture was added to water (10 mL) dropwise with stirring. The mixture was extracted with ethyl acetate. The ethyl acetate was evaporated and 55 mg of the orange solid (58.5% yield) was obtained. LCMS m/z = 286.1(M+1) (Method B) (retention time = 1.24 min).

Method E: 6-Propoxy-2-pyridin-3-yl-1H-quinazolin-4-one (iv-a) A mixture of N-(2-carbamoyl-4-propoxy-phenyl)-nicotinamide (980 mg, 3.27 mmol) in EtOH (20 mL) was treated with NaOH (654 mg, 16.37 mmol). The resulting mixture was stirred at room temperature for 18 h. After the reaction was completed, the volatiles were removed *in vacuo*. The residue was partitioned between H_2O (50 mL) and ethyl acetate (50 mL). The aqueous layer was neutralized to pH 7 by slowly adding aq. citric acid and then a precipitate formed. The precipitate was collected and dried to give 1.00 g of **iv-a** as a grey solid (quantitative yield). LCMS m/z = 282.1 (M+1) (Method B) (retention time = 1.60 min).

Method F1: 4-Chloro-6-propoxy-2-pyridin-3-yl-quinazoline (v-a)
(This method is representative of method F1, F2, F3 and F4. These three methods can be implemented in a similar way except for substitution of the appropriate chlorinating reagent, solvent and temperature) To a mixture of 6-propoxy-2-pyridin-3-yl-1H-quinazolin-4-one (1.00 g, 3.56 mmol) in $POCl_3$ (10 mL) was added *N,N*-dimethylaniline (0.1 mL). The resulting mixture was stirred at 120 °C for 2 h. After the reaction was completed, $POCl_3$ was removed *in vacuo*, and the residue was added to ice-water slowly. The pH was adjusted to around 7 by slowly adding $NaHCO_3$ (sat.) at 0 °C. The resultant solid was collected and purified by chromatography on silica gel eluted with petroleum ether / ethyl acetate (v/ v = 4: 1 to 1: 1) to give 580 mg of **v-a** as a pale yellow solid (54.7%).

Method F5: 4-chloro-6-methoxy-2-(pyridin-3-yl)quinazoline (v-c) In a sealed tube, phosphorus oxychloride (11 mL, 120 mmol) was added to 6-methoxy-2-(pyridin-3-yl)quinazolin-4(3H)-one (2.70 g, 10.66 mmol). The mixture was refluxed at 120°C for 12 h. After cooling, the remaining phosphorus oxychloride was removed *in vacuo* to leave a tan solid. This residue was added to an ice-water mixture (100 mL) with cooling and allowed to stir. The pH of the suspension was adjusted to about pH 9 via dropwise addition of 28% ammonium hydroxide, and stirring was continued for 30 mins. The resulting solid was filtered to give the desired product as a tan solid

(2.55 g, 9.39 mmol, 88%). LC-MS m/z = 272.0 (M+1) (retention time = 2.05) ^{1}H NMR (300 MHz, DMSO) δ 9.55 (s, 1H), 8.81 – 8.64 (m, 2H), 8.09 (d, *J* = 9.2 Hz, 1H), 7.78 (dd, *J* = 9.2, 2.8 Hz, 1H), 7.61 (dd, *J* = 7.9, 4.8 Hz, 1H), 7.49 (d, *J* = 2.5 Hz, 1H), 4.00 (s, 3H).

Method F6: 6-Bromo-4-chloro-8-fluoro-2-(pyridin-3-yl)quinazoline (v-d) To a suspension of 6-bromo-8-fluoro-2-(pyridin-3-yl)quinazolin-4-ol (6.16 g, 0.0192 mol) in toluene (60 mL) was added phosphorus oxychloride (5.30 ml, 0.0579 mol) at room temperature. The mixture was refluxed for 3 h. The solvent was evaporated and water was added to the residue under cooling conditions. The suspension was stirred at room temperature for 30 min, the resulting precipitate was filtered and dried to give the title compound (6.5 g, quantitative). ^{1}H NMR (400 MHz, DMSO) δ 9.58 (d, *J* = 1.6 Hz, 1H), 8.82 (dd, *J* = 4.7, 1.5 Hz, 1H), 8.80 – 8.75 (m, 1H), 8.37 (dd, *J* = 9.7, 1.9 Hz, 1H), 8.34 – 8.29 (m, 1H), 7.67 (dd, *J* = 7.8, 4.6 Hz, 1H).

Method F7: 4-Bromo-6-methoxy-2-(pyridin-3-yl)quinazoline (v-e) To a sealed tube containing 6-methoxy-2-(pyridin-3-yl)quinazolin-4(3H)-one (1.30 g, 5.13 mmol) in dichloromethane (20 mL) was added 1 M phosphorus tribromide in dichloromethane (10.3 mL, 10.3mmol) and DMF (2 mL). The reaction mixture was heated at 60°C for 4 h. After cooling, excess dichloromethane was evaporated leaving a tan residue. This solid was added to an ice-water mixture (100 mL) with cooling and allowed to stir. The pH of the suspension was adjusted to about pH 9 via dropwise addition of 28% ammonium hydroxide, and stirring was continued for 30 mins. The resulting solid was filtered to give the desired product as a tan solid (1.49 g, 4.71 mmol, 92%). LC-MS m/z = 318.3 (M+2) (retention time = 2.19).

Method G1: 2-(6-Propoxy-2-pyridin-3-yl-quinazolin-4-ylamino)-benzamide (vi-a) (This method is representative of method G1, G2, and G3. These three methods can be implemented in a similar way except for substitution of the appropriate solvent and temperature) A mixture of 4-chloro-6-propoxy-2-(pyridin-3-yl)quinazoline (90 mg, 0.3 mmol) and 2-aminobenzamide (52 mg, 0.4 mmol) in *i*-

PrOH (5 mL) was stirred at 85 °C for 18 h. The yellow precipitate was collected and washed with *i*-PrOH (10 mL). The solid was suspended in water (10 mL) and NH_3-H_2O (1 mL) was added. After filtration the solid was dried *in vacuo* to afford 31.0 mg of **vi-a** as a white solid (30.8%). LCMS m/z = 400.1 (M+1) (Method B) (retention time = 1.96 min). ^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.59 (d, *J* = 2.0 Hz, 1H), 9.58 (d, *J* = 7.6 Hz, 1H), 8.69 – 8.74 (m, 2H), 8.48 (s, 1H), 7.97 (d, *J* = 6.8 Hz, 2H), 7.90 (d, *J* = 8.8 Hz 1H), 7.74 (t, *J* = 7.6 Hz, 1H), 7.56 – 7.61 (m, 3H), 7.20 (t, *J* = 7.2 Hz, 1H), 4.16 (t, *J* = 6.4 Hz, 2H), 1.86 (dd, *J* = 14.0, 6.8 Hz, 2H), 1.07 (t, *J* = 7.2 Hz, 3H).

Method G8: 2-(6-ethoxy-2-(pyridin-3-yl)quinazolin-4-yloxy)benzamide (vii-a) (The method G8 is representative of method G6, G7, G9, G10 and G11. These six methods can be implemented in a similar way except for substitution of the appropriate base, solvent and temperature) To a 2.5 dram reaction vial was first added sodium hydride 60% (0.028 g, 0.700 mmol) and salicylamide (0.072 g, 0.525 mmol) in DMF (2 mL). The mixture was allowed to stir at room temperature for 1 h. Then, 4-chloro-6-ethoxy-2-(pyridin-3-yl)quinazoline (0.100 g, 0.350 mmol) was added to the mixture, and the reaction was allowed to proceed at room temperature overnight. LC-MS analysis of the crude mixture showed about 85% of product formed and 10% remaining starting material. Water (30 mL) was added to the mixture, and the product was extracted with chloroform (3 x 15 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The crude product was purified via ISCO (silica gel, 97.5:2.5 CH_2Cl_2/MeOH; 12 g column) to afford 13.9 mg of the desired product as a white solid (10.3%) LCMS m/z = 387 (M+1) (Method C) (retention time = 2.05 min). ^{1}H NMR (300 MHz, DMSO) δ 11.47 (s, 2H), 9.39 (s, 1H), 8.66 (d, *J* = 2.8 Hz, 1H), 8.56 – 8.47 (m, 1H), 8.01 – 7.90 (m, 2H), 7.69 – 7.55 (m, 2H), 7.55 – 7.40 (m, 2H), 7.05 (t, *J* = 7.5 Hz, 1H), 6.97 (d, *J* = 8.2 Hz, 1H), 4.23 (q, *J* = 6.9 Hz, 2H), 1.44 (t, *J* = 6.9 Hz, 3H).

Method G13: 4-(4-chlorophenyl)-N-(6-methoxy-2-(pyridin-3-yl)quinazolin-4-yl)thiazol-2-amine (vi-c) (The method G13 is representative of method G12 also.

This method can be implemented in a similar way except for substitution of the appropriate base, solvent and temperature) To a suspension of 4-chloro-6-methoxy-2-(pyridine-3-yl)quinazoline (645.2 mg, 2.375 mmol) and 2-amino-4-(4-chlorophenyl)thiazole (1050 mg, 4.98 mmol) in DMA (40 mL) was added Cs_2CO_3 (2430 mg, 7.46 mmol) at room temperature. The mixture was stirred at 80°C for 9.5 h. Water was added and a precipitate formed which was collected by filtration and washed with H_2O. Recrystallization from acetone/DMF/methanol gave 383.6 mg of the product in a 36% yield as yellow solid, >98% purity by ^{1}H NMR). ^{1}H NMR (400 MHz DMSO-d_6) δ 12.52 (s, 1H), 9.78 (d, J = 1.56 Hz, 1H), 8.91-8.88 (m, 1H), 8.74 (dd, J = 4.74, 1.60 Hz, 1H), 8.33 (brs, 1H), 8.06 (d, J = 8.56 Hz, 2H), 7.93 (d, J = 9.08 hz, 1H), 7.89 (s, 1H), 7.66-7.59 (m, 2H), 7.55 (d, J = 8.56 Hz, 2H),4.01 (s, 3H).

Method G14: 4-(6-methoxy-2-(pyridin-3-yl)quinazolin-4-ylamino)-1H-pyrazole-5-carboxamide, 2HCl (vi-d): (The method G14 is representative of method G4 and G5 also. This method can be implemented in a similar way except for substitution of the appropriate solvent and adjustment of the temperature)
To a microwave vial containing 4-bromo-6-methoxy-2-(pyridin-3-yl)quinazoline (150.0 mg, 0.47 mmol) in DMF (2 mL) was added 4-amino-1H-pyrazole-5-carboxamide (66.0 mg, 0.52 mmol) and sodium *tert*-butoxide (50 mg, 0.52 mmol). The reaction mixture was heated at 100°C for 15 mins by microwave irradiation. Water (50 mL) was added to the reaction mixture, and extracted with ethyl acetate (5 x 50 mL). The crude material was purified via ISCO (silica, 12 g column, 93% CH_2Cl_2 – 7% MeOH – 0.1% NH_4OH) giving the product as a yellow solid. The free base was then converted to the HCl salt to yield the final product as an orange solid (59.8 mg, 0.14 mmol, 22%). LC-MS m/z = 362.4 (M+1) (retention time = 1.57) ^{1}H NMR (300 MHz, DMSO) δ 11.28 (s, 1H), 9.62 (d, J = 1.7 Hz, 1H), 9.17 (d, J = 7.8 Hz, 1H), 8.93 (dd, J = 5.2, 1.3 Hz, 1H), 8.60 (s, 1H), 8.05 (s, 1H), 8.03 - 7.94 (m, 2H), 7.77 (s, 1H), 7.64 (dd, J = 9.2, 2.5 Hz 1H), 7.40 (d, J = 2.6 Hz, 1H), 3.97 (s, 3H).

Method J1: 1-(6-Methoxy-2-(pyridin-3-yl)quinazolin-4-yl)-1H-benzo[d]imidazol-2(3H)-one (vi-b) To a 50-mL two-neck round bottom flask equipped with a reflux

condenser was added a mixture of 4-chloro-6-methoxy-2-(pyridin-3-yl)quinazoline (50 mg, 0.18 mmol, 1 eq.) and 1H-benzo[d]imidazol-2(3H)-one (27 mg, 0.21 mmol, 1.1 eq.) in 5 mL of dry 1,4-dioxane. $Pd(PPh_3)_4$ (10.6 mg, 0.009 mmol, 0.05 eq) and *t*-BuOK (41 mg, 0.36 mmol, 2 eq.) were added. The resulting mixture was stirred at 100 °C under N_2 atmosphere overnight. After cooling, 20 mL of methanol was added. The mixture was filtered, the filtrate was concentrated *in vacuo* and then was purified with chromatography on silica gel (ethyl acetate/ petroleum ether from 1:4 to 1:2) to give the crude product, which was further purified with reverse phase HPLC to afford 4.8 mg of **vi-e** as a pale yellow solid (7%). MS m/z = 370.1 (M+1) (Method B) (retention time = 1.680 min). ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.51 (s, 1H), 8.78 (d, *J* = 8.0 Hz, 2H), 8.17 (d, *J* = 9.2 Hz, 1H), 7.80 (dd, *J* = 9.2, 2.8 Hz, 1H), 7.70 – 7.64 (m, 1H), 7.46 (d, *J* = 2.8 Hz, 1H), 7.41 (d, *J* = 8.0 Hz, 1H), 7.20 (d, *J* = 4.0 Hz, 2H), 7.16 – 7.08 (m, 1H), 3.89 (s, 3H).

Method J2: 6-methoxy-N-(pyridin-2-yl)-2-(pyridin-3-yl)quinazolin-4-amine dihydrochloride (vi-e) To a suspension of 4-chloro-6-methoxy-2-(pyridine-3-yl)quinazoline (600 mg, 2.208 mmol) in dioxane (40 mL) under N_2, was added tris(dibenzylideneacetone)dipalladium(0) (103.1 mg, 0.113 mmol), 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene (132.2 mg, 0.228 mmol) and cesium carbonate (1.1289 g, 3.46 mmol) at room temperature. 2-Aminopyridine (229 mg, 2.43 mmol) was added and the mixture was stirred at 100°C for 2h 30 min. Water was added and then a precipitate formed. The solid was collected and washed with water. The solid was dissolved in CH_2Cl_2. Purification was carried out using NH-silica gel to give the free base (649.3 mg). The free base was converted to the HCl salt by dissolving the compound in CH_2Cl_2 / MeOH and 1.5 ml of 4N HCl in ethyl acetate was added and then a precipitate formed. The solid was collected and dried in vacuo (at 40 degrees on and 60 degrees for ca. 3 h) and then washed with methanol. The resulting solid was dried *in vacuo* at 60 degrees to give 682mg of the desired product as the HCl salt in a 77% yield as a pale yellow solid. ^{1}H NMR (DMSO-d_6) δ 11.14 (brs, 1H), 9.58 (s, 1H), 9.13 (dd, J = 7.96 Hz, 1H), 8.93 (d, J = 5.24 Hz, 1H), 8.54 (d, J = 4.72 Hz, 1H), 8.48 (d, J = 8.32 Hz, 1H), 8.28 (brs, 1H), 8.09 (brt, J = 7.16 Hz, 1H),

8.02-7.96 (m, 2H), 7.65 (dd, J = 8.80, 2.48 Hz, 1H), 7.34 (brt, J = 6.52 Hz, 1H), 4.01 (s, 3H) . The 1H of 2HCl was not observed.

Method J3: N-(Biphenyl-4-yl)-6-methoxy-2-(pyridin-3-yl)quinazolin-4-amine hydrochloride (vi-f) To a suspension of N-(4-bromophenyl)-6-methoxy-2-(pyridin-3-yl)quinazolin-4-amine (548.7 mg, 1.347 mmol) and phenylboronic acid (270 mg, 2.21 mmol) in dioxane / H_2O (2/1) (30 mL) under N_2 was added Na_2CO_3 (485 mg, 4.58 mmol) and tetrakis(triphenylphosphine) palladium(0) (78 mg, 0.067 mmol) at room temperature. The mixture was stirred at 100°C for 1 h. Water was added and then a precipitate formed. The solid was dissolved in methanol/acetone at 60°C. The solution was filtrated through Celite to remove any extra palladium. The filtrate was concentrated down to give 493.4 mg of a solid residue in. The solid was added to CH_2Cl_2 followed by addition of 4N HCl in ethyl acetate (0.4 mL) at room temperature to form the HCl salt. The mixture was stirred at room temperature and the resulting solid was filtered and dried *in vacuo* to give 435.2 mg and a yield of 73% as the HCl salt. ^{1}H NMR (DMSO-d6) δ 10.24 (br, 1H), 9.54 (s, 1H), 8.92 (d, J = 7.52 Hz, 1H), 8.82 (d, J = 3.96 Hz, 1H), 8.10 (d, J = 2.44 Hz, 1H), 8.03 (d, J = 8.68 Hz, 2H), 7.92 (d, J = 9.08 Hz, 1H), 7.84 (d, J =8.68 Hz, 2H), 7.81 (m, 1H), 7.77-7.75 (m, 2H), 7.62 (dd, J = 9.08, 2.44 Hz, 1H), 7.50 (m, 2H), 7.38 (m, 1H), 4.01 (s, 3H) .The 1H of HCl was not observed.

The compounds in the following table were prepared in a manner analogous to that described in **Scheme 1 and 5** (prepared according to method **procedure A - J** as designated).

Table 1:

Number	Product	Salt type	Molecular Mass	^{1}H-NMR	^{1}H-NMR Solvent	LCMS	LCMS Protocol	Purity percent	Method for Coupling
1			399.45	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.59 (d, *J* = 2.0 Hz, 1H), 9.58 (d, *J* = 7.6 Hz, 1H), 8.69 – 8.74 (m, 2H), 8.46 (s, 1H), 7.97 (d, *J* = 6.8 Hz, 2H), 7.90 (d, *J* = 8.8 Hz 1H), 7.74 (t, *J* = 7.6 Hz, 1H), 7.56 – 7.61 (m, 3H), 7.20 (t, *J* = 7.2 Hz, 1H), 4.16 (t, *J* = 6.4 Hz, 2H), 1.86 (dd, *J* = 7.2, 6.8 Hz, 2H), 1.07 (t, *J* = 7.2 Hz, 3H).	DMSO	400.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1
2		HCl	398.46	^{1}H-NMR (400 MHz, DMSO-d_6): δ 13.20 (s, 1H), 9.79 (s, 1H), 9.02 – 9.08 (m, 2H), 8.67 (d, *J* = 3.2 Hz, 1H), 8.53 (s, 1H), 8.34 (d, *J* = 8.0 Hz, 1H), 8.19 (d, *J* = 6.8 Hz, 1H), 7.74 – 7.99 (m, 5H), 7.28 (t, *J* = 7.6 Hz, 1H), 4.92 (d, *J* = 4.0 Hz, 2H), 2.87 (d, *J* = 3.2 Hz, 6H).	DMSO	399.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1
3		HCl	424.50	^{1}H-NMR (400 MHz, DMSO-d_6): δ 13.07 (s, 1H), 9.64 (d, *J* = 1.6 Hz, 1H), 9.15 (d, *J* = 8.0 Hz, 1H), 8.78 (ddd, *J* = 8.0, 4.0, 2.4 Hz, 1H), 8.73 (dd, *J* = 4.4, 1.2 Hz, 1H), 8.49 (s, 1H), 8.09 (d, *J* = 8.0 Hz, 1H), 7.92 – 7.69 (m, 3H), 7.67 – 7.74 (m, 2H), 7.62 (dd, *J* = 8.0, 4.8 Hz, 1H), 7.22 (t, *J* = 7.6 Hz, 1H), 4.29 (s, 2H), 2.61 (brs, 4H), 1.70 (brs, 4H).	DMSO	425.2 (M+1)	Method B (NH4HCO3)	95	Method C, G1

193

4			422.43	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.87 (s, 1H), 9.52 (s, 1H), 8.67 (d, *J* = 5.6 Hz, 1H), 7.99 (d, *J* = 2.4 Hz, 1H), 7.94 (s, 1H), 7.86 (d, *J* = 9.2 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.50 – 7.58 (m, 3H), 7.30 (t, *J* = 34.0 Hz, 1H), 7.00 (dd, *J* = 8.4, 2.0 Hz, 1H), 4.16 (t, *J* = 6.4 Hz, 2H), 1.86 (dd, *J* = 7.2, 6.4 Hz, 2H), 1.07 (t, *J* = 7.2 Hz, 3H).	DMSO	423.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1
5		HCl	408.86	^{1}H-NMR (400 MHz, DMSO-d_6): δ10.28 (s, 1H), 9.48 (s, 1H), 8.93 (d, *J* = 6.4 Hz, 1H), 8.85 (d, *J* = 4.4 Hz, 1H), 8.18 (dd, *J* = 7.6, 2.4 Hz, 1H), 8.06 (d, *J* = 2.0 Hz, 1H), 7.85 – 7.93 (m, 3H), 7.62 (dd, *J* = 8.8, 6.4 Hz, 1H), 7.55 (t, *J* = 8.8 Hz, 1H), 4.17 (t, *J* = 6.4 Hz, 3H), 1.86 (dd, *J* = 7.6, 6.4 Hz, 2H), 1.06 (t, *J* = 7.6 Hz, 3H).	DMSO	409.1, 411.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1
6			425.31	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.93 (s, 1H), 9.51 (s, 1H), 8.68 – 8.71 (m, 2H), 8.16 (d, *J* = 2.4 Hz, 1H), 7.94 (d, *J* = 2.0 Hz, 1H), 7.86 (d, *J* = 8.8 Hz, 1H), 7.56 – 7.60 (m, 2H), 7.37 (s, 1H), 4.14 (t, *J* = 6.4 Hz, 2H), 1.84 (dd, *J* = 10.4 Hz, 7.2 Hz, 2H), 1.07 (t, *J* = 7.6 Hz, 3H).	DMSO	425.0, 427.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1
7			392.4	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.06 (s, 1H), 9.49 (s, 1H), 8.77 – 8.81 (m, 2H), 8.09 (ddd, *J* = 10.0, 7.6, 2.4 Hz, 1H), 7.88 (d, *J* = 9.2 Hz, 1H), 7.69 – 7.74 (m, 2H), 7.54 – 7.61 (m, 2H), 4.15 (t, *J* = 6.4 Hz, 2H), 1.86 (dd, *J* = 14.0, 7.6 Hz, 2H), 1.06 (t, *J* = 7.2 Hz, 3H).	DMSO	393.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1

194

8			425 31	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.05 (s, 1H), 9.51 (s, 1H), 8.75 – 8.80 (m, 2H), 8.34 (d, *J* = 2.4 Hz, 1H), 7.96 – 8.00 (m, 2H), 7.88 (d, *J* = 9.2 Hz, 1H), 7.68 – 7.75 (m, 2H), 7.59 (dd, *J* = 9.2, 2.8 Hz, 1H), 4.15 (t, *J* = 6.4 Hz, 2H), 1.86 (dd, *J* = 7.2, 6.8 Hz, 2H), 1.06 (t, *J* = 7.6 Hz, 3H).	DMSO	425 0, 427.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1
9			415.44	^{1}H-NMR (400 MHz, DMSO-d_6): δ 13.03 (s, 1H), 9.59 (d, *J* = 1.2 Hz, 1H), 9.15 (d, *J* = 8.4 Hz, 1H), 8 69 – 8 74 (m, 2H), 8.49 (s, 1H), 7 96 – 8 06 (m, 2H), 7 90 (d, *J* = 9.2 Hz, 1H), 7 56 – 7 63 (m, 3H), 7.20 (t, *J* = 8.0 Hz, 1H), 4.31 (t, *J* = 4.0 Hz, 2H), 3.79 (t, *J* = 4 8 Hz, 2H), 3.31 (s, 3H).	DMSO	416 0 (M+1)	Method B (NH4HCO3)	95	Method C, G1
10			438.43	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.86 (s, 1H), 9.53 (s, 1H), 8.66 – 8.68 (m, 2H), 8.02 (d, *J* = 2.8 Hz, 1H), 7.95 (t, *J* = 2.0 Hz, 1H), 7.86 (d, *J* = 8.8 Hz, 1H), 7.79 (d, *J* =1.2 Hz, 1H), 7.48 – 7.60 (m, 3H), 7.30 (t, *J* = 74.4 Hz, 1H), 7.00 (dd, *J* = 8.0, 2.0 Hz, 1H), 4.33 (t, *J* = 4.8 Hz, 2H), 3.79 (t, *J* = 4.4 Hz, 2H), 3.37 (s, 3H).	DMSO	439.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1
11		HCl	424.86	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.27 (s, 1H), 9.48 (s, 1H), 8.93 (d, *J* = 8.4 Hz, 1H), 8.85 (d, *J* = 4.8 Hz, 1H), 8.19 (dd, *J* = 6.8, 2.4 Hz, 1H), 8.10 (d, *J* = 2.4 Hz, 1H), 7.85 – 7.93 (m, 3H), 7.64 (dd, *J* = 9.2, 6.8 Hz, 1H), 7.55 (t, *J* = 8.8 Hz, 1H), 4.34 (t, *J* = 4.4 Hz, 2H), 3.78 (t, *J* = 4.4 Hz, 2H), 3.31 (s, 3H).	DMSO	425.1, 427.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1

195

12			397.43	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.07 (s, 1H), 9.50 (s, 1H), 8.78 (dd, *J* = 17.6, 7.6 Hz, 1H), 8.39 (s, 1H), 8.26 (dd, *J* = 8.0, 2.0 Hz, 1H), 8.02 (d, *J* = 2.0 Hz, 1H), 7.90 (d, *J* = 9.2 Hz, 1H), 7.61 – 7.73 (m, 4H), 4.34 (t, *J* = 4.8 Hz, 2H), 3.79 (t, *J* = 4.4 Hz, 2H), 3.35 (s, 3H).	DMSO	398.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1
13			408.4	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.86 (s, 1H), 9.50 (d, J = 1.6 Hz, 1H), 8.67 (dd, *J* = 4.6, 1.6 Hz, 1H), 8.64 (dt, *J* = 8.0, 1.6 Hz, 1H), 8.12 (ddd, J = 13.2, 7.2, 2.4 Hz, 1H), 7.98 (d, J = 2.8 Hz, 1H), 7.86 (d, *J* = 9.2, 1H), 7.69 – 7.72 (m, 1H), 7.52 – 7.60 (m, 3H), 4.31 (t, J = 4.0 Hz, 2H), 3.76 – 3.80 (m, 2H), 3.37 (s, 3H).	DMSO	409.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1
14			441.31	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.90 (s, 1H), 9.52 (d, *J* = 1.2 Hz, 1H), 8.64 – 8.68 (m, 1H), 8.37 (d, *J* = 2.8 Hz, 1H), 7.98 (d, *J* = 2.4 Hz, 1H), 7.96 (dd, *J* = 10.6, 2.4 Hz, 1H), 7.86 (d, *J* = 9.2 Hz, 1H), 7.74 (d, *J* = 9.2 Hz, 1H), 7.59 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.55 (dd, *J* = 8.0, 4.8 Hz, 1H), 4.31 (t, *J* = 4.08 Hz, 2H), 3.76 (t, *J* = 4.4 Hz, 2H), 3.37 (s, 3H).	DMSO	441.0, 443.0 (M+1), 221.9 (M/2 +1)	Method A (TFA)	95	Method C, G1
15			441.31	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.93 (s, 1H), 9.53 (d, *J* = 1.6 Hz, 1H), 8.66 – 8.70 (m, 2H), 8.18 (s, 1H), 8.17 (s, 1H), 7.99 (d, *J* = 2.4 Hz, 1H), 7.69 (d, *J* = 8.8 Hz, 1H), 7.61 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.56 (dd, *J* = 7.6, 4.8 Hz, 1H), 7.39 (t, *J* = 2.0 Hz, 1H), 4.33 (t, *J* = 4.8 Hz, 2H), 3.79 (t, *J* = 4.4 Hz, 2H), 3.37 (s, 3H).	DMSO	441.1, 443.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1

196

16		HCl	375 79	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.34 (s, 1H), 9.53 (d, *J* = 1.2 Hz, 1H), 9.16 (d, *J* =1.2 Hz, 1H), 8.74 (dd, *J* = 4.0, 1.6 Hz, 1H), 8.66 – 8.69 (m, 2H), 8.20 – 8.28 (m, 2H), 8.00 (d, *J* = 8.4 Hz, 1H), 7.89 – 7.93 (m, 1H), 7.55 – 7.61 (m, 2H).	DMSO	376 0, 378.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1
17			393.8	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.37 (s, 1H), 9.54 (d, *J* = 1.6 Hz, 1H), 9.09 (s, 1H), 8.69 (d, *J* = 10.0 Hz, 1H), 8.68 (d, *J* = 8.0 Hz, 1H), 8.23 – 8.27 (m, 2H), 8.11 (s, 1H), 8 78 (s, 2H), 7.50 – 7.58 (m, 3H).	DMSO	394.1, 396.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1
18		HCl	394.79	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.81 (s, 1H), 9.48 (d, *J* = 0.8 Hz, 1H), 9.28 (d, *J* = 0.8 Hz,1H), 8.69 (d, *J* = 10.0 Hz, 1H), 8.66 (d, *J* = 8.0 Hz, 1H), 8 23 – 8.27 (m, 2H), 8.11 (s, 1H), 8.78 (s, 2H), 7.50 – 7.56 (m, 3H).	DMSO	395.0, 397.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1
19			422.38	1H-NMR (400 MHz, DMSO-d_6): δ 10.11 (brs, 1H), 9.48 (s, 1H), 8.79 (d, *J* = 4.8 Hz, 1H), 8.83 (d, *J* = 8.0 Hz, 1H), 8.07 (d, *J* = 2.0 Hz, 1H), 8.02 (d, *J* = 2.4 Hz, 1H), 7.86 – 7.90 (m,1H), 1.77(d, *J* = 8.0 Hz, 1H), 7.52 – 7.62 (m, 3H), 4.27 (q, *J* = 7.2 Hz, 2H), 1.46 (t, *J* = 7.2 Hz, 3H).	DMSO	423.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1

197

20		HCl	408 81	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.73 (s, 1H), 9.52 (d, J = 1.6 Hz, 1H), 9.32 (d, J = 1.6 Hz, 1H), 9.01 (d, J = 4.8 Hz, 1H), 8.91 (d, J = 5.2 Hz, 1H), 8.39 (dd, J = 8.4, 1.6 Hz, 1H), 8.17 (dd, J = 6.8, 2.0 Hz, 1H), 8.01 (d, J = 8.8 Hz, 1H), 7.90 – 7.95 (m, 2H), 7.55 (t, J = 9.2 Hz, 1H), 3.98 (s, 3H).	DMSO	409.1, 411.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1
21			399.45	^{1}H-NMR (400 MHz, DMSO-d_6) δ 12.94 (s, 1H), 9.56 (s, 1H), 9.14 (d, J = 8.0 Hz, 1H), 8.83 – 8.66 (m, 2H), 8.48 (s, 1H), 8.06 – 7.91 (m, 2H), 7.76 – 7.58 (m, 2H), 7.35 (s, 1H), 7.27 (d, J = 2.0 Hz, 1H), 7.18 (t, J = 7.2 Hz, 1H), 4.15 (q, J = 6.8 Hz, 2H), 2.64 (s, 3H), 1.43 (t, J = 6.8 Hz, 1H).	DMSO	400.1 (M+1)	Method B (NH4HCO3)	95	Method D, G1
22			440 42	^{1}H-NMR (400 MHz, DMSO-d_6) δ 9.84 (s, 1H), 9.55 (d, J = 1.2 Hz, 1H), 8.73 – 8.60 (m, 2H), 8.14 (s, 1H), 7.91 (d, J = 8.4 Hz, 1H), 7.80 (d, J = 2.4 Hz, 1H), 7.60 (t, J = 8.0 Hz, 1H), 7.53 (dd, J = 7.6, 4.8 Hz, 1H), 7.45 (d, J = 1.6 Hz, 1H), 7.16 (d, J = 8.4 Hz, 1H), 4.23 (q, J = 6.8 Hz, 2H), 2.70 (s, 3H), 1.44 (t, J = 6.6 Hz, 3H)	DMSO	440.9 (M+1)	Method A (TFA)	95	Method D, G1
23			405.81	^{1}H-NMR (400 MHz, DMSO-d_6) δ 10.08 (s, 1H), 9.42 (s, 1H), 8.68 (d, J = 3.6 Hz, 1H), 8.55 (d, J = 8.4 Hz, 1H), 8.32 (s, 1H), 8.15 (dd, J = 6.8, 2.4 Hz, 1H), 8.04 (s, 1H), 7.93 – 7.78 (m, 1H), 7.54 (td, J = 8.3, 6.9 Hz, 2H), 4 08 (s, 3H)	DMSO	406.1, 408.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1

198

24			493.92	^{1}H-NMR (400 MHz, DMSO-d_6) δ 10.00 (s, 1H), 9.49 – 9.51 (m, 1H), 8.62 – 8.70 (m, 2H), 8.21 (dd, *J* = 6.8, 2.8 Hz, 1H), 8.03 (s, 1H), 7.87 – 7.91 (m, 1H), 7.75 (s, 1H), 7.53 – 7.59 (m, 2H), 4.02 (s, 3H), 3.64 – 3.73 (m, 4H), 3.49 – 3.56 (m, 2H), 3.14 – 3.22 (m, 2H).	DMSO	494.1, 496.1 (M+1)	Method B (NH4HCO4)	95	Method C, G1
25		TFA	369.38	^{1}H-NMR (400 MHz, DMSO-d_6): δ 11.51 (s, 1H), 8.78 (d, *J* = 8.0 Hz, 2H), 8.17 (d, *J* = 9.2 Hz, 1H), 7.80 (dd, *J* = 9.2, 2.8 Hz, 1H), 7.70 – 7.64 (m, 1H), 7.46 (d, *J* = 2.8 Hz, 1H), 7.41 (d, *J* = 8.0 Hz, 1H), 7.20 (d, *J* = 4.0 Hz, 2H), 7.16 – 7.08 (m, 1H), 3.89 (s, 3H).	DMSO	370.1 (M+1)	Method B (NH4HCO3)	95	Method C, J1
26			406.4	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.87 (s, 1H), 8.53 (dd, *J* = 4.7, 1.5 Hz, 1H), 8.23 (d, *J* = 6.8 Hz, 1H), 8.00 (d, *J* = 2.6 Hz, 1H), 7.8 (t, *J* = 2.1 Hz, 1H), 7.84 (d, *J* = 9.1 Hz, 1H), 7.73 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.58 (dd, *J* = 9.1, 2.6 Hz, 1H), 7.41 – 7.25 (m, 3H), 7.24 (t, *J* = 74.0 Hz, 1H), 6.96 (dd, *J* = 8.0, 2.2 Hz, 1H), 3.99 (s, 3H), 2.75 (s, 3H).	DMSO	409.1 (M+1)	Method B (NH4HCO3)	95	Method D, G1
27			385.42	^{1}H-NMR (400 MHz, DMSO-d_6): δ 13.09 (s, 1H), 9.08 (d, *J* = 7.8 Hz, 1H), 8.55 (dd, *J* = 4.8, 1.6 Hz, 1H), 8.49 (s, 1H), 8.22 (dd, *J* = 7.8, 1.7 Hz, 1H), 8.01 (s, 1H), 7.95 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.87 (d, *J* = 9.6 Hz, 1H), 7.66 – 7.58 (m, 3H), 7.40 (dd, *J* = 7.7, 4.8 Hz, 1H), 7.15 (dd, *J* = 11.5, 4.4 Hz, 1H), 3.99 (s, 3H), 2.77 (s, 3H).	DMSO	386.1 (M+1)	Method B (NH4HCO3)	95	Method D, G1

199

28			394.83	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.10 (s, 1H), 8.63 (d, *J* = 4.1 Hz, 1H), 8.43 (d, *J* = 7.6 Hz, 1H), 8.15 (dd, *J* = 6.8, 2.5 Hz, 1H), 8.03 (d, *J* = 2.3 Hz, 1H), 7.88 – 7.78 (m, 2H), 7.58 (ddd, *J* = 12.5, 8.3, 4.1 Hz, 2H), 7.49 (t, *J* = 9.1 Hz, 1H), 3.99 (s, 3H), 2.80 (s, 3H).	DMSO	395.1, 397.1 (M+1)	Method B (NH4HCO3)	95	Method D, G1
29		HCl	440.5	^{1}H-NMR (400 MHz, DMSO-d_6): δ 13.19 (s, 1H), 11.12 – 10.93 (m, 1H), 9.83 (d, *J* = 1.5 Hz, 1H), 9.21 (d, *J* = 7.8 Hz, 1H), 9.01 (d, *J* = 7.8 Hz, 1H), 8.93 – 8.89 (m, 1H), 8.53 (s, 1H), 8.36 (dd, *J* = 11.6, 7.9 Hz, 2H), 8.02 – 7.73 (m, 6H), 7.29 (d, *J* = 8.02 Hz, 1H), 5.01 (s, 2H), 3.95 – 3.81 (m, 4H), , 3.37 (s, 4H).	DMSO	441.2 (M+1)	Method B (NH4HCO3)	95	Method C, G1
30		HCl	449.91	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.05 (s, 1H), 9.56 (s, 1H), 8.73 – 8.66 (m, 2H), 8.47 (d, *J* = 8.1 Hz, 1H), 8.28 (dd, *J* = 6.8, 2.5 Hz, 1H), 7.99 – 7.90 (m, 2H), 7.67 – 7.50 (m, 3H), 4.16 (s, 2H), 3.62 (s, 4H), 2.53 (s, 4H).	DMSO	450.1, 452.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1

200

31			400 33	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.47 (d, J = 2.0 Hz, 2H), 8.70 (dd, J = 4.8, 1.6 Hz, 1H), 8.65 – 8.59 (m, 1H), 8.06 (s, 1H), 7.91 (dt, J = 8.1, 6.0 Hz, 1H), 7.82 (dd, J = 8.2, 1.2 Hz, 1H), 7.76 (d, J = 8.4 Hz, 1H), 7.59 (t, J = 8.2 Hz, 1H), 7.51 (ddd, J = 20.0, 10.0, 6.4 Hz, 2H), 7.21 (d, J = 8.4 Hz, 1H).	DMSO	401.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1
32		HCl	368.77	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.53 (d, J = 11.3 Hz, 1H), 9.44 (d, J = 1.2 Hz, 1H), 8.84 – 8.79 (m, 2H), 8.09 (dd, J = 6.8, 2.6 Hz, 1H), 7.97 – 7.89 (m, 1H), 7.85 – 7.75 (m, 3H), 7.57– 7.47 (m, 2H).	DMSO	369.1, 371.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1
33		HCl	359.36	^{1}H-NMR (400 MHz, DMSO-d_6): δ 12.21 (d, J = 12.1 Hz, 1H), 9.53 (d, J = 1.2 Hz, 1H), 8.99 (d, J = 8.1 Hz, 1H), 8.89 (d, J = 4.2 Hz, 1H), 8.71 (d, J = 7.9 Hz, 1H), 8.35 (s, 1H), 7.97 – 7.76 (m, 5H), 7.72 – 7.65 (m, 1H), 7.50 (dd, J = 12.1, 7.5 Hz, 1H), 7.29 (t, J = 7.1 Hz, 1H).	DMSO	360.2 (M+1)	Method B (NH4HCO3)	95	Method C, G1
34			382.34	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.49 (d, J = 1.8 Hz, 1H), 9.42 (s, 1H), 8.71 (dd, J = 4.6, 1.3 Hz, 1H), 8.65 (d, J = 7.8 Hz, 1H), 7.90 (dd, J = 15.6, 9.7 Hz, 2H), 7.73 (dd, J = 19.0, 8.26 Hz, 2H), 7.56 – 7.12 (m, 4H), 7.04 (dd, J = 8.2, 1.8 Hz, 1H).	DMSO	383.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1

201

35		HCl	400.33	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.43 (s, 1H), 9.52 (s, 1H), 8.89 (d, *J* = 8.2 Hz, 1H), 8.85 (d, *J* = 4.2 Hz, 1H), 8.78 (dd, *J* = 9.2, 5.9 Hz, 1H), 8.09 (s, 1H), 7.95 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.80 (dd, *J* = 7.9, 5.2 Hz, 1H), 7.72 – 7.58 (m, 3H), 7.21 (d, *J* = 8.4 Hz, 1H).	DMSO	401.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1
36		HCl	405.84	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.74 – 10.48 (m, 1H), 9.36 (d, *J* = 1.6 Hz, 1H), 8.95 (d, *J* = 8.2 Hz, 1H), 8.89 – 8.85 (m, 1H), 8.06 (d, *J* = 1.7 Hz, 1H), 8.02 (d, *J* = 9.15 Hz, 1H), 7.93 – 7.86 (m, 2H), 7.73 – 7.63 (m, 3H), 7.60 – 7.52 (m, 2H), 3.98 (s, 3H).	DMSO	406.1, 408.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1
37		HCl	359.36	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.61 (s, 1H), 9.00 (dd, *J* = 15.4, 8.2 Hz, 2H), 8.86 (d, *J* = 4.13 Hz, 1H), 8.52 (s, 1H), 8.04 – 7.94 (m, 3H), 7.86 – 7.70 (m, 4H), 7.26 (dd, *J* = 11.2, 4.2 Hz, 1H).	DMSO	360.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1
38		HCl	368.77	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.22 (s, 1H), 9.52 (s, 1H), 8.73 (d, *J* = 3.6 Hz, 1H), 8.69 (td, *J* = 8.0, 1.8 Hz, 1H), 8.38 (d, *J* = 8.4 Hz, 1H), 8.25 (dd, *J* = 6.8, 2.6 Hz, 1H), 7.91 (ddd, *J* = 9.0, 4.2, 2.6 Hz, 1H), 7.79 (dd, *J* = 9.8, 7.9 Hz, 1H), 7.67 (dd, *J* = 8.2, 5.2 Hz, 1H), 7.61 – 7.53 (m, 2H).	DMSO	369.0, 371.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1

202

39		HCl	400.33	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.47 (s, 1H), 9.52 (d, *J* = 1.4 Hz, 1H), 9.04 (d, *J* = 8.0 Hz, 1H), 8.92 (dd, *J* = 5.2, 1.2 Hz, 1H), 8.52 (d, *J* = 8.4 Hz, 1H), 8.07 (s, 1H), 7.97 (d, *J* = 1.2 Hz, 2H), 7.86 – 7.80 (m, 1H), 7.74 – 7.68 (m, 1H), 7.62 (t, *J* = 8.2 Hz, 1H), 7.22 (d, *J* = 8.4 Hz, 1H).	DMSO	401.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1
40			360.34	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.66 (d, *J* = 1.6 Hz, 1H), 8.82 (td, *J* = 7.9, 1.8 Hz, 1H), 8.71 (dd, *J* = 4.6, 1.6 Hz, 1H), 8.22 (d, *J* = 8.2 Hz, 1H), 7.87 (dd, *J* = 7.8, 1.9 Hz, 1H), 7.73 (dd, *J* = 9.2, 7.6 Hz, 1H), 7.59 (dt, *J* = 8.1, 5.0 Hz, 2H), 7.21 – 7.15 (m, 1H), 6.66 (d, *J* = 8.2 Hz, 1H), 6.54 (t, *J* = 7.4 Hz, 1H).	DMSO	360.9 (M+1), 382.9 (M+23)	Method B (NH4HCO3)	95	Method C, G9
41			380.08	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.56 (brs, 1H), 9.62 (d, *J* = 1.2 Hz, 1H), 9.05 (d, *J* = 8.4 Hz, 1H), 9.00 (dd, *J* = 1.6, 4.6 Hz, 1H), 8.71 (d, *J* = 9.2 Hz, 1H), 8.31 (dd, *J* = 2.0, 7.2 Hz, 1H), 8.02 – 7.99 (m, 2H), 7.66 (t, *J* = 9.2 Hz, 1H), 7.54 (s, 1H), 7.50 (dd, *J* = 2.4, 9.2 Hz, 1H), 4.11 (s, 3H).	DMSO	381.1, 383.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1
42			476.67	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.40 (s, 1H), 9.51 (s, 1H), 8.93 (d, *J* = 8.0 Hz, 1H), 8.88 (d, *J* = 4.8 Hz, 1H), 8.40 (d, *J* = 8.8 Hz, 1H), 8.35 (d, *J* = 1.6 Hz, 1H), 8.20 (dd, *J* = 4.4, 6.8 Hz, 1H), 8.04 (dd, *J* = 7.2, 8.8 Hz, 1H), 7.93 – 7.86 (m, 2H), 7.35 (t, *J* = 9.2 Hz, 1H).	DMSO	477.0, 499.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1

203

43			429.67	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.46 (s, 1H), 9.49 (s, 1H), 8.95 (d, *J* = 8.1 Hz, 1H), 8.89 (d, *J* = 4.97 Hz, 1H), 8.60 (d, *J* = 8.9 Hz, 1H), 8.19 (dd, *J* = 6.8, 2.6 Hz, 1H), 8.14 (d, *J* = 1.9 Hz, 1H), 7.96 – 7.83 (m, 3H), 7.53 (t, *J* = 9.0 Hz, 1H).	DMSO	429.0, 430.9, 433.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1
44		HCl	385.42	^{1}H-NMR (400 MHz, DMSO-d_6): δ 13.05 (s, 1H), 9.44 (d, *J* = 1.7 Hz, 1H), 9.16 – 8.91 (m, 2H), 8.03 – 7.89 (m, 3H), 7.88 – 7.82 (m, 1H), 7.75 – 7.68 (m, 1H), 7.67 – 7.60 (m, 2H), 7.25 (t, *J* = 7.6 Hz, 1H), 4.00 (s, 3H), 2.74 (s, 3H).	DMSO	386.0 (M+1) 193.4 (M/2+1)	Method A (TFA)	95	Method C, G1
45		HCl	408.4	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.37 – 10.12 (m, 1H), 9.35 (d, *J* = 1.8 Hz, 1H), 8.95 (dd, *J* = 4.6, 3.4 Hz, 1H), 8.09 (d, *J* = 2.3 Hz, 1H), 7.92 (d, *J* = 9.1 Hz, 1H), 7.87 (s, 1H), 7.84 – 7.74 (m, 2H), 7.62 (dd, *J* = 9.1, 2.6 Hz, 1H), 7.54 (t, *J* = 8.2 Hz, 1H), 7.32 (t, *J* = 74.0 Hz, 1H), 7.05 (dd, *J* = 8.3, 1.9 Hz, 1H), 4.00 (s, 3H), 2.72 (s, 3H).	DMSO	409.0 (M+1) 205.0 (M/2+1)	Method A (TFA)	95	Method C, G1

204

46		HCl	394.83	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.27 (brs, 1H), 9.32 (d, *J* = 1.7 Hz, 1H), 8.93 (d, *J* = 7.5 Hz, 1H), 8.19 (dd, *J* = 6.8, 2.5 Hz, 1H), 8.07 (d, *J* = 2.3 Hz, 1H), 7.88 – 7.92 (m, 2H), 7.84 (d, *J* = 8.1 Hz, 1H), 7.62 (dd, *J* = 9.2, 2.5 Hz, 1H), 7.54 (t, *J* = 9.1 Hz, 1H), 4.00 (s, 3H), 2.72 (s, 3H).	DMSO	395.0, 397.0 (M+1) 197.8, 198.8 (M/2+1)	Method A (TFA)	95	Method C, G1
47		HCl	378.37	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.58 – 10.30 (m, 1H), 9.32 (d, *J* = 1.9 Hz, 1H), 9.04 (d, *J* = 7.9 Hz, 1H), 8.17 – 8.04 (m, 2H), 7.95 (d, *J* = 9.0 Hz, 2H), 7.73 – 7.66 (m, 1H), 7.63 (dd, *J* = 9.2, 2.6 Hz, 1H), 7.60 – 7.50 (m, 1H), 4.01 (s, 3H), 2.76 (s, 3H).	DMSO	379.0 (M+1) 190.0 (M/2+1)	Method A (TFA)	95	Method C, G1
48		HCl	411.28	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.29 (s, 1H), 9.33 (d, *J* = 1.7 Hz, 1H), 9.04 – 8.89 (m, 1H), 8.31 (d, *J* = 2.4 Hz, 1H), 8.07 (d, *J* = 2.4 Hz, 1H), 7.97 (dd, *J* = 8.8, 2.5 Hz, 1H), 7.91 (d, *J* = 9.1 Hz, 1H), 7.85 (d, *J* = 8.6 Hz, 1H), 7.73 (d, *J* = 8.8 Hz, 1H), 7.62 (dd, *J* = 9.1, 2.5 Hz, 1H), 4.00 (s, 3H), 2.73 (s, 3H).	DMSO	411.0, 413.0 (M+1) 205.0, 206.9 (M/2+1)	Method A (TFA)	95	Method C, G1
49			411.28	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.30 (s, 1H), 9.31 (d, *J* = 1.5 Hz, 1H), 8.94 (d, *J* = 7.3 Hz, 1H), 8.13 (d, *J* = 1.7 Hz, 2H), 8.07 (d, *J* = 2.3 Hz, 1H), 7.90 (d, *J* = 9.2 Hz, 1H), 7.87 (d, *J* = 8.5 Hz, 1H), 7.61 (dd, *J* = 9.1, 2.6 Hz, 1H), 7.41 (d, *J* = 1.7 Hz, 1H), 4.00 (s, 3H), 2.72 (s, 3H).	DMSO	411.0, 413.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1

205

50		HCl	389.84	^{1}H-NMR (400 MHz, DMSO-d_6): δ 13.09 (s, 1H), 9.38 (s, 1H), 9.16 (d, *J* = 8.4 Hz, 1H), 8.83 (d, *J* = 8.3 Hz, 1H), 8.50 (s, 1H), 8.20 (d, *J* = 8.8 Hz, 1H), 8.05 – 7.99 (m, 2H), 7.97 (d, *J* = 7.9 Hz, 1H), 7.92 (s, 1H), 7.81 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.68 (t, *J* = 7.8 Hz, 1H), 7.28 (t, *J* = 7.6 Hz, 1H), 2.82 (s, 3H).	DMSO	390.1, 392.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1
51		HCl	412.82	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.49 (s, 1H), 9.35 (d, *J* = 1.7 Hz, 1H), 9.08 (dd, *J* = 8.3, 1.5 Hz, 1H), 8.75 (d, *J* = 9.0 Hz, 1H), 8.02 (d, *J* = 2.1 Hz, 1H), 7.97 (d, *J* = 8.3 Hz, 1H), 7.87 (s, 1H), 7.80 (dd, *J* = 9.0, 2.0 Hz, 2H), 7.53 (t, *J* = 8.2 Hz, 1H), 7.31 (t, *J* = 74.0 Hz, 1H), 7.06 (dd, *J* = 8.1, 2.0 Hz, 1H), 2.79 (s, 3H).	DMSO	413.0, 415.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1
52			399.25	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.49 (s, 1H), 9.32 (d, *J* = 1.7 Hz, 1H), 9.00 (d, *J* = 8.4 Hz, 1H), 8.69 (d, *J* = 8.9 Hz, 1H), 8.20 (dd, *J* = 6.8, 2.6 Hz, 1H), 8.00 (d, *J* = 2.1 Hz, 1H), 7.96 – 7.86 (m, 2H), 7.80 (dd, *J* = 8.9, 2.1 Hz, 1H), 7.53 (t, *J* = 9.1 Hz, 1H), 2.76 (s, 3H).	DMSO	399.0, 401.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1
53		HCl	382.79	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.55 (s, 1H), 9.32 (d, *J* = 1.7 Hz, 1H), 9.07 (dd, *J* = 8.2, 1.2 Hz, 1H), 8.73 (d, *J* = 8.9 Hz, 1H), 8.08 (ddd, *J* = 13.0, 7.5, 2.6 Hz, 1H), 8.00 (dd, *J* = 8.9, 5.2 Hz, 2H), 7.80 (dd, *J* = 8.9, 2.1 Hz, 1H), 7.71 (dd, *J* = 6.1, 2.9 Hz, 1H), 7.54 (dd, *J* = 19.7, 9.2 Hz, 1H), 2.78 (s, 3H)	DMSO	383.0, 385.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1

206

54		HCl	415.7	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.63 (s, 1H), 9.30 (d, *J* = 1.7 Hz, 1H), 9.07 (dd, *J* = 8.3, 1.8 Hz, 1H), 8.75 (d, *J* = 9.0 Hz, 1H), 8.29 (d, *J* = 2.4 Hz, 1H), 8.01 (d, *J* = 8.4 Hz, 1H), 7.99 (d, *J* = 2.1 Hz, 1H), 7.96 (dd, *J* = 8.9, 2.5 Hz, 1H), 7.77 (dd, *J* = 8.9, 2.1 Hz, 1H), 7.70 (d, *J* = 8.8 Hz, 1H), 2.81 (s, 3H).	DMSO	415.0, 417.0, 419.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1
55		HCl	415.7	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.54 (s, 1H), 9.32 (s, 1H), 9.01 (dd, *J* = 8.0, 1.8 Hz, 1H), 8.72 (d, *J* = 9.0 Hz, 1H), 8.11 (d, *J* = 1.8 Hz, 2H), 8.01 (d, *J* = 2.0 Hz, 1H), 7.97 (d, *J* = 8.5 Hz, 1H), 7.80 (dd, *J* = 8.9, 2.0 Hz, 1H), 2.76 (s, 3H).	DMSO	415.0, 417.0, 419.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1
56			379.36	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.16 (s, 1H), 9.47 (s, 1H), 8.79 (dd, *J* = 8.9, 7.1 Hz, 2H), 7.91 (s, 1H), 7.84 – 7.77 (m, 2H), 7.76 – 7.68 (m, 1H), 7.56 (d, *J* = 2.1 Hz, 1H), 7.51 (t, *J* = 8.2 Hz, 1H), 7.39 (dd, *J* = 8.9, 2.2 Hz, 1H), 7.29 (t, *J* = 74.0 Hz, 1H), 7.00 (dd, *J* = 8.1, 2.1 Hz, 1H), 4.23 (brs, 2H).	DMSO	380.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1
57		HCl	463.48	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.43 – 10.20 (m, 2H), 9.72 (s, 1H), 8.89 – 8.67 (m, 3H), 8.29 – 8.21 (m, 1H), 7.97 (s, 1H), 7.87 – 7.80 (m, 1H), 7.81 – 7.73 (m, 1H), 7.63 – 7.46 (m, 2H), 7.30 (t, *J* = 74.0 Hz, 1H), 7.08 – 6.98 (m, 1H), 5.00 (s, 2H), 4.05 – 3.65 (m, 4H), 3.39 – 3.36 (m, 4H).	DMSO	464.2 (M+1)	Method B (NH4HCO3)	95	Method C, G1

207

58		HCl	399 45	^{1}H-NMR (400 MHz, DMSO-d_6) δ 12.53 (s, 1H), 9.30 (d, *J* = 1.6 Hz, 1H), 9.03 – 8.96 (m, 1H), 8.94 – 8.88 (m, 1H), 8.71 (d, *J* = 8.4 Hz, 1H), 7.91 – 7.83 (m, 3H), 7.67 – 7.55 (m, 3H), 7.25 (t, *J* = 7.2 Hz, 1H), 3.98 (s, 3H), 2.80 – 2.74 (m, 6H).	DMSO	400.1 (M+1)	Method B (NH4HCO3)	95	Method D, G1
59		HCl	389.38	^{1}H-NMR (400 MHz, DMSO-d_6): δ 13.27 (s, 1H), 9.23 (s, 1H), 8.98 (d, *J* = 5.2 Hz, 1H), 8.91 (d, *J* = 8.0 Hz, 1H), 8.54 (dd, *J* = 12.0, 2.6 Hz, 1H), 8.48 (s, 1H), 8.07 (dd, *J* = 8.0, 5.6 Hz, 1H), 7.97 – 7.93 (m, 2H), 7.66 (d, *J* = 9.0 Hz, 1H), 7.37 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.13 (d, *J* = 2.0 Hz, 1H), 6.91 (dt, *J* = 8.4, 2.6 Hz, 1H), 3.80 (s, 3H).	DMSO	390.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1
60			415.70	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.13 (s, 1H), 9.48 (s, 1H), 8.87 (dd, *J* = 14.0, 6.2 Hz, 2H), 8.54 (d, *J* = 1.7 Hz, 1H), 8.10 (d, *J* = 1.8 Hz, 2H), 7.89 – 7.76 (m, 2H), 7.37 (t, *J* = 1.8 Hz, 1H), 2.70 (s, 3H).	DMSO	414.9, 416.9, 419.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1

208

61			415.70	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.10 (s, 1H), 9.44 (s, 1H), 8.86 (d, *J* = 7.8 Hz, 1H), 8.79 (d, *J* = 4.5 Hz, 1H), 8.50 (d, *J* = 1.7 Hz, 1H), 8.23 (d, *J* = 2.4 Hz, 1H), 7.89 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.83 – 7.71 (m, 2H), 7.62 (d, *J* = 8.8 Hz, 1H), 2.62 (s, 3H)	DMSO	414.9, 416.9, 418.9 (M+1)	Method B (NH4HCO3)	95	Method C, G1
62			412.82	^{1}H-NMR (400 MHz, DMSO-d_6): δ:10.02 (s, 1H), 9.58 (d, *J* = 1.8 Hz, 1H), 8.76 – 8.67 (m, 2H), 8.59 (d, *J* = 1.8 Hz, 1H), 7.96 (s, 1H), 7.82 (d, *J* = 6.6 Hz, 2H), 7.54 (ddd, *J* = 16.4, 10.0, 6.4 Hz, 2H), 7.30 (t, *J* = 74.0 Hz, 1H), 7.01 (dd, *J* = 8.0, 2.0 Hz, 1H), 2.74 (s, 3H).	DMSO	413.0, 415.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1
63			389.84	^{1}H-NMR (400 MHz, DMSO-d_6): δ 13.15 (s, 1H), 9.58 (s, 1H), 9.03 (d, *J* = 0.8 Hz, 1H), 8.76 – 8.84 (m, 2H), 8.50 (s, 1H), 7.95 – 8.03 (m, 3H), 7.80 (s, 1H), 7.70 – 7.74 (m, 2H), 7.23 (d, *J* = 7.2 Hz, 1H), 2.70 (s, 3H).	DMSO	391.0, 392.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1
64			371.82	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.31 (s, 1H), 9.48 (d, *J* = 1.2 Hz, 1H), 9.01 (d, *J* = 8.4 Hz, 1H), 8.90 (d, *J* = 4.0 Hz, 1H), 8.61 (d, *J* = 1.6 Hz, 1H), 8.33 (s, 1H), 8.27 (dd, *J* = 6.0, 2.0 Hz, 1H), 7.95 – 7.63 (m, 3H), 2.70 (s, 3H).	DMSO	372.0 373.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1

209

65			476.67	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.28 (s, 1H), 9.46 (d, *J* = 1.2 Hz, 1H), 9.01 (d, *J* = 1.2 Hz, 1H), 8.83 (dd, *J* = 8.4, 1.6 Hz, 2H), 8.19 – 8.14 (m, 2H), 7.89 – 7.49 (m, 2H).	DMSO	476.9, 478.9 (M+1)	Method B (NH4HCO3)	95	Method C, G1
66			399.25	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.03 (s, 1H), 8.54 (s, 1H), 8.71 – 8.67 (m, 2H), 8.53 (s, 1H), 8.26 (dd, *J* = 6.8 Hz, 2.4 Hz, 1H), 7.83 (s, 1H), 7.58 – 7.52 (m, 2H), 2.72 (s, 3H).	DMSO	399.0, 401.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1
67			382.79	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.04 (s, 1H), 9.51 (d, *J* = 1.2 Hz, 1H), 8.72 – 8.69 (m, 2H), 8.53 (d, *J* = 2.0 Hz, 1H), 8.08 (ddd, *J* = 9.2, 7.6, 2.4 Hz, 1H), 7.79 – 7.48 (m, 4H), 2.69 (s, 3H).	DMSO	383.0, 385.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1
68		HCl	399.45	^{1}H-NMR (400 MHz, DMSO-d6): δ 13.02 (s, 1H), 9.59 (s, 1H) , 9.09 (d, *J* = 8.0 Hz, 1H) , 8.96 (d, *J* = 8.4 Hz, 1H) , 8.91 (d, *J* = 4.61 Hz, 1H) , 8.48 (s, 1H), 7.97 (dd, *J* = 8.0, 2.8 Hz, 4H), 7.72 (t, *J* = 7.6 Hz, 1H), 7.64 – 7.61 (m, 2H), 7.26 (t, *J* = 7.6 Hz, 1H), 4.88 – 4.82 (m, 1H), 1.43 (d, *J* = 6.0 Hz, 6H).	DMSO	400.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1

210

69		HCl	422.43	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.63 (s, 1H), 9.51 (s, 1H), 9.09 (d, *J* = 7.6 Hz, 1H), 8.91 (d, *J* = 7.6 Hz, 1H), 8.23 (s, 1H), 8.03 – 7.97 (m, 1H), 7.83 – 7.80 (m, 2H), 7.64 (dd, *J* = 9.2, 2.4 Hz, 1H), 7.55 (t, *J* = 8.1 Hz, 1H), 7.32 (t, *J* = 74.0 Hz, 1H), 7.08 (d, *J* = 7.4 Hz, 1H), 5.02 – 4.97 (m, 1H), 1.39 (d, *J* = 6.0 Hz, 6H).	DMSO	423.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1
70		HCl	408.86	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.61 (s, 1H), 9.48 (s, 1H), 9.05 (d, *J* = 7.2 Hz, 1H), 8.93 (d, *J* = 5.2 Hz, 1H), 8.19 – 8.15 (m, 2H), 8.01 – 7.92 (m, 3H), 7.63 – 7.53 (m, 2H), 5.01 – 4.94 (m, 1H), 1.39 (d, *J* = 6.0 Hz, 6H).	DMSO	409.1, 411.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1
71		HCl	425.31	^{1}H NMR (400 MHz, DMSO-d_6): δ 9.92 (s, 1H), 9.52 (d, *J* = 1.2 Hz, 1H), 8.70 – 8.66 (m, 2H), 8.17 (d, *J* = 1.6 Hz, 2H), 7.98 (d, *J* = 2.4 Hz, 1H), 7.88 (d, *J* = 8.8 Hz, 1H), 7.60 – 7.56 (m, 2H), 7.39 (t, *J* = 1.8 Hz, 1H), 4.94 – 4.88 (m, 1H), 1.39 (d, *J* = 6.0 Hz, 6H).	DMSO	424.9, 426.9 (M+1)	Method B (NH4HCO3)	95	Method C, G1
72		HCl	392.4	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.28 (s, 1H), 9.49 (d, *J* = 1.2 Hz, 1H), 8.93 (d, *J* = 8.0 Hz, 1H), 8.86 – 8.84 (m, 1H), 8.10 – 8.05 (m, 2H), 7.93 – 7.85 (m, 2H), 7.71 – 7.69 (m, 2H), 7.61 – 7.52 (m, 1H), 4.97 – 4.91 (m, 1H), 1.39 (d, *J* = 6.0 Hz, 6H).	DMSO	393.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1

211

73		HCl	385.42	^{1}H-NMR (400 MHz, DMSO-d_6): δ 13.03 (s, 1H), 9.53 (d, *J* = 1.2 Hz, 1H), 9.10 (d, *J* = 8.4 Hz, 1H), 8.93 – 8.90 (m, 2H), 8.49 (s, 1H), 8.01 – 7.91 (m, 4H), 7.69 (t, *J* = 7.6 Hz, 1H), 7.59 – 7.54 (m, 2H), 7.24 (t, *J* = 7.6 Hz, 1H), 4.21 (q, *J* = 6.8 Hz, 2H), 1.46 (t, *J* = 6.9 Hz, 3H).	DMSO	386.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1
74		HCl	367.4	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.35 (s, 1H), 9.49 (s, 1H), 8.95 (d, *J* = 7.6 Hz, 1H), 8.85 (d, *J* = 4.8 Hz, 1H), 8.37 (s, 1H), 8.28 (d, *J* = 7.6 Hz, 1H), 8.08 (s, 1H), 7.94 – 7.85 (m, 2H), 7.73 – 7.60 (m, 3H), 4.28 (q, *J* = 6.8 Hz, 2H), 1.46 (t, *J* = 6.8 Hz, 3H).	DMSO	368.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1
75		HCl	394.83	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.64 (s, 1H), 9.44 (s, 1H), 8.99 (d, *J* = 8.4 Hz, 1H), 8.91 (d, *J* = 4.4 Hz, 1H), 8.17 (d, *J* = 3.2 Hz, 2H), 7.59 – 7.50 (m, 2H), 4.26 (q, *J* = 6.8 Hz, 2H), 1.44 (t, *J* = 6.8 Hz, 3H).	DMSO	395.1 397.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1
76		HCl	411.28	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.48 (s, 1H), 9.47 (s, 1H), 9.02 (d, *J* = 7.6 Hz, 1H), 8.91 (d, *J* = 4.4 Hz, 1H), 8.28 (d, *J* = 1.6 Hz, 1H), 8.13 (s, 1H), 8.01 – 7.91 (m, 3H), 7.72 (d, *J* = 8.8 Hz, 1H), 7.59 – 7.57 (m, 1H), 4.26 (q, *J* = 6.8 Hz, 2H), 1.44 (t, *J* = 6.8 Hz, 3H).	DMSO	411.0 413.0 415.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1

212

77		HCl	411.28	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.23 (s, 1H), 9.48 (s, 1H), 8.93 (d, *J* = 8.0 Hz, 1H), 8.85 (d, *J* = 4.8 Hz, 1H), 8.14 (s, 2H), 8.05 (d, *J* = 1.6 Hz, 1H), 7.92 – 7.85 (m, 2H), 7.61 (dd, *J* = 9.1, 1.8 Hz, 1H), 7.41 (s, 1H), 4.26 (q, *J* = 6.8 Hz, 2H), 1.45 (t, *J* = 6.8 Hz, 3H).	DMSO	411.0 413.1 415.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1
78		HCl	378.37	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.39 (s, 1H), 9.49 (s, 1H), 8.98 (d, *J* = 8.0 Hz, 1H), 8.68 (d, *J* = 4.8 Hz, 1H), 8.11 – 8.05 (m, 2H), 7.95 – 7.91 (m, 2H), 7.72 – 7.52 (m, 3H), 4.28 (q, *J* = 6.8 Hz, 2H), 1.45 (t, *J* = 6.8 Hz, 3H).	DMSO	379.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1
79		HCl	429.47	^{1}H-NMR (400 MHz, DMSO-d_6): δ 12.99 (s, 1H), 9.59 (d, *J* = 1.6 Hz, 1H), 9.14 (d, *J* = 7.6 Hz, 1H), 8.75 – 8.69 (m, 2H), 8.46 (s, 1H), 7.99 – 7.96 (m, 2H), 7.90 (d, *J* = 8.8 Hz,, 1H), 7.76 – 7.72 (m, 1H), 7.61 – 7.56 (m, 3H), 7.22 – 7.19 (m, 1H), 4.24 (t, *J* = 6.0 Hz, 2H), 3.56 (t, *J* = 6.0 Hz, 2H), 3.28 (s, 3H), 2.11 – 2.04 (m, 2H).	DMSO	430.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1
80		HCl	380.80	^{1}H-NMR (400 MHz, DMSO-d_6): δ 11.67 (s, 1H), 9.18 (d, *J* = 2.0 Hz, 1H), 8.90 (d, *J* = 8.4 Hz, 1H), 8.66 (dd, *J* = 8.8, 2.4 Hz, 1H), 8.35 (d, *J* = 8.4 Hz, 1H), 8.14 – 8.08 (m, 2H), 7.90 – 7.81 (m, 2H), 7.62 (t, *J* = 9.2 Hz, 1H), 7.09 (d, *J* = 8.8 Hz, 1H), 3.98 (s, 3H).	DMSO	380.9, 382.9 (M+1)	Method A (TFA)	95	Method C, G1

81		HCl	394.79	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.81 (s, 1H), 9.49 (d, *J* = 1.2 Hz, 1H), 9.28 (d, *J* = 0.8 Hz, 1H), 9.15 (d, *J* = 8.0 Hz, 1H), 9.02 (d, *J* = 5.2 Hz, 1H), 8.37 – 8.34 (m, 1H), 8.12 – 8.09 (m, 2H), 8.01 (d, *J* = 8.4 Hz, 1H), 7.95 – 7.91 (m, 1H), 7.53 (t, *J* = 9.0 Hz, 1H).	DMSO	395.0, 397.0 (M+1)	Method B (NH_4HCO_3)	95	Method C, G1
82			385.39	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.63 (d, *J* = 1.6 Hz, 1H), 9.13 (s, 1H), 8.80 – 8.75 (m, 2H), 8.21 (d, *J* = 9.2 Hz, 1H), 7.97 – 7.94 (m, 1H), 7.82 (dd, *J* = 9.2, 2.8 Hz, 1H), 7.73 (dd, *J* = 9.2, 2.4 Hz, 1H), 7.64 – 7.61 (m, 1H), 7.38 – 7.32 (m, 2H), 4.18 (q, *J* = 6.8 Hz, 2H), 3.19 (t, *J* = 7.0 Hz, 3H).	DMSO	386.1 (M+1)	Method B (NH_4HCO_3)	95	Method C, G10
83		HCl	426.39	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.43 (s, 1H), 9.49 (d, *J* = 1.6 Hz, 1H), 8.99 (d, *J* = 8.0 Hz, 1H), 8.89 (dd, *J* = 9.2, 1.6 Hz, 1H), 8.13 (d, *J* = 2.4 Hz, 1H), 8.05 (s 1H), 7.97 – 7.89 (m, 3H), 7.65 – 7.61 (m, 2H), 7.23 (d, *J* = 8.4 Hz, 1H), 4.29 (q, *J* = 6.8 Hz, 2H), 1.46 (t, *J* =7.2 Hz, 3H).	DMSO	427.1 (M+1)	Method B (NH_4HCO_3)	95	Method C, G1
84			426.47	^{1}H-NMR (400 MHz, DMSO-d_6): δ 12.00 (s, 1H), 9.55 (s, 1H), 9.12 (d, *J* = 8.0 Hz, 1H), 8.94 (d, *J* = 4.8 Hz, 1H), 8.84 (d, *J* = 8.4 Hz, 1H), 8.11 – 8.09 (m, 1H), 8.02 – 7.99 (m, 1H), 7.96 (d, *J* = 9.2 Hz, 1H), 7.82 – 7.11 (m, 1H), 7.65 (s, 1H), 7.62 – 7.59 (m, 1H), 7.30 (t, *J* = 7.2, Hz, 1H), 5.06 – 5.03 (m, 1H), 2.15 – 2.09 (m, 2H), 1.86 – 1.74 (m, 4H), 1.68 – 1.65 (m, 2H)	DMSO	427.0 (M+1)	Method B (NH_4HCO_3)	95	Method C, G1

214

85			375.81	1H-NMR (400 MHz, DMSO-d6): δ 13.09 (s, 1H), 9.58 (s, 1H), 9.12 (d, *J* = 8.4 Hz, 1H), 8.94 (d, *J* = 4.4 Hz, 1H), 8.88 (d, *J* = 8.4 Hz, 1H), 8.50 (s, 1H), 8.25 (s, 1H), 8.01 – 7.96 (m, 5H), 7.71 (t, *J* = 8.0 Hz, 1H), 7.27 (t, *J* = 8.0 Hz, 1H).	DMSO	376.0, 378.0 (M+1) 397.9 (M+23) 188.4 (M/2+1)	Method A (TFA)	95	Method C, G1
86			398.79	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.10 (s, 1H), 9.54 (s, 1H), 8.78 (s, 1H), 8.71 – 8.67 (m, 2H), 7.96 (s, 1H), 7.91 (d, *J* = 8.0 Hz, 2H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.56 – 7.51 (m, 2H), 7.30 (t, *J* = 74.0 Hz, 1H), 7.01 (dd, *J* = 2.0, 8.0 Hz, 1H).	DMSO	399.0, 401.0 (M+1) 199.9, 200.8 (M/2+1)	Method A (TFA)	95	Method C, G1
87			443.7	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.09 (s, 1H), 9.39 (s, 1H), 8.93 (d, *J* = 8.4 Hz, 1H), 8.90 (d, *J* = 5.6 Hz, 1H), 8.62 (d, *J* = 1.6 Hz, 1H), 8.11 (dd, *J* = 6.8, 2.4 Hz, 1H), 7.95 – 7.91 (m, 1H), 7.89 – 7.85 (m, 1H), 7.80 (s, 1H), 7.45 (t, *J* = 8.8 Hz, 1H), 2.66 (s, 3H).	DMSO	443.0, 445.0, 447.0 (M+1)	Method B (NH_4HCO_3)	98	Method C, G1

215

88			401.42	^{1}H-NMR (400 MHz, DMSO-d_6): δ 13.19 (s, 1H), 9.43 (d, *J* = 8.0 Hz, 1H), 8.53 (s, 1H), 8.31 (dd, *J* = 4.8, 1.6 Hz, 1H), 8.26 (dd, *J* = 1.6, 7.2 Hz, 1H), 8.03 (s, 1H), 7.96 – 7.89 (m, 1H), 7.86 (d, *J* = 9.2 Hz, 1H), 7.65 – 7.54 (m, 3H), 7.18 – 7.12 (m, 2H), 4.02 (s, 3H), 3.98 (s, 3H).	DMSO	402.1 (M+1)	Method B (NH_4HCO_3)	95	Method C, G1
89			410.83	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.79 (s, 1H), 8.52 (dd, *J* = 2.4, 7.2 Hz, 1H), 8.28 (dd, *J* = 5.6, 2.4 Hz, 1H), 8.12 (dd, *J* = 2.4, 5.2 Hz, 1H), 7.98 – 7.94 (m, 2H), 7.82 (d, *J* = 9.2 Hz, 1H), 7.56 (dd, *J* = 9.2, 2.8 Hz, 1H), 7.47 (t, *J* = 9.2 Hz, 1H), 7.14 – 7.11 (m, 1H), 4.00 (s, 3H), 3.99 (s, 3H).	DMSO	411.1, 413.1 (M+1)	Method B (NH_4HCO_3)	95	Method C, G1
90			415.44	^{1}H-NMR (400 MHz, DMSO-d_6): δ 13.03 (s, 1H), 9.21 (d, *J* = 2.2 Hz, 1H), 9.16 (d, *J* = 7.9 Hz, 1H), 8.67 (dd, *J* = 8.7, 2.4 Hz, 1H), 8.50 (s, 1H), 8.02 (s, 1H), 7.99 – 7.93 (m, 1H), 7.84 (d, *J* = 8.9 Hz, 1H), 7.78 – 7.72 (m, 1H), 7.56 (dd, *J* = 11.2, 2.1 Hz, 2H), 7.19 (t, *J* = 7.2 Hz, 1H), 6.99 (d, *J* = 8.8 Hz, 1H), 4.24 (q, *J* = 6.9 Hz, 2H), 3.96 (s, 3H), 1.46 (t, *J* = 6.9 Hz, 3H).	DMSO	416.1 (M+1)	Method B (NH_4HCO_3)	95	Method D, G1

216

91		HCl	405.84	^{1}H-NMR (400 MHz, DMSO-d_6): δ 13.28 (s, 1H), 9.55 (d, *J* = 1.7 Hz, 1H), 9.31 (d, *J* = 2.1 Hz, 1H), 8.90 (d, *J* = 8.3 Hz, 1H), 8.83 (dd, *J* = 5.0, 1.4 Hz, 1H), 8.58 (s, 1H), 8.12 (s, 1H), 8.01 (d, *J* = 8.6 Hz, 1H), 7.93 (d, *J* = 9.1 Hz, 1H), 7.82 (dd, *J* = 7.9, 5.0 Hz, 1H), 7.63 (dd, *J* = 9.1, 2.6 Hz, 1H), 7.54 (d, *J* = 2.5 Hz, 1H), 7.30 (dd, *J* = 8.5, 2.2 Hz, 1H), 3.98 (s, 3H).	DMSO	406.0, 408.0 (M+1)	Method A (TFA)	95	Method C, G2
92			429.47	^{1}H-NMR (400 MHz, DMSO-d_6): δ 12.99 (s, 1H), 9.21 (d, *J* = 2.0 Hz, 1H), 9.14 (d, *J* = 8.4 Hz, 1H), 8.67 (dd, *J* = 8.7, 2.3 Hz, 1H), 8.49 (s, 1H), 8.05 – 7.90 (m, 2H), 7.85 (d, *J* = 9.0 Hz, 1H), 7.75 (t, *J* = 7.2 Hz, 1H), 7.67 – 7.47 (m, 2H), 7.20 (t, *J* = 7.5 Hz, 1H), 6.99 (d, *J* = 8.8 Hz, 1H), 4.15 (t, *J* = 6.3 Hz, 2H), 3.96 (s, 3H), 1.07 (t, *J* = 7.4 Hz, 3H), 1.86 (dd, *J* = 14.0, 6.7 Hz, 2H).	DMSO	430.1 (M+1)	Method B (NH_4HCO_3)	95	Method D, G1
93		HCl	389.36	^{1}H-NMR (400 MHz, DMSO-d_6): δ 11.34 (s, 1H), 9.52 (d, *J* = 1.7 Hz, 1H), 8.99 (d, *J* = 7.8 Hz, 1H), 8.85 (dd, *J* = 5.2, 1.3 Hz, 1H), 8.22 (d, *J* = 8.1 Hz, 1H), 8.11 – 8.00 (m, 2H), 7.95 (d, *J* = 9.1 Hz, 1H), 7.87 (dd, *J* = 7.9, 5.3 Hz, 1H), 7.77 – 7.59 (m, 3H), 7.27 – 7.16 (m, 1H), 3.99 (s, 3H).	DMSO	390.1 (M+1)	Method B (NH_4HCO_3)	95	Method C, G3

217

94			436 29	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.62 (s, 1H), 9.17 (s, 1H), 8.77 (d, *J* = 8.0 Hz, 1H), 8.76 (d, *J* = 4.0 Hz, 1H), 8.26 – 8.07 (m, 3H), 7.83 (dd, *J* = 9.1, 2.5 Hz, 1H), 7.63 (dd, *J* = 7.5, 5.0 Hz, 1H), 7.36 (d, *J* = 2.4 Hz, 1H), 4.18 (q, *J* = 6.8 Hz, 2H), 1.39 (t, *J* = 6.9 Hz, 3H).	DMSO	436.1, 438.0 (M+1)	Method B (NH_4HCO_3)	95	Method C, G10
95			405 84	^{1}H-NMR (400 MHz, DMSO-d_6): δ 12.93 (s, 1H), 9.58 (s, 1H), 9.16 (d, *J* = 9.0 Hz, 1H), 8.70 – 8.74 (m, 2H), 8.59 (s, 1H), 8.13 (s, 1H), 8.05 (d, *J* = 2.3 Hz, 1H), 7.92 (d, *J* = 9.1 Hz, 1H), 7.82 (dd, *J* = 8.9, 2.1 Hz, 1H), 7.65 – 7.49 (m, 3H), 3.98 (s, 3H).	DMSO	406.1, 408.0 (M+1)	Method B (NH_4HCO_3)	95	Method C,G3
96			429.67	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.45 (s, 1H), 9.47 (s, 1H), 9.02 – 8.92 (m, 3H), 8.18 – 8.16 (m, 1H), 8.06 – 8.04 (m, 1H), 7.96 – 7.84 (m, 3H), 7.54 – 7.50 (m, 1H).	DMSO	429.9, 431.0, 433.0 (M+1)	Method B (NH_4HCO_3)	95	Method C,G1
97			398 79	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.25 (s, 1H), 9.58 (s, 1H), 8.85 – 8.76 (m, 2H), 8.60 (d, *J* = 7.2 Hz, 1H), 8.12 – 8.10 (m, 1H), 7.92 (s, 1H), 7.83 – 7.80 (m, 1H), 7.71 – 7.64 (m, 2H), 7.56 – 7.52 (m, 1H), 7.30 (t, *J* = 74.0 Hz, 1H), 7.05 – 7.03 (m, 1H).	DMSO	399.0, 401.0 (M+1)	Method B (NH_4HCO_3)	95	Method C,G1

218

98			385.22	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.47 (s, 1H), 9.50 (s, 1H), 9.04 (d, *J* = 8.0 Hz, 1H), 8.93 (d, *J* = 5.2 Hz, 2H), 8.64 (d, *J* = 8.8 Hz, 1H), 8.20 – 8.18 (m, 1H), 8.11 (d, *J* = 8.4 Hz, 1H), 7.97 – 7.92 (m, 2H), 7.68 – 7.64 (m, 1H), 7.53 (t, *J* = 9.2 Hz, 1H).	DMSO	385.0, 386.9 (M+1)	Method B (NH_4HCO_3)	95	Method C,G1
99			401.68	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.42 (s, 1H), 9.55 (d, *J* = 1.6 Hz, 1H), 8.96 (d, *J* = 4.0 Hz, 1H), 8.88 – 8.87 (m, 1H), 8.61 (d, *J* = 7.6 Hz, 1H), 8.32 (d, *J* = 2.4 Hz, 1H), 8.14 – 8.12 (m, 1H), 7.99 – 7.95 (m, 1H), 7.88 (dd, *J* = 8.0, 5.2 Hz, 1H), 7.74 (d, *J* = 8.8 Hz, 1H), 7.70 – 7.67 (m, 1H).	DMSO	400.9, 402.9, 404.9 (M+1)	Method B (NH_4HCO_3)	95	Method C,G1
100			368.77	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.47 (s, 1H), 9.51 (d, *J* = 1.2 Hz, 1H), 9.04 (d, *J* = 8.0 Hz, 1H), 8.92 (d, *J* = 5.6 Hz, 1H), 8.65 (d, *J* = 8.0 Hz, 1H), 8.11 – 8.05 (m, 2H), 7.97 (dd, *J* = 8.0, 4.0 Hz, 1H), 7.75 – 7.73 (m, 1H), 7.66 (t, *J* = 8.0 Hz, 1H), 7.58 – 7.51 (m, 1H).	DMSO	369.0, 371.0 (M+1)	Method B (NH_4HCO_3)	95	Method C,G1

219

101			375.09	^{1}H-NMR (400 MHz, DMSO-d_6): δ 13.18 (s, 1H), 9.61 (s, 1H), 9.02 (d, *J* = 8.4 Hz, 1H), 8.93 (d, *J* = 8.4 Hz, 1H), 8.83 (d, *J* = 4.0 Hz, 1H), 8.52 (s, 1H), 8.16 – 8.08 (m, 2H), 7.98 – 7.94 (m, 2H), 7.80 – 7.67 (m, 3H), 7.26 (t, *J* = 7.6 Hz, 1H).	DMSO	376.0, 378.0 (M+1)	Method B (NH_4HCO_3)	95	Method C,G1
102			401.68	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.47 (s, 1H), 9.49 (d, *J* = 2.0 Hz, 1H), 9.00 – 8.98 (m, 1H), 8.91 (dd, *J* = 5.2, 1.6 Hz, 1H), 8.64 – 8.62 (m, 1H), 8.12 – 8.09 (m, 3H), 7.94 (dd, *J* = 8.0, 5.2 Hz, 1H), 7.67 (t, *J* = 8.0 Hz, 1H), 7.41 (t, *J* = 2.0 Hz, 1H).	DMSO	400.9, 402.9, 404.9 (M+1)	Method B (NH_4HCO_3)	95	Method C,G1
103			434.77	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.17 (d, *J* = 1.2 Hz, 1H), 9.51 (s, 1H), 8.71 – 8.62 (m, 3H), 8.25 – 8.22 (m, 1H), 8.04 – 8.00 (m, 1H), 7.92 – 7.87 (m, 2H), 7.58 – 7.53 (m, 2H).	DMSO	435.1, 437.1 (M+1)	Method B (NH_4HCO_3)	95	Method C,G1
104			448.35	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.16 (s, 1H), 9.55 (d, *J* = 1.2 Hz, 1H), 8.72 – 8.68 (m, 3H), 8.05 (d, *J* = 9.2 Hz, 1H), 7.92 – 7.95 (m, 2H), 7.80 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.57 – 7.53 (m, 2H), 7.31 (t, *J* = 74.4 Hz, 1H), 7.03 (dd, *J* = 8.0, 1.2 Hz, 1H).	DMSO	449.1 (M+1)	Method B (NH_4HCO_3)	95	Method C,G1

220

105			425.36	^{1}H-NMR (400 MHz, DMSO-d_6): δ 13.24 (s, 1H), 9.59 (s, 1H), 9.06 (d, *J* = 8.0 Hz, 1H), 8.74 – 8.73 (m, 2H), 8.54 (s, 1H), 8.10 – 7.91 (m, 5H), 7.77 – 7.73 (m, 1H), 7.61 – 7.58 (m, 1H), 7.26 (t, *J* = 7.6 Hz, 1H).	DMSO	426.1 (M+1)	Method B (NH_4HCO_3)	95	Method C,G1
106			448.35	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.23 (s, 1H), 9.55 (d, *J* = 1.6 Hz, 1H), 8.76 (d, *J* = 9.1 Hz, 1H), 8.74 – 8.67 (m, 2H), 7.94 (t, *J* = 2.0 Hz, 1H), 7.82 – 7.78 (m, *J* = 10.3 Hz, 2H), 7.68 (dd, *J* = 9.0, 1.8 Hz, 1H), 7.59 – 7.50 (m, 2H), 7.30 (t, *J* = 74.0 Hz, 1H), 7.03 (dd, *J* = 8.2, 2.2 Hz, 1H).	DMSO	449.0 (M+1) 225.0 (M/2+1)	Method A (TFA)	95	Method C,G1
107			425.36	^{1}H-NMR (400 MHz, DMSO-d_6): δ 13.17 (s, 1H), 9.59 (s, 1H), 9.04 (d, *J* = 8.0 Hz, 1H), 8.74 – 8.70 (m,2H), 8.51 (s, 1H), 8.30 (d, *J* = 9.0 Hz, 1H), 8.02 – 7.90 (m, 2H), 7.86 – 7.69 (m, 3H), 7.65 – 7.56 (m, 1H), 7.25 (t, *J* = 9.8 Hz, 1H).	DMSO	426.0 (M+1)	Method B (NH4HCO3)	95	Method C,G1
108			434.77	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.26 (s, 1H), 9.52 (s, 1H), 8.81 – 8.59 (m, 3H), 8.24 (dd, *J* = 6.9, 2.5 Hz, 1H), 7.89 – 7.52 (m, 1H), 7.79 (s, 1H), 7.70 (d, *J* = 9.1 Hz, 1H), 7.65 – 7.50 (m, 2H).	DMSO	435.0, 437.0 (M+1) 218.1 (M/2+1)	Method A (TFA)	95	Method C,G1

221

109			455.39	^{1}H-NMR (400 MHz, DMSO-d_6): δ 13.35 (s, 1H), 9.58 (s, 1H), 9.27 (s, 1H), 8.83 – 8.70 (m, 2H), 8.62 (s, 1H), 8.18 (s, 1H), 8.11 (d, *J* = 8.8 Hz, 1H), 7.92 (d, *J* = 9.1 Hz, 1H), 7.68 – 7.58 (m, 2H), 7.54 (d, *J* = 2.5 Hz, 1H), 7.19 (dd, *J* = 8.4, 2.17 Hz, 1H), 3.98 (s, 3H).	DMSO	456.0 (M+1) 228.5 (M/2+1)	Method A (TFA)	95	Method C, J1
110			425.48	^{1}H-NMR (400 MHz, DMSO-d_6): δ 13.08 (s, 1H), 9.59 (s, 1H), 9.07 (d, *J* = 7.6 Hz, 1H), 9.02 (d, *J* = 8.0 Hz, 1H), 8.89 (d, *J* = 4.0 Hz, 1H), 8.50 (s, 1H), 7.92 – 7.99 (m, 4H), 7.73 (t, *J* = 7.6 Hz, 1H), 7.59 – 7.60 (m, 2H), 7.25 (t, *J* = 7.6 Hz, 1H), 2.12 – 2.15 (m, 2H), 5.02 – 5.03 (m, 1H), 1.67 – 1.86 (m, 6H).	DMSO	426.1 (M+1)	Method B (NH4HCO3)	95	Method C,G1
111			448.46	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.26 (s, 1H), 9.50 (d, *J* = 1.6 Hz, 1H), 8.95 (d, *J* = 7.2 Hz, 1H), 8.55 (d, *J* = 4.4 Hz, 1H), 8.08 (s, 1H), 7.94 (d, *J* = 8.8 Hz, 1H), 7.85 (d, *J* = 9.6 Hz, 2H), 7.79 (d, *J* = 8.8 Hz, 1H), 7.60 – 7.63 (m, 1H), 7.55 (t, *J* = 8.0 Hz, 1H), 7.31 (t, *J* = 74.0 Hz, 1H), 7.05 (d, *J* = 8.4 Hz, 1H), 5.14 (s, 1H), 2.03 – 2.09 (m, 2H), 1.61 – 1.81 (m, 6H).	DMSO	449.0 (M+1)	Method B (NH4HCO3)	95	Method C,G1

222

112			434.89	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.47 (s, 1H), 9.47 (s, 1H), 8.97 (d, *J* = 7.6 Hz, 1H), 8.89 (d, *J* = 4.4 Hz, 1H), 8.16 – 8.19 (m, 1H), 7.53 – 7.61 (m, 2H), 8.10 (s, 1H), 7.90 – 7.96 (m, 3H), 5.15 (s, 1H), 2.09 – 2.10 (m, 2H), 1.67 – 1.78 (m, 6H).	DMSO	435.0, 437.0 (M+1)	Method B (NH4HCO3)	95	Method C,G1
113			451.35	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.23 (s, 1H), 9.49 (s, 1H), 8.85 (d, *J* = 7.6 Hz, 1H), 8.80 (d, *J* = 4.0 Hz, 1H), 8.32 (s, 1H), 8.03 (s, 1H), 7.97 – 7.99 (m, 1H), 7.88 (d, *J* = 8.8 Hz, 1H), 7.77 – 7.79 (m, 1H), 7.75 (d, *J* = 8.8 Hz, 1H), 7.55 – 7.58 (m, 1H), 5.13 (s, 1H), 2.08 (d, *J* = 8.4 Hz, 2H), 1.79 (d, *J* = 9.6 Hz, 4H).	DMSO	451.0, 453.0 (M+1)	Method B (NH4HCO3)	95	Method C,G1
114			418.44	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.24 (s, 1H), 9.49 (s, 1H), 8.92 (d, *J* = 6.0 Hz, 1H), 8.40 (d, *J* = 6.4 Hz, 1H), 8.04 – 8.11 (m, 2H), 7.92 (d, *J* = 9.2 Hz, 1H), 7.84 – 7.91 (m, 1H), 7.69 – 7.71 (m, 1H), 7.52 – 7.61 (m, 2H), 5.13 (s, 1H), 2.06 – 2.11 (m, 2H), 1.65 – 1.81 (m, 6H).	DMSO	419.0 (M+1)	Method B (NH4HCO3)	95	Method C,G1
115			407.47	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.70 (s, 1H), 9.45 (s, 1H), 8.98 (d, *J* = 6.8 Hz, 1H), 8.89 (d, *J* = 6.0 Hz, 1H), 8.37 (s, 1H), 8.32 (d, *J* = 6.8 Hz, 1H), 8.18 (s, 1H), 7.93 (t, *J* = 9.2 Hz, 2H), 7.70 (t, *J* = 7.2 Hz, 2H), 7.56 (d, *J* = 8.8 Hz, 1H), 5.18 (s, 1H), 2.09 (s, 2H), 1.77 (m, 4H), 1.66 (m, 2H).	DMSO	408.0 (M+1)	Method B (NH4HCO3)	95	Method C,G1

223

116			401 68	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9 81 (s, 1H), 9.47 (s, 1H), 8.71 (d, *J* = 6.4 Hz, 1H), 8.62 (d, *J* = 7.6 Hz, 1H), 8.26 (s, 1H), 7.88 (t, *J* = 7.2 Hz, 3H), 7.75 – 7.73 (m, 2H), 7.57 – 7.56 (m, 1H).	DMSO	401.0, 403.0 405.0 (M+1)	Method B (NH4HCO3)	95	Method C,G1
117			368.77	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.74(s, 1H), 9.45 (d, *J* = 1.2 Hz, 1H), 8.70 (dd, *J* = 4.4, 1.6 Hz, 1H), 8.60 (d, *J* = 8.0 Hz, 1H), 8.04 – 8.00 (m, 1H), 7 88 – 7.85 (m, 2H), 7.74 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.65 – 7 63 (m, 1H), 7.57 – 7.56 (m, 2H).	DMSO	369.1, 371.1 (M+1)	Method B (NH4HCO3)	95	Method C,G1
118			436.34	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.33 (s, 1H), 8.87 – 8.20 (m, 2H), 8.27 (d, *J* = 1.6 Hz, 1H), 7.99 (d, *J* = 8.4 Hz, 1H), 7.90 – 7.72 (m, 3H), 7.39 – 7.36 (m, 2H), 3.44 (brs, 4H), 2.05 (brs, 4H).	DMSO	435.9, 437.9, 439.8 (M+1)	Method B (NH4HCO3)	95	Method C,G1
119			403.43	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.38 (s, 1H), 9.43 (d, *J* = 1.2 Hz, 1H), 8.85 – 8.80 (m, 2H), 8.07 – 8.05 (m, 1H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.81 (t, *J* = 6.8 Hz, 1H), 7.69 – 7.67 (m, 1H), 7.58 – 7.83 (m, 1H), 7.43 – 7.41(m, 2H), 3.45 (brs, 4H), 2.06 (brs, 4H).	DMSO	403.9 (M+1)	Method B (NH4HCO3)	95	Method C,G1

224

120			368.77	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.28 (s, 1H), 9.49 (s, 1H), 8.77 – 8.87 (m, 3H), 8.06 – 8.12 (m, 1H), 7.90 – 7.95 (m, 2H), 7.78 – 7.81 (m, 1H), 7.57 – 7.73 (m, 1H), 7.53 (dd, *J* = 19.6 Hz, 9.2 Hz, 1H).	DMSO	369.0, 371.1 (M+1)	Method A (TFA)	95	Method C,G1
121			401.66	1H-NMR (400 MHz, DMSO-d6): δ 10.37 (s, 1H), 9.52 (s, 1H), 8.95 (d, J = 3.2 Hz, 1H), 8.87 (m, 1H), 8.81 (s, 1H), 8.32 (d, J = 2.0 Hz, 1H), 7.95 – 7.99 (m, 3H), 7.87 – 7.89 (m, 1H), 7.72 (d, J = 8.8 Hz, 1H).	DMSO	401.0, 403.0, 405.0 (M+1)	Method B (NH4HCO3)	95	Method C,G1
122			385.22	1H-NMR (400 MHz, DMSO-d6): δ 10.09 (s, 1H), 9.50 (s, 1H), 8.69 (s, 2H), 8.64 (d, J = 8.0 Hz, 1H), 8.26 (dd, J = 10.6 Hz, 1.8 Hz, 1H), 7.89 – 7.90 (m, 3H), 7.51 – 7.57 (m, 2H).	DMSO	385.0, 387.0 (M+1)	Method B (NH4HCO3)	95	Method C,G1

225

123			357.8	1H-NMR (400 MHz, DMSO-d6): δ 10.25 (s, 1H), 9.52 (s, 1H), 8.67 – 8.76 (m, 3H), 8.44 (s, 1H), 8.27 (m, 1H), 7.96 (s, 2H), 7.66 – 7.69 (m, 2H), 7.57 – 7.59 (m, 1H).	DMSO	358.0 (M+1)	Method A (TFA)	95	Method C,G1
124			411.86	1H-NMR (400 MHz, DMSO-d6): δ 10.53 (s, 1H), 9.54 (s, 1H), 9.08 (d, J = 8.4 Hz, 1H), 8.94 – 8.90 (m, 2H), 8.15 (d, J = 8.4 Hz, 2H), 8.00 – 7.93 (m, 5H), 7.39 (s, 2H).	DMSO	412.0, 414.0 (M+1)	Method A (TFA)	95	Method C,G1
125			411.86	1H-NMR (400 MHz, DMSO-d6): δ 10.64 (s, 1H), 9.54 (s, 1H), 9.22 (s, 1H), 8.92 – 8.96 (m, 2H), 8.70 (s, 1H), 8.10 (s, 1H), 8.03 – 8.05 (m, 1H), 7.95 (s, 2H), 7.69 (s, 2H), 7.53 (s, 2H).	DMSO	412.0, 414.0 (M+1)	Method A (TFA)	95	Method C,G1

226

126			364.35	1H-NMR (400 MHz, DMSO-d6): δ 10.65 (s, 1H), 9.47 (s, 1H), 9.02 (d, J = 7.6 Hz, 1H), 8.92 (s, 1H), 8.21 (s, 1H), 8.08 – 8.10 (m, 1H), 7.95 – 7.97 (m, 2H), 7.74 – 7.75 (m, 1H), 7.54 – 7.62 (m, 2H), 4.00 (s, 3H).	DMSO	365.1 (M+1), 183.1 (M/2+1)	Method A (TFA)	95	Method C,G1
127			397.26	1H-NMR (400 MHz, DMSO-d6): δ 10.56 (s, 1H), 9.46 (s, 1H), 9.02 (d, J = 8.0 Hz, 1H), 8.91 – 8.92 (m, 1H), 8.28 (d, J = 2.4 Hz, 1H), 8.16 – 8.17 (m, 1H), 7.92 – 8.03 (m, 3H), 7.72 (d, J = 8.8 Hz, 1H), 7.56 – 7.61 (m, 1H), 4.00 (s, 3H).	DMSO	397.0, 399.0 (M+1), 200.1 (M/2+1)	Method A (TFA)	95	Method C,G1
128			407.45	1H-NMR (400 MHz, DMSO-d6): δ 10.32 (s, 1H), 9.55 (s, 1H), 8.92 – 8.84 (m, 2H), 8.16 – 8.09 (m, 3H), 7.95 – 7.89 (m, 3H), 7.83 – 7.79 (m, 1H), 7.62 – 7.58 (m, 1H), 7.36 (s, 2H), 3.40 (s, 3H).	DMSO	408.1 (M+1)	Method A (TFA)	95	Method C,G1
129			362.81	1H-NMR (400 MHz, DMSO-d6): δ 10.06 (s, 1H), 9.51 (s, 1H), 8.82 – 8.85 (m, 2H), 8.10 – 8.11 (m, 1H), 8.05 (d , J = 2.0 Hz, 1H), 7.98 – 7.93 (m, 2H), 7.75 – 7.77 (m, 1H), 7.59 – 7.61 (m, 1H), 7.52 (t , J = 8.0 Hz, 1H), 7.27 – 7.28 (m, 1H), 3.99 (s, 3H).	DMSO	363.0, 365.0 (M+1), 182.1 (M/2+1)	Method A (TFA)	95	Method C,G1

227

130			380.8	1H-NMR (300 MHz, DMSO-d6): δ 10.02 (s, 1H), 9.50 (s, 1H), 7.78 – 8.79 (m, 2H), 8.19 – 8.24 (m, 1H), 7.86 – 8.00 (m, 3H), 7.52 – 7.70 (m, 3H), 3.98 (s, 3H).	DMSO	381.1, 383.1 (M+1), 191.1 (M/2+1)	Method A (TFA)	95	Method C,G1
131			371.39	1H-NMR (300 MHz, DMSO-d6): δ 13.08 (s, 1H), 9.59 (s, 1H), 9.07 (d, J = 8.1 Hz, 1H), 8.96(d, J = 8.1 Hz, 1H), 8.83 (d, J = 3.9 Hz, 1H), 8.49(s, 1H), 7.89 – 7.99 (m, 3H), 7.80 – 7.84 (m, 1H), 7.72 (t, J = 7.8 Hz, 1H), 7.60 – 7.63 (m, 2H), 7.23 (t, J = 7.5 Hz, 1H), 3.98 (s, 3H).	DMSO	371.9 (M+1)	Method A (TFA)	95	Method C,G1
132			362.81	1H-NMR (400 MHz, DMSO-d6): δ 10.12 (s, 1H), 9.28 (s, 1H), 8.69 (d, J = 4.0 Hz, 1H), 8.59 (d, J = 8.4 Hz, 1H), 8.00 (d, J = 2.8 Hz, 1H), 7.87 (d, J = 9.2 Hz, 1H), 7.68 – 7.70 (m, 2H), 7.57 – 7.63 (m, 2H), 7.46 – 7.53 (m, 1H), 7.40 – 7.44 (m, 1H), 3.86 (s, 3H).	DMSO	363.0, 365.1 (M+1), 182.1 (M/2+1)	Method A (TFA)	95	Method C,G1
133			348.35	1H-NMR (400 MHz, DMSO-d6): δ 9.46 (s, 1H), 9.11 (s, 1H), 8.79 – 8.76 (m, 2H), 8.00 – 7.94 (m, 1H), 7.83 – 7.73 (m, 3H), 7.62 – 7.48 (m, 3H), 3.00 (s, 3H).	DMSO	349.1 (M+1), 175.1 (M/2+1)	Method A (TFA)	95	Method C,G1

228

134			381.26	1H-NMR (400 MHz, DMSO-d6): δ 9.48 (s, 1H), 9.13 (s, 1H), 8.75 – 8.77 (m, 2H), 8.18 (s, 1H), 7.72 – 7.85 (m, 5H), 7.49 – 7.50 (m, 1H), 3.00 (s, 3H).	DMSO	381.0, 383.0, 385.0 (M+1)	Method A (TFA)	95	Method C,G1
135			364.8	1H-NMR (400 MHz, DMSO-d6): δ 9.43 (m, 2H), 8.94 – 8.89 (m, 2H), 8.08 – 8.06 (m, 1H), 7.92 – 7.81 (m, 4H), 7.57 – 7.53 (m, 2H), 3.03 (s, 3H).	DMSO	365.0, 367.0 (M+1), 183.1 (M/2+1)	Method A (TFA)	95	Method C,G1
136			337.38	1H-NMR (400 MHz, DMSO-d6): δ 9.52 – 9.44 (m, 2H), 8.98 (d, J = 8.0 Hz, 1H), 8.92 (d, J = 4.4 Hz, 1H), 8.36 – 8.19 (m, 2H), 8.02 – 7.84 (m, 3H), 7.73 – 7.69 (m, 2H), 7.55 (d, J = 6.8 Hz, 1H), 3.04 (s, 3H).	DMSO	338.1 (M+1), 169.6 (M/2+1)	Method A (TFA)	95	Method C,G1
137			364.35	1H-NMR (400 MHz, DMSO-d6): δ 9.97 (s, 1H), 9.51 (s, 1H), 8.69 – 8.66 (m, 2H), 8.16 – 8.08 (m, 2H), 7.75 – 7.73 (m, 1H), 7.61 – 7.53 (m, 3H), 7.40 (d, J = 7.6 Hz, 1H), 4.01 (s, 3H).	DMSO	183.1 (M/2+1) 365.1 (M+1)	Method A (TFA)	95	Method C,G1

229

138			397.26	1H-NMR (400 MHz, DMSO-d6): δ 10.01 (s, 1H), 9.53 (s, 1H), 8.67 – 8.70 (m, 2H), 8.41 (d, J = 2.4 Hz, 1H), 8.10 (d, J = 8.4 Hz, 1H), 7.95 – 7.99 (m, 1H), 7.73 (d, J = 8.8 Hz, 1H), 7.56 – 7.63 (m, 2H), 7.42 (d, J = 8.4 Hz, 1H), 4.02 (s, 3H).	DMSO	397.0, 399.0 (M+1)	Method A (TFA)	95	Method C,G1
139			380.8	1H-NMR (400 MHz, DMSO-d6): δ 10.21 (s, 1H), 9.48 (s, 1H), 8.99 (d, J = 8.0 Hz, 1H), 8.89 (d, J = 4.8 Hz, 1H), 8.15 – 8.22 (m, 2H), 7.92 – 7.95 (m, 2H), 7.62 (t, J = 8.0 Hz, 1H), 7.52 (t, J = 8.8 Hz, 1H), 7.43 (d, J = 8.0 Hz, 1H), 4.02 (s, 3H).	DMSO	191.1 (M/2+1) 381.1, 383.1 (M+1)	Method A (TFA)	95	Method C,G1
140			401.68	1H-NMR (400 MHz, DMSO-d6): δ 10.11 (s, 1H), 8.50 (m, 1H), 8.63 – 8.70 (m, 3H), 8.14 (d, J = 2.0 Hz, 2H), 7.92 (m, 2H), 7.57 (m, 1H), 7.38 (t, J = 1.6 Hz, 1H).	DMSO	401.0, 403.0 (M+1)	Method B (NH4HCO3)	95	Method C,G1
141			348.35	1H-NMR (400 MHz, DMSO-d6): δ 9.46 (s, 1H), 9.11 (s, 1H), 8.76 – 8.70 (m, 2H), 7.95 – 7.99 (m, 1H), 7.78 – 7.60 (m, 3H), 7.54 – 7 .44 (m, 3H), 3.00 (s, 3H).	DMSO	175.1 (M/2+1) 349.1 (M+1)	Method A (TFA)	95	Method C,G1

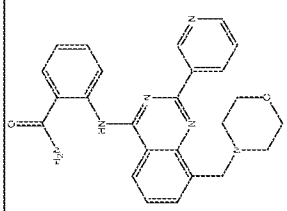
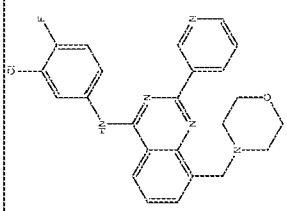
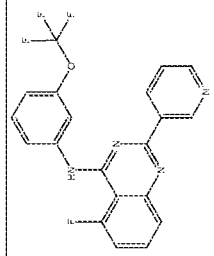
230

142			397.26	1H-NMR (400 MHz, DMSO-d6): δ 10.30 (s, 1H), 8.39 (s, 1H), 8.83 (s, 2H), 8.03 – 8.12 (m, 3H), 7.79 – 7.81 (m, 2H), 7.50 – 7.51 (m, 1H), 7.32 (s, 1H), 3.96 (s, 3H).	DMSO	397.0, 399.0, 401.0 (M+1)	Method B (NH4HCO3)	95	Method C,G1
143			452.34	1H-NMR (400 MHz, DMSO-d6): δ 9.86 (s, 1H), 9.51 (s, 1H), 8.65 – 8.66 (m, 2H), 8.34 – 8.35 (m, 1H), 7.95 – 7.96 (m, 1H), 7.72 – 7.80 (m, 4H), 7.54 (m, 1H), 3.84 (m, 4H), 3.56 (m, 4H).	DMSO	452.1, 454.0 (M+1)	Method B (NH4HCO3)	95	Method C,G1
144			435.88	1H-NMR (400 MHz, DMSO-d6): δ 9.83 (s, 1H), 9.49 (s, 1H), 8.62 – 8.65 (m, 2H), 8.21 – 8.23 (m, 1H), 7.89 – 7.91 (m, 1H), 7.76 – 7.81 (m, 1H), 7.72 – 7.73 (m, 2H), 7.51 – 7.54 (m, 2H), 3.84 (t, J = 4.0 Hz, 4H), 3.36 (m, 4H).	DMSO	436.1, 438.1 (M+1)	Method B (NH4HCO3)	95	Method C,G1
145			419.43	1H-NMR (400 MHz, DMSO-d6): δ 10.50 (s, 1H), 9.45 (s, 1H), 8.83 – 8.90 (m, 2H), 8.06 – 8.08 (m, 1H), 7.70-7.93 (m, 5H), 7.56 (dd, J = 19.6, 9.6 Hz, 1H), 3.82 – 3.83 (m, 4H), 3.39 – 3.41 (m, 4H).	DMSO	420.1 (M+1)	Method B (NH4HCO3)	95	Method C,G1

231

146			408.46	1H-NMR (400 MHz, DMSO-d6): δ 10.54 (s, 1H), 9.44 (s, 1H), 8.90 (d, J = 6.0 Hz, 1H), 8.84 (d, J = 4.4 Hz, 1H), 8.34 (s, 1H), 8.27 (d, J = 7.2 Hz, 1H), 7.67 – 7.92 (m, 6H), 3.82 – 3.83 (m, 4H), 3.39 – 3.40 (m, 4H).	DMSO	409.2 (M+1)	Method B (NH4HCO3)	95	Method C,G1
147			452.34	1H-NMR (400 MHz, DMSO-d6): δ 10.42 (s, 1H), 9.42 (s, 1H), 8.85 – 8.87 (m, 2H), 8.11 (s, 2H), 7.73 – 7.88 (m, 4H), 7.38 (s, 1H), 3.82 – 3.83 (m, 4H), 3.39 – 3.40 (m, 4H).	DMSO	452.1, 454.1, 456.1 (M+1)	Method B (NH4HCO3)	95	Method C,G1
148			426.47	1H-NMR (400 MHz, DMSO-d6): δ 12.93 (s, 1H), 9.57 (m, 1H), 9.12 (d, J = 8.4 Hz, 1H), 8.66 – 8.72 (m, 2H), 8.56 (s, 1H), 8.02 (d, J = 6.8 Hz, 1H), 7.96 (s, 1H), 7.72 – 7.84 (m, 3H), 7.56 – 7.57 (m, 1H), 7.40 (m, 1H), 7.19 (t, J = 8.0 Hz, 1H), 3.84 (t, J = 4.4 Hz, 4H), 3.35 (t, J = 4.4 Hz, 4H).	DMSO	427.2 (M+1)	Method B (NH4HCO3)	95	Method C,G1

232

149			393.84	1H-NMR (400 MHz, DMSO-d6): δ 9.71 (s, 1H), 9.48 (s, 1H), 8.62 – 8.63 (m, 2H), 8.23 (m, 1H), 7.92 (m, 1H), 7.77 (d, J = 9.6 Hz, 1H), 7.51 – 7.56 (m, 3H), 7.42 (m, 1H), 3.12 (s, 6H).	DMSO	394.1, 396.1 (M+1)	Method B (NH4HCO3)	95	Method C,G1
150			377.39	1H-NMR (400 MHz, DMSO-d6): δ 9.72 (s, 1H), 9.46 (m, 1H), 8.60 – 8.63 (m, 2H), 8.08 – 8.14 (m, 1H), 7.77 (d, J = 9.2 Hz, 1H), 7.69 – 7.71 (m, 1H), 7.50 – 7.57 (m, 3H), 7.42 – 7.43 (m, 1H), 3.12 (s, 6H).	DMSO	378.2 (M+1)	Method B (NH4HCO3)	95	Method C,G1
151			410.3	1H-NMR (400 MHz, DMSO-d6): δ 9.72 (s, 1H), 9.49 (s, 1H), 8.60 – 8.64 (m, 2H), 8.17 (s, 2H), 7.76 (d, J = 8.8 Hz, 1H), 7.51 – 7.53 (m, 2H), 7.37 (s, 1H), 7.32 (s, 1H), 3.11 (s, 6H).	DMSO	410.1, 412.0, 414.1 (M+1)	Method B (NH4HCO3)	95	Method C,G1

152			410.3	1H-NMR (400 MHz, DMSO-d6): δ 10.44 (s, 1H), 9.45 (s, 1H), 8.83 – 8.91 (m, 2H), 8.26 – 8.27 (m, 1H), 7.72 – 7.99 (m, 4H), 7.57 – 7.61 (m, 2H), 3.14 (s, 6H).	DMSO	410.1, 412.1, 414.0 (M+1)	Method B (NH4HCO3)	95	Method C,G1
153			366.42	1H-NMR (400 MHz, DMSO-d6): δ 9.82 (s, 1H), 9.48 (s, 1H), 8.55 – 8.64 (m, 2H), 8.41 (s, 1H), 8.28 (d, J = 8.0 Hz, 1H), 7.79 (d, J = 9.6 Hz, 1H), 7.69 (t, J = 8.0 Hz, 1H), 7.50 – 7.61 (m, 3H), 7.43 (m, 1H), 3.12 (s, 6H).	DMSO	367.1 (M+1)	Method B (NH4HCO3)	95	Method C,G1
154			435.23	1H-NMR (400 MHz, DMSO-d6): δ 10.57 (s, 1H), 9.53 (s, 1H), 8.86 – 8.94 (m, 3H), 8.32 – 8.33 (m, 1H), 8.21 (s, 1H), 7.97 – 8.01 (m, 2H), 7.84 – 7.88 (m, 1H), 7.73 (d, J = 8.8 Hz, 1H).	DMSO	435.1, 437.1, 439.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1
155			402.32	1H-NMR (400 MHz, DMSO-d6): δ 10.32 (s, 1H), 9.51 – 9.52 (m, 1H), 8.65 – 8.78 (m, 3H), 8.19 (s, 1H), 8.11 (m, 1H), 7.97 (d, J = 8.0 Hz, 1H), 7.71 (m, 1H), 7.55 – 7.59 (m, 2H).	DMSO	403.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1

234

156			435.23	1H-NMR (400 MHz, DMSO-d6): δ 10.65 (s, 1H), 9.46(s, 1H), 8.88 – 8.97 (m, 3H), 8.17 (s, 1H), 8.10 – 8.11 (m, 2H), 7.97 (s, 1H), 7.95 (s, 1H), 7.39 (s, 1H).	DMSO	435.1, 437.0, 439.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1
157			418.77	1H-NMR (400 MHz, DMSO-d6): δ 10.62 (s, 1H), 9.52 (s, 1H), 8.99 (d, J = 8.0 Hz, 1H), 8.88 – 8.90 (m, 2H), 8.20 – 8.23 (m, 2H), 8.01 (d, J = 8.0 Hz, 1H), 7.92 – 7.95 (m, 2H), 7.54 (t, J = 9.2 Hz, 1H).	DMSO	419.1, 421.1 (M+1)	Method B (NH4HCO3)	95	Method C, G
158			409.36	1H-NMR (400 MHz, DMSO-d6): δ 13.24 (s, 1H), 9.56 (s, 1H), 9.10 (d, J = 8.4 Hz, 1H), 8.96 (s, 1H), 8.67 (d, J = 8.0 Hz, 1H), 8.54 (s, 1H), 8.33 (d, J = 8.8 Hz, 1H), 8.18 (s, 1H), 7.95 – 8.01 (m, 4H), 7.70 (t, J = 7.6 Hz, 1H), 7.27 (t, J = 7.2 Hz, 1H).	DMSO	410.1 (M+1)	Method B (NH4HCO3)	95	Method C, G

235

159			391.35	1H-NMR (400 MHz, DMSO-d6): δ 10.82 (s, 1H), 8.50 (s, 1H), 9.04 (d, J = 6.0 Hz, 1H), 8.96 (d, J = 8.8 Hz, 2H), 8.37 (s, 1H), 8.30 – 8.28 (m, 1H), 8.21(s, 1H), 7.98 (d, J = 7.6 Hz, 2H), 7.68 – 7.69 (m, 2H).	DMSO	392.2 (M+1)	Method B (NH4HCO3)	95	Method C, G
160			450.34	1H-NMR (400 MHz, DMSO-d6): δ 10.40 (s, 1H), 9.54 – 9.55 (m, 1H), 8.82 – 8.84 (m, 1H), 8.67 – 8.73 (m, 2H), 8.15 – 8.21 (m, 2H), 7.93 – 8.00 (m, 2H), 7.54 – 7.64 (m, 2H), 7.21 (d, J = 8.0 Hz, 1H).	DMSO	451.1 (M+1)	Method B (NH4HCO3)	95	Method C, G
161			416.78	1H-NMR (400 MHz, DMSO-d6): δ 10.10 (s, 1H), 9.49 (s, 1H), 8.62 – 8.72 (m, 3H), 8.13 (s, 1H), 7.68 – 7.92 (m, 3H), 7.51 – 7.60 (m, 2H), 7.14 – 7.16 (m, 1H).	DMSO	417.1, 419.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1

162			375.81	1H-NMR (400 MHz, DMSO-d6): δ 13.13 (s, 1H), 9.53 (s, 1H), 9.01 (d, J = 8.0 Hz, 1H), 8.68 – 8.72 (m, 2H), 8.50 (s, 1H), 8.10 (d, J = 8.8, 1H), 7.88 – 7.97 (m, 3H), 7.70 – 7.72 (m, 2H), 7.57 – 7.59 (m, 1H), 7.22 (t, J = 7.6, 1H).	DMSO	376.0, 378.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1
163			376.8	1H-NMR (400 MHz, DMSO-d6): δ 12.07(s, 1H), 9.56 (s, 1H), 8.84 (d, J = 8.4 Hz, 1H), 8.71 – 8.73 (m, 2H), 8.34 (s, 1H), 7.96 – 8.09(m, 3H), 7.59 – 7.80 (m, 2H), 7.29 (t, J = 7.2 Hz, 1H).	DMSO	377.0, 379.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1
164			394.37	1H-NMR (400 MHz, DMSO-d6): δ 9.90 (s, 1H), 9.53 (s, 1H), 8.67 (d, J = 5.2 Hz, 2H), 7.99 (d, J = 2.4 Hz, 1H), 7.94 (m, 1H), 7.87 (d, J = 9.2 Hz, 1H), 7.80 (d, J = 8.4 Hz, 1H), 7.49 – 7.59 (m, 3H), 7.31 (t, J = 74.0 Hz, 1H), 7.00 (d, J = 8.0 Hz, 1H), 3.99 (s, 3H).	DMSO	395 1 (M+1)	Method B (NH4HCO3)	95	Method C, G1

237

165		HCl	458.51	1H-NMR (400 MHz, DMSO-d6): δ 9.42 (s, 1H), 8.98 (d, J = 8.4 Hz, 1H), 8.68 – 8.71 (m, 2H), 7.94 (d, J = 7.6 Hz, 1H), 7.70 (t, J = 8.0 Hz, 1H), 7.57 (t, J = 5.6 Hz, 1H), 7.53 (s, 1H), 7.38 (s, 1H), 7.19 (t, J = 7.2 Hz, 1H), 4.52 (s, 2H), 4.00 (s, 3H), 3.63 (s, 2H), 2.89 (s, 6H).	DMSO	459.1 (M+1) 230.2 (M/2+1)	Method A (TFA)	95	Method C, G1
166			467.92	1H-NMR (400 MHz, DMSO-d6): δ 9.71 (s, 1H), 9.50 (d, J = 1.6 Hz, 1H), 8.62 – 8.67 (m, 2H), 8.20 (dd, J = 6.8, 2.4 Hz, 1H), 7.86 – 7.89 (m, 2H), 7.51 – 7.55 (m, 2H), 7.31 (s, 1H), 4.24 (t, J = 6.0 Hz, 2H), 3.98 (s, 3H), 2.77 (t, J = 5.6 Hz, 2H), 2.29 (s, 6H).	DMSO	468.1 (M+1) 234.6 (M/2+1)	Method B (NH4HCO3)	95	Method C, G1
167		HCl	428.82	1H-NMR (400 MHz, DMSO-d6): δ 10.41 (s, 1H), 9.50 (d, J = 1.6 Hz, 1H), 8.98 (d, J = 8.4 Hz, 1H), 8.88 (dd, J = 5.2, 1.6 Hz, 1H), 8.13 (d, J = 2.8 Hz, 1H), 8.00 (t, J = 2.0 Hz, 1H), 7.89 – 7.95 (m, 3H), 7.62 (dd, J = 9.2, 3.2 Hz, 1H), 7.36 (t, J = 73.6 Hz, 1H), 7.16 (d, J = 2.0 Hz, 1H), 4.01 (s, 3H).	DMSO	429.1, 431.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1
168			385.42	1H-NMR (400 MHz, DMSO-d6): δ 13.03 (s, 1H), 9.62 (d, J = 1.6 Hz, 1H), 9.20 (d, J = 8.4 Hz, 1H), 8.74 – 8.77 (m, 1H), 8.70 (dd, J = 4.4, 1.6 Hz, 1H), 8.48 (s, 1H), 7.96 – 7.99 (m, 2H), 7.72 – 7.76 (m, 1H), 7.57 – 7.60 (m, 1H), 7.47 (m, 1H), 7.41 (m, 1H), 7.17 – 7.21 (m, 1H), 3.95 (s, 3H), 2.72 (s, 3H).	DMSO	386.1 (M+1)	Method B (NH4HCO3)	95	Method D, G1

169		HCl	368.77	1H-NMR (400 MHz, DMSO-d6): δ 10.31 (s, 1H), 9.47 (s, 1H), 8.86 – 8.93 (m, 2H), 8.54 (dd, J = 10.0, 2.8 Hz, 1H), 8.21 (dd, J = 6.8, 2.4 Hz, 1H), 7.82 – 8.00 (m, 4H), 7.52 (t, J = 9.2 Hz, 1H).	DMSO	369.0, 371.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1
170		HCl	400.33	1H-NMR (400 MHz, DMSO-d6): δ 10.35 (s, 1H), 9.53 (s, 1H), 8.99 (d, J = 8.0 Hz, 1H), 8.89 (d, J = 4.0 Hz, 1H), 8.60 (dd, J = 10.4, 3.2 Hz, 1H), 7.97 – 8.09 (m, 3H), 7.86 – 7.92 (m, 2H), 7.62 (t, J = 8.0 Hz, 1H), 7.21 (d, J = 8.0 Hz, 1H).	DMSO	401.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1
171			359.36	1H-NMR (400 MHz, DMSO-d6): δ 13.06 (s, 1H), 9.58 (s, 1H), 9.07 (d, J = 8.4 Hz, 1H), 8.72 (d, J = 5.6 Hz, 2H), 8.52 (s, 1H), 7.96 – 8.02 (m, 3H), 7.83 – 7.87 (m, 2H), 7.74 (t, J = 8.0 Hz, 1H), 7.59 (t, J = 6.0 Hz, 1H), 7.23 (t, J = 7.6 Hz, 1H).	DMSO	360.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1

239

172		HCl	382.34	1H-NMR (400 MHz, DMSO-d6): δ 10.30 (s, 1H), 9.53 (d, J = 1.2 Hz, 1H), 8.98 (d, J = 8.0 Hz, 1H), 8.86 (d, J = 4.4 Hz, 1H), 8.62 (dd, J = 10.0, 2.8 Hz, 1H), 8.01 – 8.05 (m, 1H), 7.84 – 7.92 (m, 4H), 7.50 – 7.56 (m, 1H), 7.32 (t, J = 74.0 Hz, 1H), 7.03 (dd, J = 8.0, 2.0 Hz, 1H).	DMSO	383.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1
173			346.35	1H-NMR (400 MHz, DMSO-d6): δ 10.09 (s, 1H), 9.51 (s, 1H), 8.79 – 8.76 (m, 2H), 8.38 (s, 1H), 8.16 – 8.11 (m, 1H), 7.86 – 7.66 (m, 4H), 7.59 – 7.50 (m, 1H), 2.57 (s, 3H).	DMSO	349.1 (M+1), 175.1 (M/2+1)	Method A (TFA)	95	Method C, G1
174			364.8	1H-NMR (300 Hz, CD3OD): δ 9.50 (d, J = 1.2 Hz, 1H), 9.14 (d, J = 8.4 Hz, 1H), 8.94 (d, J = 4.8 Hz, 1H), 8.35 (s, 1H), 8.09 – 7.99 (m, 2H), 7.93 (s, 2H), 7.78 – 7.73 (m, 1H), 7.39 (t, J = 9.0 Hz, 1H), 2.64 (s, 3H).	CD3OD	365.1, 367.1 (M+1)	Method A (TFA)	95	Method C, G1
175			381.26	1H-NMR (400 MHz, DMSO-d6): δ 10.13 (s, 1H), 9.51 (s, 1H), 8.84 – 8.79 (m, 2H), 8.36 – 8.34 (m, 2H), 7.96 (dd, J = 8.8, 2.5 Hz, 1H), 7.85 – 7.70 (m, 4H), 2.55 (s, 3H).	DMSO	381.0, 383.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1

240

176			346.81	1H-NMR (300 Hz, CD3OD): δ 9.48 (d, J = 1.2 Hz, 1H), 8.99 – 8.95 (m, 1H), 8.82 – 8.80 (m, 1H), 8.30 – 8.29 (m, 1H), 7.90 – 7.81 (m, 5H), 7.52 – 7.46 (m, 2H), 2.62 (s, 3H).	CD3OD	347.0, 349.1 (M+1)	Method A (TFA)	95	Method C, G1
177			346.81	1H-NMR (400 MHz, DMSO-d6): δ 10.12 (s, 1H), 9.52 (s, 1H), 8.84 – 8.78 (m, 2H), 8.42 (s, 1H), 8.16 – 8.15 (m, 1H), 7.94 – 7.91 (m, 1H), 7.85 (d, J = 8.4 Hz, 1H), 7.79 (d, J = 8.1 Hz, 1H), 7.75 – 7.71 (m, 1H), 7.50 (t, J = 8.1 Hz, 1H), 7.27 – 7.23 (m, 1H), 2.56 (s, 3H).	DMSO	347.1, 349.1 (M+1)	Method A (TFA)	95	Method C, G1
178			380.37	1H-NMR (400 MHz, DMSO-d6): δ 10.60 (s, 1H), 9.50 (d, J = 2.1 Hz, 1H), 9.00 (d, J = 8.1 Hz, 1H), 8.90 (dd, J = 5.1, 1.2 Hz, 1H), 8.55 (s, 1H), 8.43 (s, 1H), 8.25 (d, J = 7.8 Hz, 1H), 7.96 – 7.90 (m, 2H), 7.84 (d, J = 8.1 Hz, 1H), 7.27 (t, J = 8.2 Hz, 1H), 7.57 (d, J = 7.8 Hz, 1H), 2.62 (s, 3H).	DMSO	381.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1

241

179			414.81	1H-NMR (400 MHz, DMSO-d6): δ 10.59 (s, 1H), 9.50 (s, 1H), 9.02 (d, J = 8.4 Hz, 1H), 8.92 (d, J = 5.2 Hz, 1H), 8.59 (d, J = 2.8 Hz, 1H), 8.54 (s, 1H), 8.34 (dd, J = 8.6, 2.6 Hz, 1H), 7.96 – 7.90 (m, 2H), 7.81 (d, J = 8.8 Hz, 2H), 2.56 (s, 3H).	DMSO	415.1, 417.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1
180			401 37	1H-NMR (400 MHz, DMSO-d6): δ 13.91 (s, 1H), 10.38 (s, 1H), 9.59 (s, 1H), 8.79 – 8.76 (m, 1H), 8.73 (d, J = 4.8 Hz, 1H), 8.61 (d, J = 2.4 Hz, 1H), 8.44 (s, 1H), 8.33 (dd, J = 9.0, 2.6 Hz, 1H), 8.20 (d, J = 8.8 Hz, 1H), 7.88 (d, J = 8.4 Hz, 1H), 7.81 (dd, J = 8.4, 1.2 Hz, 1H), 7.60 – 7.57 (m, 1H), 2.58 (s, 3H).	DMSO	402.0 (M+1)	Method A (TFA)	95	Method C, G1
181			381.26	1H-NMR (400 MHz, DMSO-d6): δ 10.40 (s, 1H), 9.47 (s, 1H), 8.98 (d, J = 7.5 Hz, 1H), 8.91 (d, J = 4.5 Hz, 1H), 8.48 (s, 1H), 8.12 (d, J = 2.1 Hz, 2H), 7.97 – 7.93 (m, 1H), 7.88 (d, J = 8.4 Hz, 1H), 7.80 (d, J = 7.8 Hz, 1H), 7.40 (s, 1H), 2.55 (s, 3H).	DMSO	381.0, 383.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1

242

182			390.82	1H-NMR (400 MHz, DMSO-d6): δ 12.25 (s, 1H), 9.54 (s, 1H), 9.25 (s, 1H), 8.84 – 8.80 (m, 2H), 8.09 (d, J = 8.0 Hz, 1H), 7.96 (s, 1H), 7.88 (d, J = 8.0 Hz, 1H), 7.81 (d, J = 9.2 Hz, 1H), 7.77 – 7.75 (m, 1H), 7.29 (d, J = 8.4 Hz, 1H), 2.56 (s, 3H).	DMSO	391.1, 393.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1
183			366.34	1H-NMR (400 MHz, DMSO-d6): δ 9.98 (s, 1H), 9.50 (d, J = 1.6 Hz, 1H), 8.69 (dd, J = 4.8, 1.6 Hz, 1H), 8.66 – 8.63 (m, 1H), 8.30 (s, 1H), 7.99 – 7.95 (m, 2H), 7.82 (d, J = 8.4 Hz, 1H), 7.76 (dd, J = 8.6, 1.4 Hz, 1H), 7.58 – 7.55 (m, 1H), 2.55 (s, 3H).	DMSO	367.1 (M+1), 184.1 (M/2+1)	Method A (TFA)	95	Method C, G1
184			415.7	1H-NMR (400 MHz, DMSO-d6): δ 10.09 (s, 1H), 9.51 (s, 1H), 8.75 – 8.72 (m, 2H), 8.38 (s, 2H), 8.32 (s, 1H), 7.83 (d, J = 8.8 Hz, 1H), 7.77 (d, J = 8.0 Hz, 1H), 7.66 – 7.64 (m, 1H), 2.55 (s, 3H).	DMSO	414.8, 416.8 (M+1)	Method B (NH4HCO3)	95	Method C, G1

185			354.4	1H-NMR (400 MHz, DMSO-d6): δ 10.26 (s, 1H), 9.56 (s, 1H), 8.93 (d, J = 8.0 Hz, 1H), 8.81 (d, J = 4.0 Hz, 1H), 8.65 (s, 1H), 8.46 (s, 1H), 8.21 (d, J = 8.0 Hz, 1H), 7.86 (d, J = 8.4 Hz, 1H), 7.88 – 7.88 (m, 3H), 7.65 (t, J = 7.6 Hz, 1H), 2.65 (s, 3H), 2.58 (s, 3H).	DMSO	355.1 (M+1), 178.1 (M/2+1)	Method A (TFA)	95	Method C, G1
186			356.38	1H-NMR (400 MHz, DMSO-d6): δ 12.18 (s, 1H), 9.57 (s, 1H), 9.07 (d, J = 8.4 Hz, 1H), 8.71 (d, J = 5.6 Hz, 2H), 8.10 (d, J = 8.0 Hz, 1H), 7.99 (s, 1H), 7.86 – 7.76 (m, 3H), 7.56 (t, J = 6.2 Hz, 1H), 7.23 (t, J = 7.4 Hz, 1H), 2.55 (s, 3H).	DMSO	357.1 (M+1)	Method A (TFA)	95	Method C, G1
187			337.36	1H-NMR (400 MHz, DMSO-d6): δ 10.10 (s, 1H), 9.51 (s, 1H), 8.65 – 8.70 (m, 2H), 8.45 (s, 1H), 8.38 (s, 1H), 8.28 (d, J = 8.0 Hz, 1H), 7.83 (d, J = 8.8 Hz, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.69 (t, J = 7.8 Hz, 1H), 7.62 (d, J = 7.2 Hz, 1H), 7.54 – 7.57 (m, 1H), 2.56 (s, 3H).	DMSO	338.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1
188			355.39	1H-NMR (400 MHz, DMSO-d6): δ 13.11 (s, 1H), 9.61 (s, 1H), 9.09 (d, J = 8.8 Hz, 1H), 8.89 (d, J = 8.0 Hz, 1H), 8.81 (s, 1H), 8.50 (s, 1H), 8.01 – 7.98 (m, 2H), 7.96 (dd, J = 7.8, 1.0 Hz, 1H), 7.86 (d, J = 8.8 Hz, 1H), 7.76 – 7.72 (m, 3H), 7.23 (t, J = 7.4 Hz, 1H), 2.56 (s, 3H),	DMSO	356.2 (M+1)	Method B (NH4HCO3)	95	Method C, G1

244

189			385.42	1H-NMR (400 MHz, DMSO-d6): δ 12.62 (s, 1H), 9.58 (s, 1H), 9.03 (d, J = 8.4 Hz, 1H), 8.92 (d, J = 4.0 Hz, 1H), 8.74 – 8.69 (m, 2H), 7.92 – 7.87 (m, 2H), 7.72 (t, J = 7.6 Hz, 1H), 7.66 – 7.56 (m, 3H), 7.23 (t, J = 7.6 Hz, 1H), 4.00 (s, 3H), 2.84 (d, J = 4.4 Hz, 3H).	DMSO	386.2 (M+1)	Method B (NH4HCO3)	95	Method C, G1
190			461.51	1H-NMR (400 MHz, DMSO-d6): δ 12.40 (s, 1H), 9.57 (d, J = 1.2 Hz, 1H), 9.48 (t, J = 6.0 Hz, 1H), 8.89 (d, J = 8.8 Hz, 1H), 8.73 – 8.68 (m, 2H), 7.96 (dd, J = 8.0, 1.2 Hz, 1H), 7.89 (d, J = 8.8 Hz, 1H), 7.76 – 7.72 (m, 1H), 7.61 – 7.55 (m, 3H), 7.34 – 7.20 (m, 6H), 4.52 (d, J = 5.6 Hz, 2H), 3.93 (s, 3H).	DMSO	462.2 (M+1)	Method B (NH4HCO3)	95	Method C, G1
191			368.77	1H NMR (300 MHz, DMSO-d6): δ 10.32 (s, 1H), 9.55 – 9.45 (m, 1H), 8.93 – 8.76 (m, 2H), 8.63 (d, J = 8.9 Hz, 1H), 8.10 (ddd, J = 13.2, 7.5, 2.6 Hz, 1H), 7.97 (d, J = 2.1 Hz, 1H), 7.80 – 7.67 (m, 3H), 7.62 – 7.49 (m, 1H).	DMSO	369.0, 371.0 (M+1)	Method B (NH4HCO3)	97	Method C, G1

245

192			401.68	1H NMR (300 MHz, DMSO-d6): δ 10.36 (s, 1H), 9.58 – 9.43 (m, 1H), 8.90 – 8.79 (m, 2H), 8.65 (d, J = 9.0 Hz, 1H), 8.33 (d, J = 2.4 Hz, 1H), 8.01 – 7.90 (m, 2H), 7.82 – 7.68 (m, 3H).	DMSO	401.0, 403.0, 405.0 (M+1)	Method B (NH4HCO3)	97	Method C, G1
193			367.23	1H NMR (300 MHz, DMSO-d6): δ 10.19 (s, 1H), 9.53 (d, J = 2.1 Hz, 1H), 8.78 – 8.56 (m, 3H), 8.17 (t, J = 2.0 Hz, 1H), 7.96 (d, J = 2.1 Hz, 1H), 7.93 – 7.85 (m, 1H), 7.75 (dd, J = 8.9, 2.2 Hz, 1H), 7.58 (ddd, J = 8.0, 4.8, 0.7 Hz, 1H), 7.51 (t, J = 8.1 Hz, 1H), 7.26 (ddd, J = 8.0, 2.0, 0.8 Hz, 1H).	DMSO	367.0, 369.0 (M+1)	Method B (NH4HCO3)	98	Method C, G1
194			376.80	1H NMR (300 MHz, DMSO-d6): δ 13.11 (s, 1H), 10.27 (s, 1H), 9.58 (d, J = 2.1 Hz, 1H), 8.87 – 8.62 (m, 4H), 8.21 – 8.10 (m, 1H), 7.96 (d, J = 2.1 Hz, 1H), 7.82 – 7.68 (m, 2H), 7.64 – 7.53 (m, 2H).	DMSO	377.0, 379.0 (M+1)	Method A (TFA)	95	Method C, G1

246

195			401.68	1H NMR (300 MHz, DMSO-d6): δ 10.32 (s, 1H), 9.52 – 9.49 (m, 1H), 8.85 – 8.73 (m, 2H), 8.61 (d, J = 9.0 Hz, 1H), 8.18 – 8.08 (m, 2H), 7.99 – 7.95 (m, 1H), 7.77 (dd, J = 8.9, 2.2 Hz, 1H), 7.71 (dd, J = 7.8, 5.0 Hz, 1H), 7.42 – 7.39 (m, 1H).	DMSO	401.0, 403.0, 405.0 (M+1)	Method B (NH4HCO3)	97	Method C, G1
196			386.76	1H-NMR (300 MHz, DMSO-d6): δ 10.43 (s, 1H), 9.49 (d, J = 1.9 Hz, 1H), 8.95 – 8.82 (m, 2H), 8.64 (d, J = 9.0 Hz, 1H), 8.01 – 7.82 (m, 4H), 7.78 (dd, J = 8.9, 2.2 Hz, 1H).	DMSO	387.0, 389.1 (M+1)	Method B (NH4HCO3)	97	Method C, G1
197			411.86	1H NMR (400 MHz, DMSO-d6): δ 10.50 (brs, 1H), 9.56 (s, 1H), 9.08 – 8.93 (m, 1H), 8.92 – 8.82 (m, 1H), 8.73 (d, J = 8.9 Hz, 1H), 8.21 – 8.11 (m, 2H), 8.02 (d, J = 1.9 Hz, 1H), 7.98 – 7.77 (m, 4H), 7.38 (s, 2H).	DMSO	412.1, 414.1 (M+1)	Method B (NH4HCO3)	97	Method C, G1

247

198			385 22	1H NMR (400 MHz, DMSO-d6): δ 10.25 (s, 1H), 9.51 (d, J = 1.4 Hz, 1H), 8.77 – 8.69 (m, 2H), 8.60 (d, J = 9.0 Hz, 1H), 8.27 – 8.20 (m, 1H), 7.97 (d, J = 2.1 Hz, 1H), 7.90 (ddd, J = 9.0, 4.3, 2.6 Hz, 1H), 7.76 (dd, J = 8.9, 2.1 Hz, 1H), 7.64 (dd, J = 8.0, 4.9 Hz, 1H), 7.55 (t, J = 9.1 Hz, 1H).	DMSO	385.0, 387.0 (M+1)	Method B (NH4HCO3)	100	Method C, G1
199			357.80	1H NMR (400 MHz, DMSO-d6): δ 10.36 (s, 1H), 9.53 – 9.49 (m, 1H), 8.81 – 8.70 (m, 2H), 8.64 (d, J = 8.9 Hz, 1H), 8.45 – 8.36 (m, 1H), 8.29 – 8.21 (m, 1H), 7.98 (d, J = 2.1 Hz, 1H), 7.77 (dd, J = 8.9, 2.1 Hz, 1H), 7.74 – 7.61 (m, 3H).	DMSO	357.9, 359.9 (M+1)	Method B (NH4HCO3)	99	Method C, G1
200			435.23	1H-NMR (400 MHz, DMSO-d6): δ 10.44 (s, 1H), 9.53 (s, 1H), 8.84 - 8.74 (m, 2H), 8.69 – 8.61 (m, 2H), 8.26 (dd, J = 8.8, 2.6 Hz, 1H), 7.99 (d, J = 2.1 Hz, 1H), 7.83 (d, J = 8.8 Hz, 1H), 7.78 (dd, J = 8.9, 2.1 Hz, 1H), 7.70 (dd, J = 7.7, 5.3 Hz, 1H).	DMSO	435.0, 437.0 (M+1)	Method B (NH4HCO3)	99	Method C, G1

248

201			400.78	1H-NMR (400 MHz, DMSO-d6): δ 10.45 (s, 1H), 9.53 (d, J = 1.5 Hz, 1H), 8.85 (d, J = 8.1 Hz, 1H), 8.82 (dd, J = 5.0, 1.4 Hz, 1H), 8.69 (d, J = 9.0 Hz, 1H), 8.49 (s, 1H), 8.21 (d, J = 8.0 Hz, 1H), 7.99 (d, J = 2.1 Hz, 1H), 7.83 – 7.67 (m, 3H), 7.56 (d, J = 7.8 Hz, 1H).	DMSO	401.1, 403.0 (M+1)	Method B (NH4HCO3)	99	Method C, G1
202			375.79	1H-NMR (400 MHz, DMSO-d6): δ 10.47 (s, 1H), 9.49 (s, 1H), 8.87 – 8.77 (m, 2H), 8.63 (d, J = 8.9 Hz, 1H), 8.42 (dd, J = 5.8, 2.7 Hz, 1H), 8.26 (ddd, J = 9.1, 4.9, 2.8 Hz, 1H), 7.98 (d, J = 2.1 Hz, 1H), 7.83 – 7.72 (m, 2H), 7.66 (t, J = 9.1 Hz, 1H).	DMSO	375.9, 377.9 (M+1)	Method B (NH4HCO3)	99	Method C, G1
203			348.35	1H-NMR (400 MHz, DMSO-d6): δ 10.42 (s, 1H), 9.51 (s, 1H), 8.91 (d, J = 6.8 Hz, 1H), 8.86 (d, J = 4.4 Hz, 1H), 8.57 (d, J = 8.3 Hz, 1H), 8.11 (ddd, J = 13.0, 7.5, 2.5 Hz, 1H), 7.90 – 7.68 (m, 3H), 7.65 – 7.46 (m, 2H), 2.56 (s, 3H).	DMSO	349.1 (M+1)	Method B (NH4HCO3)	100	Method C, G1

249

204			381.26	1H-NMR (400 MHz, DMSO-d6): δ 10.05 (s, 1H), 9.54 (s, 1H), 8.75 – 8.65 (m, 2H), 8.46 (d, J = 8.5 Hz, 1H), 8.42 (d, J = 2.4 Hz, 1H), 7.98 (dd, J = 8.8, 2.4 Hz, 1H), 7.72 (d, J = 9.1 Hz, 2H), 7.57 (dd, J = 7.9, 4.9 Hz, 1H), 7.53 (d, J = 8.5 Hz, 1H), 2.55 (s, 3H).	DMSO	381.0, 383.0 (M+1)	Method B (NH4HCO3)	100	Method C, G1
205			364.35	1H-NMR (400 MHz, DMSO-d6): δ 9.98 (s, 1H), 9.53 (s, 1H), 8.79 – 8.58 (m, 2H), 8.49 (d, J = 9.0 Hz, 1H), 8.13 (ddd, J = 9.2, 7.1, 1.7 Hz, 1H), 7.84 – 7.65 (m, 1H), 7.67 – 7.46 (m, 2H), 7.41 – 7.23 (m, 2H), 3.97 (s, 3H).	DMSO	365.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1
206			364.80	1H-NMR (400 MHz, DMSO-d6): δ 10.32 (s, 1H), 9.50 (d, J = 1.4 Hz, 1H), 8.92 – 8.77 (m, 2H), 8.53 (d, J = 8.5 Hz, 1H), 8.24 (dd, J = 6.8, 2.5 Hz, 1H), 7.98 – 7.87 (m, 1H), 7.83 – 7.70 (m, 2H), 7.60 – 7.50 (m, 2H), 2.56 (s, 3H).	DMSO	365.1, 367.1 (M+1)	Method B (NH4HCO3)	100	Method C, G1

250

207			381.26	1H-NMR (400 MHz, DMSO-d6): δ 10.21 (s, 1H), 9.53 (s, 1H), 8.87 – 8.73 (m, 2H), 8.50 (d, J = 8.5 Hz, 1H), 8.17 (d, J = 1.7 Hz, 2H), 7.77 (s, 1H), 7.72 (dd, J = 7.8, 5.1 Hz, 1H), 7.57 (dd, J = 8.4, 0.9 Hz, 1H), 7.39 (t, J = 1.6 Hz, 1H), 2.56 (s, 3H).	DMSO	381.1, 383.0 (M+1)	Method B (NH4HCO3)	99	Method C, G1
208			337.38	1H-NMR (400 MHz, DMSO-d6): δ 10.12 (s, 1H), 9.53 (d, J = 1.6 Hz, 1H), 8.77 – 8.63 (m, 2H), 8.53 – 8.42 (m, 2H), 8.28 (d, J = 8.3 Hz, 1H), 7.75 (s, 1H), 7.69 (t, J = 7.9 Hz, 1H), 7.62 (d, J = 7.7 Hz, 1H), 7.60 – 7.51 (m, 2H), 2.55 (s, 3H).	DMSO	338.2 (M+1)	Method B (NH4HCO3)	100	Method C, G1
209			355.39	1H-NMR (400 MHz, DMSO-d6): δ 13.09 (s, 1H), 9.60 (s, 1H), 9.02 (d, J = 8.4 Hz, 1H), 8.96 (d, J = 8.4 Hz, 1H), 8.85 (d, J = 4.0 Hz, 1H), 8.49 (s, 1H), 8.13 (d, J = 8.4 Hz, 1H), 7.97 (d, J = 7.8 Hz, 1H), 7.92 (s, 1H), 7.83 (dd, J = 8.0, 5.2 Hz, 1H), 7.80 (s, 1H), 7.73 (t, J = 7.4 Hz, 1H), 7.61 (d, J = 8.0 Hz, 1H), 7.25 (t, J = 7.6 Hz, 1H), 2.56 (s, 3H).	DMSO	356.1 (M+1)	Method B (NH4HCO3)	99	Method C, G1

251

210			375.81	1H-NMR (400 MHz, DMSO-d6): 13.13 (s, 1H), 9.59 (s, 1H), 9.03 – 8.89 (m, 3H), 8.50 (s, 1H), 8.21 – 8.19 (d, J = 8.6 Hz, 1H), 7.99 – 7.87 (m, 4H), 7.82 – 7.79 (dd, J = 8.8, 2.3 Hz, 1H), 7.74 – 7.70 (m, 1H), 7.28 – 7.24 (m, 1H).	DMSO	376.1, 378.1 (M+1)	Method B (NH4HCO3)	98	Method C, G1
211			444.79	1H-NMR (400 MHz, DMSO-d6): δ 13.68 (brs, 1H), 11.98 (s, 1H), 9.49 (s, 1H), 8.83 – 8.64 (m, 2H), 8.11 – 7.90 (m, 3H), 7.81 (d, J = 2.0 Hz, 1H), 7.75 – 7.62 (m, 2H), 7.22 (t, J = 7.6 Hz, 1H).	DMSO	444.9, 446.9 (M+1)	Method B (NH4HCO3)	100	Method C, G1
212		HCl	466.79	1H-NMR (400 MHz, DMSO-d6): δ 10.36 (s, 1H), 9.62 (s, 1H), 8.90 (dd, J = 8.2, 1.3 Hz, 1H), 8.69 (d, J = 9.0 Hz, 1H), 8.05 (d, J = 8.2 Hz, 1H), 7.99 (d, J = 2.1 Hz, 1H), 7.92 – 7.86 (m, 1H), 7.86 – 7.79 (m, 1H), 7.77 (dd, J = 8.9, 2.1 Hz, 1H), 7.53 (t, J = 8.2 Hz, 1H), 7.30 (t, J = 73.3 Hz, 1H), 7.04 (dd, J = 8.1, 2.1 Hz, 1H).	DMSO	466.9, 468.9 (M+1)	Method B (NH4HCO3)	100	Method C, G1

252

213			469.67	1H-NMR (400 MHz, DMSO-d6): δ 10.31 (s, 1H), 9.57 (s, 1H), 8.85 (dd, J = 8.1, 1.3 Hz, 1H), 8.60 (d, J = 9.0 Hz, 1H), 8.35 – 8.23 (m, 1H), 8.06 (d, J = 8.2 Hz, 1H), 8.00 – 7.90 (m, 2H), 7.80 – 7.65 (m, 2H).	DMSO	468.9, 470.8 (M+1)	Method B (NH4HCO3)	100	Method C, G1
214			436.77	1H-NMR (400 MHz, DMSO-d6): δ 10.35 (s, 1H), 9.56 (s, 1H), 8.84 (d, J = 8.3 Hz, 1H), 8.64 (d, J = 9.0 Hz, 1H), 8.14 – 7.99 (m, 2H), 7.95 (d, J = 2.1 Hz, 1H), 7.81 – 7.65 (m, 2H), 7.59 – 7.48 (m, 1H).	DMSO	436.9, 438.9 (M+1)	Method B (NH4HCO3)	100	Method C, G1
215			440.37	1H-NMR (400 MHz, DMSO-d6): δ 13.81 (brs, 1H), 11.97 (s, 1H), 9.57 (s, 1H), 9.01 – 8.91 (m, 1H), 8.84 (d, J = 8.3 Hz, 1H), 8.06 (dd, J = 7.9, 1.4 Hz, 1H), 8.01 (d, J = 8.2 Hz, 1H), 7.82 (d, J = 9.1 Hz, 1H), 7.79 – 7.70 (m, 1H), 7.52 (dd, J = 9.1, 2.6 Hz, 1H), 7.49 – 7.44 (m, 1H), 7.20 (t, J = 7.6 Hz, 1H), 3.94 (s, 3H).	DMSO	441.1 (M+1)	Method B (NH4HCO3)	100	Method C, G1

253

216			396.80	1H-NMR (400 MHz, DMSO-d6): δ 11.89 (s, 1H), 9.80 (s, 1H), 8.34 (dd, J = 9.6, 2.6 Hz, 1H), 8.22 (s, 1H), 8.11 (dd, J = 6.9, 2.6 Hz, 1H), 7.88 (d, J = 2.7 Hz, 1H), 7.84 – 7.77 (m, 1H), 7.74 (d, J = 9.1 Hz, 1H), 7.56 – 7.43 (m, 2H), 6.44 (d, J = 9.6 Hz, 1H), 3.95 (s, 3H).	DMSO	397.1, 399.1 (M+1)	Method B (NH4HCO3)	100	Method D, G1
217			410.37	1H-NMR (400 MHz, DMSO-d6): δ 11.89 (s, 1H), 9.80 (s, 1H), 8.36 (dd, J = 9.6, 2.6 Hz, 1H), 8.25 (d, J = 2.2 Hz, 1H), 7.92 (d, J = 2.6 Hz, 1H), 7.80 – 7.67 (m, 3H), 7.53 – 7.46 (m, 2H), 7.27 (t, J = 74.0 Hz, 1H), 6.98 (dd, J = 8.2, 2.0 Hz, 1H), 6.43 (d, J = 9.6 Hz, 1H), 3.96 (s, 3H).	DMSO	411.1 (M+1)	Method B (NH4HCO3)	100	Method D, G1
218			387.39	1H-NMR (400 MHz, DMSO-d6): δ 12.98 (s, 1H), 12.58 – 12.05 (m, 1H), 8.55 (s, 2H), 8.41 (s, 1H), 8.33 (dd, J = 9.7, 2.5 Hz, 1H), 8.11 – 7.98 (m, 1H), 7.97 – 7.86 (m, 2H), 7.79 – 7.64 (m, 3H), 7.44 – 7.29 (m, 1H), 6.52 (d, J = 9.7 Hz, 1H), 3.98 (s, 3H).	DMSO	388.2 (M+1)	Method B (NH4HCO3)	100	Method D, G1
219			389.38	1H-NMR (400 MHz, DMSO-d6): δ 12.73 (s, 1H), 9.56 (s, 1H), 9.10 (dd, J = 8.9, 5.4 Hz, 1H), 8.79 – 8.63 (m, 2H), 8.50 (s, 1H), 8.08 (s, 1H), 7.95 – 7.76 (m, 2H), 7.68 – 7.45 (m, 4H), 3.97 (s, 3H).	DMSO	390.1 (M+1)	Method B (NH4HCO3)	98	Method C, G1

254

220			369.80	1H-NMR (400 MHz, DMSO-d6): δ 14.87 (brs, 1H), 10.08 (brs, 1H), 8.85 – 7.66 (m, 6H), 7.69 – 6.63 (m, 3H), 3.96 (s, 3H).	DMSO	397.1, 399.1 (M+1)	Method B (NH4HCO3)	100	Method C, G1
221			387.39	1H-NMR (400 MHz, DMSO-d6): δ 14.80 (brs, 1H), 13.19 (s, 1H), 8.68 (d, J = 7.3 Hz, 1H), 8.44 (s, 1H), 8.38 (d, J = 8.0 Hz, 1H), 8.13 (d, J = 9.1 Hz, 1H), 8.10 – 8.03 (m, 1H), 7.95 (d, J = 7.8 Hz, 1H), 7.90 (s, 1H), 7.86 (s, 1H), 7.78 – 7.65 (m, 2H), 7.43 (t, J = 7.5 Hz, 1H), 6.78 (t, J = 6.8 Hz, 1H), 3.99 (s, 3H).	DMSO	388.1 (M+1)	Method B (NH4HCO3)	100	Method C, G1
222			410.37	1H-NMR (400 MHz, DMSO-d6): δ 15.33 (brs, 1H), 13.47 (brs, 1H), 11.69 (s, 1H), 8.62 (dd, J = 7.5, 2.1 Hz, 1H), 8.45 (d, J = 2.3 Hz, 1H), 8.17 (d, J = 9.2 Hz, 1H), 8.07 (dd, J = 6.2, 2.1 Hz, 1H), 7.81 – 7.66 (m, 3H), 7.61 (t, J = 8.1 Hz, 1H), 7.32 (t, J = 74.0 Hz, 1H), 7.26 – 7.16 (m, 1H), 6.80 – 6.69 (m, 1H), 4.03 (s, 3H).	DMSO	411.1 (M+1)	Method B (NH4HCO3)	100	Method C, G1

255

223			401.22	1H-NMR (400 MHz, DMSO-d6): δ 11.22 (brs, 1H), 8.47 (d, J = 8.8 Hz, 1H), 8.30 (dd, J = 9.6, 2.3 Hz, 1H), 8.27 – 8.18 (m, 1H), 8.11 (dd, J = 6.8, 2.4 Hz, 1H), 7.90 – 7.73 (m, 2H), 7.60 (dd, J = 8.8, 1.8 Hz, 1H), 7.47 (t, J = 9.1 Hz, 1H), 6.44 (d, J = 9.6 Hz, 1H).	DMSO	401.0, 403.0 (M+1)	Method B (NH4HCO3)	100	Method C, G1
224			414.79	1H-NMR (400 MHz, DMSO-d6): δ 12.00 (s, 1H), 10.07 (s, 1H), 8.54 (d, J = 8.9 Hz, 1H), 8.34 (dd, J = 9.6, 2.6 Hz, 1H), 8.30 (d, J = 2.3 Hz, 1H), 7.87 – 7.69 (m, 3H), 7.62 (dd, J = 8.9, 2.1 Hz, 1H), 7.48 (t, J = 8.2 Hz, 1H), 7.26 (t, J = 74.0 Hz, 1H), 7.00 (dd, J = 8.1, 2.0 Hz, 1H), 6.44 (d, J = 9.6 Hz, 1H).	DMSO	415.1, 417.1 (M+1)	Method B (NH4HCO3)	100	Method C, G1
225			432.78	1H-NMR (400 MHz, DMSO-d6): δ 12.06 (s, 1H), 10.15 (s, 1H), 8.55 (d, J = 9.0 Hz, 1H), 8.34 (dd, J = 9.6, 2.5 Hz, 1H), 8.29 (s, 1H), 7.97 (s, 1H), 7.88 (d, J = 8.0 Hz, 1H), 7.84 (d, J = 2.1 Hz, 1H), 7.65 (dd, J = 8.8, 2.1 Hz, 1H), 7.57 (t, J = 8.2 Hz, 1H), 7.17 (d, J = 7.8 Hz, 1H), 6.44 (d, J = 9.6 Hz, 1H).	DMSO	433.0, 435.0 (M+1)	Method B (NH4HCO3)	100	Method C, G1
226			428.36	1H-NMR (400 MHz, DMSO-d6): δ 12.28 (brs, 1H), 8.47 – 8.06 (m, 3H), 8.06 – 7.76 (m, 3H), 7.67 – 7.59 (m, 2H), 7.28 (s, 1H), 6.47 (d, J = 9.7 Hz, 1H), 3.98 (s, 3H).	DMSO	429.1 (M+1)	Method B (NH4HCO3)	94	Method D, G1

256

227			401.42	1H-NMR (400 MHz, DMSO-d6): δ 12.97 (s, 1H), 12.27 (s, 1H), 8.73 – 8.56 (m, 1H), 8.53 (s, 1H), 8.42 (s, 1H), 8.33 (dd, J = 9.7, 2.6 Hz, 1H), 8.04 – 7.86 (m, 3H), 7.74 – 7.59 (m, 3H), 7.34 (t, J = 8.7 Hz, 1H), 6.52 (d, J = 9.7 Hz, 1H), 4.23 (q, J = 6.9 Hz, 2H), 1.45 (t, J = 6.9 Hz, 3H).	DMSO	402.2 (M+1)	Method B (NH4HCO3)	100	Method D, G1
228			465 91	1H-NMR (400 MHz, DMSO-d6): δ 8.43 – 8.31 (m, 2H), 8.27 (s, 1H), 8.14 (dd, J = 6.7, 2.3 Hz, 1H), 7.89 – 7.70 (m, 3H), 7.47 (t, J = 9.1 Hz, 1H), 6.44 (d, J = 9.6 Hz, 1H), 3.62 (d, J = 9.3 Hz, 6H), 2.42 (s, 4H).	DMSO	466.1, 468.1 (M+1)	Method B (NH4HCO3)	97	Method D, G1
229			436.41	1H-NMR (400 MHz, DMSO-d6): δ 10.28 (brs, 1H), 9.47 (s, 1H), 8.91 (d, J = 7.2 Hz, 1H), 8.84 (d, J = 5.2 Hz, 1H), 8.08 – 8.06 (m, 2H), 7.91 (d, J = 7.6 Hz, 1H), 7.85 (t, J = 8 Hz, 1H), 7.65 – 7.60 (m, 2H), 7.54 – 7.52 (m, 1H), 4.17 (t, J = 7.6 Hz, 2H), 1.86 (q, J = 6.8 Hz, 2H), 1.08 – 1.03 (m, 3H).	DMSO	423.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1
230			403.41	1H-NMR (400 MHz, DMSO-d6): δ 13.42 (s, 1H), 9.53 (s, 1H), 9.10 (d, J = 12.8 Hz, 1H), 8.70 – 8.65 (m, 2H), 8.50 (s, 1H), 8.07 – 8.04 (m, 2H), 7.86 (d, J = 8.8 Hz, 1H), 7.60 – 7.55 (m, 2H), 7.48 (s, 1H), 7.06 – 7.01 (m, 1H), 4.21 (q, J = 6.8 Hz, 2H), 1.45 (t, J = 7.2 Hz, 3H).	DMSO	403.9 (M+1)	Method A (TFA)	95	Method C, G1

257

231			440.42	1H-NMR (400 MHz, DMSO-d6): δ 10.57 (s, 1H), 9.48 (s, 1H), 9.01 (d, J = 7.6 Hz, 1H), 8.90 (d, J = 5.2 Hz,1H), 8.19 (s, 1H), 8.04 (s, 1H), 7.98 (d, J = 8.8 Hz, 2H), 7.93 (t, J = 5.6 Hz, 1H), 7.64 – 7.60 (m, 2H), 7.22 (d, J = 8.4 Hz, 1H), 4.19 (t, J = 6.4 Hz,1H), 1.87 – 1.81 (m, 2H), 1.06 (t, J = 7.2 Hz, 3H).	DMSO	440.9 (M+1)	Method A (TFA)	95	Method C, G1
232			359.12	1H-NMR (400 MHz, DMSO-d6): δ 13.10 (s, 1H), 9.54 (s, 1H), 8.96 (d, J = 8.4 Hz, 1H), 8.82 – 8.80 (m, 2H), 8.52 (s, 1H), 8.22 – 8.17 (m, 1H), 7.97 – 7.93 (m, 2H), 7.70 – 7.59 (m, 4H), 7.21 (t, J = 8.0 Hz, 1H).	DMSO	360.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1
233			381.26	1H-NMR (400 MHz, DMSO-d6): δ 9.48 (s, 1H), 9.08 (s, 1H), 8.67 – 8.70 (m, 1H), 8.64 (d, J = 8.0 Hz, 1H), 7.98 (s, 2H), 7.76 – 7.78 (m, 2H), 7.55 – 7.57 (m, 1H), 7.43 – 7.46 (m, 1H), 7.36 (s, 1H), 2.99 (s, 3H).	DMSO	381.0, 383.0, 385.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1
234		HCl	408.4	1H-NMR (400 MHz, DMSO-d6): δ 10.38 (s, 1H), 9.51 (s, 1H), 9.00 (d, J = 7.2 Hz, 1H), 8.88 (d, J = 4.8 Hz, 1H), 8.13 (s, 1H), 7.96 (d, J = 7.2 Hz, 1H), 7.86 – 7.91 (m, 2H), 7.86 (s, 1H), 7.80 (d, J = 8.4 Hz, 1H), 7.63 (d, J = 2.4 Hz, 1H), 7.62 (dd, J = 9.2, 2.0 Hz, 1H), 7.55 (t, J = 8.4 Hz, 1H), 7.31 (t, J = 74.0 Hz, 1H), 7.05 (d, J = 8.0 Hz, 1H), 4.28 (q, J = 6.8 Hz, 2H), 1.46 (t, J = 6.8 Hz, 3H).	DMSO	409.2 (M+1)	Method B (NH4HCO3)	95	Method C, G1

235			412.36	1H-NMR (400 MHz, DMSO-d6): δ 10.81 (s, 1H), 9.49 (s, 1H), 9.02 (d, J = 8.4 Hz, 1H), 8.91 (dd, J = 5.2, 1.2 Hz, 1H), 8.31 (d, J = 2.0 Hz, 1H), 8.06 (s, 1H), 8.01 (d, J = 8.8 Hz, 2H), 7.94 – 7.91 (m, 1H), 7.64 – 7.60 (m, 2H), 7.22 (d, J = 8.4 Hz,1H), 4.02 (s, 3H).	DMSO	412.9 (M+1)	Method A (TFA)	95	Method C, G1
236			395.46	1H-NMR (400 MHz, DMSO-d6): δ 9.64 (s, 1H), 8.90 (s, 1H), 8.77 (dd, J = 13.5, 6.2 Hz, 2H), 8.19 (d, J = 9.2 Hz, 1H), 7.81 (dd, J = 9.2, 2.4 Hz, 1H), 7.72 – 7.56 (m, 3H), 7.33 (d, J = 2.0 Hz, 1H), 4.15 (q, J = 6.8 Hz, 2H), 2.39 (s, 3H), 2.35 (s, 3H), 1.38 (t, J = 6.8 Hz, 3H).	DMSO	396.2 (M+1)	Method B (NH4HCO3)	98	Method C, J1
237			376.8	1H-NMR (400 MHz, DMSO-d6): δ 11.64 (brs, 1H), 11.31(brs, 1H), 9.45 (s, 1H), 8.82 – 8.69 (m, 1H), 8.61 (s, 1H), 8.15 (d, J = 2.0 Hz, 1H), 8.04 – 7.91 (m, 1H), 7.81 (dd, J = 8.9, 2.1 Hz, 1H), 7.70 – 7.55 (m, 1H), 7.47 (s, 1H), 7.06 (s, 1H), 6.98 (d, J = 8.2 Hz, 1H).	DMSO	376.9, 378.9 (M+1)	Method B (NH4HCO3)	95	Method C, G8

259

238			412.23	1H-NMR (400 MHz, DMSO-d6): δ 10.70 (s, 1H), 9.62 (d, J = 2.4 Hz, 1H), 9.51 (d, J = 1.6 Hz, 1H), 8.76 – 8.79 (m, 2H), 8.57 (dd, J = 6.8, 2.0 Hz, 1H), 8.29 (d, J = 2.4 Hz, 1H), 8.01 (d, J = 8.8 Hz, 1H), 7.94 (dd, J = 6.8, 2.0 Hz, 1H), 7.71 (m, 2H).	DMSO	412.0, 414.0, 416.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1
239			381.26	1H-NMR (400 MHz, DMSO-d6): 10.04 (s, 1H), 9.59 (d, J = 1.2 Hz, 1H), 8.74 – 8.70 (m, 2H), 8.42 – 8.39 (m, 2H), 7.98 (dd, J = 2.4 Hz, 1H), 7.79 (d, J = 7.2 Hz, 1H), 7.72 (d, J = 8.8 Hz, 1H), 7.59 – 7.55 (m, 2H), 2.75 (s, 3H).	DMSO	381, 383 (M+1)	Method B (NH4HCO3)	95	Method C, G1
240			348.35	1H-NMR (400 MHz, DMSO-d6): 10.00 (s, 1H), 9.57 (d, J = 1.2 Hz, 1H), 8.72 – 8.70 (m, 2H), 8.38 (d, J = 8.4 Hz, 1H), 8.17 – 8.12 (m, 1H), 7.79 – 7.74 (m, 2H), 7.59 – 7.50 (m, 3H), 2.74 (s, 3H).	DMSO	349.2 (M+1)	Method B (NH4HCO3)	95	Method C, G1
241			355.39	1H-NMR (400 MHz, DMSO-d6): 11.10 (s, 1H), 9.60 (d, J = 1.6 Hz,1H), 9.16 (d, J = 8.4 Hz, 1H), 8.82 – 8.72 (m, 2H), 8.50 (s, 1H), 8.04 (d, J = 8.4 Hz, 1H), 7.97 – 7.92 (m, 2H), 7.77 – 7.72 (m, 2H), 7.63 – 7.60 (m, 2H), 7.24 – 7.19 (m, 1H), 2.76 (s, 3H).	DMSO	356.2 (M+1)	Method B (NH4HCO3)	95	Method C, G1

260

242			337.4	1H-NMR (400 MHz, DMSO-d6): 10.12 (s,1H), 9.57 (s, 1H), 8.73 – 8.70 (m, 2H), 8.46 (s, 1H), 8.41 (d, J = 8.4 Hz, 1H), 8.28 (d, J = 8.0 Hz, 1H), 7.80 (d, J = 7.6 Hz, 1H), 7.72 – 7.56 (m, 4H), 2.76 (s, 3H).	DMSO	338.2 (M+1)	Method B (NH4HCO3)	95	Method C, G1
243			396.37	1H-NMR (400 MHz, DMSO-d6): 10.07 (s, 1H), 9.59 (s, 1H), 8.75 – 8.69 (m, 2H), 8.44 (d, J = 8.0 Hz, 1H), 8.20 (s, 1H), 7.97 – 7.94 (m, 1H), 7.89 (d, J = 7.2 Hz, 1H), 7.62 – 7.54 (m, 3H), 7.16 (d, J = 8.4 Hz, 1H), 2.76 (s, 3H).	DMSO	397.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1
244			378.37	1H-NMR (400 MHz, DMSO-d6): 9.98 (s, 1H), 9.60 (s, 1H), 8.75 – 8.69 (m, 2H), 8.44 (d, J = 8.0 Hz, 1H), 7.98 (s, 1H), 7.84 (d, J = 7.6 Hz, 1H), 7.79 (d, J = 6.8 Hz, 1H), 7.58 – 7.00 (m, 4H), 6.98 (d, J = 2.0 Hz, 1H), 2.76 (s, 3H).	DMSO	379.2(M+1)	Method B (NH4HCO3)	95	Method C, G1

261

245			360.34	1H-NMR (400 MHz, DMSO-d6): δ 11.95 – 11.11 (m, 2H), 9.43 (d, J = 1.6 Hz, 1H), 8.71 (dd, J = 4.7, 1.5 Hz, 1H), 8.56 (td, J = 8.0, 1.9 Hz, 1H), 8.15 (dd, J = 9.2, 5.3 Hz, 1H), 8.08 (dd, J = 9.4, 2.7 Hz, 1H), 8.02 – 7.68 (m, 2H), 7.54 (dd, J = 7.90, 4.81 Hz, 1H), 7.50 – 7.40 (m, 1H), 7.04 (t, J = 7.1 Hz, 1H), 6.96 (d, J = 8.1 Hz, 1H).	DMSO	360.8 (M+1)	Method B (NH4HCO3)	95	Method C, G8
246			393.8	1H-NMR (400 MHz, DMSO-d6): δ 13.29 (s, 1H), 9.54 (s, 1H), 9.29 (s, 1H), 8.06 (d, J = 0.9 Hz, 1H), 7.99 (d, J = 8.5 Hz, 2H), 7.82 (dd, J = 26.4, 8.4 Hz, 2H), 7.58 (dd, J = 7.9, 4.8 Hz, 1H), 7.28 (d, J = 8.0 Hz, 1H), 8.72 (d, J = 3.6 Hz, 1H), 8.67 (d, J = 7.8 Hz, 1H), 8.64 – 8.53 (m, 1H).	DMSO	394.0, 396.0 (M+1)	Method B (NH4HCO3)	95	Method C, J1
247				1H-NMR (400 MHz, DMSO-d6): δ 13.36 (brs, 1H), 9.54 (s, 1H), 9.36 – 9.08 (m, 1H), 8.12 (d, J = 8.8 Hz, 2H), 8.08 – 7.96 (m, 1H), 7.94 – 7.78 (m, 2H), 7.57 (dd, J = 7.8, 4.8 Hz, 1H), 7.29 – 7.16 (m, 1H), 8.94 – 8.49 (m, 3H).	DMSO	444.1 (M+1)	Method B (NH4HCO3)	95	Method C, J1
248			376.8	1H-NMR (400 MHz, DMSO-d6): δ 9.57 (s, 1H), 8.71 (d, J = 5.6 Hz, 2H), 8.40 (d, J = 1.8 Hz, 1H), 8.01 – 7.97 (m, 2H), 7.89 (dd, J = 7.8, 1.5 Hz, 1H), 7.63 – 7.51 (m, 1H), 7.29 (t, J = 7.4 Hz, 1H), 6.79 (d, J = 8.4 Hz, 1H), 6.76 – 6.74 (m, 1H).	DMSO	377.0, 379.0 (M+1)	Method B (NH4HCO3)	95	Method C, G8

262

249			426.35	1H-NMR (400 MHz, DMSO-d6): δ 9.70 (d, J = 1.5 Hz, 1H), 8.74 (td, J = 8.0, 1.9 Hz, 1H), 8.71 (dd, J = 4.7, 1.7 Hz, 1H), 8.50 (d, J = 9.0 Hz, 1H), 7.88 (dd, J = 7.8, 1.9 Hz, 1H), 7.76 (d, J = 1.1 Hz, 1H), 7.20 – 7.11 (m, 1H), 7.64 – 7.56 (m, 2H)., 6.70 – 6.60 (m, 1H), 6.52 (dd, J = 10.6, 3.9 Hz, 1H).	DMSO	427.1 (M+1)	Method B (NH4HCO3)	95	Method C, G8
250			360.34	1H-NMR (400 MHz, DMSO-d6): δ 9.69 (s, 1H), 8.83 (d, J = 7.4 Hz, 1H), 8.71 (d, J = 3.9 Hz, 1H), 8 49 (t, J = 7.2 Hz, 1H), 7.85 (d, J = 7.8 Hz, 1H), 7.63 – 7.51 (m, 3H), 7 14 (t, J = 7.0 Hz, 1H), 6 61 (d, J = 8.0 Hz, 1H), 6.46 (t, J = 7.2 Hz, 1H).	DMSO	360 8 (M+1)	Method B (NH4HCO3)	95	Method C, G8
251			400.43	1H-NMR (400 MHz, DMSO-d6): δ 12.92 (s, 1H), 9.04 (d, J = 8.3 Hz, 1H), 8.66 (dd, J = 7.7, 1.7 Hz, 1H), 8.48 (s, 1H), 8.10 (dd, J = 4.6, 1.7 Hz, 1H), 8.01 – 7.94 (m, 2H), 7.89 (d, J = 8.9 Hz, 1H), 7.72 (t, J = 7.7 Hz, 1H), 7.55 (m, 2H), 7.20 (t, J = 7.5 Hz, 1H), 6.74 (dd, J = 7.7, 4.7 Hz, 1H), 4.24 (q, J = 6.9 Hz, 2H), 1.46 (t, J = 6.9 Hz, 3H).	DMSO	401.0 (M+1)	Method B (NH4HCO3)	95	Method C,G1
252			483 44	1H-NMR (400 MHz, DMSO-d6): δ 13.28 (s, 1H), 9.54 (s, 1H), 9.28 (s, 1H), 8.70 – 8.66 (m, 2H), 8.59 (s, 1H), 8.11 (d, J = 8.8 Hz, 2H), 7 90 (d, J = 8.9 Hz, 1H), 7.64 – 7.49 (m, 3H), 7.18 (d, J = 8 2 Hz, 1H), 4 14 (t, J = 6.2 Hz, 2H), 1 86 (q, J = 6.8 Hz, 2H), 1.07 (t, J = 7.2 Hz, 3H).	DMSO	484.0 (M+1)	Method B (NH4HCO3)	95	Method C, J1

263

253				1H-NMR (400 MHz, DMSO-d6): δ 13.24 (s, 1H), 9.56 (s, 1H), 9.39 (d, J = 2.1 Hz, 1H), 8.77 - 8.73 (m, 2H), 8.55 (s, 1H), 8.09 (s, 1H), 8.00 (d, J = 8.6 Hz, 1H), 7.90 (d, J = 9.1 Hz, 1H), 7.65 (dd, J = 7.9, 4.9 Hz, 1H), 7.59 (dd, J = 9.1, 2.5 Hz, 1H), 4.24 (q, J = 6.9 Hz, 2H), 1.46 (t, J = 6.9 Hz, 3H).	DMSO	420.0, 422.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1
254			469 42	1H-NMR (400 MHz, DMSO-d6): δ 13.34 (s, 1H), 9.60 (s, 1H), 9.35 (s, 1H), 8.77 (d, J = 3.5 Hz, 1H), 8.72 (d, J = 7.9 Hz, 1H), 8.67 (s, 1H), 8.22 (s, 1H), 8.17 (d, J = 8.8 Hz, 1H), 7.94 (d, J = 9.1 Hz, 1H), 7.69 – 7.58 (m, 2H), 7.55 (s, 1H), 7.24 (d, J = 8.5 Hz, 1H), 4.29 (q, J = 7.0 Hz, 2H), 1.53 (t, J = 6.9 Hz, 3H).	DMSO	470.2 (M+1)	Method B (NH4HCO3)	95	Method C, G1
255			403.41	1H-NMR (400 MHz, DMSO-d6): δ 11.43 (s, 1H), 9.53 (s, 1H), 8.68 – 8.66 (m, 2H), 8.56 (d, J = 8.3 Hz, 1H), 8.23 (s, 1H), 8.12 (s, 1H), 7.88 (d, J = 9.1 Hz, 1H), 7.72 – 7.64 (m, 1H), 7.61 – 7.47 (m, 3H), 7.17 – 7.08 (m, 1H), 4.23 (q, J = 6.9 Hz, 2H), 1.46 (t, J = 6.9 Hz, 3H).	DMSO	404.2 (M+1)	Method B (NH4HCO3)	95	Method C, G1

264

Number	Product	Salt Type	Molecular Mass	^{1}H NMR	^{1}H NMR Solvent	LCMS	Retention Time (min)	LCMS Protocol	Purity percent	Method of Coupling
256		HCl	456.723	^{1}H NMR (300 MHz, DMSO) δ 9.55 (s, 1H), 9.09 (d, *J* = 8.0 Hz, 1H), 9.01 – 8.76 (m, 2H), 8.50 (s, 1H), 8.37 (s, 1H), 8.13 – 7.91 (m, 4H), 7.65 (d, *J* = 8.9 Hz, 1H), 7.69 (t, *J* = 7.7 Hz, 1H), 7.25 (t, *J* = 7.6 Hz, 1H).	DMSO	420 (M+1)	1.89	Method D	100	Method G1
257		HCl	524.39	1H NMR (300 MHz, DMSO) δ 10.68 (s, 1H), 9.50 (s, 1H), 9.08 (d, J = 8.1 Hz, 1H), 8.92 (d, J = 5.2 Hz, 1H), 8.28 (s, 1H), 8.11 (s, 1H), 8.06 – 7.93 (m, 2H), 7.87 (d, J = 7.6 Hz, 1H), 7.70 – 7.51 (m, 2H), 7.19 (d, J = 7.6 Hz, 1H), 4.28 (t, J = 9.1 Hz, 2H), 4	DMSO	452 (M+1)	1.34	Method D	100	Method G1
258		HCl	474.89	1H NMR (300 MHz, DMSO) δ 10.36 (s, 1H), 9.52 (s, 1H), 9.00 (d, J = 8.2 Hz, 1H), 8.89 (d, J = 4.4 Hz, 1H), 8.12 (s, 1H), 8.02 – 7.78 (m, 4H), 7.64 (d, J = 9.2 Hz, 1H), 7.54 (t, J = 8.2 Hz, 1H), 7.07 (d, J = 7.7 Hz, 1H), 4.08 – 3.87 (m, 5H), 3.46 (s, 3H)	DMSO	439 (M+1)	2.21	Method C	98	Method G1

265

259		HCl	460.86	1H NMR (300 MHz, DMSO) δ 10.61 (s, 1H), 9.51 (s, 1H), 9.10 (d, J = 8.2 Hz, 1H), 8.94 (d, J = 4.9 Hz, 1H), 8.22 (s, 1H), 8.08 – 7.94 (m, 2H), 7.93 – 7.78 (m, 2H), 7.65 (d, J = 9.1 Hz, 1H), 7.53 (t, J = 8.2 Hz, 1H), 7.08 (d, J = 7.3 Hz, 1H), 4.01 (s, 3H), 3	DMSO	425 (M+1)	1.64	Method C	98	Method G1
260		HCl	429.67	No Data		428.9 (M+1)	2.35	Method C	100	Method G1
261		HCl	443.24	1H NMR (300 MHz, DMSO) δ 10.35 (s, 1H), 9.52 (d, J = 1.5 Hz, 1H), 8.97 (dd, J = 6.6, 1.8 Hz, 2H), 8.91 – 8.83 (m, 1H), 8.07 (dd, J = 8.9, 2.0 Hz, 1H), 7.85 (dd, J = 14.6, 8.2 Hz, 4H), 7.54 (dd, J = 11.7, 4.6 Hz, 1H), 7.31 (s, 1H), 7.10 – 6.99 (m, 1H)	DMSO	442.96 (M+1)	2.36	Method C	100	Method G1
262		HCl	426.39	1H NMR (300 MHz, DMSO) δ 10.71 (s, 1H), 9.47 (s, 1H), 9.01 (d, J = 8.2 Hz, 1H), 8.90 (d, J = 4.0 Hz, 1H), 8.23 (s, 1H), 8.08 – 7.86 (m, 4H), 7.61 (t, J = 8.2 Hz, 2H), 7.22 (d, J = 7.6 Hz, 1H), 4.28 (d, J = 7.0 Hz, 2H), 1.44 (t, J = 6.9 Hz, 3H).	DMSO	427.1 (M+1)	2.47	Method C	93	Method G1

266

263		HCl	446.13	1H NMR (300 MHz, DMSO) δ 10.35 (s, 1H), 9.47 (s, 1H), 8.90 (s, 3H), 8.27 (s, 1H), 8.02 (d, J = 8.9 Hz, 1H), 7.94 (d, J = 8.8 Hz, 1H), 7.61 (d, J = 9.0 Hz, 2H), 7.66 (d, J = 8.8 Hz, 1H).	DMSO	494.0 (M+1)	2.29	Method C	91	Method G1
264			395.46	1H NMR (300 MHz, DMSO) δ 9.63 (s, 1H), 8.88 (s, 1H), 8.83 – 8.71 (m, 2H), 8.18 (d, J = 9.2 Hz, 1H), 7.80 (dd, J = 9.2, 2.3 Hz, 1H), 7.69 – 7.57 (m, 3H), 7.32 (d, J = 2.1 Hz, 1H), 4.14 (q, J = 6.6 Hz, 2H), 2.39 (s, 3H), 2.35 (s, 3H), 1.37 (t, J = 6.9 Hz, 3	DMSO	396.10 (M+1)	2.3	Method C	100	Method G12
265		HCl	469.53	1H NMR (300 MHz, DMSO) δ 12.13 (s, 1H), 9.54 (s, 1H), 8.99 (d, J = 7.4 Hz, 1H), 8.85 (s, 2H), 8.61 (d, J = 8.2 Hz, 1H), 7.95 (d, J = 9.1 Hz, 1H), 7.86 (d, J = 7.3 Hz, 2H), 7.68 (dd, J = 15.1, 7.8 Hz, 3H), 7.32 (d, J = 6.8 Hz, 1H), 4.00 (s, 3H), 3.71 (d, J	DMSO	470.1 (M+1)	2.15	Method C	100	Method G1
266		HCl	455.51	1H NMR (300 MHz, DMSO) δ 12.07 (s, 1H), 9.52 (s, 1H), 8.82 – 8.65 (m, 4H), 7.88 (dd, J = 8.1, 5.0 Hz, 2H), 7.73 – 7.55 (m, 4H), 7.27 (t, J = 7.2 Hz, 1H), 3.98 (m, 1H), 3.82 (d, J = 10.4 Hz, 2H), 3.35 (t, J = 11.7 Hz, 2H), 1.68 (d, J = 10.3 Hz, 2H), 1.55 –	DMSO	456.1 (M+1)	2.09	Method C	100	Method G1

267

267		HCl	406.36	1H NMR (300 MHz, DMSO) δ 10.57 (s, 1H), 9.45 (d, J = 1.5 Hz, 1H), 8.99 (d, J = 8.0 Hz, 1H), 8.89 (d, J = 3.9 Hz, 1H), 8.16 (d, J = 2.3 Hz, 1H), 8.05 (d, J = 2.0 Hz, 1H), 7.94 (t, J = 7.4 Hz, 2H), 7.63 (ddd, J = 9.3, 6.9, 2.3 Hz, 2H), 7.52 (d, J = 8.7 Hz,	DMSO	409.1 (M+1)	2.3	Method C	100	Method G1
268		HCl	367.4	1H NMR (300 MHz, DMSO) δ 11.12 (s, 1H), 9.81 (s, 1H), 9.43 – 9.37 (m, 1H), 8.56 (ddd, J = 8.0, 4.8, 1.4 Hz, 2H), 8.09 (d, J = 2.5 Hz, 1H), 7.89 (d, J = 2.2 Hz, 1H), 7.80 (s, 1H), 7.72 (d, J = 7.9 Hz, 1H), 7.53 – 7.41 (m, 3H), 7.17 (t, J = 7.5 Hz, 1H), 7.0	DMSO	368.1 (M+1)	1.98	Method C	100	Method G1
269			386.4	^{1}H NMR (300 MHz, DMSO) δ 11.47 (s, 2H), 9.39 (s, 1H), 8.66 (d, *J* = 2.8 Hz, 1H), 8.56 – 8.47 (m, 1H), 8.01 – 7.90 (m, 2H), 7.69 – 7.55 (m, 2H), 7.55 – 7.40 (m, 2H), 7.05 (t, *J* = 7.5 Hz, 1H), 6.97 (d, *J* = 8.2 Hz, 1H), 4.23 (q, *J* = 6.9 Hz, 2H), 1.44 (t, *J* =	DMSO	387.0 (M+1)	2.05	Method C	100	Method G6
270			407.45	^{1}H NMR (300 MHz, DMSO) δ 10.52 (s, 1H), 9.44 (s, 1H), 8.92 (d, *J* = 7.4 Hz, 1H), 8.86 (d, *J* = 5.1 Hz, 1H), 8.46 (d, *J* = 6 4 Hz, 1H), 8.01 (d, *J* = 8.7 Hz, 2H), 7.92 – 7.74 (m, 6H), 7.68 (dd, *J* = 9.2, 2.4 Hz, 1H), 7.48 (t, *J* = 7.8 Hz, 1H), 3.98 (s, 4H).	DMSO	408.0 (M+1)	1.92	Method C	100	Method G1, with two drops of conc. HCl

268

271		HCl	385.42	^{1}H NMR (300 MHz, DMSO) δ 9.75 (s, 1H), 9.66 (s, 1H), 9.39 (s, 1H), 8.61 (d, *J* = 3.1 Hz, 1H), 8.54 (d, *J* = 8.2 Hz, 1H), 7.85 (s, 1H), 7.82 (s, 2H), 7.71 (d, *J* = 7.4 Hz, 1H), 7.54 (d, *J* = 9.1 Hz, 1H), 7.46 (dd, *J* = 7.5, 5.2 Hz, 1H), 7.35 – 7.23 (m, 2H), 3.9	DMSO	386.1 (M+1)	1.79	Method C	96	Method G2
272		HCl	413.47	^{1}H NMR (300 MHz, DMSO) δ 12.30 (s, 1H), 9.57 (d, *J* = 2.1 Hz, 1H), 8.89 (d, *J* = 8.0 Hz, 1H), 8.77 – 8.67 (m, 2H), 8.63 (d, *J* = 7.7 Hz, 1H), 7.94 – 7.83 (m, 2H), 7.71 (t, *J* = 7.1 Hz, 1H), 7.66 – 7.52 (m, 3H), 7.25 (t, *J* = 7.4 Hz, 1H), 4.24 – 4.06 (m, 1H), 3	DMSO	414.2 (M+1)	2.36	Method C	100	Method G1
273		HCl	387.46	^{1}H NMR (300 MHz, DMSO) δ 10.96 (s, 1H), 10.29 (s, 1H), 9.85 (s, 1H), 9.51 (d, *J* = 2.0 Hz, 1H), 8.71 – 8.62 (m, 2H), 8.47 (dd, *J* = 8.2, 0.9 Hz, 1H), 7.89 (d, *J* = 9.1 Hz, 1H), 7.67 – 7.62 (m, 2H), 7.60 (d, *J* = 2.5 Hz, 1H), 7.57 (d, *J* = 2.6 Hz, 1H), 7.55 – 7	DMSO	388.1 (M+1)	2.01	Method C	95	Method G1
274		HCl	399.45	^{1}H NMR (300 MHz, DMSO) δ 12.45 (s, 1H), 9.57 (d, *J* = 1.3 Hz, 1H), 8.96 (dd, *J* = 8.4, 0.9 Hz, 1H), 8.89 (t, *J* = 5.2 Hz, 1H), 8.75 – 8.66 (m, 2H), 7.94 – 7.84 (m, 2H), 7.72 (t, *J* = 7.9 Hz, 1H), 7.65 – 7.52 (m, 3H), 7.24 (t, *J* = 7.6 Hz, 1H), 4.00 (s, 3H), 3.	DMSO	400.3 (M+1)	2.21	Method C	100	Method G1

269

275		HCl	453.42	^{1}H NMR (300 MHz, DMSO) δ 11.70 (s, 1H), 9.54 (d, *J* = 2.0 Hz, 1H), 9.40 (t, *J* = 6.1 Hz, 1H), 8.79 (d, *J* = 7.7 Hz, 1H), 8.73 – 8.63 (m, 2H), 7.89 (d, *J* = 9.8 Hz, 2H), 7.76 (t, *J* = 7.1 Hz, 1H), 7.64 – 7.50 (m, 3H), 7.30 (t, *J* = 7.1 Hz, 1H), 4.16 – 4.01 (m, 2	DMSO	454.0 (M+1)	2.28	Method C	100	Method G1
276			421.25	^{1}H NMR (300 MHz, DMSO) δ 9.26 (d, *J* = 2.2 Hz, 1H), 8.71 – 8.62 (m, 2H), 8.46 (dt, *J* = 8.0, 1.9 Hz, 1H), 8.21 (dd, *J* = 8.9, 2.3 Hz, 1H), 8.03 (d, *J* = 8.9 Hz, 1H), 7.89 (s, 1H), 7.78 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.72 – 7.62 (m, 1H), 7.56 – 7.45 (m, 3H), 7.32	DMSO	423.0 (M+1)	1.85	Method C	94	Method G1
277		HCl	447.49	^{1}H NMR (300 MHz, DMSO) δ 11.25 (s, 1H), 10.46 (s, 1H), 9.45 (s, 1H), 8.93 (d, *J* = 7.9 Hz, 1H), 8.82 (d, *J* = 3.9 Hz, 1H), 8.22 (d, *J* = 8.1 Hz, 1H), 7.97 – 7.79 (m, 4H), 7.73 (t, *J* = 7.1 Hz, 1H), 7.62 (dd, *J* = 9.1, 2.5 Hz, 1H), 7.53 – 7.39 (m, 3H), 7.19 (t,	DMSO	448.1 (M+1)	2.67	Method C	100	Method G1
278		HCl	399.45	^{1}H NMR (300 MHz, DMSO) δ 12.59 (s, 1H), 9.57 (d, *J* = 1.4 Hz, 1H), 9.03 (dd, *J* = 8.4, 0.9 Hz, 1H), 8.91 (d, *J* = 4.6 Hz, 1H), 8.76 – 8.64 (m, 2H), 7.88 (t, *J* = 7.8 Hz, 2H), 7.72 (t, *J* = 7.9 Hz, 1H), 7.63 – 7.53 (m, 3H), 7.22 (td, *J* = 7.9, 1.1 Hz, 1H), 4.28	DMSO	400.1 (M+1)	2.5	Method C	100	Method G1

270

279		HCl	399.45	^{1}H NMR (300 MHz, DMSO) δ 9.99 (s, 1H), 9.37 (d, *J* = 1.4 Hz, 1H), 8.61 (dd, *J* = 4.7, 1.7 Hz, 1H), 8.58 – 8.51 (m, 1H), 7.84 (dd, *J* = 9.0, 5.3 Hz, 3H), 7.65 – 7.42 (m, 4H), 7.38 (t, *J* = 7.5 Hz, 1H), 3.95 (s, 3H), 2.74 (s, 6H).	DMSO	400.1 (M+1)	2.2	Method C	100	Method G1
280		HCl	439.51	^{1}H NMR (300 MHz, DMSO) δ 12.05 (s, 1H), 9.51 (d, *J* = 1.6 Hz, 1H), 9.04 (d, *J* = 8.1 Hz, 1H), 8.88 (dd, *J* = 5.2, 1.3 Hz, 1H), 8.60 (d, *J* = 7.0 Hz, 1H), 8.44 (d, *J* = 8.0 Hz, 1H), 8.00 – 7.87 (m, 2H), 7.83 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.77 (d, *J* = 1.9 Hz, 1H),	DMSO	440.1 (M+1)	2.52	Method C	100	Method G1
281		HCl	403.41	^{1}H NMR (300 MHz, DMSO) δ 10.98 (s, 1H), 9.50 (s, 1H), 8.72 - 8.55 (m, 3H), 8.38 (d, *J* = 8.2 Hz, 1H), 7.87 (d, *J* = 8.9 Hz, 1H), 7.72 - 7.45 (m, 4H), 7.19 - 7.07 (m, 1H), 3.96 (s, *J* = 5.2 Hz, 3H), 2.73 (d, *J* = 4.5 Hz, 3H).	DMSO	404.1 (M+1)	2.18	Method C	100	Method G1
282		HCl	417.44	^{1}H NMR (300 MHz, DMSO) δ 10.96 (s, 1H), 9.50 (d, *J* = 1.9 Hz, 1H), 8.71 – 8.55 (m, 3H), 8.38 (d, *J* = 8.2 Hz, 1H), 7.86 (d, *J* = 9.0 Hz, 1H), 7.66 (dd, *J* = 14.8, 8.3 Hz, 1H), 7.60 – 7.47 (m, 3H), 7.21 – 7.05 (m, 1H), 4.24 (q, *J* = 6.9 Hz, 2H), 2.73 (d, *J* = 4.	DMSO	419.1 (M+1)	2.38	Method C	100	Method G1
283		HCl	439.39	^{1}H NMR (300 MHz, DMSO) δ 13.10 (s, 1H), 9.68 (d, *J* = 1.1 Hz, 1H), 9.52 (d, *J* = 1.4 Hz, 1H), 8.75 - 8.58 (m, 3H), 8.26 (s, 1H), 8.15 (d, *J* = 8.2 Hz, 1H), 7.85 (d, *J* = 9.1 Hz, 1H), 7.59 - 7.47 (m, 3H), 7.45 (d, *J* = 2.5 Hz, 1H), 3.95 (s, 3H).	DMSO	440.1 (M+1)	2.25	Method C	100	Method G1

271

284		HCl	453.42	^{1}H NMR (300 MHz, DMSO) δ 13.08 (s, 1H), 9.70 (s, 1H), 9.55 (d, *J* = 1.3 Hz, 1H), 8.77 - 8.60 (m, 3H), 8.26 (s, 1H), 8.15 (d, *J* = 8.5 Hz, 1H), 7.88 (d, *J* = 9.1 Hz, 1H), 7.62 - 7.39 (m, 4H), 4.21 (q, *J* = 7.1 Hz, 2H), 1.45 (t, *J* = 6.9 Hz, 3H).	DMSO	454.1 (M+1)	2.43	Method C	95	Method G1
285		HCl	410.43	^{1}H NMR (300 MHz, DMSO) δ 12.87 (s, 1H), 9.50 (d, *J* = 1.5 Hz, 2H), 8.73 - 8.59 (m, 3H), 8.26 (s, 1H), 8.07 (d, *J* = 8.2 Hz, 1H), 7.85 (d, *J* = 9.1 Hz, 1H), 7.64 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.59 - 7.49 (m, 2H), 7.42 (d, *J* = 2.4 Hz, 1H), 4.19 (q, *J* = 6.9 Hz, 2H	DMSO	411.1 (M+1)	2.16	Method C	95	Method G1
286		HCl	397.43	^{1}H NMR (300 MHz, DMSO) δ 13.63 (s, 1H), 9.55 (s, 1H), 9.13 (d, *J* = 8.3 Hz, 1H), 8.75 - 8.56 (m, 3H), 7.84 (d, *J* = 9.8 Hz, 1H), 7.69 - 7.48 (m, 4H), 7.01 (d, *J* = 7.4 Hz, 1H), 3.94 (s, 3H), 3.46 - 3.36 (m, 2H), 2.96 (t, *J* = 5.7 Hz, 2H).	DMSO	398.3 (M+1)	2.12	Method C	100	Method G1
287		HCl	411.46	^{1}H NMR (300 MHz, DMSO) δ 13.61 (s, 1H), 9.56 (s, 1H), 9.14 (d, *J* = 8.1 Hz, 1H), 8.75 - 8.60 (m, 3H), 7.84 (d, *J* = 9.8 Hz, 1H), 7.70 - 7.46 (m, 4H), 7.02 (d, *J* = 7.2 Hz, 1H), 4.19 (q, *J* = 6.9 Hz, 3H), 3.48 - 3.37 (m, 2H), 2.96 (t, *J* = 6.1 Hz, 2H), 1.44 (t,	DMSO	412.4 (M+1)	2.4	Method C	100	Method G1

272

288		HCl	383.4	^{1}H NMR (300 MHz, DMSO) δ 11.62 (s, 1H), 9.60 (d, *J* = 1.5 Hz, 1H), 9.02 (s, 1H), 8.88 (d, *J* = 8.0 Hz, 1H), 8.80 - 8.65 (m, 2H), 7.90 (d, *J* = 9.0 Hz, 1H), 7.75 (t, *J* = 7.9 Hz, 1H), 7.66 - 7.51 (m, 3H), 7.27 (d, *J* = 7.6 Hz, 1H), 4.47 (s, 2H), 3.97 (s, 3H).	DMSO	384.1 (M+1)	2.01	Method C	95	Method G1
289		HCl	421.4	^{1}H NMR (300 MHz, DMSO) δ 12.07 (s, 1H), 9.48 (d, J = 1.6 Hz, 1H), 8.76 - 8.55 (m, 3H), 8.34 (s, 1H), 8.14 (s, 1H), 7.87 (d, J = 9.1 Hz, 1H), 7.62 - 7.49 (m, 2H), 7.38 (d, J = 2.5 Hz, 1H), 7.14 (ddd, J = 11.5, 9.0, 2.6 Hz, 1H), 4.19 (q, J = 6.9 Hz, 2H), 1.	DMSO	422.2 (M+1)	2.35	Method C	100	Method G1
290		HCl	412.44	^{1}H NMR (300 MHz, DMSO) δ 9.82 (s, 1H), 9.50 (d, J = 2.0 Hz, 1H), 8.68 - 8.58 (m, 2H), 7.98 (d, J = 2.5 Hz, 1H), 7.85 (d, J = 1.8 Hz, 1H), 7.80 (d, J = 9.1 Hz, 1H), 7.55 - 7.43 (m, 3H), 7.23 (d, J = 8.4 Hz, 1H), 3.96 (s, 3H), 3.37 (d, J = 4.2 Hz, 6H).	DMSO	413.0 (M+1)	1.79	Method C		Method G1
291		HCl	426.47	^{1}H NMR (300 MHz, DMSO) δ 9.78 (s, 1H), 9.50 (d, J = 2.0 Hz, 1H), 8.68 - 8.57 (m, 2H), 7.97 (d, J = 2.5 Hz, 1H), 7.85 (d, J = 1.8 Hz, 1H), 7.79 (d, J = 9.1 Hz, 1H), 7.55 - 7.43 (m, 3H), 7.22 (d, J = 8.4 Hz, 1H), 4.22 (q, J = 6.9 Hz, 2H), 3.37 (d, J = 4.3 H	DMSO	427.1 (M+1)	1.92	Method C		Method G1

273

292			404.39	^{1}H NMR (300 MHz, DMSO) δ 9.36 (d, *J* = 1.4 Hz, 1H), 8.66 (d, *J* = 2.7 Hz, 1H), 8.52 (d, *J* = 7.8 Hz, 1H), 7.97 (d, *J* = 8.9 Hz, 2H), 7.64 (d, *J* = 13.5 Hz, 2H), 7.50 (dd, *J* = 7.7, 4.2 Hz, 1H), 6.86 (t, *J* = 6.8 Hz, 1H), 6.70 (dd, *J* = 11.8, 1.7 Hz, 1H), 4.22 (q,	DMSO	405.1 (M+1)	1.98	Method C	95	Method G6
293			406.82	^{1}H NMR (300 MHz, DMSO) δ 9.23 (d, *J* = 1.4 Hz, 1H), 8.63 (d, *J* = 3.6 Hz, 1H), 8.43 (d, *J* = 8.0 Hz, 1H), 8.00 (d, *J* = 9.1 Hz, 1H), 7.92 (s, 1H), 7.81 – 7.65 (m, 4H), 7.55 (dd, *J* = 8.4, 2.1 Hz, 1H), 7.48 (dd, *J* = 6.7, 3.8 Hz, 1H), 7.37 (s, 1H), 3.97 (s, 3H).	DMSO	407.1 (M+1)	1.88	Method C	100	Method G8
294		HCl	406.46	^{1}H NMR (300 MHz, DMSO) δ 10.11 (s, 1H), 9.39 (d, *J* = 1.4 Hz, 1H), 8.63 (dd, *J* = 4.7, 1.7 Hz, 1H), 8.59 – 8.53 (m, 1H), 8.50 (dd, *J* = 8.2, 0.8 Hz, 1H), 8.03 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.96 – 7.84 (m, 2H), 7.65 – 7.46 (m, 4H), 3.94 (s, 3H), 3.25 (s, 3H).	DMSO	407.1 (M+1)	2.13	Method C	95	Method G1

274

Number	Starting Material 1	Starting Material 2	Product	Salt Type	^{1}H NMR	^{1}H NMR Solvent	Purity percent	Method of Coupling
295					^{1}H NMR (400 MHz, DMSO) δ 13.12 (s, 1H), 9.90 (s, 1H), 9.47 (d, *J* = 1.4 Hz, 1H), 8.70 – 8.54 (m, 2H), 8.20 – 8.15 (m, 1H), 8.14 (s, 1H), 8.01 (d, *J* = 2.6 Hz, 1H), 7.88 – 7.75 (m, 2H), 7.65 (d, *J* = 8.9 Hz, 1H), 7.59 – 7.44 (m, 2H), 3.98 (s, 3H).	DMSO	>98	G1
296					^{1}H NMR (400 MHz, DMSO) δ 10.04 (s, 1H), 9.54 – 9.47 (m, 1H), 9.36 (s, 1H), 8.72 (d, *J* = 2.0 Hz, 1H), 8.69 – 8.59 (m, 2H), 8.19 (d, *J* = 8.8 Hz, 1H), 8.08 – 7.97 (m, 2H), 7.86 (d, *J* = 9.1 Hz, 1H), 7.61 – 7.47 (m, 2H), 3.99 (s, 3H).	DMSO	>98	G1
297					^{1}H NMR (400 MHz, DMSO) δ 9.64 (s, 1H), 9.55 – 9.45 (m, 1H), 8.72 – 8.60 (m, 2H), 7.95 (d, *J* = 2.7 Hz, 1H), 7.82 (d, *J* = 9.1 Hz, 1H), 7.58 – 7.48 (m, 3H), 7.34 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.96 (d, *J* = 8.7 Hz, 1H), 4.39 – 4.23 (m, 4H), 3.97 (s, 3H).	DMSO	>98	G1
298					^{1}H NMR (400 MHz, DMSO) δ 11.21 (s, 1H), 9.79 (s, 1H), 9.53 (d, *J* = 1.4 Hz, 1H), 8.75 – 8.56 (m, 2H), 8.07 (s, 1H), 8.03 (d, *J* = 2.7 Hz, 1H), 7.82 (d, *J* = 9.1 Hz, 1H), 7.61 (d, *J* = 8.5 Hz, 1H), 7.56 – 7.47 (m, 2H), 7.43 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.39 – 7.34 (m, 1H), 6.50 – 6.41 (m, 1H), 3.99 (s, 3H).	DMSO	>98	G1

275

299					^{1}H NMR (400 MHz, DMSO) δ 9.54 (s, 1H), 9.42 – 9.34 (m, 1H), 8.61 (dd, *J* = 4.7, 1.7 Hz, 1H), 8.57 – 8.47 (m, 1H), 7.93 (d, *J* = 2.7 Hz, 1H), 7.81 (d, *J* = 9.1 Hz, 1H), 7.56 – 7.44 (m, 2H), 7.19 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.00 – 6.91 (m, 1H), 6.86 (dd, *J* = 8.2, 1.6 Hz, 1H), 4.34 – 4.17 (m, 4H), 3.95 (s, 3H).	DMSO	>98	G1
300					^{1}H NMR (400 MHz, DMSO) δ 10.76 (s, 1H), 10.01 (s, 1H), 9.17 – 9.06 (m, 1H), 8.53 (dd, *J* = 4.7, 1.7 Hz, 1H), 8.36 – 8.27 (m, 1H), 8.05 (d, *J* = 2.7 Hz, 1H), 7.84 (d, *J* = 9.1 Hz, 1H), 7.60 – 7.48 (m, 2H), 7.36 (ddd, *J* = 8.0, 4.8, 0.8 Hz, 1H), 7.32 – 7.28 (m, 1H), 7.25 (d, *J* = 6.8 Hz, 1H), 7.16 – 7.04 (m, 1H), 6.54 (dd, *J* = 3.0, 1.9 Hz, 1H), 3.98 (s, 3H).	DMSO	>98	G1
301					^{1}H NMR (400 MHz, DMSO) δ 10.02 (s, 1H), 9.48 (d, *J* = 1.5 Hz, 1H), 9.33 (d, *J* = 1.0 Hz, 1H), 8.69 – 8.59 (m, 2H), 8.37 (d, *J* = 1.7 Hz, 1H), 8.10 (dd, *J* = 9.0, 2.1 Hz, 1H), 8.00 (d, *J* = 2.7 Hz, 1H), 7.90 (d, *J* = 9.0 Hz, 1H), 7.86 (d, *J* = 9.1 Hz, 1H), 7.57 (dd, *J* = 9.1, 2.7 Hz, 1H), 7.54 – 7.47 (m, 1H), 3.99 (s, 3H).	DMSO	>98	G1
302					^{1}H NMR (400 MHz, DMSO) δ 10.52 (s, 1H), 9.16 (dd, *J* = 2.2, 0.8 Hz, 1H), 8.60 (dd, *J* = 4.7, 1.7 Hz, 1H), 8.45 – 8.36 (m, 1H), 8.03 (d, *J* = 2.7 Hz, 1H), 7.97 – 7.90 (m, 2H), 7.88 (d, *J* = 7.0 Hz, 1H), 7.77 (dd, *J* = 9.0, 7.1 Hz, 1H), 7.61 (dd, *J* = 9.1, 2.7 Hz, 1H), 7.44 (ddd, *J* = 8.0, 4.8, 0.8 Hz, 1H), 4.01 (s, 3H).	DMSO	>98	G1

276

303					^{1}H NMR (400 MHz, DMSO) δ 9.86 (s, 1H), 9.60 – 9.56 (m, 1H), 8.72 – 8.67 (m, 1H), 8.65 (dd, *J* = 4.8, 1.7 Hz, 1H), 8.26 – 8.21 (m, 1H), 8.05 (d, *J* = 2.7 Hz, 1H), 7.83 (d, *J* = 9.1 Hz, 1H), 7.62 (d, *J* = 8.4 Hz, 1H), 7.56 – 7.50 (m, 2H), 7.46 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.35 (d, *J* = 3.1 Hz, 1H), 6.46 (dd, *J* = 3.1, 0.8 Hz, 1H), 3.99 (s, 3H), 3.86 (s, 3H).	DMSO	>98	G1
304					^{1}H NMR (400 MHz, DMSO) δ 9.96 (s, 1H), 9.51 – 9.45 (m, 1H), 8.68 – 8.59 (m, 2H), 8.57 – 8.52 (m, 1H), 8.02 – 7.86 (m, 3H), 7.87 – 7.80 (m, 1H), 7.58 – 7.46 (m, 2H), 3.98 (s, 3H), 2.63 (s, 3H).	DMSO	>98	G1
305					^{1}H NMR (400 MHz, DMSO) δ 9.94 (s, 1H), 9.51 – 9.43 (m, 1H), 8.68 – 8.58 (m, 2H), 8.39 (d, *J* = 2.0 Hz, 1H), 7.99 (d, *J* = 2.7 Hz, 1H), 7.87 – 7.80 (m, 2H), 7.78 (d, *J* = 8.6 Hz, 1H), 7.54 (dd, *J* = 9.1, 2.7 Hz, 1H), 7.51 (ddd, *J* = 8.0, 4.8, 0.8 Hz, 1H), 4.19 (s, 3H), 3.98 (s, 3H).	DMSO	>98	G1
306					^{1}H NMR (400 MHz, DMSO) δ 9.72 (s, 1H), 9.52 – 9.47 (m, 1H), 8.67 – 8.60 (m, 2H), 7.98 (d, *J* = 2.7 Hz, 1H), 7.82 (d, *J* = 9.1 Hz, 1H), 7.78 – 7.74 (m, 1H), 7.68 – 7.62 (m, 1H), 7.55 – 7.48 (m, 2H), 7.32 (d, *J* = 8.1 Hz, 1H), 3.97 (s, 3H), 2.99 – 2.86 (m, 4H), 2.15 – 2.04 (m, 2H).	DMSO	>98	G1

277

307					^{1}H NMR (400 MHz, $CDCl_3$) δ 9.74 (s, 1H), 9.37 – 9.31 (m, 1H), 8.60 (dd, *J* = 4.7, 1.7 Hz, 1H), 8.53 – 8.46 (m, 1H), 7.95 (d, *J* = 2.7 Hz, 1H), 7.82 (d, *J* = 9.1 Hz, 1H), 7.52 (dd, *J* = 9.1, 2.7 Hz, 1H), 7.47 (ddd, *J* = 8.0, 4.8, 0.8 Hz, 1H), 7.34 (d, *J* = 7.0 Hz, 1H), 7.31 – 7.24 (m, 1H), 7.22 (d, *J* = 7.1 Hz, 1H), 3.96 (s, 3H), 2.99 (t, *J* = 7.3 Hz, 2H), 2.82 (t, *J* = 7.4 Hz, 2H), 2.06 – 1.96 (m, 2H).	DMSO	>98	G1
306				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.45 (s, 1H), 9.50 – 9.44 (m, 1H), 8.94 – 8.87 (m, 1H), 8.83 (dd, *J* = 5.1, 1.5 Hz, 1H), 8.54 (d, *J* = 2.0 Hz, 1H), 8.13 (d, *J* = 2.4 Hz, 1H), 8.02 (d, *J* = 8.7 Hz, 1H), 7.97 – 7.89 (m, 2H), 7.83 (dd, *J* = 8.0, 5.2 Hz, 1H), 7.63 (dd, *J* = 9.1, 2.7 Hz, 1H), 4.01 (s, 3H), 2.83 (s, 3H).	DMSO	>98	G1
309				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.64 (s, 1H), 9.47 (d, *J* = 1.5 Hz, 1H), 8.94 (d, *J* = 8.1 Hz, 1H), 8.86 (dd, *J* = 5.2, 1.5 Hz, 1H), 8.54 – 8.48 (m, 1H), 8.23 – 8.16 (m, 1H), 8.04 – 7.94 (m, 2H), 7.92 – 7.83 (m, 2H), 7.78 (d, *J* = 5.4 Hz, 1H), 7.65 (dd, *J* = 9.1, 2.6 Hz, 1H), 7.51 (dd, *J* = 5.4, 0.7 Hz, 1H), 4.02 (s, 3H).	DMSO	>98	G1
310				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.86 (s, 1H), 9.43 (d, *J* = 1.6 Hz, 1H), 8.94 (d, *J* = 7.5 Hz, 1H), 8.89 (dd, *J* = 5.2, 1.5 Hz, 1H), 8.30 – 8.20 (m, 1H), 8.13 – 7.99 (m, 3H), 7.94 – 7.84 (m, 1H), 7.74 (d, *J* = 1.3 Hz, 2H), 7.67 (dd, *J* = 9.1, 2.5 Hz, 1H), 7.08 (d, *J* = 2.2 Hz, 1H), 4.02 (s, 3H).	DMSO	>98	G1

278

311				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.53 (s, 1H), 9.48 (d, *J* = 1.5 Hz, 1H), 8.93 (d, *J* = 7.7 Hz, 1H), 8.85 (dd, *J* = 5.2, 1.5 Hz, 1H), 8.44 (d, *J* = 1.9 Hz, 1H), 8.20 – 8.15 (m, 1H), 8.13 (d, *J* = 8.7 Hz, 1H), 7.97 (d, *J* = 9.1 Hz, 1H), 7.92 (dd, *J* = 8.7, 2.0 Hz, 1H), 7.86 (dd, *J* = 7.8, 5.1 Hz, 1H), 7.64 (dd, *J* = 9.1, 2.6 Hz, 1H), 4.02 (s, 3H), 2.65 (s, 3H).	DMSO	>98	G1
312				3 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.85 (s, 1H), 9.54 (d, *J* = 1.5 Hz, 1H), 9.47 (s, 1H), 9.32 (s, 1H), 9.03 (d, *J* = 8.0 Hz, 1H), 8.93 – 8.87 (m, 1H), 8.86 – 8.78 (m, 2H), 8.44 (dd, *J* = 8.8, 1.9 Hz, 1H), 8.14 (d, *J* = 2.1 Hz, 1H), 8.10 (d, *J* = 8.7 Hz, 1H), 7.99 – 7.89 (m, 2H), 7.78 – 7.71 (m, 1H), 7.55 (d, *J* = 8.7 Hz, 1H).	DMSO	>98	G1
313				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 11.07 (s, 1H), 9.54 (d, *J* = 1.6 Hz, 1H), 9.51 (d, *J* = 2.0 Hz, 1H), 9.46 – 9.39 (m, 1H), 9.10 – 9.01 (m, 1H), 8.97 – 8.88 (m, 2H), 8.86 (dd, *J* = 5.3, 1.3 Hz, 1H), 8.63 – 8.55 (m, 1H), 8.48 (dd, *J* = 8.8, 1.9 Hz, 1H), 8.15 (d, *J* = 8.7 Hz, 1H), 8.04 – 7.90 (m, 4H), 7.79 (d, *J* = 5.4 Hz, 1H), 7.52 (dd, *J* = 5.4, 0.7 Hz, 1H).	DMSO	>98	G1
314	HCl			HCl	^{1}H NMR (400 MHz, DMSO) δ 10.49 (s, 1H), 9.46 (d, *J* = 1.5 Hz, 1H), 8.93 (d, *J* = 7.9 Hz, 1H), 8.85 (dd, *J* = 5.2, 1.5 Hz, 1H), 8.24 (s, 1H), 8.16 (d, *J* = 2.5 Hz, 1H), 8.05 (d, *J* = 2.2 Hz, 1H), 7.96 (d, *J* = 9.1 Hz, 1H), 7.87 (dd, *J* = 8.1, 5.3 Hz, 1H), 7.77 (d, *J* = 8.4 Hz, 1H), 7.72 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.64 (dd, *J* = 9.1, 2.6 Hz, 1H), 7.03 (dd, *J* = 2.2, 1.0 Hz, 1H), 4.02 (s, 3H).	DMSO	>98	G1

279

315				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.72 (s, 1H), 9.46 (d, *J* = 1.5 Hz, 1H), 8.96 (d, *J* = 8.2 Hz, 1H), 8.87 (dd, *J* = 5.2, 1.5 Hz, 1H), 8.50 (d, *J* = 1.8 Hz, 1H), 8.21 (d, *J* = 2.4 Hz, 1H), 8.06 – 7.96 (m, 2H), 7.93 – 7.84 (m, 2H), 7.78 (d, *J* = 5.4 Hz, 1H), 7.63 (dd, *J* = 9.1, 2.6 Hz, 1H), 7.51 (dd, *J* = 5.4, 0.7 Hz, 1H), 4.29 (q, *J* = 7.0 Hz, 2H), 1.46 (t, *J* = 7.0 Hz, 3H).	DMSO	>98	G1
316					^{1}H NMR (400 MHz, DMSO) δ 10.04 (s, 1H), 9.60 – 9.52 (m, 1H), 8.75 – 8.63 (m, 2H), 8.16 (d, *J* = 2.0 Hz, 1H), 8.04 – 7.95 (m, 2H), 7.93 – 7.83 (m, 2H), 7.63 – 7.53 (m, 2H), 6.32 (d, *J* = 1.2 Hz, 1H), 4.01 (s, 3H), 2.47 (s, 3H).	DMSO	>98	G1 (0.1 N HCl added)
317					^{1}H NMR (400 MHz, DMSO) δ 11.82 (s, 1H), 10.06 (s, 1H), 9.53 – 9.46 (m, 1H), 8.81 – 8.70 (m, 2H), 8.04 (d, *J* = 2.6 Hz, 1H), 7.88 (d, *J* = 9.1 Hz, 1H), 7.81 (d, *J* = 2.1 Hz, 1H), 7.67 (dd, *J* = 7.9, 5.0 Hz, 1H), 7.57 (dd, *J* = 9.1, 2.7 Hz, 1H), 7.53 (dd, *J* = 8.7, 2.1 Hz, 1H), 7.39 (d, *J* = 8.6 Hz, 1H), 4.00 (s, 3H).	DMSO	>98	G1 (0.1 N HCl added)
318					^{1}H NMR (400 MHz, DMSO) δ 9.89 (s, 1H), 9.57 – 9.48 (m, 1H), 8.72 – 8.58 (m, 2H), 8.01 (d, *J* = 2.1 Hz, 1H), 7.99 (d, *J* = 2.7 Hz, 1H), 7.85 (d, *J* = 9.1 Hz, 1H), 7.59 – 7.49 (m, 3H), 7.43 (d, *J* = 8.6 Hz, 1H), 3.98 (s, 3H), 3.41 (s, 3H).	DMSO	>98	G1 (0.1 N HCl added)
319					^{1}H NMR (400 MHz, DMSO) δ 9.88 (s, 1H), 9.52 – 9.44 (m, 1H), 8.71 – 8.59 (m, 2H), 8.02 – 7.91 (m, 2H), 7.63 (d, *J* = 9.1 Hz, 1H), 7.66 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.58 – 7.48 (m, 2H), 7.36 (d, *J* = 8.4 Hz, 1H), 3.96 (s, 3H), 3.40 (s, 3H).	DMSO	>98	G1 (0.1 N HCl added)

320					^{1}H NMR (400 MHz, DMSO) δ 10.01 (s, 1H), 9.58 – 9.51 (m, 1H), 9.45 (s, 1H), 8.75 (d, *J* = 1.9 Hz, 1H), 8.71 – 8.63 (m, 2H), 8.25 (d, *J* = 8.7 Hz, 1H), 8.08 – 8.00 (m, 2H), 7.86 (d, *J* = 9.1 Hz, 1H), 7.61 – 7.50 (m, 2H), 4.00 (s, 3H).	DMSO	>98	G1 (0.1 N HCl added)
321					^{1}H NMR (400 MHz, DMSO) δ 10.43 (s, 1H), 9.72 (s, 1H), 9.51 – 9.45 (m, 1H), 8.67 – 8.57 (m, 2H), 7.96 (d, *J* = 2.7 Hz, 1H), 7.81 (d, *J* = 9.1 Hz, 1H), 7.73 – 7.68 (m, 1H), 7.64 (dd, *J* = 8.3, 2.1 Hz, 1H), 7.56 – 7.48 (m, 2H), 6.93 (d, *J* = 8.3 Hz, 1H), 3.97 (s, 3H), 3.58 (s, 2H).	DMSO	>98	G1 (0.1 N HCl added)
322					^{1}H NMR (400 MHz, DMSO) δ 9.95 (s, 1H), 9.54 – 9.45 (m, 1H), 8.67 (dd, *J* = 4.7, 1.7 Hz, 1H), 8.66 – 8.60 (m, 1H), 8.15 (d, *J* = 2.4 Hz, 1H), 7.94 (d, *J* = 2.6 Hz, 1H), 7.89 – 7.83 (m, 2H), 7.63 – 7.52 (m, 3H), 3.98 (s, 3H).	DMSO	>98	G1 (0.1 N HCl added)
323					^{1}H NMR (400 MHz, DMSO) δ 10.99 (s, 1H), 9.75 (s, 1H), 9.55 – 9.49 (m, 1H), 8.69 – 8.62 (m, 2H), 7.96 (d, *J* = 2.7 Hz, 1H), 7.83 (d, *J* = 9.1 Hz, 1H), 7.58 – 7.49 (m, 3H), 7.35 (dd, *J* = 8.7, 2.5 Hz, 1H), 7.06 (d, *J* = 8.6 Hz, 1H), 4.62 (s, 2H), 3.97 (s, 3H).	DMSO	>98	G1 (0.1 N HCl added)
324				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.24 (s, 1H), 9.58 – 9.51 (m, 1H), 8.92 – 8.84 (m, 1H), 8.80 (dd, *J* = 5.0, 1.5 Hz, 1H), 8.16 (d, *J* = 2.0 Hz, 1H), 8.07 (d, *J* = 2.6 Hz, 1H), 7.98 (dd, *J* = 8.8, 2.1 Hz, 1H), 7.91 (d, *J* = 9.1 Hz, 1H), 7.83 – 7.72 (m, 2H), 7.61 (dd, *J* = 9.1, 2.6 Hz, 1H), 6.37 (s, 1H), 4.75 (d, *J* = 1.2 Hz, 2H), 4.01 (s, 3H), 3.47 (s, 3H).	DMSO	>98	G1 (0.1 N HCl added)

281

325				HCl	^{1}H NMR (400 MHz, DMSO) δ 12.01 (s, 1H), 10.15 (s, 1H), 9.58 (d, *J* = 1.5 Hz, 1H), 8.94 – 8.86 (m, 1H), 8.78 (dd, *J* = 5.0, 1.5 Hz, 1H), 8.07 (d, *J* = 2.6 Hz, 1H), 8.04 – 7.98 (m, 1H), 7.91 (dd, *J* = 9.3, 2.2 Hz, 2H), 7.78 – 7.69 (m, 2H), 7.66 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.61 (dd, *J* = 9.1, 2.7 Hz, 1H), 6.44 (d, *J* = 9.5 Hz, 1H), 4.01 (s, 3H).	DMSO	>98	G1 (0.1 N HCl added)
326				HCl	^{1}H NMR (400 MHz, DMSO) δ 12.19 (s, 1H), 10.21 (s, 1H), 9.58 – 9.51 (m, 1H), 8.94 – 8.86 (m, 1H), 8.81 (dd, *J* = 5.1, 1.6 Hz, 1H), 8.10 (d, *J* = 2.6 Hz, 1H), 7.96 – 7.88 (m, 2H), 7.79 (dd, *J* = 7.9, 5.1 Hz, 1H), 7.68 – 7.56 (m, 3H), 4.00 (s, 3H).	DMSO	>98	G1 (0.1 N HCl added)
327				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.43 (s, 1H), 9.57 – 9.50 (m, 1H), 9.07 – 8.98 (m, 1H), 8.88 (dd, *J* = 5.2, 1.4 Hz, 1H), 8.16 (d, *J* = 2.5 Hz, 1H), 8.06 (d, *J* = 1.9 Hz, 1H), 8.00 – 7.89 (m, 2H), 7.75 (d, *J* = 8.5 Hz, 1H), 7.67 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.63 (dd, *J* = 9.1, 2.6 Hz, 1H), 4.02 (s, 3H), 3.47 (s, 3H).	DMSO	>98	G1 (0.1 N HCl added)
328				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.66 (s, 1H), 10.24 (s, 1H), 9.45 (d, *J* = 1.6 Hz, 1H), 9.05 – 8.95 (m, 1H), 8.92 (dd, *J* = 5.2, 1.5 Hz, 1H), 8.25 – 8.16 (m, 1H), 8.09 – 7.99 (m, 1H), 7.98 – 7.89 (m, 1H), 7.71 – 7.60 (m, 3H), 6.98 (d, *J* = 8.3 Hz, 1H), 4.00 (s, 3H), 2.99 (t, *J* = 7.5 Hz, 2H), 2.57 – 2.52 (m, 2H).	DMSO	>98	G1 (0.1 N HCl added)

282

329				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 12.05 (s, 1H), 10.98 (s, 1H), 9.50 (d, *J* = 1.6 Hz, 1H), 9.32 (s, 1H), 9.03 (d, *J* = 8.2 Hz, 1H), 8.98 (d, *J* = 1.7 Hz, 1H), 8.92 (dd, *J* = 5.3, 1.4 Hz, 1H), 8.53 (d, *J* = 2.6 Hz, 1H), 8.46 (dd, *J* = 8.8, 1.8 Hz, 1H), 8.30 (s, 1H), 8.13 (d, *J* = 2.1 Hz, 1H), 8.09 (d, *J* = 8.7 Hz, 1H), 7.95 (dd, *J* = 7.7, 5.3 Hz, 1H), 7.82 (dd, *J* = 8.6, 2.1 Hz, 1H), 7.26 (d, *J* = 8.6 Hz, 1H), 4.06 (s, 3H).	DMSO	>98	G1 (0.1 N HCl added)
330				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.40 (s, 1H), 9.54 (d, *J* = 1.5 Hz, 1H), 9.05 – 8.97 (m, 1H), 8.87 (dd, *J* = 5.2, 1.5 Hz, 1H), 8.15 – 8.06 (m, 3H), 8.00 – 7.87 (m, 3H), 7.81 (d, *J* = 8.5 Hz, 1H), 7.64 (dd, *J* = 9.1, 2.7 Hz, 1H), 6.43 (d, *J* = 9.4 Hz, 1H), 4.02 (s, 3H).	DMSO	>98	G1 (0.1 N HCl added)
331				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 12.05 (s, 1H), 10.77 (s, 1H), 9.51 (d, *J* = 1.5 Hz, 1H), 9.43 – 9.35 (m, 1H), 9.31 – 9.21 (m, 1H), 9.04 – 8.93 (m, 1H), 8.88 (dd, *J* = 5.2, 1.5 Hz, 1H), 8.61 (dd, *J* = 5.1, 1.4 Hz, 1H), 8.73 (d, *J* = 8.4 Hz, 1H), 8.42 (dd, *J* = 8.8, 1.6 Hz, 1H), 8.13 (d, *J* = 2.1 Hz, 1H), 8.09 (d, *J* = 8.7 Hz, 1H), 7.94 – 7.83 (m, 2H), 7.80 (dd, *J* = 8.6, 2.2 Hz, 1H), 7.27 (d, *J* = 8.6 Hz, 1H).	DMSO	>98	G1 (0.1 N HCl added)
332				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.57 (s, 1H), 9.55 (d, *J* = 1.6 Hz, 1H), 9.09 – 9.01 (m, 1H), 8.90 (dd, *J* = 5.3, 1.5 Hz, 1H), 8.65 – 8.59 (m, 1H), 8.24 – 8.16 (m, 2H), 8.14 (dd, *J* = 9.6, 0.8 Hz, 1H), 8.03 – 7.92 (m, 2H), 7.65 (dd, *J* = 9.1, 2.7 Hz, 1H), 4.03 (s, 3H).	DMSO	>98	G1 (0.1 N HCl added)

283

333				HCl	^{1}H NMR (400 MHz, DMSO) δ 11.81 (s, 1H), 10.31 (s, 1H), 9.58 (d, *J* = 1.5 Hz, 1H), 9.08 (d, *J* = 7.9 Hz, 1H), 8.67 (dd, *J* = 5.2, 1.5 Hz, 1H), 8.13 (d, *J* = 2.6 Hz, 1H), 8.04 (d, *J* = 2.0 Hz, 1H), 7.98 – 7.88 (m, 2H), 7.81 (d, *J* = 8.8 Hz, 1H), 7.69 (dd, *J* = 8.8, 2.1 Hz, 1H), 7.63 (dd, *J* = 9.1, 2.7 Hz, 1H), 6.36 (s, 1H), 4.02 (s, 3H), 2.46 (d, *J* = 1.1 Hz, 3H).	DMSO	>98	G1 (0.1 N HCl added)
334				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.51 (s, 1H), 9.53 (d, *J* = 1.6 Hz, 1H), 9.08 – 9.02 (m, 1H), 8.90 (dd, *J* = 5.3, 1.5 Hz, 1H), 8.63 – 8.59 (m, 1H), 8.22 – 8.10 (m, 3H), 8.00 – 7.92 (m, 2H), 7.63 (dd, *J* = 9.1, 2.6 Hz, 1H), 4.30 (q, *J* = 7.0 Hz, 2H), 1.46 (t, *J* = 7.0 Hz, 3H).	DMSO	>98	G1 (0.1 N HCl added)
335				HCl	^{1}H NMR (400 MHz, DMSO) δ 11.99 (s, 1H), 10.34 (s, 1H), 9.62 – 9.52 (m, 1H), 9.11 (d, *J* = 8.2 Hz, 1H), 8.90 (d, *J* = 4.4 Hz, 1H), 8.13 (d, *J* = 2.6 Hz, 1H), 8.06 (d, *J* = 1.8 Hz, 1H), 8.00 – 7.88 (m, 3H), 7.75 (d, *J* = 8.6 Hz, 1H), 7.68 – 7.60 (m, 2H), 6.46 (d, *J* = 9.5 Hz, 1H), 4.29 (q, *J* = 7.0 Hz, 2H), 1.46 (t, *J* = 7.0 Hz, 3H).	DMSO	>98	G1 (0.1 N HCl added)
336				HCl	^{1}H NMR (400 MHz, DMSO) δ 11.02 (s, 1H), 10.49 (s, 1H), 9.50 (d, *J* = 1.6 Hz, 1H), 9.02 (d, *J* = 8.1 Hz, 1H), 8.90 (dd, *J* = 5.2, 1.5 Hz, 1H), 8.15 (d, *J* = 2.3 Hz, 1H), 8.00 (d, *J* = 9.1 Hz, 1H), 7.93 (dd, *J* = 7.8, 5.4 Hz, 1H), 7.63 (dd, *J* = 9.1, 2.6 Hz, 1H), 7.54 (d, *J* = 2.4 Hz, 1H), 7.35 (dd, *J* = 8.7, 2.5 Hz, 1H), 7.08 (d, *J* = 8.6 Hz, 1H), 4.64 (s, 2H), 4.26 (q, *J* = 6.9 Hz, 2H), 1.45 (t, *J* = 7.0 Hz, 3H).	DMSO	>98	G1 (0.1 N HCl added)

284

337				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.36 (s, 1H), 10.25 (s, 1H), 9.50 (d, *J* = 1.6 Hz, 1H), 8.98 (d, *J* = 8.1 Hz, 1H), 8.86 (dd, *J* = 5.2, 1.5 Hz, 1H), 8.10 (d, *J* = 2.4 Hz, 1H), 7.94 (d, *J* = 9.1 Hz, 1H), 7.87 (dd, *J* = 7.7, 5.2 Hz, 1H), 7.61 (dd, *J* = 9.1, 2.6 Hz, 1H), 7.47 (d, *J* = 1.9 Hz, 1H), 7.36 (dd, *J* = 8.1, 2.1 Hz, 1H), 7.28 (d, *J* = 8.1 Hz, 1H), 4.27 (q, *J* = 7.0 Hz, 2H), 2.93 (t, *J* = 7.5 Hz, 2H), 2.56 – 2.52 (m, 2H), 1.45 (t, *J* = 7.0 Hz, 3H).	DMSO	>98	G1 (0.1 N HCl added)
338					^{1}H NMR (400 MHz, DMSO) δ 10.25 (s, 1H), 9.50 – 9.39 (m, 1H), 9.03 (dd, *J* = 2.1, 0.7 Hz, 1H), 8.52 (dd, *J* = 4.7, 1.7 Hz, 1H), 8.48 (d, *J* = 6.0 Hz, 1H), 8.31 – 8.24 (m, 1H), 8.16 (d, *J* = 8.2 Hz, 1H), 8.12 (d, *J* = 2.7 Hz, 1H), 8.04 (d, *J* = 7.3 Hz, 1H), 7.91 – 7.78 (m, 3H), 7.58 (dd, *J* = 9.1, 2.7 Hz, 1H), 7.35 (ddd, *J* = 8.0, 4.8, 0.7 Hz, 1H), 4.01 (s, 3H).	DMSO	>98	J2
339					^{1}H NMR (400 MHz, DMSO) δ 10.23 (s, 1H), 9.37 (dd, *J* = 2.1, 0.7 Hz, 1H), 8.62 (dd, *J* = 4.7, 1.7 Hz, 1H), 8.57 – 8.49 (m, 1H), 7.93 (d, *J* = 2.7 Hz, 1H), 7.89 (d, *J* = 9.1 Hz, 1H), 7.58 (dd, *J* = 9.1, 2.7 Hz, 1H), 7.47 (ddd, *J* = 8.0, 4.8, 0.8 Hz, 1H), 7.40 – 7.30 (m, 3H), 3.98 (s, 3H).	DMSO	>98	J2
340					^{1}H NMR (400 MHz, DMSO) δ 11.31 (s, 1H), 9.56 (s, 1H), 9.54 (dd, *J* = 2.1, 0.7 Hz, 1H), 8.80 – 8.66 (m, 2H), 8.14 (d, *J* = 9.2 Hz, 1H), 7.77 (dd, *J* = 9.2, 2.8 Hz, 1H), 7.58 (ddd, *J* = 8.0, 4.8, 0.8 Hz, 1H), 7.36 (d, *J* = 2.8 Hz, 1H), 7.03 – 6.94 (m, 1H), 6.68 (dd, *J* = 7.8, 0.8 Hz, 1H), 6.56 (dd, *J* = 8.2, 0.8 Hz, 1H), 3.86 (s, 3H).	DMSO	>98	J2

285

341					^{1}H NMR (400 MHz, DMSO) δ 10.00 (s, 1H), 9.54 – 9.49 (m, 1H), 8.75 (s, 1H), 8.69 – 8.62 (m, 2H), 8.50 (d, *J* = 1.7 Hz, 1H), 8.02 (d, *J* = 2.7 Hz, 1H), 7.91 – 7.85 (m, 2H), 7.83 (dd, *J* = 8.6, 1.9 Hz, 1H), 7.60 – 7.51 (m, 2H), 4.00 (s, 3H).	DMSO	>98	J2
342					^{1}H NMR (400 MHz, DMSO) δ 10.08 (s, 1H), 9.34 – 9.27 (m, 1H), 8.60 (dd, *J* = 4.7, 1.7 Hz, 1H), 8.51 – 8.44 (m, 1H), 7.94 (d, *J* = 2.7 Hz, 1H), 7.88 (d, *J* = 9.1 Hz, 1H), 7.58 (dd, *J* = 9.1, 2.7 Hz, 1H), 7.56 – 7.51 (m, 1H), 7.51 – 7.47 (m, 2H), 7.45 (ddd, *J* = 8.0, 4.8, 0.8 Hz, 1H), 3.98 (s, 3H).	DMSO	>98	J2
343					^{1}H NMR (400 MHz, DMSO) δ 10.99 (s, 1H), 9.93 (s, 1H), 9.26 (d, *J* = 1 4 Hz, 1H), 8.59 (dd, *J* = 4.8, 1.7 Hz, 1H), 8.50 – 8.43 (m, 1H), 8.01 (d, *J* = 2 7 Hz, 1H), 7.98 (d, *J* = 9 5 Hz, 1H), 7.85 (d, *J* = 9.1 Hz, 1H), 7.65 (d, *J* = 8 4 Hz, 1H), 7.55 (dd, *J* = 9.1, 2.7 Hz, 1H), 7.49 – 7.42 (m, 1H), 7.36 (d, *J* = 8.3 Hz, 1H), 6.55 (dd, *J* = 9.5, 1.7 Hz, 1H), 3.98 (s, 3H), 2.33 (s, 3H).	DMSO	>98	J2
344				HCl	^{1}H NMR (400 MHz, DMSO) δ 9.34 – 9.28 (m, 1H), 8.81 – 8.75 (m, 1H), 8.74 – 8.65 (m, 1H), 8.06 (d, *J* = 9.2 Hz, 1H), 7.93 (d, *J* = 2.7 Hz, 1H), 7.85 (d, *J* = 8.8 Hz, 1H), 7.80 – 7.72 (m, 2H), 7.69 (d, *J* = 2.8 Hz, 1H), 7.59 (dd, *J* = 8.8, 2.7 Hz, 1H), 4.00 (s, 3H).	DMSO	>98	G8 using DMF instead of THF

345				HCl	^{1}H NMR (400 MHz, DMSO) δ 9.35 – 9.29 (m, 1H), 8.87 – 8.78 (m, 2H), 8.19 (d, *J* = 9.4 Hz, 1H), 8.09 (d, *J* = 9.2 Hz, 1H), 7.94 (d, *J* = 8.5 Hz, 1H), 7.86 (dd, *J* = 8.0, 5.3 Hz, 1H), 7.77 (dd, *J* = 9.1, 2.9 Hz, 1H), 7.72 (d, *J* = 2.8 Hz, 1H), 7.67 (d, *J* = 2.3 Hz, 1H), 7.54 (dd, *J* = 8.5, 2.3 Hz, 1H), 6.56 (d, *J* = 9.6 Hz, 1H), 4.02 (s, 3H).	DMSO	>98	G12 at room temperature
346				HCl	^{1}H NMR (400 MHz, DMSO) δ 11.98 (s, 1H), 9.29 (d, *J* = 1.7 Hz, 1H), 8.88 – 8.78 (m, 2H), 8.08 (d, *J* = 9.2 Hz, 1H), 7.97 (d, *J* = 9.6 Hz, 1H), 7.88 (dd, *J* = 8.1, 5.4 Hz, 1H), 7.81 (d, *J* = 2.6 Hz, 1H), 7.78 – 7.72 (m, 2H), 7.67 (dd, *J* = 8.9, 2.6 Hz, 1H), 7.48 (d, *J* = 8.9 Hz, 1H), 6.60 (d, *J* = 9.5 Hz, 1H), 4.02 (s, 3H).	DMSO	>98	G12 at room temperature
347				HCl	^{1}H NMR (400 MHz, DMSO) δ 9.33 – 9.26 (m, 1H), 8.87 – 8.67 (m, 2H), 8.06 (d, *J* = 9.1 Hz, 1H), 7.91 – 7.79 (m, 1H), 7.75 (dd, *J* = 9.1, 2.9 Hz, 1H), 7.71 (d, *J* = 2.8 Hz, 1H), 7.67 – 7.61 (m, 2H), 7.56 – 7.51 (m, 2H), 4.01 (s, 3H).	DMSO	>98	G12 at room temperature
348				HCl	^{1}H NMR (400 MHz, DMSO) δ 9.28 (d, *J* = 2.0 Hz, 1H), 8.85 – 8.67 (m, 2H), 8.06 (d, *J* = 9.0 Hz, 1H), 7.88 – 7.77 (m, 1H), 7.77 – 7.69 (m, 2H), 7.62 – 7.54 (m, 2H), 7.51 – 7.45 (m, 2H), 7.44 – 7.37 (m, 1H), 4.02 (d, *J* = 3.9 Hz, 3H).	DMSO	>98	G12 at room temperature
349				HCl	^{1}H NMR (400 MHz, DMSO) δ 9.23 (dd, *J* = 2.1, 0.7 Hz, 1H), 8.80 (dd, *J* = 5.2, 1.6 Hz, 1H), 8.72 – 8.64 (m, 1H), 8.09 (d, *J* = 9.1 Hz, 1H), 7.84 – 7.71 (m, 4H), 7.66 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.61 – 7.54 (m, 1H), 7.52 – 7.45 (m, 1H), 4.02 (s, 3H).	DMSO	>98	G12 at room temperature

287

350				HCl	^{1}H NMR (400 MHz, DMSO) δ 9.22 (d, *J* = 1.7 Hz, 1H), 8.87 – 8.79 (m, 1H), 8.77 – 8.67 (m, 1H), 8.06 (d, *J* = 9.2 Hz, 1H), 7.92 – 7.79 (m, 1H), 7.74 (dd, *J* = 9.1, 2.9 Hz, 1H), 7.70 (d, *J* = 2.8 Hz, 1H), 7.45 – 7.37 (m, 2H), 7.33 – 7.27 (m, 1H), 7.17 – 7.09 (m, 1H), 4.01 (s, 3H), 3.71 (s, 3H).	DMSO	>98	G12 at room temperature
351				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 12.03 (s, 1H), 10.69 (s, 1H), 9.65 (d, *J* = 1.8 Hz, 1H), 9.26 – 9.21 (m, 1H), 9.20 – 9.12 (m, 1H), 8.99 – 8.88 (m, 2H), 8.52 (d, *J* = 2.6 Hz, 1H), 8.49 – 8.42 (m, 1H), 8.25 – 8.17 (m, 1H), 8.15 – 8.08 (m, 2H), 8.02 – 7.96 (m, 1H), 7.93 (d, *J* = 9.4 Hz, 1H), 7.77 (d, *J* = 8.5 Hz, 1H), 7.72 (dd, *J* = 8.5, 1.9 Hz, 1H), 6.47 (d, *J* = 9.6 Hz, 1H), 4.04 (s, 3H).	DMSO	>98	G1
352				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 12.04 (s, 1H), 10.92 (s, 1H), 9.65 (d, *J* = 1.7 Hz, 1H), 9.58 – 9.50 (m, 1H), 9.46 – 9.39 (m, 1H), 9.27 – 9.18 (m, 1H), 9.01 – 8.92 (m, 2H), 8.88 (dd, *J* = 5.3, 1.2 Hz, 1H), 8.48 (dd, *J* = 8.8, 1.9 Hz, 1H), 8.20 – 8.10 (m, 2H), 8.09 – 8.01 (m, 2H), 7.93 (d, *J* = 9.5 Hz, 1H), 7.81 – 7.72 (m, 2H), 6.47 (d, *J* = 9.5 Hz, 1H).	DMSO	>98	G1
353				HCl	1H NMR (300 MHz, DMSO) δ 10.90 (s, 1H), 9.63 (s, 1H), 8.89 (d, J = 8.0 Hz, 1H), 8.76 (d, J = 4.0 Hz, 1H), 8.19 (d, J = 2.1 Hz, 1H), 7.89 (d, J = 9.1 Hz, 1H), 7.83 (d, J = 7.9 Hz, 1H), 7.78 – 7.65 (m, 2H), 7.63 – 7.49 (m, 2H), 7.47 – 7.33 (m, 2H), 3.98 (s, 3H).	DMSO	>98	G1

288

354				HCl	1H NMR (300 MHz, DMSO) δ 11.44 (s, 1H), 9.58 (d, J = 1.8 Hz, 1H), 9.16 (d, J = 8.2 Hz, 1H), 8.96 (dd, J = 5.3, 1.3 Hz, 1H), 8.29 (d, J = 2.5 Hz, 1H), 8.13 (d, J = 9.2 Hz, 1H), 7.99 (dd, J = 8.0, 5.4 Hz, 1H), 7.72 – 7.49 (m, 2H), 7.44 – 7.27 (m, 3H), 7.12 (s, 1H), 3.99 (s, 3H), 2.52 (s, 3H).	DMSO	>98	G1
355				HCl	1H NMR (300 MHz, DMSO) δ 11.38 (s, 1H), 9.53 (s, 1H), 9.18 (d, J = 8.1 Hz, 1H), 8.97 (d, J = 5.3 Hz, 1H), 8.21 (s, 1H), 8.14 – 8.02 (m, 1H), 7.92 (d, J = 9.1 Hz, 1H), 7.60 (d, J = 9.1 Hz, 1H), 6.90 (s, 1H), 3.99 (s, 3H).	DMSO	>98	G1
356				HCl	1H NMR (300 MHz, DMSO) δ 11.30 (s, 1H), 9.59 (d, J = 1.8 Hz, 1H), 9.19 (d, J = 8.2 Hz, 1H), 8.97 (dd, J = 5.3, 1.2 Hz, 1H), 8.24 (d, J = 2.5 Hz, 1H), 8.11 – 7.93 (m, 2H), 7.76 – 7.54 (m, 4H), 7.40 (t, J = 7.6 Hz, 1H), 7.26 (s, 1H), 7.21 (d, J = 7.4 Hz, 1H), 3.98 (s, 3H), 2.41 (s, 3H).	DMSO	>98	G1
357				HCl	1H NMR (300 MHz, DMSO) δ 11.21 (s, 1H), 9.59 (d, J = 1.7 Hz, 1H), 9.22 (d, J = 8.1 Hz, 1H), 9.02 – 8.95 (m, 1H), 8.23 (d, J = 2.5 Hz, 1H), 8.13 – 7.96 (m, 3H), 7.85 (d, J = 8.7 Hz, 2H), 7.72 (d, J = 8.7 Hz, 2H), 7.60 (dd, J = 9.1, 2.6 Hz, 1H), 7.31 (s, 1H), 3.98 (s, 3H).	DMSO	>98	G1
358				HCl	1H NMR (300 MHz, DMSO) δ 10.87 (s, 1H), 9.65 – 9.55 (m, 1H), 8.93 (dt, J = 8.0, 1.8 Hz, 1H), 8.81 (dd, J = 5.0, 1.6 Hz, 1H), 8.18 (d, J = 2.6 Hz, 1H), 7.94 – 7.82 (m, 4H), 7.78 (dd, J = 8.0, 5.0 Hz, 1H), 7.60 – 7.46 (m, 4H), 7.44 – 7.35 (m, 1H), 7.32 (s, 1H), 3.98 (s, 3H).	DMSO	>98	G1

289

359				HCl	H NMR (300 MHz, DMSO) δ 11.29 (s, 1H), 9.59 (s, 1H), 9.20 (d, J = 8.1 Hz, 1H), 9.01 – 8.94 (m, 1H), 8.25 (s, 1H), 8.12 – 7.98 (m, 2H), 7.90 – 7.75 (m, 2H), 7.62 (d, J = 9.1 Hz, 1H), 7.21 (s, 1H), 7.08 (d, J = 8.6 Hz, 2H), 3.99 (s, 3H), 3.84 (s, 3H).	DMSO	>98	G1
360				HCl	1H NMR (300 MHz, DMSO) δ 11.29 (s, 1H), 9.60 (s, 1H), 9.21 (d, J = 8.0 Hz, 1H), 8.99 (d, J = 5.3 Hz, 1H), 8.26 (d, J = 2.2 Hz, 1H), 8.11 – 7.99 (m, 2H), 7.77 (d, J = 8.0 Hz, 2H), 7.62 (dd, J = 9.1, 2.4 Hz, 1H), 7.32 (d, J = 8.1 Hz, 2H), 7.26 (s, 1H), 3.99 (s, 3H), 2.37 (s, 3H).	DMSO	>98	G1
361				HCl	1H NMR (300 MHz, DMSO) δ 11.00 (s, 1H), 9.55 (d, J = 1.7 Hz, 1H), 8.96 (dt, J = 8.1, 1.7 Hz, 1H), 8.86 (dd, J = 5.1, 1.5 Hz, 1H), 8.19 (d, J = 2.6 Hz, 1H), 7.97 (d, J = 9.2 Hz, 1H), 7.83 (dt, J = 9.5, 4.8 Hz, 1H), 7.55 (dd, J = 9.1, 2.6 Hz, 1H), 6.72 (s, 1H), 3.95 (d, J = 7.0 Hz, 3H), 2.35 (d, J = 3.5 Hz, 3H).	DMSO	>98	G1
362				HCl	H NMR (300 MHz, DMSO) δ 11 21 (s, 1H), 9.58 (d, J = 1 5 Hz, 1H), 9 21 – 9.06 (m, 1H), 8.95 (d, J = 4.3 Hz, 1H), 8.22 (d, J = 2.3 Hz, 1H), 8.09 – 7.92 (m, 2H), 7.70 – 7.51 (m, 3H), 7.24 – 7.17 (m, 1H), 7.13 (s, 1H), 3.99 (s, 3H).	DMSO	>98	G1
363				HCl	1H NMR (300 MHz, DMSO) δ 11.07 (s, 1H), 9.60 (s, 1H), 9.13 (d, J = 6.5 Hz, 1H), 8.93 (d, J = 5.1 Hz, 1H), 8.23 (s, 1H), 8.05 – 7.85 (m, 4H), 7.67 – 7.54 (m, 1H), 7.43 – 7.23 (m, 3H), 3.99 (s, 3H).	DMSO	>98	G1

290

364				2 HCl	1H NMR (300 MHz, DMSO) δ 11.16 (s, 1H), 9.57 (d, J = 1.5 Hz, 1H), 9.14 (d, J = 8.1 Hz, 1H), 8.93 (d, J = 5.2 Hz, 1H), 8.18 (d, J = 2.4 Hz, 1H), 8.03 – 7.89 (m, 4H), 7.61 – 7.54 (m, 2H), 7.32 (s, 1H), 3.97 (s, 3H).	DMSO	>98	G1
365				2 HCl	1H NMR (300 MHz, DMSO) δ 11.29 (s, 1H), 9.58 (d, J = 1.6 Hz, 1H), 9.27 (d, J = 8.2 Hz, 1H), 9.06 – 8.99 (m, 1H), 8.18 (d, J = 2.5 Hz, 1H), 8.10 (dd, J = 8.1, 5.5 Hz, 1H), 8.02 (d, J = 9.1 Hz, 1H), 7.91 (dd, J = 10.7, 1.8 Hz, 1H), 7.80 – 7.65 (m, 2H), 7.57 (dd, J = 9.1, 2.6 Hz, 1H), 7.29 (s, 1H), 3.96 (s, 3H).	DMSO	>98	G1
366				2 HCl	1H NMR (300 MHz, DMSO) δ 11.17 (s, 1H), 9.60 (s, 1H), 9.24 (d, J = 8.2 Hz, 1H), 8.98 (d, J = 5.1 Hz, 1H), 8.22 (d, J = 2.5 Hz, 1H), 8.11 – 8.04 (m, 1H), 8.02 – 7.91 (m, 2H), 7.82 – 7.68 (m, 2H), 7.62 (dd, J = 9.1, 2.5 Hz, 1H), 7.36 (s, 1H), 4.01 (d, J = 11.0 Hz, 3H).	DMSO	>98	G1
367				2 HCl	1H NMR (300 MHz, DMSO) δ 11.53 (s, 1H), 9.58 (d, J = 1.6 Hz, 1H), 9.20 (d, J = 8.2 Hz, 1H), 8.98 (dd, J = 5.3, 1.3 Hz, 1H), 8.25 (d, J = 2.5 Hz, 1H), 8.12 (d, J = 9.1 Hz, 1H), 8.04 – 7.95 (m, 1H), 7.80 – 7.68 (m, 2H), 7.63 – 7.57 (m, 1H), 7.56 – 7.48 (m, 1H), 7.31 (s, 1H), 3.99 (d, J = 6.7 Hz, 3H).	DMSO	>98	G1

291

368				2 HCl	1H NMR (300 MHz, DMSO) δ 11.24 (s, 1H), 9.59 (d, J = 1.7 Hz, 1H), 9.26 (d, J = 8.3 Hz, 1H), 9.00 (d, J = 4.2 Hz, 1H), 8.23 (d, J = 2.6 Hz, 1H), 8.16 (d, J = 2.0 Hz, 1H), 8.09 (dd, J = 8.1, 5.4 Hz, 1H), 8.01 (d, J = 9.2 Hz, 1H), 7.91 (dd, J = 8.4, 2.1 Hz, 1H), 7.77 (d, J = 8.4 Hz, 1H), 7.62 (dd, J = 9.1, 2.5 Hz, 1H), 7.37 (s, 1H), 3.98 (s, 3H).	DMSO	>98	G1
369				HCl	1H NMR (300 MHz, DMSO) δ 11.33 (s, 1H), 9.62 (s, 1H), 9.27 (d, J = 8.4 Hz, 1H), 9.01 (d, J = 5.2 Hz, 1H), 8.29 – 8.19 (m, 3H), 8.13 – 8.01 (m, 2H), 7.79 – 7.73 (m, 2H), 7.63 (dd, J = 9.1, 2.6 Hz, 1H), 7.42 (s, 1H), 3.99 (s, 3H).	DMSO	>98	G1
370				HCl	1H NMR (300 MHz, DMSO) δ 11.31 (s, 1H), 9.55 (d, J = 1.7 Hz, 1H), 9.07 (d, J = 7.9 Hz, 1H), 8.92 (d, J = 4.0 Hz, 1H), 8.26 (d, J = 2.5 Hz, 1H), 8.04 (d, J = 9.1 Hz, 1H), 7.98 - 7.68 (m, 5H), 7.63 (dd, J = 9.2, 2.5 Hz, 1H), 7.13 (s, 1H), 4.00 (s, 3H).	DMSO	>98	G1
371				2 HCl	1H NMR (300 MHz, CDCl3) δ 11.29 (s, 1H), 9.57 (d, J = 1.8 Hz, 1H), 9.07 (d, J = 8.1 Hz, 1H), 8.93 (dd, J = 5.2, 1.3 Hz, 1H), 8.25 (d, J = 2.5 Hz, 1H), 8.07 – 7.97 (m, 2H), 7.92 (dd, J = 8.0, 5.3 Hz, 1H), 7.67 – 7.51 (m, 4H), 7.28 (s, 1H), 3.99 (s, 3H).	DMSO	>98	G1

292

372				2 HCl	1H NMR (300 MHz, DMSO) δ 11.32 (s, 1H), 9.60 (d, J = 1.7 Hz, 1H), 9.27 (d, J = 8.1 Hz, 1H), 9.03 (d, J = 5.4 Hz, 1H), 8.22 (d, J = 2.5 Hz, 1H), 8.12 (dd, J = 8.1, 5.7 Hz, 1H), 8.03 (d, J = 8.8 Hz, 3H), 7.59 (dd, J = 9.1, 2.5 Hz, 1H), 7.52 (d, J = 8.1 Hz, 2H), 7.32 (s, 1H), 3.98 (d, J = 6.7 Hz, 3H).	DMSO	>98	G1
373				2 HCl	1H NMR (300 MHz, DMSO) δ 11.38 (s, 1H), 9.61 (d, J = 1.6 Hz, 1H), 9.26 (d, J = 8.2 Hz, 1H), 9.02 (d, J = 5 3 Hz, 1H), 8.23 (d, J = 2.4 Hz, 1H), 8 12 – 8.01 (m, 2H), 7.95 (d, J = 8 0 Hz, 1H), 7.89 (s, 1H), 7.71 – 7.56 (m, 2H), 7 45 – 7 33 (m, 2H), 4 10 – 3 90 (m, 3H).	DMSO	>98	G1
374				2 HCl	1H NMR (300 MHz, DMSO) δ 11.29 (s, 1H), 9.56 (s, 1H), 9.12 (d, J = 7.7 Hz, 1H), 8.94 (d, J = 4.9 Hz, 1H), 8.26 (d, J = 2.3 Hz, 1H), 8.07 – 7.90 (m, 2H), 7.71 – 7.57 (m, 2H), 7.51 (s, 1H), 7.47 – 7.37 (m, 1H), 7.17 (s, 1H), 3.99 (s, 3H), 2.53 (s, 3H).	DMSO	>98	G1
375				2 HCl	1H NMR (300 MHz, DMSO) δ 13.13 – 11.88 (m, 1H), 9.66 (d, J = 1 4 Hz, 1H), 9.36 (d, J = 8.2 Hz, 1H), 9.00 (d, J = 5.4 Hz, 1H), 8.38 (d, J = 2.2 Hz, 1H), 8.14 (dd, J = 8.1, 5.6 Hz, 1H), 8.01 (d, J = 7.5 Hz, 2H), 7.89 (d, J = 9 1 Hz, 1H), 7.76 (s, 1H), 7.64 – 7.35 (m, 9H), 5.23 (s, 2H).	DMSO	>98	J NaOtBu, Pd(OAc)2, Tri-t-butylphosphonium tetrafluoroborate, Toluene
376				2 HCl	1H NMR (300 MHz, DMSO) δ 12.49 (s, 1H), 9.63 (s, 1H), 9.27 (d, J = 8.1 Hz, 1H), 8.96 (d, J = 5.4 Hz, 1H), 8.34 (s, 1H), 8.07 (dd, J = 8.1, 5.6 Hz, 1H), 7.99 (d, J = 8.3 Hz, 2H), 7.85 (d, J = 9.1 Hz, 1H), 7.80 (s, 1H), 7.64 – 7.35 (m, 9H), 5.21 (s, 2H).	DMSO	>98	J NaOtBu, Pd(OAc)2, Tri-t-butylphosphonium tetrafluoroborate, Toluene

293

377				2 HCl	1H NMR (300 MHz, DMSO) δ 9.56 (d, J = 1.8 Hz, 1H), 9.30 – 9.21 (m, 1H), 9.01 (dd, J = 5.5, 1.2 Hz, 1H), 8.18 – 8.03 (m, 2H), 7.76 – 7.64 (m, 2H), 7.55 – 7.45 (m, 2H), 7.33 (dd, J = 8.6, 2.3 Hz, 1H), 4.69 (t, J = 7.9 Hz, 2H), 3.92 (s, 3H), 3.26 (t, J = 7.8 Hz, 2H).	DMSO	>98	G8
378				2 HCl	1H NMR (300 MHz, DMSO) δ 9.54 (d, J = 1.9 Hz, 1H), 8.70 – 8.65 (m, 2H), 7.95 (d, J = 9.2 Hz, 1H), 7.66 – 7.50 (m, 2H), 7.45 – 7.36 (m, 2H), 7.27 (t, J = 8.0 Hz, 1H), 7.07 (d, J = 7.9 Hz, 1H), 4.61 (t, J = 8.1 Hz, 2H), 3.87 (s, 3H), 3.36 – 3.17 (m, 5H).	DMSO	>98	G8 at 50°C
379				2 HCl	1H NMR (400 MHz, DMSO) δ 9.54 (d, J = 1.9 Hz, 1H), 9.28 – 9.18 (m, 1H), 8.99 (dd, J = 5.5, 1.3 Hz, 1H), 8.18 – 8.02 (m, 2H), 7.69 (dd, J = 9.2, 2.7 Hz, 1H), 7.58 – 7.46 (m, 2H), 7.39 (dd, J = 8.2, 5.9 Hz, 1H), 6.96 – 6.85 (m, 1H), 4.71 (t, J = 8.0 Hz, 2H), 3.92 (s, 3H), 3.22 (t, J = 7.8 Hz, 2H).	DMSO	>98	G8 at 50°C
380				2 HCl	1H NMR (300 MHz, DMSO) δ 9.55 (d, J = 1.8 Hz, 1H), 9.11 (d, J = 8.1 Hz, 1H), 8.93 (dd, J = 5.3, 1.4 Hz, 1H), 8.10 – 7.93 (m, 2H), 7.76 (dd, J = 8.7, 4.7 Hz, 1H), 7.67 (dd, J = 9.2, 2.6 Hz, 1H), 7.52 (d, J = 2.6 Hz, 1H), 7.28 (dd, J = 8.4, 2.6 Hz, 1H), 7.12 (td, J = 9.0, 2.7 Hz, 1H), 4.70 (t, J = 7.9 Hz, 2H), 3.92 (s, 3H), 3.26 (t, J = 7.5 Hz, 2H).	DMSO	>98	G8 at 50°C

294

381				HCl	1H NMR (300 MHz, DMSO) δ 9.66 (d, J = 2.0 Hz, 1H), 9.15 – 9.06 (m, 1H), 8.91 (dd, J = 5.2, 1.5 Hz, 1H), 8.27 – 8.17 (m, 2H), 8.01 (d, J = 8.9 Hz, 1H), 7.94 (dd, J = 8.2, 5.2 Hz, 1H), 7.88 – 7.78 (m, 2H), 7.42 (d, J = 2.7 Hz, 1H), 7.35 (dd, J = 8.8, 2.2 Hz, 1H), 6.96 (d, J = 3.5 Hz, 1H), 3.91 (s, 3H).	DMSO	>98	G8 at 50°C
382				HCl	1H NMR (300 MHz, DMSO) δ 9.56 (d, J = 1.6 Hz, 1H), 9.26 (d, J = 8.2 Hz, 1H), 9.05 – 8.98 (m, 1H), 8.20 – 8.02 (m, 2H), 7.69 (dd, J = 9.2, 2.7 Hz, 1H), 7.53 – 7.40 (m, 2H), 7.32 (dd, J = 14.0, 8.0 Hz, 1H), 6.92 (t, J = 8.5 Hz, 1H), 4.71 (t, J = 7.9 Hz, 2H), 3.91 (s, 3H), 3.28 (t, J = 7.8 Hz, 2H).	DMSO	>98	G8 at 50°C
383				2 HCl	1H NMR (300 MHz, DMSO) δ 9.66 (d, J = 1.5 Hz, 1H), 9.23 – 9.09 (m, 1H), 8.93 (dd, J = 5.3, 1.5 Hz, 1H), 8.31 – 8.16 (m, 2H), 8.08 – 7.93 (m, 2H), 7.82 (dd, J = 9.2, 2.8 Hz, 1H), 7.56 (dd, J = 9.4, 2.5 Hz, 1H), 7.43 (d, J = 2.7 Hz, 1H), 7.19 (td, J = 9.2, 2.7 Hz, 1H), 7.02 – 6.89 (m, 1H), 3.91 (s, 3H).	DMSO	>98	G8 at 50°C
384				2 HCl	1H NMR (300 MHz, DMSO) δ 9.66 (d, J = 1.6 Hz, 1H), 9.23 – 9.09 (m, 1H), 8.94 (dd, J = 5.3, 1.5 Hz, 1H), 8.26 – 8.14 (m, 2H), 8.00 (dd, J = 8.1, 5.3 Hz, 1H), 7.90 – 7.73 (m, 3H), 7.45 (d, J = 2.7 Hz, 1H), 7.25 – 7.10 (m, 1H), 6.98 (d, J = 3.5 Hz, 1H), 3.92 (s, 3H).	DMSO	>98	G8 at 50°C

295

385				2 HCl	1H NMR (300 MHz, DMSO) δ 9.54 (d, J = 1.8 Hz, 1H), 9.21 (dt, J = 8.2, 1.6 Hz, 1H), 8.98 (dd, J = 5.5, 1.3 Hz, 1H), 8.20 – 8.00 (m, 2H), 7.68 (dd, J = 9.2, 2.7 Hz, 1H), 7.55 – 7.31 (m, 3H), 7.00 – 6.78 (m, 1H), 4.69 (t, J = 7.9 Hz, 2H), 4.19 (q, J = 7.0 Hz, 2H), 3.22 (t, J = 7.9 Hz, 2H), 1.41 (t, J = 6.9 Hz, 3H).	DMSO	>98	G8 at 50°C
386				2 HCl	1H NMR (300 MHz, DMSO) δ 9.42 (d, J = 1.5 Hz, 1H), 9.06 (d, J = 8.1 Hz, 1H), 8.93 (d, J = 5.4 Hz, 1H), 8.09 – 7.99 (m, 2H), 7.68 (dd, J = 9.1, 2.7 Hz, 1H), 7.53 (d, J = 2.6 Hz, 1H), 7.30 – 7.16 (m, 3H), 4.66 (t, J = 7.9 Hz, 2H), 3.98 (s, 3H), 3.29 (t, J = 7.7 Hz, 2H).	DMSO	>98	G8 at 50°C
387				2 HCl	1H NMR (300 MHz, DMSO) δ 9.37 (d, J = 1.4 Hz, 1H), 9.11 (d, J = 8.2 Hz, 1H), 8.99 (d, J = 4.9 Hz, 1H), 8.14 (dd, J = 8.2, 5.6 Hz, 1H), 8.06 (d, J = 9.2 Hz, 1H), 7.70 (dd, J = 9.2, 2.6 Hz, 1H), 7.51 (d, J = 2.7 Hz, 1H), 7.45 – 7.36 (m, 2H), 7.26 – 7.15 (m, 1H), 4.83 (d, J = 9.5 Hz, 1H), 4.49 – 4.36 (m, 2H), 4.00 (s, 3H), 3.48 – 3.28 (m, 1H), 3.27 – 3.05 (m, 1H).	DMSO	>98	G8 at 50°C
388				2 HCl	1H NMR (400 MHz, DMSO) δ 9.56 (d, J = 1.9 Hz, 1H), 9.31 – 9.19 (m, 1H), 9.00 (dd, J = 5.5, 1.3 Hz, 1H), 8.21 – 8.02 (m, 2H), 7.73 – 7.64 (m, 2H), 7.47 (dd, J = 5.4, 2.4 Hz, 2H), 7.32 (dd, J = 8.6, 2.3 Hz, 1H), 4.67 (t, J = 8.0 Hz, 2H), 4.18 (q, J = 7.0 Hz, 2H), 3.26 (t, J = 7.8 Hz, 2H), 1.41 (t, J = 6.9 Hz, 3H).	DMSO	>98	G8 at 50°C

296

389				2 HCl	1H NMR (400 MHz, DMSO) δ 9.54 (d, J = 1.8 Hz, 1H), 9.25 (dt, J = 8.2, 1.6 Hz, 1H), 9.04 (dd, J = 5.5, 1.1 Hz, 1H), 8.26 (d, J = 2.1 Hz, 1H), 8.16 (dd, J = 8.0, 5.6 Hz, 1H), 8.11 – 7.96 (m, 2H), 7.91 (d, J = 8.6 Hz, 1H), 7.47 (d, J = 2.1 Hz, 1H), 7.34 (dd, J = 8.6, 2.3 Hz, 1H), 4.68 (t, J = 7.9 Hz, 2H), 3.25 (t, J = 7.8 Hz, 2H).	DMSO	>98	G8 at 50°C
390				HCl	^{1}H NMR (400 MHz, DMSO) δ 9.37 (d, *J* = 1.4 Hz, 1H), 8.82 (dd, *J* = 5.1, 1.5 Hz, 1H), 8.76 (dd, *J* = 8.1 Hz, 1H), 8.62 (d, *J* = 1.9 Hz, 1H), 8.46 (dd, *J* = 8.8, 2.1 Hz, 1H), 8.20 (d, *J* = 8.7 Hz, 1H), 7.91 (dd, *J* = 6.3, 2.6 Hz, 1H), 7.80 (dd, *J* = 6.0, 5.1 Hz, 1H), 7.71 – 7.59 (m, 2H), 7.52 – 7.36 (m, 3H), 7.10 – 7.01 (m, 1H), 3.89 (s, 3H).	DMSO	>98	G8 with DMF instead of THF
391				HCl	1H NMR (400 MHz, DMSO) δ 9.38 (d, J = 1.4 Hz, 1H), 8.82 (d, J = 5.1 Hz, 1H), 8.76 (d, J = 7.9 Hz, 1H), 8.63 (d, J = 1.8 Hz, 1H), 8.46 (dd, J = 8.8, 2.2 Hz, 1H), 8.20 (d, J = 8.7 Hz, 1H), 7.97 (d, J = 2.7 Hz, 1H), 7.87 (d, J = 8.8 Hz, 1H), 7.84 – 7.76 (m, 1H), 7.64 (dd, J = 8.8, 2.7 Hz, 1H), 7.52 – 7.39 (m, 3H), 7.10 – 7.02 (m, 1H), 3.88 (s, 3H).	DMSO	>98	G8 with DMF instead of THF
392				HCl	^{1}H NMR (400 MHz, DMSO) δ 9.39 (t, *J* = 3.2 Hz, 1H), 8.93 – 8.82 (m, 2H), 8.62 (d, *J* = 1.8 Hz, 1H), 8.47 (dd, *J* = 8.8, 2.2 Hz, 1H), 8.21 (d, *J* = 9.0 Hz, 1H), 7.91 (dd, *J* = 8.1, 5.3 Hz, 1H), 7.84 – 7.77 (m, 1H), 7.73 – 7.63 (m, 1H), 7.53 – 7.40 (m, 4H), 7.09 – 7.03 (m, 1H), 3.87 (d, *J* = 6.5 Hz, 3H).	DMSO	>98	G8 with DMF instead of THF

297

393				HCl	^{1}H NMR (400 MHz, DMSO) δ 11.71 (s, 1H), 11.10 (s, 1H), 9.42 (d, *J* = 1.9 Hz, 1H), 8.90 – 8.69 (m, 2H), 8.62 (d, *J* = 1.7 Hz, 1H), 8.40 (dd, *J* = 8.8, 1.9 Hz, 1H), 8.14 (d, *J* = 8.7 Hz, 1H), 7.92 (d, *J* = 7.7 Hz, 1H), 7.84 – 7.69 (m, 1H), 7.57 – 7.40 (m, 3H), 7.11 – 7.02 (m, 2H), 6.96 (d, *J* = 8.3 Hz, 1H), 3.89 (s, 3H).	DMSO	>98	G8 with DMF instead of THF
394				HCl	^{1}H NMR (400 MHz, DMSO) δ 9.43 – 9.29 (m, 1H), 8.75 – 8.64 (m, 2H), 8.60 – 8.48 (m, 1H), 8.47 – 8.32 (m, 1H), 8.21 – 8.01 (m, 2H), 7.86 – 7.74 (m, 2H), 7.64 (d, *J* = 8.6 Hz, 1H), 7.59 – 7.34 (m, 4H), 7.13 – 7.01 (m, 1H), 6.87 (d, *J* = 8.7 Hz, 1H), 3.90 (t, *J* = 5.3 Hz, 3H).	DMSO	>98	G8 with DMF instead of THF
395				HCl	^{1}H NMR (400 MHz, DMSO) δ 9.24 (dd, *J* = 2.2, 0.8 Hz, 1H), 8.76 (dd, *J* = 5.0, 1.7 Hz, 1H), 8.61 – 8.54 (m, 1H), 8.49 (dd, *J* = 1.8, 1.1 Hz, 1H), 8.21 – 8.12 (m, 2H), 7.75 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.70 – 7.62 (m, 2H), 7.62 – 7.53 (m, 1H), 7.53 – 7.44 (m, 1H).	DMSO	>98	G8 with DMF instead of THF
396				HCl	^{1}H NMR (400 MHz, DMSO) δ 11.71 (s, 1H), 11.10 (s, 1H), 9.42 (d, *J* = 1.9 Hz, 1H), 8.90 – 8.69 (m, 2H), 8.62 (d, *J* = 1.7 Hz, 1H), 8.40 (dd, *J* = 8.8, 1.9 Hz, 1H), 8.14 (d, *J* = 8.7 Hz, 1H), 7.92 (d, *J* = 7.7 Hz, 1H), 7.84 – 7.69 (m, 1H), 7.57 – 7.40 (m, 3H), 7.11 – 7.02 (m, 2H), 6.96 (d, *J* = 8.3 Hz, 1H), 3.89 (s, 3H).	DMSO	>98	G12

397				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.40 (s, 1H), 9.50 (d, *J* = 1.6 Hz, 1H), 8.99 (d, *J* = 8.2 Hz, 1H), 8.88 (dd, *J* = 5.3, 1.5 Hz, 1H), 8.30 (d, *J* = 2.5 Hz, 1H), 8.14 – 8.06 (m, 1H), 7.99 – 7.88 (m, 2H), 7.78 – 7.66 (m, 2H), 7.61 – 7.51 (m, 3H), 7.50 – 7.34 (m, 3H), 5.34 (s, 2H).	DMSO	>98	Method G1
398					^{1}H NMR (400 MHz, DMSO) δ 9.96 (s, 1H), 9.52 (d, *J* = 1.4 Hz, 1H), 8.68 (dd, *J* = 9.9 Hz, 1H), 8.65 (d, *J* = 9.9 Hz, 1H), 8.16 (dd, *J* = 2.5, 5.4 Hz, 2H), 7.68 – 7.41 (m, 2H), 7.78 – 7.66 (m, 8H), 7.39 – 7.19 (m, 1H), 5.30 (s, 2H).	DMSO	>98	Method G1
399					1H NMR (DMSO-d6) ppm 12.52 (s, 1H), 9.78 (d, J = 1.56 Hz, 1H), 8.91-8.88 (m, 1H), 8.74 (dd, J = 4.74, 1.60 Hz, 1H), 8.33 (brs, 1H), 8.06 (d, J = 8.56 Hz, 2H), 7.93 (d, J = 9.08 hz, 1H), 7.89 (s, 1H), 7.66-7.59 (m, 2H), 7.55 (d, J = 8.56 Hz, 2H),4.01 (s, 3H).	DMSO	>98	G13
400				2 HCl	1H NMR (DMSO-d6) ppm 12.80-12.40 (br, 1H), 9.77 (d, J = 1.84 Hz, 1H), 9.32 (d, J = 8.04 Hz, 1H), 8.97 (dd, J = 5.36, 1 40 Hz, 1H), 8.34 (d, J = 2.68 Hz, 1H), 8.09-8.06 (m, 3H), 7.97 (d, J = 9 12 Hz, 1H), 7.91 (s, 1H), 7 64 (dd, J = 9 12, 2.68 Hz, 1H), 7.55 (d, J = 8.60 Hz, 2H), 4.01 (s, 3H) . The 1H of 2HCl was not observed.	DMSO	>98	G13

299

401				2 HCl	1H NMR (DMSO-d6) ppm 11.14 (brs, 1H), 9.58 (s, 1H), 9.13 (dd, J = 7.96 Hz, 1H), 8.93 (d, J = 5.24 Hz, 1H), 8.54 (d, J = 4.72 Hz, 1H), 8.48 (d, J = 8.32 Hz, 1H), 8.28 (brs, 1H), 8.09 (brt, J = 7.16 Hz, 1H), 8.02-7.96 (m, 2H), 7.65 (dd, J = 8.80, 2.48 Hz, 1H), 7.34 (brt, J = 6.52 Hz, 1H), 4.01 (s, 3H) . The 1H of 2HCl was not observed.	DMSO	>98	J2
402				2 HCl	1H NMR (DMSO-d6) ppm 10.89 (s, 1H), 9.57 (d, J = 1.60 Hz, 1H), 9.04 (d, J = 8.04 Hz, 1H), 8.88 (dd, J = 5.16, 1.40 Hz, 1H), 8.55 (dd, J = 2.64, 0.52 Hz, 1H), 8.50 (d, J = 8.92 Hz, 1H), 8.22 (d, J = 2.68 Hz, 1H), 8.08 (d, J = 8.92, 2.68 Hz, 1H), 7.94-7.90 (m, 2H), 7.61 (dd, J = 9.08, 2.68 Hz, 1H), 3.99 (s, 3H). The 1H of 2HCl was not observed.	DMSO	DMSO	J2
403				2 HCl	1H NMR (DMSO-d6) ppm 10.53 (s, 1H), 9.38 (s, 1H), 8.99 (d, J = 8.08 Hz, 1H), 8.88 (d, J = 4.60 Hz, 1H), 8.11 (brs, 1H), 8.01-7.95 (m, 2H), 7.90 (d, J = 8.60 Hz, 2H), 7.66 (dd, J = 9.12, 2.68 Hz, 1H), 7.50 (d, J = 8.60 Hz, 2H), 6.93 (s, 1H), 4.00 (s, 3H), 3.80 (s, 3H) . The 1H of 2HCl was not observed.	DMSO	>98	J2
404				HCl	1H NMR (DMSO-d6) ppm 11.81 (brs, 1H), 9.64 (s, 1H), 9.00 (d, J = 7.48 Hz, 1H), 8.85 (brs, 1H), 8.14 (d, J = 2.56 Hz, 1H), 8.00 (d, J = 8.60 Hz, 2H), 7.96 (d, J = 9.08 Hz, 1H), 7.86 (br, 1H), 7.66-7.63 (m, 3H), 7.25 (s, 1H), 4.00 (s, 3H) . The 1H of HCl was not observed.	DMSO	>98	J2

300

405				HCl	1H NMR (DMSO-d6) ppm 11.80 (brs, 1H), 9.65 (brs, 1H), 9.04 (d, J = 7.92 Hz, 1H), 8.88 (brs, 1H), 8.14 (d, J = 2.60 Hz, 1H), 8.05-8.02 (m, 2H), 7.96 (d, J = 9.12 Hz, 1H), 7.89 (m, 1H), 7.64 (dd, J = 9.12, 2.60 Hz, 1H), 7.42 (t, J = 8.84 Hz, 2H), 7.23 (s, 1H), 3.99 (s, 3H) . The 1H of HCl was not observed.	DMSO	>98	J2
406				HCl	1H NMR (DMSO-d6) ppm 10.31 (s, 1H), 9.37 (s, 1H), 8.88 (m, 2H), 8.04 (d, J = 2.60 Hz, 1H), 7.94 (d, J = 9.12 Hz, 1H), 7.91 (m, 1H), 7.64 (dd, J = 9.12, 2.68 Hz, 1H), 7.56 (d, J = 1.88 Hz, 1H),6.40 (d, J = 1.88Hz, 1H), 3.98 (s, 3H), 3.74 (s, 3H) . The 1H of HCl was not observed.	DMSO	>98	J2
407				2 HCl	1H NMR (DMSO-d6) ppm 12.89 (brs, 1H), 9.56 (s, 1H), 8.92 (d, J = 4.92 Hz, 2H), 8.04 (d, J = 8.84 Hz, 1H), 7.98 (d, J = 2.88 Hz, 1H), 7.84 (br, 1H), 7.71-7.66 (m, 3H), 7.45-7.39 (m, 2H), 4.00 (s, 3H), 3.94 (s, 3H) . The 1H of 2HCl was not observed.	DMSO	>98	J2
408				HCl	1H NMR (DMSO-d6) ppm 10.39 (s, 1H), 9.38 (s, 1H), 8.90 (d, J = 8.00 Hz, 1H), 8.84 (d, J = 4.76 hz, 1H), 8.06 (d, J = 2.68 Hz, 1H), 7.95 (d, J = 9.16 Hz, 1H), 7.90-7.88 (m, 3H), 7.65 (dd, J = 9.16, 2.68 Hz, 1H), 7.44 (brt, J = 7.40 Hz, 2H), 7.35 -7.31 (m, 1H), 6.88 (s, 1H), 3.99 (s, 3H), 3.80 (s, 3H) . The 1H of HCl was not observed.	DMSO	>98	J2 Temperature at 100 °C

301

409				HCl	1H NMR (DMSO-d6) ppm 10.44 (brs, 1H), 9.01 (s, 1H), 8.68 (brs, 1H), 8.39 (brs, 1H), 8.23 (s, 1H), 8.07 (brs, 1H), 7.84 (d, J = 9.04 Hz, 1H), 7.70-7.54 (m, 2H), 7.44 (brd, J = 7.32 Hz, 2H), 7.15 (brt, J = 7.56 Hz, 2H), 7.00 (brt, 7.40 Hz, 1H), 3.97 (s, 3H), 3.93 (s, 3H) . The 1H of HCl was not observed.	DMSO	>98	J2 Temperature at 100 °C
410				HCl	1H NMR (DMSO-d6) ppm 11.13 (s, 1H),9.59 (d, J = 1.64 Hz, 1H), 9.03 (brs, 1H), 8.88 (brs, 1H), 8.63 (d, J = 2.52 Hz, 1H), 8.23 (d, J = 2.32 Hz, 1H), 7.93-7.82 (brm, 4H), 7.61-7.53 (m, 3H), 7.35-7 31 (brm, 2H), 4.00 (s, 3H) . The 1H of HCl was not observed.	DMSO	>98	J2 Temperature at 100 °C
411					1H NMR (DMSO-d6) ppm 9.54 (s, 1H), 8.79 (s, 1H), 8.69 (d, J = 7.60 Hz, 1H), 7.89 (brd, J = 8.96 Hz, 2H), 7.68-7.58 (m, 4H), 7.38-7.30 (m, 2H), 3.98 (s, 3H). The 1H of NH- was not observed.	DMSO	>98	J2 Temperature at 100 °C
412				HCl	1H NMR (DMSO-d6) ppm 9.70 (s, 1H), 9.05 (d, J = 7.88 Hz, 1H), 8.85 (brd, J = 4 44 Hz, 1H), 8.24 (brs, 1H), 8.04 (d, J = 8.44 Hz, 2H), 7.94 (d, J = 9.00 Hz, 1H), 7.84 (m, 1H), 7.66 (d, J = 8.44 Hz, 2H), 7.62 (dd, J = 9.00, 2.64 Hz, 1H), 3.99 (s, 3H). The 1H of HCl and NH- were not observed.	DMSO	>98	G12 Temperature at 100°C

302

413					1H NMR (CDCl3) ppm 15.18 (brs, 1H), 9.57 (d, J = 2.32 Hz, 1H), 8.86 (dd, J = 4.80, 1.56 Hz, 1H), 8.59-8.56 (m, 1H), 7.78-7.73 (m, 4H), 7.55-7.52 (m, 1H), 7.43 (d, J = 8.56 Hz, 2H), 7.38 (dd, J = 8.88, 2.96 Hz, 1H), 7.34 (s, 1H), 3.97 (s, 3H), 3.30 (s, 3H), 3.11 (s, 3H).	CDCl3	>98	J2 Temperature at 100 °C

303

Number	Starting Material 1	Starting Material 2	Product	Salt type	^{1}H NMR	^{1}H NMR Solvent	Purity percent	Method of Coupling	LCMS	Retention Time	LCMS Method
414				2 HCl	1H NMR (DMSO-d6) ppm 9.72 (s, 1H), 9.16 (brs, 1H), 8.93 (d, J = 4.36 Hz, 1H), 8.14 (br, 1H), 7.96 (brm, 2H), 7.63 (dd, J = 9.08, 2.56 Hz, 1H), 7.00 (s, 1H), 3.98 (s, 3H), 2.37 (s, 3H).The 1H of 2HCl and NH- were not observed.	DMSO	>98	G12 Temperature at 100°C			
415				2 HCl	1H NMR (DMSO-d6) ppm 12.60 (brs, 1H), 9.78 (s, 1H), 9.12 (d, J = 8.00 Hz, 1H), 8.86 (brs, 1H), 8.35 (brd, J = 2.60 Hz, 1H), 8.01 (d, J = 8.56 Hz, 2H), 7.96 (d, J = 9.08 Hz, 1H), 7.92 (s, 1H), 7.86 (m, 1H), 7.69 (d, J = 8.56 Hz, 2H), 7.63 (dd, J = 9.08, 2.60 Hz, 1H), 4.02 (s, 3H) . The 1H of HCl was not observed.	DMSO	>98	G12 Temperature at 100°C			
416				HCl	1H NMR (DMSO-d6) ppm 12.80-12.40 (br, 1H), 9.79 (d, J = 1.64 Hz, 1H), 9.16 (d, J = 7.88 Hz, 1H), 8.88 (d, J = 3.88 Hz, 1H), 8.36 (brd, J = 2.64 Hz, 1H), 8.06-8.04 (m, 2H), 7.96 (d, J = 9.08 Hz, 1H), 7.90 (m, 1H), 7.85 (s, 1H), 7.63 (dd, J = 9.08, 2.64 Hz, 1H), 7.49 (m, 2H), 7.38 (m, 1H), 4.02 (s, 3H). The 1H of HCl was not observed.	DMSO	>98	G12 Temperature at 100°C			

417				HCl	1H NMR (DMSO-d6) ppm 12.80 (s, 1H), 9.74 (d, J = 1.60 Hz, 1H), 9.01 (brs, 1H), 8.83 (brs, 1H), 8.31 (d, J = 2.64 Hz, 1H), 8.15 (d, J = 1.00 Hz, 1H), 7.96 (d, J = 9.12 Hz, 1H), 7.78 (br, 1H), 7.64 (dd, J = 9.12, 2.64 Hz, 1H), 3.99 (s, 3H). The 1H of HCl was not observed.	DMSO	>98	G12 Temperature at 100°C			
418				HCl	1H NMR (DMSO-d6) ppm 12.60 (br, 1H), 9.79 (d, J = 1.72 Hz, 1H), 9.19 (d, J = 8.00 Hz, 1H), 8.93 (dd, J = 5.16 , 1.44 Hz, 1H), 8.23 (brs, 1H), 8.10 (s, 1H), 7.99 (m, 1H), 7.95 (d, J = 9.08 Hz, 1H), 7.77-7.75 (br, 2H), 7.62 (dd, J = 9.08, 2.72 Hz, 1H), 7.50 (m, 2H), 7.37 (m, 1H), 3.99 (s, 3H). The 1H of HCl was not observed.	DMSO	>98	G12 Temperature at 100°C			
419				HCl	1H NMR (DMSO-d6) ppm 12.56 (s, 1H), 9.78 (s, 1H), 9.09 (d, J = 8.20 Hz, 1H), 8.84 (d, J = 3.96 Hz, 1H), 8.35 (d, J = 2.60 Hz, 1H), 8.10-8.07 (m, 2H), 7.95 (d, J = 9.12 Hz, 1H), 7.83 (brt, J = 6.60 Hz, 2H), 7.63 (dd, J = 9.12, 2.60 Hz, 1H), 7.32 (m, 2H), 4.02 (s, 3H) .The 1H of HCl was not observed.	DMSO	>98	G12 Temperature at 100°C			
420				HCl	1H NMR (DMSO-d6) ppm 9.74 (s, 1H), 9.04 (d, J = 6.68 Hz, 1H), 8.86 (brs, 1H), 8.29 (brs, 1H), 8.05 (brs, J = 7.44 Hz, 2H), 7.97 (d, J = 9.08 Hz, 1H), 7.89 (br, 1H), 7.67-7.58 (m, 4H), 4.00 (s, 3H) .The 1H of HCl and NH- were not observed.	DMSO	>98	G12 Temperature at 100°C			

305

421					1H NMR (DMSO-d6) ppm 9.88 (s, 1H), 9.51 (dd, J = 2.16, 0.8 Hz, 1H), 8.68-8.64 (m, 2H), 7.98 (d, J = 2.40 Hz, 1H), 7.91 (d, J = 8.84 Hz, 2H), 7.86 (d, J = 9.12 Hz, 1H), 7.68 (d, J = 8.84 Hz, 2H), 7.58-7.53 (m, 2H), 3.98 (s, 3H).	DMSO	>98	G1			
422				HCl	1H NMR (DMSO-d6) ppm 10.24 (br, 1H), 9.54 (s, 1H), 8.92 (d, J = 7.52 Hz, 1H), 8.82 (d, J = 3.96 Hz, 1H), 8.10 (d, J = 2.44 Hz, 1H), 8.03 (d, J = 8.68 Hz, 2H), 7.92 (d, J = 9.08 Hz, 1H), 7.84 (d, J =8.68 Hz, 2H), 7.81 (m, 1H), 7.77-7.75 (m, 2H), 7.62 (dd, J = 9.08, 2.44 Hz, 1H), 7.50 (m, 2H), 7.38 (m, 1H), 4.01 (s, 3H) .The 1H of HCl was not observed.	DMSO	>98	J3 using Na_2CO_3 instead of K_2CO_3			
423				HCl	1H NMR (DMSO-d6) ppm 9.72 (s, 1H), 9.09 (d, J = 8.00 Hz, 1H), 8.89 (d, J = 4.24 Hz, 1H), 8.26 (brs, 1H), 8.12-8.09 (m, 2H), 7.96 (d, J = 9.12 Hz, 1H), 7.91 (m, 1H), 7.64 (dd, J = 9.12, 2.64 Hz, 1H), 7.45 (t, J = 8.80 Hz, 2H), 3.99 (s, 3H).The 1H of HCl and NH- were not observed.	DMSO	>98	G13 using K_2CO_3 instead of Cs_2CO_3			

306

424				HCl	1H NMR (DMSO-d6) ppm 10.30-10.15 (br, 1H), 9.54 (s, 1H), 8.91 (brs, 1H), 8.82 (brs, 1H), 8.10 (brs, 1H), 8.04 (d, J = 8.56 Hz, 2H), 7.92 (d, J = 9.6 Hz, 1H), 7.85 (d, J = 8.56 Hz, 2H), 7.80 (m, 1H), 7.79 (d, J = 8.56 Hz, 2H), 7.65-7.59 (brm, 1H), 7.55 (d, J = 8.56 Hz, 2H), 4.01 (s, 3H) .The 1H of HCl was not observed.	DMSO	>98	J3			
425				HCl	1H NMR (DMSO-d6) ppm 9.91 (s, 1H), 9.53 (d, J = 1.84 Hz, 1H), 8.69 (d, J = 5.56 Hz, 2H), 8.31 (t, J = 1.88 Hz, 1H), 7.99 (d, J = 2.68 Hz, 1H), 7.98-7.94 (m, 1H), 7.87 (d, J = 9.08 Hz, 1H), 7.60-7.54 (m, 2H), 7.46 (t, J = 8.04 Hz, 1H), 7.39-7.35 (m, 1H), 3.99 (s, 3H) .The 1H of HCl was not observed.	DMSO	>98	G1			
426				HCl	1H NMR (DMSO-d6) ppm 10.25 (br, 1H), 9.52 (s, 1H), 8.89 (brs, 1H), 8.88 (brs, 1H), 8.22 (brs, 1H), 8.11 (brs, 1H), 7.98-7.92 (brm, 2H), 7.80-7.70 (brm, 3H), 7.63-7,.69 (brm, 2H), 7.55- 7.50 (brm, 3H), 7.41 (m, 1H), 4.00 (s, 3H). The 1H of HCl was not observed.	DMSO	>98	G13 using K_2CO_3 instead of Cs_2CO_3 at 120 °C			

307

427				HCl	1H NMR (DMSO-d6) ppm 10.31 (br, 1H), 9.51 (brs, 1H), 8.92 (brd, J = 7.44 Hz, 1H), 8.84 (brs, 1H), 8.22 (brs, 1H), 8.12 (brd, J = 2.28 Hz, 1H), 8.00-7.93 (brm, 2H), 7.83-7.77 (brm, 3H), 7.64-7.54 (brm, 5H), 4.01 (s, 3H) . The 1H of HCl was not observed.	DMSO	>98	J3 using Na_2CO_3 instead of K_2CO_3			
428				4 HCl	1H NMR (DMSO-d6) ppm 9.73 (d, J = 1.72 Hz, 1H), 9.06 (d, J = 8.08 Hz, 1H), 8.88 (d, J = 3.72 Hz, 1H), 8.28 (brs, 1H), 8.01-7.96 (m, 3H), 7.88 (m, 1H), 7.81 (d, J = 8.60 Hz, 2H), 7.65 (dd, J = 9.08, 2.64 Hz, 1H), 4.00 (s, 3H). The 1H of 4HCl and NH- were not observed.	DMSO	>98	G13 using K_2CO_3 instead of Cs_2CO_3			
429				HCl	1H NMR (DMSO-d6) ppm 12.60 (br, 1H), 9.78 (d, J = 1.76 Hz, 1H), 9.28 (d, J = 8.04 Hz, 1H), 8.95 (dd, J = 5.20 , 1.20 Hz, 1H), 8.36 (d, J = 2.28 Hz, 1H), 8.04-7.93 (m, 4H), 7.77 (s, 1H), 7.64 (dd, J = 9.12, 2.68 Hz, 1H), 7.30 (d, J = 8.04 Hz, 2H), 4.02 (s, 3H), 2.36 (s, 3H) . The 1H of HCl was not observed.	DMSO	>98	G13 using K_2CO_3 instead of Cs_2CO_3			

308

430				2 HCl	1H NMR (DMSO-d6) ppm 12.70-12.40 (br, 1H), 9.71 (s, 1H), 9.27 (d, J = 8.20 Hz, 1H), 8.94 (d, J = 4.24 Hz, 1H), 8.34 (d, J = 2.64 Hz, 1H), 8.13 (t, J = 1.80 Hz, 1H), 8.04-7.95 (m, 4H), 7.63 (dd, J = 9.08, 2.68 Hz, 1H), 7.52 (t, J = 7.88 Hz, 1H), 7.44-7.42 (m, 1H), 4.02 (s, 3H). The 1H of 2HCl was not observed.	DMSO	>98	G13 using K_2CO_3 instead of Cs_2CO_3			
431				HCl	1H NMR (DMSO-d6) ppm 12.57 (br, 1H), 9.80 (brs, 1H), 9.04 (d, J = 7.36 Hz, 1H), 8.82 (brs, 1H), 8.34 (brs, 1H), 7.99 (brd, J = 7.28 Hz, 1H), 7.95 (d, J = 9.08 Hz, 1H), 7.82 (brs, 1H), 7.76 (brm, 1H), 7.62 (m, 2H), 7.50-7.41 (m, 2H), 4.00 (s, 3H). The 1H of HCl was not observed.	DMSO	>98	G13 using K_2CO_3 instead of Cs_2CO_3			
432				HCl	1H NMR (DMSO-d6) ppm 10.40 (br, 1H), 9.23 (s, 1H), 8.80 (d, J = 4.68 Hz, 1H), 8.66 (brd, J = 8.20 Hz, 1H), 7.92 (brs, 1H), 7.87 (brd, J = 9.28 Hz, 1H), 7.78 (brm, 1H), 7.63-7.52 (m, 5H), 7.47-7.44 (m, 2H), 7.21-7.12 (m, 3H), 3.91 (s, 3H). . The 1H of HCl was not observed.	DMSO	>98	G13 using K_2CO_3 instead of Cs_2CO_3			

309

433				HCl	1H NMR (DMSO-d6) ppm 12.34 (br, 1H), 9.75 (s, 1H), 9.01 (d, J = 7.52 Hz, 1H), 8.81 (brs, 1H), 8.40-8.20 (br, 1H), 7.92 (d, J = 9.08 Hz, 1H), 7.77 (m, 1H), 7.60 (dd, J = 9.08, 2.72 Hz, 1H), 6.95 (br, 1H), 3.98 (s, 3H), 2.67 (m, 1H), 2.05 (m, 2H), 1.83-1.70 (m, 3H), 1.54-1.23 (m, 5H) . The 1H of HCl was not observed.	DMSO	>98	G13 using K_2CO_3 instead of Cs_2CO_3			
434				2 HCl	1H NMR (DMSO-d6) ppm 12.58 (br, 1H), 9.79 (s, 1H), 9.19 (d, J = 7.32 Hz, 1H), 8.90 (d, J = 5.6 Hz, 1H), 8.36 (s,1H), 7.96 (d, J = 9.08 Hz, 1H), 7.94 (m, 1H), 7.88 (s, 1H), 7.65-7.62 (m, 3H), 7.40 (t, J = 8.16 Hz, 1H), 6.96-6.93 (m, 1H), 4.02 (s,3H), 3.84 (s, 3H) . The 1H of 2HCl was not observed.	DMSO	>98	G13 using K_2CO_3 instead of Cs_2CO_3			
435				2 HCl	1H NMR (DMSO-d6) ppm 12.80-12.40 (br, 1H), 9.79 (d, J = 1.44 Hz, 1H), 9.26 (d, J = 8.24 Hz, 1H), 8.93 (d, J = 4.08 Hz, 1H), 8.36 (d, J = 2.28 Hz, 1H), 8.02-7.96 (m, 4H), 7.68 (s, 1H), 7.64 (dd, J = 9.12, 2.68 Hz, 1H), 7.05 (d, J = 8.92 Hz, 2H), 4.02 (s, 3H), 3.82 (s, 3H). The 1H of 2HCl was not observed.	DMSO	>98	G13 using K_2CO_3 instead of Cs_2CO_3			

310

436				HCl	1H NMR (DMSO-d6) ppm 12.52 (br, 1H), 9.79 (s, 1H), 9.23 (d, J = 8.00 Hz, 1H), 8.91 (d, J = 4.12 Hz, 1H), 8.35 (brs, 1H), 8.25 (d, J = 7.6 Hz, 1H), 7.96 (d, J = 9.08 Hz, 1H), 7.93 (m, 1H), 7.85 (s, 1H), 7.64 (dd, J = 9.08, 2.68 Hz, 1H), 7.39-7.35 (m, 1H), 7.18 (d, J = 7.72 Hz, 1H), 7.11-7.07 (m, 1H), 4.02 (s, 3H), 3.96 (s, 3H). The 1H of HCl was not observed.	DMSO	>98	G13 using K_2CO_3 instead of Cs_2CO_3			
437					1H NMR (DMSO-d6) ppm 9.94 (s, 1H), 9.27 (d, J = 1.92 Hz, 1H), 8.59 (dd, J = 4.72, 1.68 Hz, 1H), 8.45 (dt, J = 8.04, 1.8 Hz, 1H), 7.96 (d, J = 2.72 Hz, 1H), 7.84 (d, J = 8.28 Hz, 2H), 7.67 (d, J = 8.00 Hz, 1H), 7.55 (m, 2H), 7.46-7.43 (m, 1H), 7.33 (m, 1H), 3.96 (s, 3H).	DMSO	>98	G13 using K_2CO_3 instead of Cs_2CO_3 at 120 °C			
438				HCl	1H NMR (DMSO-d6) ppm 10.48 (br, 1H), 9.23 (s,1H), 8.83 (brd, J = 3.68 Hz, 1H), 8.70 (brd, J = 7.36 Hz, 1H), 7.95 (brs, 1H), 7.91 (d, J = 9.12 Hz, 1H), 7.82 (m, 1H), 7.63-7.51 (m, 5H), 7.48 (d, J = 8.52 Hz, 2H), 7.26 (d, J = 8.52 Hz, 2H), 3.93 (s, 3H). The 1H of HCl was not observed.	DMSO	>98	J3 using Na_2CO_3 instead of K_2CO_3			

311

439				HCl	1H NMR (DMSO-d6) ppm 12.60 (br, 1H), 9.78 (s,1H), 9.17 (d, J = 7.96 Hz, 1H), 8.88 (d, J = 4.20 Hz, 1H), 8.35 (d, J = 2.60 Hz, 1H), 8.24-8.21 (m, 1H), 7.96 (d, J = 9.08 Hz, 1H), 7.91-7.88 (brm, 1H), 7.74 (d, J = 2.48 Hz, 1H), 7.63 (dd, J = 9.08, 2.60 Hz, 1H), 7.47-7.41 (m, 1H), 7.36 8m, 2H), 4.02 (s, 3H). The 1H of HCl was not observed.	DMSO	>98	G13 at 100 °C			
440				HCl	1H NMR (DMSO-d6) ppm 12.60-12.45 (br, 1H), 9.79 (d, J = 1.52 Hz, 1H), 9.15 (d, J = 8.36 Hz, 1H), 8.88 (d, J = 5.04 Hz, 1H), 8.35(d, J = 2.44 Hz, 1H), 7.96 (d, J = 9.12 Hz, 1H), 7.89 (brt, J = 7.08 Hz, 2H), 7.82 (brm, 1H), 7.81 (s, 1H), 7.63 (dd, J = 9.12, 2.44 Hz, 1H), 7.37 (t, J = 7.64 Hz, 1H), 7.19 (d, J = 7.48 Hz, 1H), 4.02 (s, 3H), 2.40 (s, 3H). The 1H of HCl was not observed.	DMSO	>98	G13 at 100 °C			
441				HCl	1H NMR (DMSO-d6) ppm 12.60 (br, 1H), 9.77 (s, 1H), 9.25 (d, J = 8.08 Hz, 1H), 8.93 (d, J = 4.28 Hz, 1H), 8.34 (d, J = 2.60 Hz, 1H), 8.01-7.84 (m, 5H), 7.63 (dd, J = 9.12, 2.60 Hz, 1H), 7.56-7.51 (m, 1H), 7.21 (m, 1H). The 1H of HCl was not observed.	DMSO	>98	G13 at 100 °C			

312

442				2 HCl	1H NMR (DMSO-d6) ppm 12.66 (brs, 1H), 9.78 (d, J = 1.68 Hz, 1H), 9.27 (d, J = 8.08 Hz, 1H), 8.94 (dd, J = 5.20 , 1.40 Hz, 1H), 8.36 (d, J = 2.56 Hz, 1H), 8.17 (d, J = 8.84 Hz, 2H), 8.01 (m, 1H), 7.97 (d, J = 9.08 Hz, 1H), 7.93 (s, 1H), 7.64 (dd, J = 9.08, 2.56 Hz, 1H), 7.49 (brd, J = 8.84 Hz, 2H), 4.02 (s, 3H). The 1H of 2HCl was not observed.	DMSO	>98	G13 at 100 °C			
443				2 HCl	1H NMR (DMSO-d6) ppm 12.64 (br, 1H), 9.79 (s, 1H), 9.13 (d, J = 7.56 Hz, 1H), 8.87 (d, J = 5.08 Hz, 1H), 8.36 (d, J = 2.60Hz, 1H), 8.27 (d, J = 8.00 Hz, 2H), 8.08 (s, 1H), 7.96 (d, J = 9.12 Hz, 1H), 7.87 (m, 1H), 7.86 (d, J = 8.00 Hz, 2H), 7.64 (dd, J = 9.12, 2.60 Hz, 1H), 4.02 (s, 3H). The 1H of 2HCl was not observed.	DMSO	>98	G13 at 100 °C			
444				2 HCl	1H NMR (MeOD-d4) ppm 9.79 (s, 1H), 9.37 (br, 1H), 8.49 (dd, J = 5.28, 1.32 Hz, 1H), 8.12 (m, 1H), 8.09 (d, J = 2.72 Hz, 1H), 7.98 (d, J = 9.16 Hz, 1H), 7.68 (dd, J = 9.16, 2.72 Hz, 1H), 7.58 (d, J = 7.12 Hz, 1H), 7.42-7.30 (m, 3H), 7.30 (s, 1H), 4.05 (s, 3H), 2.50 (s, 3H). The 1H of 2HCl was not observed.	MeOD	>98	G13			

313

445				2 HCl	1H NMR (DMSO-d6) ppm 12.59 (br, 1H), 9.78 (d, J = 1.48 Hz, 1H), 9,19 (d, J = 8.00 Hz, 1H), 8.90 (dd, J = 5.16, 1.48 Hz, 1H), 8.34 (d, J = 2.60 Hz, 1H), 8.10-8.04 (m, 1H), 7.97-7.88 (m, 4H), 7.64 (dd, J = 2.60 Hz, 1H), 7.59-7.52 (m, 1H), 4.02 (s, 3H) . The 1H of 2HCl was not observed.	DMSO	>98	G13			
446				HCl	1H NMR (DMSO-d6) ppm 12.61 (br, 1H), 9.78 (d, J = 1.72 Hz, 1H), 9.20 (d, J = 7.92 Hz, 1H), 8.90 (d, J = 4.00 Hz, 1H), 8.35 (d, J = 2.60 Hz, 1H), 8.27-8.21 (m, 1H), 7.96 (d, J = 9.12 Hz, 1H), 7.93 (m, 1H), 7.71 (d, J = 2.56 Hz, 1H), 7.64 (dd, J = 9.12, 2.60 Hz, 1H), 7.43 (m, 1H), 7.27 (m, 1H), 4.02 (s, 1H) . The 1H of HCl was not observed.	DMSO	>98	G13			
447				2 HCl	1H NMR (DMSO-d6) ppm 12.57 (br, 1H), 9.77 (d, J = 1.76 Hz, 1H), 9.25 (d, J = 8.08 Hz, 1H), 8.93 (dd, J = 5.16, 1.2 Hz, 1H), 8.34 (d, J = 2.60 Hz, 1H), 8.29 (t, J = 1.76 Hz, 1H), 8.05 (dd, J = 7.84, 1.12 Hz, 1H), 8.02-7.98 (m, 1H), 7.99 (s, 1H), 7.96 (d, J = 9.08 Hz, 1H), 7.64 (dd, J = 9.08, 2.60 Hz, 1H), 7.58-7.56 (m, 1H), 7.45 (t, J = 7.84 Hz, 1H), 4.02 (s, 3H). The 1H of 2HCl was not observed.	DMSO	>98	G13			

314

448				HCl	1H NMR (DMSO-d6) ppm 12.62 (br, 1H), 9.77 (d, J = 1.52 Hz, 1H), 9.10 (d, J = 8.16 Hz, 1H), 8.85 (dd, J = 5.00, 1.56 Hz, 1h), 8.34 (d, J = 2.60 Hz, 1H), 8.24 (d, J = 8.60 Hz, 2H), 8.13 (s, 1H), 7.96 (d, J = 8.60 Hz, 2H), 7.96 (d, J = 9.08 Hz, 1H), 7.86-7.83 (brm, 1H), 7.63 (dd, J = 9.08, 2.60 Hz, 1H), 4.02 (s, 3H). The 1H of HCl was not observed.	DMSO	>98	G13			
449				2 HCl	1H NMR (DMSO-d6) ppm 12.56 (brs, 1H), 9.79 (brs, 1H), 9.11 (d, J = 8.04 Hz, 1H), 8.87 (brs, 1H), 8.43 (brs, 1H), 8.34 (brs, 2H), 8.09 (s, 1H), 7.96 (d, J = 9.08 Hz, 1H), 7.87 (brs, 1H), 7.74 (brd, J = 5.00 Hz, 2H), 7.64 (dd, J = 9.08, 2.48 Hz, 1H), 4.03 (s, 3H) . The 1H of 2HCl was not observed.	DMSO	>98	G13 at 100 °C			
450				2 HCl	1H NMR (DMSO-d6) ppm 12.63 (br, 1H), 9.80 (d, J = 1.72 Hz, 1H), 9.27 (d, J = 8.16 Hz, 1H), 8.93 (dd, J = 5.20 , 1.36 Hz, 1H), 8.33 (d, J = 2.24 Hz, 1H), 7.99 (m, 1H), 7.98 (d, J = 9.08 Hz, 1H), 7.88 (brd, J = 7.72 Hz, 1H), 7.71-7.75 (m, 2H), 7.70 -7.63 (m, 2H), 7.45 (s, 1H), 3.98 (s, 3H). The 1H of 2HCl was not observed.	DMSO	>98	G13 at 100 °C			

315

451				HCl	1H NMR (DMSO-d6) ppm 12.70 (br, 1H), 9.79 (d, J = 1.60 Hz, 1H), 9.30 (d, J = 7.56 Hz, 1H), 8.95 (d, J = 4.96 Hz, 1H), 8.34 (d, J = 2.20 Hz, 1H), 8.02 (m, 1H), 7.98 (d, J = 9.12 Hz, 1H), 7.85-7.77 (m, 2H), 7.73 (s, 1H), 7.64 (dd, J = 9.12, 2.68 Hz, 1H), 7.52 (m, 1H), 7.36 (m, 1H), 4.00 (s, 3H). The 1H of HCl was not observed.	DMSO	>98	G13			
452				HCl	1H NMR (DMSO-d6) ppm 12.64 (br, 1H), 9.78 (d, J = 1.72 Hz, 1H), 9.19 (d, J = 7.92 Hz, 1H), 8.90 (d, J = 3.88 Hz, 1H), 8.36 (d, J = 2.64 Hz, 1H), 8.02-7.91 (m, 3H), 7.83 (d, J = 2.40 hz, 1H), 7.64 (dd, J = 9.08, 2.64 Hz, 1H), 7.46 (m, 1H), 7.36 (m, 1H), 4.02 (s, 3H). The 1H of HCl was not observed.	DMSO	>98	G13			
453				2 HCl	1H NMR (DMSO-d6) ppm 12.62 (br, 1H), 9.77 (d, J = 1.84 Hz, 1H), 9.30 (d, J = 8.00 Hz, 1H), 8.46 (dd, J = 5.36, 1.48 Hz, 1H), 8.48 (br, 1H), 8.39-8.33 (m, 2H), 8.08 (s, 1H), 8.05 (m, 1H), 7.97 (d, J = 9.12 Hz, 1H), 7.85-7.83 (m, 1H), 7.71 (t, J = 7.84 Hz, 1H), 7.64 (dd, J = 9.12, 2.60 Hz, 1H), 4.02 (s, 3H). The 1H of 2HCl was not observed.	DMSO	>98	G13			

316

454				2 HCl	1H NMR (DMSO-d6) ppm 12.65 (br, 1H), 9.79 (d, J = 1.72 Hz, 1H), 9.25 (d, J = 8.04 Hz, 1H), 8.92 (d, J = 5.36 Hz, 1H), 8.36 (d, J = 2.60 Hz, 1H), 8.24-8.22 (,m, 1H), 7.97 (d, J = 9.08 Hz, 1H), 7.96 (m, 1H), 7.69 (s, 1H), 7.65 (dd, J = 9.08, 2.60 Hz, 1H), 7.55 (m, 3H), 4.02 (s, 3H). The 1H of 2HCl was not observed.	DMSO	>98	G13			
455				HCl	1H NMR (DMSO-d6) ppm 12.52 (br, 1H), 9.78 (d, J = 1.48 Hz, 1H), 9.03 (d, J = 6.6 Hz, 1H), 8.81 (d, J = 4.72 Hz, 1H), 8.34 (d, J = 2.56 Hz, 1H), 8.09 (d, J = 7.88 Hz, 1H), 8.03 (brs, 2H), 7.96 (d, J = 9.12 Hz, 1H), 7.78 (br, 1H),7.65 (m, 2H), 7.38 (m, 1H), 4.02 (s, 3H). The 1H of HCl was not observed.	DMSO	>98	G13			
456				2 HCl	1H NMR (DMSO-d6) ppm 12.45 (br, 1H), 9.78 (d, J = 1.64 Hz, 1H), 9.15 (br, 1H), 8.89 (d, J = 4.52 Hz, 1H), 8.30 (brs, 1H), 7.94 (d, J = 9.08 Hz, 1H), 7.90 (brm, 1H), 7.76 (m, 2H), 7.62 (dd, J = 9.08, 2.64 Hz, 1H), 7.51 (m, 2H), 7.40 (m, 1H), 3.99 (s, 3H), 2.61 (s, 3H). The 1H of 2HCl was not observed.	DMSO	>98	G13			

317

457				HCl	1H NMR (DMSO-d6) ppm 12.55 (br, 1H), 9.78 (d, J = 1.48 Hz, 1H), 9.08 (d, J = 8.48 Hz, 1H), 8.84 (dd, J = 5.04, 1.56 Hz, 1H), 8.34 (d, J = 2.72 Hz, 1H), 8.09 (s, 1H), 7.96 (d, J = 9.12 Hz, 1H), 7.84 (m, 1H), 7.77 (m, 2H), 7.64 (dd, J = 9.12, 2.72 Hz, 1H), 7.25 (m, 1H), 4.02 (s, 3H). The 1H of HCl was not observed.	DMSO	>98	G13			
458				HCl	1H NMR (DMSO-d6) ppm 12.55 (br, 1H), 9.77 (d, J = 1.56 Hz, 1H), 9.14 (d, J = 8.00 Hz, 1H), 8.87 (dd, J = 5.08, 1.48 Hz, 1H), 8.34 (d, J = 2.60 Hz, 1H), 7.98 (m, 1H), 7.96 (d, J = 9.08 Hz, 1H), 7.89-7.86 (brm, 1H), 7.83 (d, J = 2.44 Hz, 1H), 7.64 (dd, J = 9.08, 2.60 Hz, 1H), 7.47-7.41 (m, 1H), 7.29 (m, 1H), 4.02 (s, 3H).The 1H of HCl was not observed.	DMSO	>98	G13			
459				HCl	1H NMR (DMSO-d6) ppm 12.66 (br, 1H), 9.79 (d, J = 1.60 Hz, 1H), 9.25 (d, J = 7.16 Hz, 1H), 8.92 (d, J = 5.20 Hz, 1H), 8.35 (d, J = 2.56 Hz, 1H), 7.98 (d, J = 9.12 Hz, 1H), 7.97 (m, 1H), 7.68 (s, 1H), 7.64 (dd, J = 9.12, 2.56 Hz, 1H), 7.55 (m, 1H), 7.27 (m, 2H), 3.99 (s, 3H).The 1H of HCl was not observed.	DMSO	>98	G13			

318

460				2 HCl	1H NMR (DMSO-d6) ppm 9.73 (s, 1H), 9.17 (brs, 1H), 8.92 (dd, J = 5.16, 1.4 Hz, 1H), 8.30-8.10 (br, 1H), 7.97 (d, J = 9.04 Hz, 1H), 7.96 (m, 1H), 7.63 (dd, J = 9.04, 2.72 Hz, 1H), 7.02 (s, 1H), 3.98 (s, 3H), 2.57 (d, J = 7.16 Hz, 2H), 2.08 (m, 1H), 0.94 (d, J = 6.60 Hz, 6H) .The 1H of HCl and NH- were not observed.	DMSO	>98	G13			
461				2 HCl	1H NMR (DMSO-d6) ppm 12.80-12.20 (br, 1H), 9.78 (d, J = 1.76 Hz, 1H), 9.28 (d, J = 8.04 Hz, 1H), 8.96 (dd, J =5.28, 1.32 Hz, 1H), 8.29 (brs, 1H), 8.07-8.03 (brm, 1H), 7.95 (d, J = 9.12 Hz, 1H), 7.79 (d, J = 8.60 Hz, 2H), 7.62 (dd, J = 9.12, 2.64 Hz, 1H), 7.57 (d, J = 8.60 Hz, 2H), 3.99 (s, 3H), 2.61 (brs, 3H). The 1H of 2HCl was not observed.	DMSO	>98	G13			
462				2 HCl	1H NMR (DMSO-d6) ppm 12.80-12.20 (br, 1H),. 9.74 (s, 1H), 9.19 (d, J = 4.96 Hz, 1H), 8.91 (dd, J = 5.2, 1.4 Hz, 1H), 8.22 (brs, 1H), 7.96 (br, 1H), 7.95 (d, J = 9.08 Hz, 1H), 7.61 (dd, J = 9.08, 2.68 Hz, 1H), 7.35-7.31 (m, 4H), 7.23 (m, 1H), 7.09 (brs, 1H), 4.07 (brs, 2H), 3.96 (brs, 3H). The 1H of 2HCl was not observed.	DMSO	>98	G13			

319

463				2 HCl	1H NMR (DMSO-d6) ppm 12.50 (br, 1H), 9.78 (d, J = 1.76 Hz, 1H), 9.25 (brs, 1H), 8.96 (brd, J = 4.68 Hz, 1H), 8.29 (brs, 1H), 8.04 (brs, 1H), 7.96 (d, J = 9.20 Hz, 1H), 7.70 (brm, 2H), 7.63 (dd, J = 9.20, 2.68 Hz, 1H), 7.51 (brm, 2H), 7.41 (brm, 1H), 3.99 (s, 3H), 3.02 (q, J = 7.40 Hz, 2H), 1.49 (t, J = 7.40 Hz, 3H). The 1H of 2HCl was not observed.	DMSO	>98	G13			
464				2 HCl	1H NMR (DMSO-d6) ppm 12.53 (br, 1H), 9.78 (d, J = 1.76 Hz, 1H), 9.20 (d, J = 8.36 Hz, 1H), 8.94 (dd, J = 5.2, 1.4 Hz., 1H), 8.29 (brs, 1H), 8.00 (brm, 1H), 7.96 (d, J = 9.12 Hz, 1H), 7.66 - 7.61 (m, 3H), 7.52 (brm, 2H), 7.43 (t, J 7.40 Hz, 1H), 3.98 (s, 3H), 1.43 (d, J = 6.8 Hz, 6H). The 1H of 2HCl was not observed. The CH proton of iPr group was not observed because of overlapping the H2O peak.	DMSO	>98	G13			
465				2 HCl	1H NMR (DMSO-d6) ppm 12.59 (brs, 1H), 9.77 (d, J - 1.72 Hz, 1H), 9.25 (d, J = 7.76 Hz, 1H), 8.96 (d, J = 4.04 Hz, 1H), 8.29 (br, 1H), 8.04 (m, 1H), 7.96 (d, J = 9.12 Hz, 1H), 7.69 (brd, J = 7.12 Hz, 2H), 7.63 (dd, J = 9.12, 2.68 Hz, 1H), 7.51 (t, J = 7.36 Hz, 2H), 7.42 (t, J = 7.36 Hz, 1H), 3.99 (s, 3H), 2.96 (t, J = 7.52 Hz, 2H), 1.78 (m, 2H), 1.01 (t, J = 7.24 Hz, 3H). The 1H of 2HCl was not observed.	DMSO	>98	G13			

320

466				2 HCl	1H NMR (DMSO-d6) ppm 12.96 (brs, 1H), 9.74 (d, J = 2.04 Hz, 1H), 9.11 (d, J = 7.96 Hz, 1H), 8.90 (d, J = 4.96 Hz, 1H), 8.31 (brd, J = 2.64 Hz, 1H), 7.97 (d, J = 9.12 Hz,1H), 7.87 (brm, 1H), 7.83- 7.80 (m, 2H), 7.64 (dd, J = 9.12, 2.62 Hz, 1H), 7.48 (m, 3H), 4.25 (q, J =7.04 Ha, 2H), 3.98 (s, 3H), 1.29 (t, J = 7.04 Hz, 3H). The 1H of 2HCl was not observed.	DMSO	>98	G13			
467				HCl	1H NMR (DMSO-d6) ppm 12.63 (br, 1H), 9.76 (d, J= 1.76 Hz, 1H), 9.29 (d, J =8.16 Hz, 1H), 8.95 (dd, J = 5.28, 1.36 Hz, 1H), 8.32 (brd, J =2.60 Hz, 1H), 8.07 (d, J = 8.52 Hz, 2H), 8.08-8.00 (m, 1H), 7.95 (d, J = 9.12 Hz, 1H), 7.90 (s, 1H), 7.61 (dd, J = 9.12, 2.60 Hz, 1H), 7.55 (d, J = 8.52 Hz, 2H), 4.24 (q, J =6.88 Hz,2H), 1.47 (t, J = 6.88 Hz, 3H). The 1H of HCl was not observed.	DMSO	>98	G13			
468				2 HCl	1H NMR (DMSO-d6) ppm 12.58 (brs, 1H), 9.76 (d, J = 1.80 Hz, 1H), 9.27 (d, J = 8.16 Hz, 1H), 8.94 (dd, J = 5.20, 1.32 Hz, 1H), 8.32 (d, J = 2.48 Hz, 1H), 8.09-8.01 (m, 2H), 7.96-7.89 (m, 3H), 7.62-7.52 (m, 2H), 4.29 (q, J = 6.88 Hz, 2H), 1.47 (t, J = 6.88 Hz, 3H) . The 1H of 2HCl was not observed.	DMSO	>98	G13			

321

469				2 HCl	1H NMR (DMSO-d6) ppm 9.72 (s, 1H), 9.13 (brd, J = 5.52 Hz, 1H), 8.92 (d, J = 3.52 Hz, 1H), 8.16 (brs, 1H), 7.95 (brd, J = 9.08 Hz, 2H), 7.62 (dd, J = 2.4 Hz, 1H), 7.39 (brs, 1H), 3.97 (s, 3H), 2.47 (s, 3H). The 1H of 2HCl and NH- were not observed.	DMSO	>98	G13			
470				HCl	1H NMR (DMSO-d6) ppm 12.58 (brs, 1H), 9.76 (d, J = 1.68 Hz, 1H), 9.17 (d, J = 8.12 Hz, 1H), 8.89 (dd, J = 5.12, 1.48 Hz, 1H), 8.32 (d, J = 2.56 Hz, 1H), 8.01-8.00 (m, 1H), 7.94 (d, J = 9.08 Hz, 1H), 7.930-7.90 (m, 1H), 7.81 (d, J = 2.4 Hz, 1H), 7.60 (dd, J = 9.08, 2.40 Hz, 1H), 7.50-7.43 (m, 1H), 7.38-7.33 (m, 1H), 4.28 (q, J = 7.00 Hz, 2H), 1.47 (t, J = 7.00 Hz, 3H). The 1H of HCl was not observed.	DMSO	>98	G13			
471				2 HCl	1H NMR (DMSO-d6) ppm12.53 (brs, 1H), 9.73 (d, J = 1.76 Hz, 1H), 9.29 (d, J = 8.16 Hz, 1H), 8.95 (dd, J = 5.32, 1.36 Hz, 1H), 8.29 (d, J = 2.56 Hz, 1H), 8.05-8.02 (brm, 1H), 7.97-7.92 (m, 1H), 7.93 (d, J = 9.08 Hz, 1H), 7.78 (d, J = 2.36 Hz, 1H), 7.60 (dd, J = 9.08, 2.6 Hz, 1H), 7.46- 7.40 (m, 1H), 7.31-7.25 (m, 1H), 4.27 (q, J = 6.92 Hz, 2H), 1.47 (t, J =6.92 Hz, 3H) . The 1H of 2HCl was not observed.	DMSO	>98	G13			

322

472				3 HCl	1H NMR (DMSO-d6) ppm 12.61 (brs, 1H), 9.76 (d, J = 1.8 Hz, 1H), 9.29 (d, J = 8.16 Hz, 1H), 8.95 (dd, J = 5.24, 1.2 Hz, 1H), 8.32 (d, J =2.52 Hz, 1H), 8.24-8.20 (m, 1H), 8.05-8.01 (brm, 1H),7.95 (d, J = 9.08 Hz, 1H), 7.68 (d, J =2.52 HZ, 1H), 7.61 (dd, J = 9.08, 2.52 Hz, 1H), 7.46-7.40 (m, 1H), 7.28-7.24 (m, 1H), 4.28 (q, J = 6.92 Hz, 2H), 1.47 (t, J = 6.92 Hz, 3H). The 1H of 3HCl was not observed.	DMSO	>98	G13			
473				2 HCl	1H NMR (DMSO-d6) ppm 12.63 (brs, 1H), 9.78 (d, J = 1.68 Hz, 1H), 9.32 (d, J = 8.12 Hz, 1H), 8.97 (d, J = 5.24 Hz, 1H), 8.35 (d, J = 2.16 Hz, 1H), 8.08-8.04 (m, 3H), 7.96 (d, J = 9.08 Hz, 1H), 7.85 (s, 1H), 7.62 (dd, J = 9.08, 2.52 Hz, 1H), 7.49 (t, J = 7.44 Hz, 2H), 7.38 (t, J = 7.28 Hz, 1H), 4.30 (q, J = 6.96 Hz, 2H), 1.47 (t, J = J = 6.96 Hz, 3H) . The 1H of 2HCl was not observed.	DMSO	>98	G13			
474					1H NMR (DMSO-d6) ppm 12.68 (s, 1H), 9.73 (d, J = 1.64 Hz, 1H), 8.87-8.84 (m, 1H), 8.75-8.73 (m, 1H), 8.33 (brs, 1H), 8.24 (brs, 1H), 7.93 (d, J = 9.16 Hz, 1H), 7.64-7.59 (m, 2H), 4.34 (q, J = 7.08 Hz, 2H), 3.98 (s, 3H), 1.34 (t, J = 7.08 Hz, 3H).	DMSO	>98	G13			

323

475				HCl	^{1}H NMR (300 MHz, DMSO) δ 10.35 (s, 1H), 9.42 (s, 1H), 8.99 - 8.76 (m, 2H), 8.11 (d, J = 6.7 Hz, 1H), 7.99 - 7.75 (m, 3H), 7.67 - 7.43 (m, 2H), 7.23 (d, J = 8.2 Hz, 1H), 4.14 (s, 3H).	DMSO	98	G1	381 (M+1)	2.07	Method A (Formic acid)
476				HCl	1H NMR (300 MHz, DMSO) δ 13.78 (s, 1H), 9.62 (d, J = 1.7 Hz, 1H), 9.21 (d, J = 8.1 Hz, 1H), 8.98 (d, J = 4.2 Hz, 1H), 8.07 (dd, J = 7.9, 5.3 Hz, 1H), 7.83 (d, J = 9.1 Hz, 2H), 7.63 - 7.50 (m, 4H), 7.41 (d, J = 6.5 Hz, 2H), 7.14 (d, J = 2.5 Hz, 1H), 5.30 (s, 1H), 3.91 (s, 3H), 2.15 (s, 3H).	DMSO	95	Method G1	468.1 (M+1)		Method C
477				HCl	1H NMR (300 MHz, DMSO) δ 13.78 (s, 1H), 9.64 (d, J = 1.5 Hz, 1H), 9.11 (d, J = 8.2 Hz, 1H), 8.90 (d, J = 3.8 Hz, 1H), 7.95 (dd, J = 10.6, 2.6 Hz, 1H), 7.84 (d, J = 9.1 Hz, 2H), 7.60 - 7.48 (m, 4H), 7.38 (d, J = 6.5 Hz, 2H), 7.17 (d, J = 2.4 Hz, 1H), 5.28 (s, 1H), 4.14 (q, J = 6.9 Hz, 2H), 2.15 (s, 3H), 1.42 (t, J = 6.9 Hz, 3H).	DMSO	95	Method G1	482.1 (M+1)		Method C
478				HCl	1H NMR (300 MHz, DMSO) δ 12.59 (s, 1H), 9.56 (s, 1H), 8.70 (d, J = 5.8 Hz, 2H), 8.58 (d, J = 5.2 Hz, 1H), 7.95 (d, J = 5.2 Hz, 2H), 7.87 (d, J = 9.1 Hz, 2H), 7.64 - 7.49 (m, 2H), 7.40 (d, J = 2.4 Hz, 1H), 4.21 (q, J = 6.8 Hz, 2H), 1.44 (t, J = 6.9 Hz, 3H).	DMSO	99	Method G1	392.1 (M+1)		Method C

324

479				HCl	1H NMR (300 MHz, DMSO) δ 13.75 (s, 1H), 9.60 (s, 1H), 8.98 (s, 1H), 8.82 (d, J = 3.6 Hz, 1H), 7.82 (d, J = 9.0 Hz, 3H), 7.52 (d, J = 9.3 Hz, 1H), 7.15 (s, 1H), 6.94 - 6.62 (s, 1H), 4.13 (d, J = 6.9 Hz, 2H), 2.90 (d, J = 21.9 Hz, 4H), 2.41 (s, 2H), 1.43 (t, J = 6.9 Hz, 3H).	DMSO	95	Method G1	432.1 (M+1)		Method C
480				HCl	1H NMR (300 MHz, DMSO) δ 12.50 (s, 1H), 9.56 (s, 1H), 8.89 (s, 1H), 8.68 (d, J = 5.3 Hz, 2H), 8.00 – 7.79 (m, 3H), 7.73 (d, J = 7.2 Hz, 4H), 7.62 – 7.38 (m, 9H), 7.34 (d, J = 2.2 Hz, 2H), 4.18 (dd, J = 13.5, 6.5 Hz, 2H), 1.43 (t, J = 6.9 Hz, 3H).	DMSO	99	Method G1	468.1 (M+1)		Method C
481				HCl	1H NMR (300 MHz, DMSO) δ 12.51 (s, 1H), 9.54 (s, 1H), 8.86 (s, 1H), 8.74 - 8.61 (m, 2H), 7.90 (s, J = 15.7 Hz, 2H), 7.83 (d, J = 9.1 Hz, 1H), 7.72 (d, J = 7.1 Hz, 2H), 7.63 - 7.40 (m, 6H), 7.33 (d, J = 2.3 Hz, 1H), 3.92 (s, 3H).	DMSO	99	Method G1	454.1 (M+1)		Method C
482				HCl	1H NMR (300 MHz, DMSO) δ 13.70 (s, 1H), 9.70 (d, J = 2.1 Hz, 1H), 8.81 (d, J = 8.0 Hz, 1H), 8.70 (dd, J = 4.8, 1.7 Hz, 1H), 7.90 (d, J = 9.1 Hz, 1H), 7.66 - 7.53 (m, 2H), 7.29 (d, J = 2.2 Hz, 1H), 3.95 (s, 3H), 2.78 (d, J = 12.9 Hz, 4H), 1.78 (s, 4H).	DMSO	99	Method G1	432.1 (M+1)		Method C

325

483				HCl	1H NMR (300 MHz, DMSO) δ 13.64 (s, 1H), 9.68 (s, 1H), 8.79 (d, J = 7.9 Hz, 1H), 8.69 (d, J = 4.7 Hz, 1H), 7.86 (d, J = 9.0 Hz, 1H), 7.63 – 7.50 (m, 2H), 7.24 (s, 1H), 4.18 (q, J = 6.7 Hz, 2H), 2.76 (d, J = 10.4 Hz, 4H), 1.78 (s, 4H), 1.43 (t, J = 6.9 Hz, 3H).	DMSO	99	Method G1	446.1 (M+1)		Method C
484				HCl	1H NMR (300 MHz, DMSO) δ 12.82 (s, 1H), 9.67 (d, J = 2.1 Hz, 1H), 8.77 (dt, J = 8.1, 2.0 Hz, 1H), 8.71 (dd, J = 4.8, 1.7 Hz, 1H), 7.87 (d, J = 9.1 Hz, 1H), 7.83 (s, 1H), 7.60 - 7.53 (m, 3H), 7.48 (s, 1H), 7.20 (d, J = 2.6 Hz, 1H), 4.20 (q, J = 6.9 Hz, 2H), 2.90 (d, J = 4.7 Hz, 3H), 1.44 (t, J = 6.9 Hz, 3H).	DMSO	95	Method G1	422.1 (M+1)		Method C
485				HCl	1H NMR (300 MHz, DMSO) δ 9.66 (s, 1H), 9.44 (d, J = 1.4 Hz, 1H), 8.64 - 8.55 (m, 2H), 7.90 (s, 1H), 7.81 (d, J = 9.1 Hz, 1H), 7.76 (d, J = 2.5 Hz, 1H), 7.69 (s, 2H), 7.54 - 7.45 (m, 2H), 4.19 (q, J = 7.0 Hz, 2H), 4.04 (s, 3H), 1.42 (t, J = 6.9 Hz, 3H).	DMSO	99	Method G1	390.1 (M+1)		Method C
486				2 HCl	1H NMR (300 MHz, DMSO) δ 9.57 (d, J = 1.5 Hz, 1H), 9.07 (d, J = 4.6 Hz, 1H), 8.94 (dd, J = 5.2, 1.4 Hz, 1H), 8.04 (d, J = 9.1 Hz, 1H), 7.97 (dd, J = 6.7, 6.0 Hz, 1H), 7.67 (dd, J = 9.1, 2.8 Hz, 1H), 7.55 (d, J = 2.7 Hz, 1H), 7.36 (dd, J = 6.4, 2.3 Hz, 2H), 7.14 - 7.03 (m, 2H), 3.74 (s, 3H), 3.69 (s, 3H).	DMSO	99	Method G1	382.5 (M+1)		Method C

326

487				2 HCl	1H NMR (300 MHz, DMSO) δ 12.59 (s, 1H), 9.58 (d, J = 2.0 Hz, 1H), 8.94 (d, J = 8.2 Hz, 1H), 8.84 (d, J = 5.2 Hz, 1H), 8.73 (s, 1H), 8.09 (s, 1H), 7.95 (s, 3H), 7.82 (dd, J = 8.4, 5.4 Hz, 2H), 7.75 (d, J = 7.4 Hz, 2H), 7.59 - 7.42 (m, 3H).	DMSO	99	Method G1	458.4 (M+1)		Method C
488				2 HCl	1H NMR (300 MHz, DMSO) δ 13.79 (s, 1H), 9.49 (d, J = 1.5 Hz, 1H), 8.96 (d, J = 8.0 Hz, 1H), 8.86 (d, J = 3.7 Hz, 1H), 7.95 - 7.71 (m, 4H), 7.65 (d, J = 1.6 Hz, 1H), 6.76 (s, 1H), 2.85 (d, J = 22.5 Hz, 4H), 2.44 - 2.29 (m, 2H).	DMSO	93	Method G1	422.4 (M+1)		Method C
489				2 HCl	1H NMR (300 MHz, DMSO) δ 9.53 (d, J = 1.8 Hz, 1H), 9.04 (d, J = 7.9 Hz, 1H), 8.93 (d, J = 3.9 Hz, 1H), 7.95 (dd, J = 8.0, 5.2 Hz, 1H), 7.90 - 7.78 (m, 2H), 7.70 (d, J = 1.7 Hz, 1H), 2.29 (s, 3H), 2.24 (s, 3H).	DMSO	94	Method G1	410.3 (M+1)		Method C
490					1H NMR (300 MHz, DMSO) δ 13.07 (s, 1H), 9.93 (d, J = 1.8 Hz, 1H), 9.64 (d, J = 1.6 Hz, 1H), 8.90 - 8.78 (m, 1H), 8.76 - 8.62 (m, 2H), 8.29 (s, 1H), 8.18 (d, J = 8.3 Hz, 1H), 7.89 (d, J = 9.1 Hz, 1H), 7.71 (dd, J = 8.3, 1.9 Hz, 1H), 7.65 (s, 1H), 7.57 (dd, J = 9.1, 2.5 Hz, 1H), 7.53 - 7.44 (m, 2H), 7.01 (s, 1H), 4.21 (q, J = 6.9 Hz, 2H), 3.34 (s, 3H), 1.44 (t, J = 6.9 Hz, 3H).	DMSO	99	Method G1	464.2 (M+1)		Method C

327

491					1H NMR (300 MHz, DMSO) δ 9.78 (s, 1H), 9.50 (d, J = 2.0 Hz, 1H), 8.68 - 8.57 (m, 2H), 7.97 (d, J = 2.5 Hz, 1H), 7.85 (d, J = 1.8 Hz, 1H), 7.79 (d, J = 9.1 Hz, 1H), 7.55 - 7.43 (m, 3H), 7.22 (d, J = 8.4 Hz, 1H), 4.22 (q, J = 6.9 Hz, 2H), 3.37 (d, J = 4.3 Hz, 6H), 1.43 (t, J = 6.9 Hz, 3H).	DMSO	99	Method G1	427.5 (M+1)		Method C
492					1H NMR (300 MHz, DMSO) δ 11.48 (s, 1H), 10.97 (s, 1H), 9.28 (d, J = 1.5 Hz, 1H), 8.64 (dd, J = 4.6, 1.7 Hz, 1H), 8.40 (d, J = 8.1 Hz, 1H), 7.94 - 7.80 (m, 3H), 7.53 - 7.35 (m, 2H), 7.02 (t, J = 7.5 Hz, 1H), 6.90 (d, J = 8.2 Hz, 1H), 4.04 (s, H).	DMSO	99	Method F5, G13	391.1 (M+1)		Method C
493				2 HCl	1H NMR (300 MHz, DMSO) δ 11.28 (s, 1H), 9.62 (d, J = 1.7 Hz, 1H), 9.17 (d, J = 7.8 Hz, 1H), 8.93 (dd, J = 5.2, 1.3 Hz, 1H), 8.60 (s, 1H), 8.05 (s, 1H), 8.03 - 7.94 (m, 2H), 7.77 (s, 1H), 7.64 (dd, J = 9.2, 2.5 Hz 1H), 7.40 (d, J = 2.6 Hz, 1H), 3.97 (s, 3H).	DMSO	99	Method G14	362.4 (M+1)		Method C
494					^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.14 (s, 1H), 9.54 (s, 1H), 8.70 – 8.67 (m, 2H), 8.48 (s, 1H), 8.16 (s, 1H), 7.96 – 7.89 (m, 3H), 7.60 (t, *J* = 8.0 Hz, 1H), 7.55 – 7.52 (m, 1H), 7.17 (d, *J* = 8.8 Hz, 1H), 3.71 (s, 2H), 2.72 – 2.65 (m, 8H).	DMSO	95	Method G1	498.1 (M+1)	t = 2.128 min	Method B (NH4HCO3)

328

495					^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.71 (s, 1H), 9.37 (s, 1H), 8.93 (s, 1H), 8.67 (d, *J* = 3.2 Hz, 1H), 8.48 (d, *J* = 8.0 Hz, 1H), 7.93 (s, 1H), 7.39 (d, *J* = 8.0 Hz, 1H), 7.65 (m, 2H), 7.04 (d, *J* = 8.0 Hz, 1H), 2.95 (t, *J* = 8.0 Hz, 2H), 2.64 (t, *J* = 8.0 Hz, 2H).	DMSO	95	Method G1	402.0 (M+1)	t = 1.746 min	Method B (NH4HCO3)
496					^{1}H-NMR (400 MHz, DMSO-d_6): δ 11.38 (s, 1H), 9.51 (s, 1H), 8.67 – 8.60 (m, 3H), 8.24 – 8.10 (m, 2H), 7.88 – 7.83 (m, 2H), 7.58 – 7.55 (m, 3H), 7.33 (dd, *J* = 7.2, 4.8 Hz, 1H), 3.97 (s, 3H).	DMSO	95	Method J1	373.0 (M+1)	t = 1.523 min	Method B (NH4HCO3)
497				2HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.92 (s, 1H), 9.30 (s, 1H), 8.60 (d, *J* = 3.4 Hz, 1H), 8.48 (d, *J* = 8.0 Hz, 1H), 8.40 (d, *J* = 4.4 Hz, 1H), 7.87 (d, *J* = 2.2 Hz, 1H), 7.84 (d, *J* = 9.1 Hz, 1H), 7.59 – 7.40 (m, 5H), 4.24 (q, *J* = 6.9 Hz, 2H), 2.55 (d, *J* = 4.5 Hz, 3H), 1.45 (t, *J* = 6.9 Hz, 3H).	DMSO	95	Method G1	418.2 (M+1)	1.782 min	Method B (NH_4HCO_3)
498					^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.14 (s, 1H), 9.54 (d, *J* = 2.0 Hz, 1H), 8.70 – 8.67 (m, 2H), 8.50 (s, 1H), 8.15 (s, 1H), 7.94 – 7.92 (m, 3H), 7.61 (t, *J* = 8.0 Hz, 1H), 7.55 (dd, J = 8.0, 4.8 Hz, 1H), 7.18 (d, *J* = 8.0 Hz, 1H), 3.90 (s, 2H), 3.17 (s, 4H), 2.98 (s, 4H).	DMSO	95	Method G1	530.0 (M+1)	1.856 min	Method B (NH_4HCO_3)

329

499				2HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 13.19 (s, 1H), 9.65 (s, 1H), 9.17 (d, *J* = 8.2 Hz, 1H), 8.97 (d, *J* = 4.5 Hz, 1H), 8.93 (s, 1H), 8.81 (d, *J* = 8.2 Hz, 1H), 8.45 (s, 1H), 8.40 (dd, *J* = 8.7, 1.7 Hz, 1H), 8.16 (d, *J* = 8.7 Hz, 1H), 7.99 (dd, *J* = 16.0, 10.4 Hz, 3H), 7.74 (t, *J* = 7.4 Hz, 1H), 7.32 (t, *J* = 7.6 Hz, 1H), 3.38 (s, 3H).	DMSO	95	Method G1	420.1 (M+1)	t = 1.478 min	Method B (NH_4HCO_3)
501				HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 13.46 (s, 1H), 9.46 (s, 1H), 8.97 (d, *J* = 7.9 Hz, 1H), 8.93 (d, *J* = 4.4 Hz, 1H), 8.77 (d, *J* = 12.1 Hz, 1H), 8.55 (s, 1H), 8.16 – 7.91 (m, 4H), 7.83 (t, *J* = 7.5 Hz, 1H), 7.73 (d, *J* = 9.3 Hz, 1H), 7.05 (t, *J* = 6.9 Hz, 1H).	DMSO	95	Method G1	378.1 (M+1)	t = 1.873 min	Method B (NH_4HCO_3)
502					^{1}H-NMR (400 MHz, DMSO-d_6): δ 13.00 (s, 1H), 9.83 (s, 1H), 9.17 (d, *J* = 8.0 Hz, 1H), 9.00 (d, *J* = 8.0 Hz, 1H), 8.73 – 8.72 (m, 1H), 8.49 (s, 1H), 7.96 (d, *J* = 8.4 Hz, 1H), 7.92 (s, 1H), 7.76 (t, *J* = 7.2 Hz, 1H), 7.63 – 7.53 (m, 3H), 7.28 (d, *J* = 7.6 Hz, 1H), 7.22 (t, *J* = 7.6 Hz, 1H).	DMSO	95	Method G1	358.0 (M+1)	t = 1.644 min	Method B (NH_4HCO_3)

503					^{1}H-NMR (400 MHz, DMSO-d_6): δ 11.34 (s, 1H), 9.50 (s, 1H), 8.69 (d, *J* = 3.6 Hz, 1H), 8.65 (d, *J* = 7.6 Hz, 1H), 8.40 (d, *J* = 8.4 Hz, 1H), 8.15 (s, 1H), 8.10 (s, 1H), 8.00 – 7.97 (m, 1H), 7.91 – 7.84 (m, 2H), 7.69 – 7.66 (m, 1H), 7.55 – 7.52 (m, 1H), 7.16 (t, *J* = 9.2 Hz, 1H).	DMSO	95	Method G1	378.0 (M+1)	t = 1.780 min	Method B (NH_4HCO_3)
504				HCl	1H-NMR (300 MHz, DMSO): δ 10.48 (s, 1H), 9.57 (s, 1H), 9.13 (d, J = 7.6 Hz, 1H), 8.97 – 8.80 (m, 2H), 8.31 (s, 1H), 8.19 (s, 1H), 8.10 (d, J = 6.5 Hz, 1H), 7.97 (d, J = 9.1 Hz, 2H), 7.83 (d, J = 7.7 Hz, 1H), 7.66 (t, J = 7.9 Hz, 2H), 7.47 (d, J = 5.4 Hz, 1H), 4.02 (s, 3H).	DMSO	95	Method G1	396.1 (M+1)		Method C
505					^{1}H NMR (400 MHz, DMSO) δ 15.71 (s, 1H), 10.01 (s, 1H), 9.59 – 9.51 (m, 1H), 8.73 – 8.62 (m, 2H), 8.60 – 8.54 (m, 1H), 8.13 – 7.96 (m, 2H), 7.93 – 7.82 (m, 2H), 7.62 – 7.49 (m, 2H), 4.01 (s, 3H).	DMSO	>98	G1			
506					^{1}H NMR (400 MHz, DMSO) δ 10.77 (s, 1H), 9.75 (s, 1H), 9.55 – 9.46 (m, 1H), 8.73 – 8.60 (m, 2H), 7.96 (d, *J* = 2.7 Hz, 1H), 7.83 (d, *J* = 9.1 Hz, 1H), 7.63 (d, *J* = 2.1 Hz, 1H), 7.58 – 7.47 (m, 3H), 6.99 (d, *J* = 8.5 Hz, 1H), 4.64 (s, 2H), 3.97 (s, 3H).	DMSO	>98	G1 (0.1 N HCl added)			

331

507					^{1}H NMR (400 MHz, DMSO) δ 12.54 (s, 1H), 9.85 (s, 1H), 9.51 (s, 1H), 8.70 – 8.60 (m, 2H), 8.27 – 8.16 (m, 2H), 8.03 (d, *J* = 2.5 Hz, 1H), 7.83 (d, *J* = 9.1 Hz, 1H), 7.72 – 7.59 (m, 2H), 7.56 – 7.47 (m, 2H), 3.99 (s, 3H).	DMSO	>98	G1			
508					^{1}H NMR (400 MHz, DMSO) δ 9.87 (s, 1H), 9.50 – 9.47 (m, 1H), 8.66 – 8.61 (m, 2H), 8.21 (s, 1H), 8.16 (d, *J* = 1.6 Hz, 1H), 8.02 (d, *J* = 2.7 Hz, 1H), 7.83 (d, *J* = 9.1 Hz, 1H), 7.74 (dd, *J* = 8.7, 1.9 Hz, 1H), 7.67 (d, *J* = 8.6 Hz, 1H), 7.56 – 7.47 (m, 2H), 3.99 (s, 3H), 3.90 (s, 3H).	DMSO	>98	G1			
509					^{1}H NMR (400 MHz, DMSO) δ 9.90 (s, 1H), 9.47 (dd, *J* = 2.1, 0.8 Hz, 1H), 8.67 – 8.60 (m, 2H), 8.15 (d, *J* = 2.1 Hz, 1H), 7.97 (d, *J* = 2.7 Hz, 1H), 7.88 – 7.81 (m, 2H), 7.57 – 7.49 (m, 2H), 7.44 (d, *J* = 8.7 Hz, 1H), 3.98 (s, 3H), 3.47 (s, 3H).	DMSO	>98	G1 (0.1 N HCl added)			
510					^{1}H NMR (400 MHz, DMSO) δ 10.76 (s, 1H), 10.62 (s, 1H), 9.71 (s, 1H), 9.53 – 9.48 (m, 1H), 8.68 – 8.62 (m, 2H), 7.98 (d, *J* = 2.6 Hz, 1H), 7.81 (d, *J* = 9.1 Hz, 1H), 7.63 (d, *J* = 1.8 Hz, 1H), 7.55 – 7.49 (m, 2H), 7.37 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.01 (d, *J* = 8.3 Hz, 1H), 3.97 (s, 3H).	DMSO	>98	G1 (0.1 N HCl added)			

332

511					^{1}H NMR (400 MHz, DMSO) δ 9.96 (s, 1H), 9.49 (dd, *J* = 2.1, 0.8 Hz, 1H), 8.79 (s, 1H), 8.67 – 8.61 (m, 2H), 8.39 – 8.36 (m, 1H), 8.02 (d, *J* = 2.7 Hz, 1H), 7.90 – 7.84 (m, 3H), 7.56 (dd, *J* = 9.1, 2.7 Hz, 1H), 7.54 – 7.50 (m, 1H), 3.99 (s, 3H).	DMSO	>98	J2			
512					^{1}H NMR (400 MHz, DMSO) δ 9.87 (s, 1H), 9.48 (dd, *J* = 2.1, 0.8 Hz, 1H), 8.67 – 8.61 (m, 2H), 8.10 – 8.08 (m, 1H), 8.00 (d, *J* = 2.7 Hz, 1H), 7.84 (d, *J* = 9.1 Hz, 1H), 7.65 – 7.63 (m, 2H), 7.57 – 7.49 (m, 2H), 4.22 (s, 3H), 3.99 (s, 3H).	DMSO	>98	G1			
513					^{1}H NMR (400 MHz, DMSO) δ 9.92 (s, 1H), 9.49 (dd, *J* = 2.1, 0.8 Hz, 1H), 8.67 – 8.60 (m, 2H), 8.22 (d, *J* = 1.8 Hz, 1H), 8.00 (d, *J* = 2.7 Hz, 1H), 7.85 (d, *J* = 9.1 Hz, 1H), 7.70 – 7.64 (m, 1H), 7.60 (d, *J* = 8.5 Hz, 1H), 7.57 – 7.49 (m, 2H), 4.21 (s, 3H), 3.98 (s, 3H).	DMSO	>98	J2			
514				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.97 (s, 1H), 9.43 (d, *J* = 1.6 Hz, 1H), 8.98 – 8.91 (m, 1H), 8.89 (dd, *J* = 5.2, 1.3 Hz, 1H), 8.43 (s, 1H), 8.27 (s, 1H), 8.13 – 8.04 (m, 2H), 7.92 – 7.85 (m, 1H), 7.73 (d, *J* = 9.2 Hz, 1H), 7.70 – 7.63 (m, 2H), 4.21 (s, 3H), 4.02 (s, 3H).	DMSO	>98	G1			

333

515				HCl	^{1}H NMR (400 MHz, DMSO) δ 11.90 (s, 1H), 10.45 (s, 1H), 9.46 (d, *J* = 1.7 Hz, 1H), 8.97 – 8.89 (m, 1H), 8.85 (dd, *J* = 5.2, 1.5 Hz, 1H), 8.16 – 8.10 (m, 2H), 8.03 – 7.97 (m, 2H), 7.94 (d, *J* = 9.1 Hz, 1H), 7.90 – 7.82 (m, 1H), 7.63 (dd, *J* = 9.1, 2.6 Hz, 1H), 7.44 (d, *J* = 8.8 Hz, 1H), 6.58 (d, *J* = 9.4 Hz, 1H), 4.00 (s, 3H).	DMSO	>98	G1 (0.1 N HCl added)			
516					^{1}H NMR (400 MHz, DMSO) δ 9.90 (s, 1H), 9.53 – 9.50 (m, 1H), 8.68 – 8.63 (m, 2H), 8.27 (d, *J* = 2.0 Hz, 1H), 8.01 (d, *J* = 2.7 Hz, 1H), 7.96 (d, *J* = 8.6 Hz, 1H), 7.85 (d, *J* = 9.1 Hz, 1H), 7.81 (dd, *J* = 8.7, 2.1 Hz, 1H), 7.58 – 7.50 (m, 2H), 4.20 (s, 3H), 3.99 (s, 3H).	DMSO	>98	G1			
517				HCl	^{1}H NMR (300 MHz, DMSO) δ 11.35 (s, 1H), 9.58 (d, *J* = 1.6 Hz, 1H), 9.24 (d, *J* = 8.2 Hz, 1H), 9.05 – 8.97 (m, 1H), 9.05 – 8.95 (m, 1H), 8.21 (d, *J* = 2.4 Hz, 1H), 8.11 – 8.02 (m, 3H), 7.90 (d, *J* = 7.8 Hz, 1H), 7.58 (dd, *J* = 8.8, 2.0 Hz, 2H), 7.52 – 7.46 (m, 1H), 7.28 (s, 1H), 3.98 (d, *J* = 9.2 Hz, 3H).	DMSO	>98	G1			
518				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 11.32 (s, 1H), 9.60 (s, 1H), 9.23 (d, *J* = 8.0 Hz, 1H), 8.98 (d, *J* = 5.4 Hz, 1H), 8.26 (s, 1H), 8.06 (dd, *J* = 13.2, 7.3 Hz, 2H), 7.63 (d, *J* = 9.1 Hz, 1H), 7.50 – 7.36 (m, 4H), 7.32 (s, 1H), 7.06 – 6.90 (m, 1H), 3.99 (s, 3H), 3.86 (s, 3H).	DMSO	>98	G1			

334

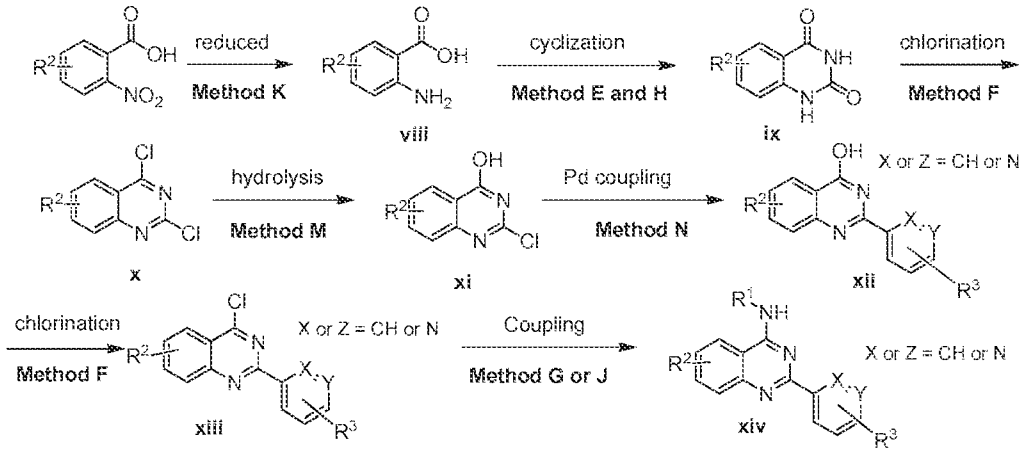
519				2HCl	1H NMR (300 MHz, DMSO) δ 13.17 (s, 1H), 11.46 (s, 1H), 9.19 (d, J = 1.7 Hz, 1H), 8.95 – 8.78 (m, 2H), 8.31 (d, J = 2.6 Hz, 1H), 8.18 (d, J = 9.2 Hz, 1H), 7.86 (dd, J = 7.9, 5.4 Hz, 1H), 7.77 – 7.54 (m, 3H), 7.44 (dd, J = 11.4, 3.9 Hz, 1H), 7.20 – 7.02 (m, 1H), 4.01 (s, 3H).	DMSO	>98	G1			
520				HCl	^{1}H NMR (300 MHz, DMSO) δ 11.10 (s, 1H), 9.59 (d, *J* = 1.8 Hz, 1H), 9.15 (d, *J* = 8.0 Hz, 1H), 8.93 (d, *J* = 3.9 Hz, 1H), 8.22 (d, *J* = 2.6 Hz, 1H), 7.99 (t, *J* = 7.4 Hz, 2H), 7.72 (dd, *J* = 8.4, 4.7 Hz, 2H), 7.63 – 7.50 (m, 2H), 7.35 (s, 1H), 7.27 – 7.18 (m, 1H), 3.99 (s, 3H).	DMSO	>98	G1			
521				HCl	^{1}H NMR (300 MHz, DMSO) δ 11.51 (s, 1H), 9.63 (d, *J* = 1.9 Hz, 1H), 9.18 (d, *J* = 8.1 Hz, 1H), 8.98 (dd, *J* = 5.2, 1.2 Hz, 1H), 8.31 (d, *J* = 2.5 Hz, 1H), 8.17 (d, *J* = 9.1 Hz, 1H), 8.01 (dd, *J* = 8.0, 5.3 Hz, 1H), 7.84 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.66 (dd, *J* = 9.1, 2.5 Hz, 1H), 7.48 – 7.35 (m, 2H), 7.21 (d, *J* = 8.2 Hz, 1H), 7.10 (t, *J* = 7.5 Hz, 1H), 3.99 (d, *J* = 6.3 Hz, 6H).	DMSO	>98	G1			
1758				3HCl	1H NMR (DMSO-d6) ppm 13.00-12.40 (br, 1H), 9.79 (d, J = 1.68 Hz, 1H), 9.30 (d, J = 8.20 Hz, 1H), 8.95 (dd, J = 5.32, 1.44 Hz, 1H), 8.71 (d, J = 4.24 Hz, 1H), 8.37 (brd, J = 2.56 Hz, 1H), 8.25-8.21 (m, 2H), 8.11-8.02 (m, 2H), 7.98 (d, J = 9.12 Hz, 1H), 7.66 (dd, J = 9.12, 2.68 Hz, 1H), 7.53-7.50 (m, 1H), 4.03 (s, 3H). The 1H of 3HCl was not observed.	DMSO	>98	G13			

335

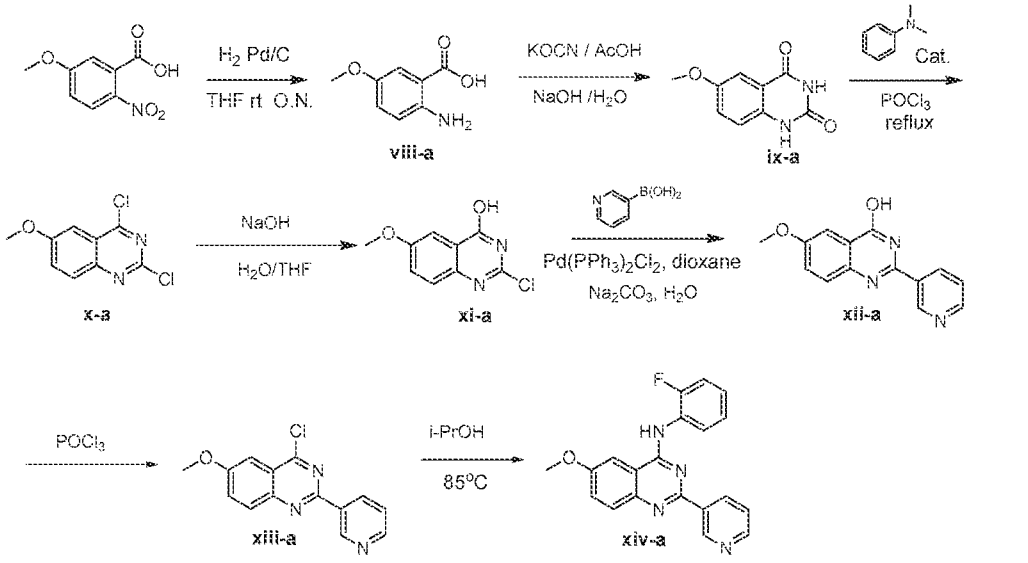
1759				3HCl	1H NMR (DMSO-d6) ppm 10.35 (br, 1H), 9.37 (d, J = 1.6 Hz, 1H), 8.96 (d, J = 7.28 Hz, 1H), 8.90 (d, J = 4.2 Hz, 1H), 8.04 (s, 1H), 7.98 (m, 1H), 7.95 (d, J = 9.16 Hz, 1H), 7.64 (dd, J = 9.16, 2.56 Hz, 1H), 6.18 (s, 1H), 3.98 (s, 3H), 3.66 (s, 3H), 2.24 (s, 3H). The 1H of 3HCl was not observed.	DMSO	>98	J2			

336

Scheme 6: General route for the synthesis of compounds with general formula xiv



Scheme 7: Representative synthesis of pyridine of formula xiv-a (see Scheme 6)



Method K: 2-Amino-5-methoxybenzoic acid (viii-a) 5-Methoxy-2-nitrobenzoic acid (30.0 g, 152.2 mmol) was hydrogenated over Pd/C (10%, 300 mg) in THF (250 mL) at room temperature under H_2 balloon. The mixture was stirred for 18 h. After the reaction was completed, the catalyst was removed by filtration over Celite and the filtrate was concentrated to afford 25.0 g of 2-amino-5-methoxybenzoic acid as a brown solid (98%). LCMS m/z = 168.1 (M+1), 150.1 (M-17) (Method B) (retention

time = 0.53 min) ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.31 (d, *J* = 2.8 Hz, 1H), 6.61 (dd, *J* = 8.8, 3.2 Hz, 1H), 6.44 (d, *J* = 8.8 Hz, 1H), 3.60 (s, 3H).

Method H: 6-Methoxyquinazoline-2,4(1*H*, 3H)-dione (ix-a) 2-Amino-5-methoxybenzoic acid (13.0 g, 77.8mmol, 1.0 eq.) was suspended in water (200 mL) and glacial acetic acid (5.2 mL) at 35 °C. A freshly prepared solution of potassium cyanate (8.21 g, 101.4 mmol, 1.3 eq.) in water (86 mL) was added dropwise to the stirred mixture. After 4 h, NaOH (104.0 g, 2600 mL, 33.4 eq.) was added in portions, keeping the reaction temperature below 40 °C. A clear solution was obtained momentarily before a precipitate formed. After cooling, the precipitate was filtered off and dissolved in hot water which was acidified to pH 5. The precipitate was collected and washed with water, dried by lyophilization to afford 9.63 g of 6-methoxyquinazoline-2, 4(1*H*, 3H)-dione as a white solid (65%). LCMS m/z = 193.1 (M+1) (Method B) (retention time = 1.22 min). ^{1}H-NMR (400 MHz, DMSO-d_6) : δ 11.26 (s, 1H), 11.01 (s, 1H), 7.31 – 7.25 (m, 2H), 7.10 (d, 1H, *J* = 8.8 Hz), 3.77 (s, 3H).

Method F1: 2,4-Dichloro-6-methoxyquinazoline (x-a) To a mixture of 6-methoxyquinazoline-2,4(1*H*, 3*H*)-dione (9.63 g, 50.2 mmol) in $POCl_3$ (150 mL) was added *N,N*-dimethylaniline (0.5 mL). The resulting mixture was stirred at 120°C for 2 h. After the reaction was completed, $POCl_3$ was removed *in vacuo*, and the residue was added to ice-water slowly. The pH was adjusted to ~ 7 by slowly adding $NaHCO_3$ (sat.) at 0°C, then a precipitate formed. The solid was collected and dried *in vacuo* to give 11.2 g of 2,4-dichloro-6-methoxyquinazoline in a 98% yield as a brown solid. LCMS m/z = 229.1, 231.0 (M+1) (Method B) (retention time = 1.87 min). ^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.89 (d, *J* = 9.2 Hz, 1H), 7.71 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.38 (d, *J* = 1.6 Hz, 1H), 3.91 (s, 3H).

Method M: 2-Chloro-6-methoxyquinazolin-4-ol (xi-a) A mixture of 2,4-dichloro-6-methoxyquinazoline (4.20 g, 18.5 mmol, 1.0 eq.) in THF (60 mL) and H_2O (60 mL) was treated with NaOH (4.00 g, 100 mmol, 5.4 eq.). The resulting mixture was stirred

at 40°C for 2 h. The reaction color turned to dark green and then a precipitate formed. After the reaction was completed, the mixture was cooled to room temperature. The precipitate was filtered off and the filtrate was concentrated down to 60 mL. The pH was then adjusted to 6 by adding 2N HCl in water. The precipitate which formed was collected and dried *in vacuo* to give 4.00 g of 2-chloro-6-methoxyquinazolin-4-ol as a grey solid (98%). LCMS m/z = 211.1, 213.0 (M+1) (Method B) (retention time = 1.11 min).

Method N: 6-Methoxy-2-(pyridin-3-yl) quinazolin-4-ol (xii-a) To a mixture of 2-chloro-6-methoxyquinazolin-4-ol (1.20 g, 5.7 mmol, 1.0 eq.), pyridin-3-ylboronic acid (1.27 g, 8.6 mmol, 1.5 eq.), K_2CO_3 (2.37 g, 17.1 mmol, 3.0 eq.) in dioxane (100 mL) and H_2O (10 mL) was added $Pd(PPh_3)_2Cl_2$ (230 mg, 0.29 mmol, 0.05 eq.) under N_2 atmosphere. The resulting mixture was stirred at 105 °C under N_2 atmosphere overnight. After reaction was completed, the mixture was cooled to room temperature, and the resultant precipitate was removed by filtration. The filtrate was concentrated *in vacuo* and the residue was partitioned between H_2O (30 mL) and ethyl acetate (100 mL x 3). The combined organic layers were washed with brine, dried over $MgSO_4$. After filtration and evaporation, the crude product was obtained, which was combined with the filter cake and dried *in vacuo* to give 1.35 g of 6-methoxy-2-(pyridin-3-yl) quinazolin-4-ol as a gray solid. LCMS m/z = 254.1 (M+1) (Method B) (retention time = 1.39 min). The crude product was used for the next step without further purification.

Method F1: 4-Chloro-6-methoxy-2-(pyridin-3-yl)quinazoline (xiii-a) To a mixture of 6-methoxy-2-(pyridin-3-yl) quinazolin-4-ol (600 mg, 2.37 mmol) in $POCl_3$ (5 mL) was added *N,N*-dimethylaniline (1 drop). The resulting mixture was stirred at 120°C for 30 min. After the reaction was completed, $POCl_3$ was removed *in vacuo*, and the residue was added to ice-water slowly. The pH was adjusted to ~ 7 by slowly adding $NaHCO_3$ (sat.) at 0°C and then a precipitate formed. The solid was collected and was purified by chromatography on silica gel eluted with petroleum ether/ ethyl acetate (v / v = 4:1 to 1:1) to give 260 mg of 4-chloro-6-methoxy-2-(pyridin-3-yl)quinazoline as

a pale yellow solid (40.4%). LCMS m/z = 272.1, 274.0 (M +1) (Method B) (retention time = 1.90 min).

Method G1: N-(2-Fluorophenyl)-6-methoxy-2-(pyridin-3-yl)quinazolin-4-amine (xiv-a) A mixture of 4-chloro-6-methoxy-2-(pyridin-3-yl)quinazoline (80 mg, 0.293 mmol, 1.0 eq.) and 2-fluoroaniline (65 mg, 0.58 mmol, 2 eq.) in *i*-PrOH (5 mL) was stirred at 85 °C for 18 h. After the reaction was completed, the mixture was filtered, and the filter cake was washed with H_2O (10 mL) and diethyl ether (10 mL). After drying, the crude product was purified by PREP-HPLC (Condition C: Gradient: B = 5%-50%, Target Peak: at 7.2 min) to give 16.5 mg of N-(2-fluorophenyl)-6-methoxy-2-(pyridin-3-yl)quinazolin-4-amine as a yellow solid, yield 16.4%. LCMS m/z = 347.0 (M +1) (Method A) (retention time = 1.31 min). ^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.08 (s, 1H), 9.33 (s, 1H), 8.72 (d, *J* = 4.4 Hz, 1H), 8.66 (d, *J* = 8.0 Hz, 1H), 8.80 (d, *J* = 1.2 Hz, 1H), 7.88 (d, *J* = 9.2 Hz, 1H), 7.70 – 7.65 (m, 2H), 7.58 (dd, *J* = 8.8, 1.2 Hz, 1H), 7.44 – 7.35 (m, 3H), 3.97 (s, 3H).

The compounds in the following table were prepared in a manner analogous to that described in **Scheme 6** substituting with appropriate nitro benzoic acid, boronic acid and aniline

Table 2:

Number	Product	Salt type	Molecular Mass	^{1}H-NMR	^{1}H-NMR Solvent	LCMS	LCMS Protocol	Purity percent	Method for Coupling
522			455.34	1H-NMR (400 MHz, DMSO-d6): δ 9.76 (s, 1H), 9.52 – 9.51 (m, 1H), 8.63 – 8.66 (m, 2H), 8.32 (d, J = 2.4 Hz, 1H), 7.94 – 7.91 (m, 2H), 7.72 (d, J = 8.8 Hz, 1H), 7.54 (q, J = 3.2 Hz, 1H), 7.32 (s, 1H), 4.87 – 4.90 (m, 1H), 3.96 (s, 3H), 1.38 (d, J = 6.0 Hz, 6H).	DMSO	454.9, 457.0 (M+1), 228.8 (M/2 +1)	Method A (TFA)	95	Method N, G1
523			438.88	1H-NMR (400 MHz, DMSO-d6): δ 9.68 (s, 1H), 9.49 (d, J = 2.0 Hz, 1H), 8.60 – 8.66 (m, 2H), 8.18 (dd, J = 6.4, 2.4 Hz, 1H), 7.84 – 7.88 (m, 2H), 7.50 – 7.54 (m, 2H), 7.31 (s, 1H), 4.85 – 4.88 (m, 1H), 3.96 (s, 3H), 1.38 (d, J = 6.4 Hz, 6H).	DMSO	439.1, 441.1 (M+1), 220.1, 220.8 (M/2 +1)	Method A (TFA)	95	Method N, G1
524			422.43	1H-NMR (400 MHz, DMSO-d6): δ 9.76 (s, 1H), 9.48 (s, 1H), 8.60 – 8.65 (m, 2H), 8.04 – 8.10 (m, 1H), 7.92 (s, 1H), 7.49 – 7.66 (m, 3H), 7.30 (s, 1H), 4.86 – 4.92 (m, 1H), 3.96 (s, 3H), 1.37 (d, J = 6.0 Hz, 6H)	DMSO	423.2 (M+1), 212.2 (M/2 +1)	Method A (TFA)	95	Method N, G1

341

525		HCl	429.47	1H-NMR (400 MHz, DMSO-d6): δ 12.96 (s, 1H), 9.60 (d, J = 8.0 Hz, 1H), 9.14 (d, J = 8.0 Hz, 1H), 8.68 – 8.74 (m, 2H), 8.46 (s, 1H), 7.95 – 7.96 (m, 2H), 7.74 – 7.70 (m, 1H), 7.59 – 7.54 (m, 2H), 7.36 (s, 1H), 7.19 – 7.15 (m, 1H), 4.76 – 4.82 (m, 1H), 3.99 (s, 3H), 1.44 (d, J = 6.0 Hz, 6H).	DMSO	430.2 (M+1) 215.7 (M/2 +1)	Method A (TFA)	95	Method N, G1
526			452.45	1H-NMR (400 MHz, DMSO-d6): δ 9.70 (s, 1H), 9.52 – 9.53 (m, 1H), 8.64 – 8.67 (m, 2H), 7.89 – 7.94 (m, 2H), 7.73 – 7.74 (m, 1H), 7.48 – 7.53 (m, 3H), 7.32 (t, J = 83.6 Hz, 1H), 6.96 – 6.99 (m, 1H), 4.89 – 4.92 (m, 1H), 3.98 (s, 3H), 1.38 (d, J = 6.0 Hz, 6H).	DMSO	453.1 (M+1)	Method B (NH4HCO3)	95	Method N, G1
527			455.34	1H-NMR (400 MHz, DMSO-d6): δ 9.53 (s, 1H), 9.52 (d, J = 1.6 Hz, 1H), 8.64 – 8.68 (m, 2H), 8.12 – 8.13 (m, 2H), 7.90 (s, 1H), 7.54 – 7.58 (m, 1H), 7.34 – 7.36 (m, 2H), 4.86 – 4.92 (m, 1H), 3.96 (s, 3H), 1.40 (d, J = 6.0 Hz, 6H).	DMSO	455.0, 457.0 (M+1)	Method B (NH4HCO3)	95	Method N, G1

342

528			455.34	1H-NMR (400 MHz, DMSO-d6): δ 9.76 (s, 1H), 9.52 (d, J = 1.2 Hz, 1H), 8.64 – 8.67 (m, 2H), 8.32 (d, J = 2.8 Hz, 1H), 7.94 (dd, J = 8.8, 2.4 Hz, 1H), 7.86 (s, 1H), 7.72 (d, J = 8.8 Hz, 1H), 7.53 – 7.56 (m, 1H), 7.32 (s, 1H), 4.14 (t, J = 6.4 Hz, 2H), 3.99 (s, 3H), 1.85 – 1.92 (m, 2H), 1.06 (t, J = 7.2 Hz, 3H).	DMSO	455.1, 457.1 (M+1) 229.1 (M/2 +1)	Method A (TFA)	95	Method N, G1
529			438.88	1H-NMR (400 MHz, DMSO-d6): δ 9.72 (s, 1H), 9.50 (d, J = 1.6 Hz, 1H), 8.62 – 8.66 (m, 2H), 8.20 (dd, J = 6.4, 2.4 Hz, 1H), 7.85 – 7.89 (m, 2H), 7.50 – 7.55 (m, 2H), 7.31 (s, 1H), 4.13 (t, J = 6.4 Hz, 2H), 3.98 (s, 3H), 1.82 – 1.90 (m, 2H), 1.06 (t, J = 7.6 Hz, 3H).	DMSO	439.1, 441.1 (M+1) 220.1, 220.8 (M/2+1)	Method A (TFA)	95	Method N, G1
530			422.43	1H-NMR (400 MHz, DMSO-d6): δ 9.74 – 9.76 (m, 1H), 9.52 (d, J = 1.6 Hz, 1H), 8.64 – 8.69 (m, 2H), 8.08 – 8.14 (m, 1H), 7.90 (s, 1H), 7.68 – 7.70 (m, 1H), 7.52 – 7.60 (m, 2H), 7.34 (s, 1H), 4.16 (t, J = 6.4 Hz, 2H), 4.01 (s, 3H), 1.85 – 1.94 (m, 2H), 1.09 (t, J = 7.2 Hz, 3H).	DMSO	423.0 (M+1) 445.0 (M+23) 212.1 (M/2+1)	Method A (TFA)	95	Method N, G1
531		HCl	429.47	1H-NMR (400 MHz, DMSO-d6): δ 12.86 (s, 1H), 9.59 (d, J = 1.6 Hz, 1H), 9.05 (d, J = 8.4 Hz, 1H), 8.85 (d, J = 8.0 Hz, 1H), 8.76 – 8.78 (m, 1H), 8.44 (s, 1H), 7.96 (dd, J = 8.0, 1.6 Hz, 2H), 7.70 – 7.73 (m, 2H), 7.53 (s, 1H), 7.37 (s, 1H), 6.96 – 7.22 (m, 1H), 4.16 (t, J = 6.4 Hz, 2H), 4.01 (s, 3H), 1.86 – 1.90 (m, 2H), 1.07 (t, J = 7.2 Hz, 3H).	DMSO	430.1 (M+1)	Method B (NH4HCO3)	95	Method N, G1

343

532			452 45	1H-NMR (400 MHz, DMSO-d6): δ 9.67 (s, 1H), 9 50 (d, J = 4.0 Hz, 1H), 8.62 -- 8.65 (m, 2H), 7.89 -- 7.92 (m, 3H), 7.44 -- 7.54 (m, 1H), 7.29 -- 7.31 (m, 3H), 7.26 (t, J = 74.0 Hz, 1H), 4.14 (t, J = 6.8 Hz, 2H), 3.98 (s, 3H), 1.84 -- 1.90 (m, 2H), 1.06 (t, J = 7.2 Hz, 3H).	DMSO	453.1 (M+1) 227.2 (M/2+1)	Method A (TFA)	95	Method N, G1
533		HCl	454 88	1H-NMR (400 MHz, DMSO-d6): δ 9.73 (s, 1H), 9 50 (d, J = 2.4 Hz, 1H), 8.62 -- 8.67 (m, 2H), 8.20 (dd, J = 7.2 Hz, 2.8 Hz, 1H), 7.85 -- 7.89 (m, 2H), 7.51 -- 7.57 (m, 2H), 7.33 (s, 1H), 4.31 (t, J = 4.0 Hz, 2H), 3.99 (s, 3H) 3.80 (t, J = 4 8 Hz, 2H), 3.37 (s, 3H).	DMSO	455.1, 457.1 (M+1)	Method B (NH4HCO3)	95	Method N, G1
534			445.47	1H-NMR (400 MHz, CD3OD): δ 9.34 (s, 1H), 8.92 (d, J = 6.0 Hz, 1H), 8.73 (m, 2H), 7.84 (s, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.54 (t, J = 8.0 Hz, 1H), 7.32 (s, 1H), 7.15 (s, 2H), 4.21 (s, 2H), 3.92 (s, 3H), 3.78 (t, J = 4.4 Hz, 2H), 3.40 (s, 3H).	CD3OD	446.2, 447.2 (M+1)	Method B (NH4HCO3)	95	Method N, G1

344

535		HCl	468.45	1H-NMR (400 MHz, DMSO-d6): δ 9.72 (s, 1H), 9.53 (s, 1H), 8.66 (d, J = 5.6 Hz, 2H), 7.91 (d, J = 6.4 Hz, 2H), 7.75 (d, J = 7.2 Hz, 1H), 7.51 (dd, J = 7.6 Hz, 2H), 7.34 (s, 1H), 7.30 (t, J = 74.0 Hz, 1H), 6.97 (dd, J = 8.0, 2.0 Hz, 1H), 4.32 (t, J = 4.4 Hz, 2H), 3.99 (s, 3H), 3.80 (t, J = 4.4 Hz, 2H), 3.37 (s, 3H)	DMSO	469.1 (M+1)	Method B (NH4HCO3)	95	Method N, G1
536			468.91	1H-NMR (400 MHz, DMSO-d6): δ 10.42 (s, 1H), 9.47 (s, 1H), 8.96 (d, J = 6.4 Hz, 1H), 8.90 (d, J = 5.2 Hz, 1H), 8.11 (dd, J = 6.8 Hz, 2.4 Hz, 1H), 8.05 (s, 2H), 7.85 – 7.94 (m, 2H), 7.55 (t, J = 9.2 Hz, 1H), 7.47 (s, 1H) 4.26 (t, J = 6.4 Hz, 2H), 4.01 (s, 3H), 3.55 (t, J = 6.0 Hz, 2H), 3.29 (s, 3H), 2.06 – 2.13 (m, 2H).	DMSO	469.0, 471.0 (M+1) 234.9, 235.6 (M/2+1)	Method A (TFA)	95	Method N, G1
537			397 26	1H-NMR (400 MHz, DMSO-d6): δ 10.08 (s, 1H), 9 54 (s, 1H), 8.76 (s, 2H), 8.49 (d, J = 7.0 Hz, 1H), 8.36 (s, 1H), 7.95 (d, J = 7 5 Hz, 1H), 7 66 – 7.23 (m, 2H), 7.33 (s, 2H), 3.98 (s, 3H).	DMSO	397.1, 399.0 (M+1)	Method B (NH4HCO3)	95	Method N, G1

345

538			397.26	1H-NMR (400 MHz, DMSO-d6): δ 10.00 (s, 1H), 8.54 (d, J = 1.3 Hz, 1H), 8.71 – 8.56 (m, 2H), 8.47 (d, J = 9.2 Hz, 1H), 8.17 (s, 1H), 8.16 (s, 1H), 7.59 – 7.56 (m, 1H), 7.35 – 7.30 (m, 3H), 3.98 (s, 3H).	DMSO	397.0, 399.0 (M+1)	Method B (NH4HCO3)	95	Method N, G1
539			364.35	1H-NMR (400 MHz, DMSO-d6): δ 9.94 (s, 1H), 9.53 (d, J = 1.6 Hz, 1H), 8.70 – 8.65 (m, 2H), 8.47 (d, J = 8.4 Hz, 1H), 8.12 (ddd, J = 13.2, 7.6, 2.8 Hz, 1H), 7.72 – 7.70 (m, 1H), 7.58 – 7.49 (m, 2H), 7.32 – 7.27 (m, 2H), 3.97 (s, 3H)	DMSO	365.2 (M+1)	Method B (NH4HCO3)	95	Method N, G1
540			353.38	1H-NMR (400 MHz, DMSO-d6): δ 10.06 (s, 1H), 9.53 (d, J = 1.6 Hz, 1H), 8.71 – 8.66 (m, 2H), 8.50 – 8.43 (m, 2H), 8.26 – 8.24 (m, 1H), 7.70 – 7.54 (m, 3H), 7.34 – 7.30 (m, 2H), 3.98 (s, 3H)	DMSO	354.2 (M+1)	Method B (NH4HCO3)	95	Method N, G1

346

541			394.37	1H-NMR (400 MHz, DMSO-d6): δ 9.93 (s, 1H), 9.54 (s, 1H), 8.68 (d, J = 5.2 Hz, 2H), 8.51 (d, J = 9.2 Hz, 1H), 7.96 (s, 1H), 7.79 (d, J = 7.6 Hz, 1H), 7.55 – 7.10 (m, 5H), 6.96 (dd, J = 8.0, 2.0 Hz, 1H), 3.96 (s, 3H).	DMSO	395.1 (M+1)	Method B (NH4HCO3)	95	Method N, G1
542			371.39	1H-NMR (400 MHz, DMSO-d6): δ 12.97 (s, 1H), 9.60 (s, 1H), 9.10 (d, J = 8.4 Hz, 1H), 8.75 – 8.71 (m, 2H), 8.48 (s, 1H), 8.07 (d, J = 9.6 Hz, 1H), 7.95 – 7.90 (m, 2H), 7.74 – 7.70 (m, 1H), 7.58 (dd, J = 8.0, 4.8 Hz, 1H), 7.35 – 7.33 (m, 2H), 7.19 (t, J = 7.2 Hz, 1H), 3.97 (s, 3H).	DMSO	372.1 (M+1)	Method B (NH4HCO3)	95	Method N, G1
543			431.7	1H-NMR (400 MHz, DMSO-d6): δ 10.03 (s, 1H), 9.49 – 9.48 (m, 1H), 8.69 – 8.67 (m, 1H), 8.63 – 8.59 9m, 1H), 8.31 (d, J = 2.4 Hz, 1H), 8.04 (s, 1H), 8.00 (s, 1H), 7.93 – 7.90 (m, 1H), 7.74 (d, J = 8.8 Hz, 1H), 7.56 – 7.53 (m, 1H), 4.07 (s, 3H).	DMSO	430.9, 432.9, 434.9 (M+1)	Method B (NH4HCO3)	95	Method N, G1

347

544			431.7	1H-NMR (400 MHz, DMSO-d6): δ 9.94 (s, 1H), 9.46 (d, J = 3.2 Hz, 1H), 8.68 (dd, J = 4.8, 2.0 Hz, 1H), 8.60 – 8.57 (m, 1H), 8.09 (s, 1H), 8.08 (s, 1H), 7.97 (s, 2H), 7.54 (dd, J = 8.8, 4.8 Hz, 1H), 7.36 (t, J = 2.0 Hz, 1H), 4.05 (s, 3H).	DMSO	430.9, 432.9, 434.9 (M+1)	Method B (NH4HCO3)	95	Method N, G1
545			415.25	1H-NMR (400 MHz, DMSO-d6): δ 10.02 (s, 1H), 9.47 (s, 1H), 8.70 – 8.62 (m, 2H), 8.19 – 8.17 (m, 1H), 8.04 (s, 1H), 8.00 (s, 1H), 7.84 – 7.88 (m, 1H), 7.59 – 7.53 (m, 2H), 4.07 (s, 3H).	DMSO	415.1, 417.0, 419.0 (M+1)	Method B (NH4HCO3)	95	Method N, G1
546			398.79	1H-NMR (400 MHz, DMSO-d6): δ 10.01 (s, 1H), 9.47 (d, J = 1.6 Hz, 1H), 8.69 – 8.67 (m, 1H), 8.62 – 8.59 (m, 1H), 8.08 – 8.04 (m, 2H), 8.00 (s, 1H), 7.65 – 7.53 (m, 3H), 4.07 (s, 3H).	DMSO	399.1, 401.1 (M+1)	Method B (NH4HCO3)	95	Method N, G1

547			428.82	1H-NMR (400 MHz, DMSO-d6): δ 10.32 (s, 1H), 9.45 (d, J = 1.2 Hz, 1H), 8.89 (d, J = 8.0 Hz, 1H), 8.83 (d, J = 4.0 Hz, 1H), 8.21 (s, 1H), 8.00 (s, 1H), 7.85 – 7.78 (m, 3H), 7.55 – 7.51 (m, 1H), 7.31 (t, J = 72.8 Hz, 1H), 7.05 – 7.03 (m, 1H), 4.07 (s, 3H).	DMSO	429.1, 431.1 (M+1)	Method B (NH4HCO3)	95	Method N, G1
548			387.82	1H-NMR (400 MHz, DMSO-d6): δ 10.62 (s, 1H), 9.38 (s, 1H), 8.97 – 8.90 (m, 2H), 8.32 – 8.26 (m, 3H), 7.97 – 7.94 (m, 2H), 7.69 – 7.65 (m, 2H), 4.08 (s, 3H).	DMSO	387.9, 390.0 (M+1)	Method B (NH4HCO3)	95	Method N, G1
549			405.84	1H-NMR (400 MHz, DMSO-d6): δ 12.98 (s, 1H), 9.36 (s, 1H), 8.94 – 8.77 (m, 3H), 8.48 (s, 1H), 7.98 – 7.83 (m, 4H), 7.59 – 7.14 (m, 2H), 7.17 (s, 1H), 3.96 (s, 3H).	DMSO	405.9, 408.0 (M+1)	Method B (NH4HCO3)	95	Method N, G1
550			436.12	1H-NMR (400 MHz, DMSO-d6): δ 10.24 (s, 1H), 9.39 (s, 1H), 8.87 (s, 1H), 8.81 (d, J = 4.4 Hz, 1H), 8.73 (d, J = 8.0 Hz, 1H), 8.24 (s, 1H), 8.01 (s, 1H), 7.88 (d, J = 8.8 Hz, 1H), 7.76 – 7.73 (m, 1H), 7.66 (d, J = 8.8 Hz, 1H).	DMSO	434.9, 436.9, 438.8 (M+1)	Method B (NH4HCO3)	95	Method N, G1

349

551			410.26	1H-NMR (400 MHz, DMSO-d6): δ 13.15 (s, 1H), 9.46 (s, 1H), 8.87 (d, J = 8.4 Hz, 1H), 8.74 (d, J = 3.6 Hz, 1H), 8.68 (d, J = 7.2 Hz, 1H), 8.49 (s, 1H), 8.23 (s, 1H), 8.02 (s, 2H), 7.94 (d, J = 8.0 Hz, 1H), 7.69 – 7.61 (m, 2H), 7.23 – 7.20 (m, 1H).	DMSO	410.0, 412.0, 413.9 (M+1) 432.0 (M+22)	Method A (TFA)	95	Method N, G1
552			433.24	1H-NMR (400 MHz, DMSO-d6): δ 10.30 (s, 1H), 9.53 (s, 1H), 9.02 (s, 1H), 8.83 – 8.80 (m, 2H), 8.20 (s, 1H), 7.91 (s, 1H), 7.81 – 7.79 (m, 1H), 7.74 – 7.71 (m, 1H), 7.56 – 7.52 (m, 1H), 7.30 (t, J = 73.6 Hz, 1H), 7.05 (d, J = 8.8 Hz, 1H).	DMSO	432.9, 434.9 (M+1)	Method B (NH4HCO3)	95	Method N, G1
553			419.67	1H-NMR (400 MHz, DMSO-d6): δ 10.43 (s, 1H), 9.40 (s, 1H), 8.97 (s, 1H), 8.89 – 8.85 (m, 2H), 8.15 – 8.14 (m, 1H), 8.05 (s, 1H), 7.89 – 7.87 (m, 2H), 7.51 – 7.47 (m, 1H).	DMSO	419.0, 421.0, 423.0 (M+1)	Method B (NH4HCO3)	95	Method N, G1

350

554			403 21	1H-NMR (400 MHz, DMSO-d6): δ 10.39 (s, 1H), 9.40 (s, 1H), 8.96 (s, 1H), 8.84 – 8.89 (m, 2H), 8.04 – 8.00 (m, 2H), 7.88 (s, 1H), 7.69 – 7.67 (m, 1H), 7.54 – 7.47 (m, 1H).	DMSO	402.9, 404.9 (M+1)	Method B (NH4HCO3)	95	Method N, G1
555			436 12	1H-NMR (400 MHz, DMSO-d6): δ 10.26 (s, 1H), 8.28 (s, 1H), 8.88 (d, J = 4 8 Hz, 1H), 8.85 (s, 1H), 8.76 (d, J = 8 0 Hz, 1H), 7.97 (s, 1H), 7.96 (s, 1H), 7.90 – 7.86 (m, 2H), 7.29 (s, 1H).	DMSO	434.9, 436.9, 438.9 (M+1)	Method A (TFA)	95	Method N, G1

351

556			441.31	1H-NMR (400 MHz, DMSO-d6): δ 9.74 (s, 1H), 9.50 (s, 1H), 8.66 – 8.64 (m, 2H), 8.31 (s, 1H), 7.90 (d, J = 8.8 Hz, 1H), 7.84 (s, 1H), 7.68 (d, J = 8.8 Hz, 1H), 7.52 (dd, J = 7.4, 5.0 Hz, 1H), 7.29 (s, 1H), 4.22 (q, J = 6.8 Hz, 2H), 3.97 (s, 3H), 1.45 (t, J = 6.8 Hz, 3H).	DMSO	441.0, 443.0 (M+1)	Method B (NH4HCO3)	95	Method N, G1
557			424 86	1H-NMR (400 MHz, DMSO-d6) δ 9.93 (s, 1H),9.48 (s, 1H),8.74 – 8.73 (m, 2H), 8.18 – 8.16 (m, 1H), 7.90 – 7.85 (m, 2H), 7.67 – 7.65 (m, 1H), 7.53 (t, J = 9 Hz, 1H), 7.33 (s, 1H), 4.24 (q, J = 7.2 Hz, 2H), 3.98 (s, 3H), 1.46 (t, J = 7.2 Hz, 3H).	DMSO	425.0, 427.0 (M+1)	Method B (NH4HCO3)	95	Method N, G1
558			408.4	1H-NMR (400 MHz, DMSO-d6): δ 9.68 (s, 1H), 9.49 (s, 1H), 8.66 – 8.61 (m, 2H), 8.10 – 8.04 (m, 1H), 7.84 (s, 1H), 7.66 – 7.64 (m, 1H), 7.56 – 7.49 (m, 2H), 7.30 (s, 1H), 4.23 (q, J = 6.8 Hz, 2H), 3.98 (s, 3H), 1.46 (t, J= 6.8 Hz, 3H).	DMSO	409.0 (M+1)	Method B (NH4HCO3)	95	Method N, G1
559			397.43	1H-NMR (400 MHz, DMSO-d6): δ 10.27 (s, 1H), 9.43 (s, 1H), 8.82 – 8.78 (m, 2H), 8.32 (s, 1H), 8.23 (d, J = 7.6 Hz, 1H), 7.98 (s, 1H), 7.77 – 7.73 (m, 1H), 7.68 – 7.60 (m, 2H), 7.35 (s, 1H), 4.23 (q, J = 6.8 Hz, 2H), 3.96 (s, 3H), 1.44 (t, J = 6.8 Hz, 3H).	DMSO	398.1 (M+1)	Method B (NH4HCO3)	95	Method N, G1

352

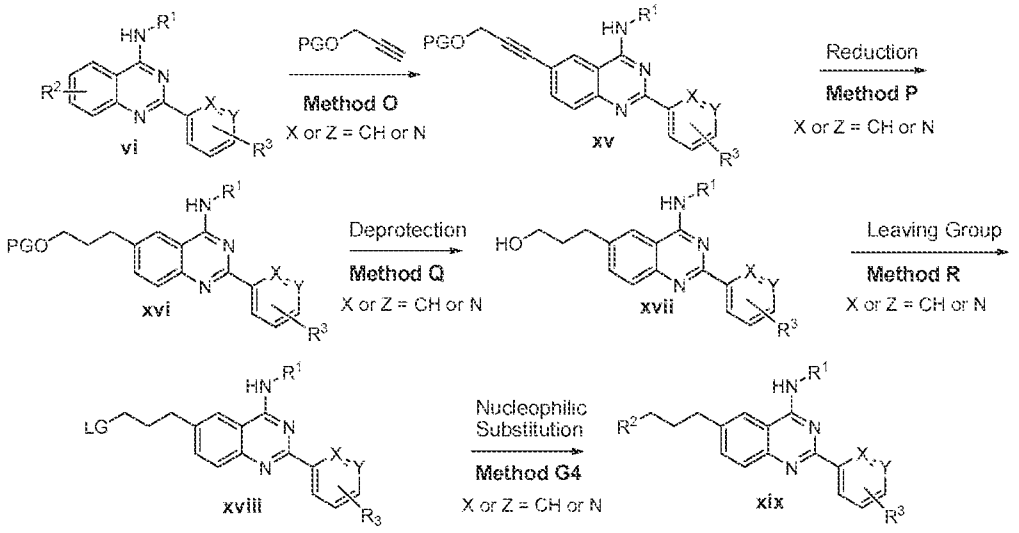
560			410 83	1H-NMR (400 MHz, DMSO-d6): δ 9.89 (s, 1H), 9.48 (s, 1H), 8.74 (d, J = 6.0 Hz, 2H), 8.16 (dd, J = 6.8, 2.4 Hz, 1H), 7.85 – 7.88 (m, 2H), 7.67 (t, J = 6.4 Hz, 1H), 7.53 (t, J = 8.7 Hz, 1H), 7.32 (s, 1H), 3.98 (s, 6H).	DMSO	411.1, 413.1 (M+1)	Method A (TFA)	95	Method N, G1
561			394 37	1H-NMR (400 MHz, DMSO-d6): δ 9.92 (s, 1H), 9.49 (s, 1H), 8.77 (d, J = 6.4 Hz, 2H), 8.02 – 8.08 (m, 1H), 7.90 (s, 1H), 7.70 – 7.74 (m, 1H), 7.64 – 7.66 (m, 1H), 7.52 – 7.59 (m, 1H), 7.33 (s, 1H), 3.99 (s, 3H), 3.98 (s, 3H).	DMSO	395.0 (M+1), 198.1 (M/2+1)	Method A (TFA)	95	Method N, G1
562			383.4	1H-NMR (400 MHz, DMSO-d6): δ 9.87 (s, 1H), 9.50 (d, J = 1.6 Hz, 1H), 8.63 – 8.68 (m, 2H), 8.38 (s, 1H), 8.23 (d, J = 8.4 Hz, 1H), 7.89 (s, 1H), 7.69 (t, J = 7.8 Hz, 1H), 7.61 (d, J = 7.6 Hz, 1H), 7.52 – 7.56 (m, 1H), 7.33 (s, 1H), 4.00 (s, 3H), 3.98 (s, 3H).	DMSO	384 2 (M+1)	Method B (NH4HCO3)	95	Method N, G1
563			427.28	1H-NMR (400 MHz, DMSO-d6): δ 9.70 (s, 1H), 9.50 (d, J = 1.6 Hz, 1H), 8.66 (d, J = 4.8 Hz, 1H), 8.62 (d, J = 8.0 Hz, 1H), 8.11 (d, J = 1.2 Hz, 2H), 7.79 (s, 1H), 7.53 (dd, J = 7.6, 4.8 Hz, 1H), 7.31 (s, 1H), 7.28 (s, 1H), 3.97 (s, 6H).	DMSO	427.1, 429.1, 431.0 (M+1)	Method B (NH4HCO3)	95	Method N, G1

353

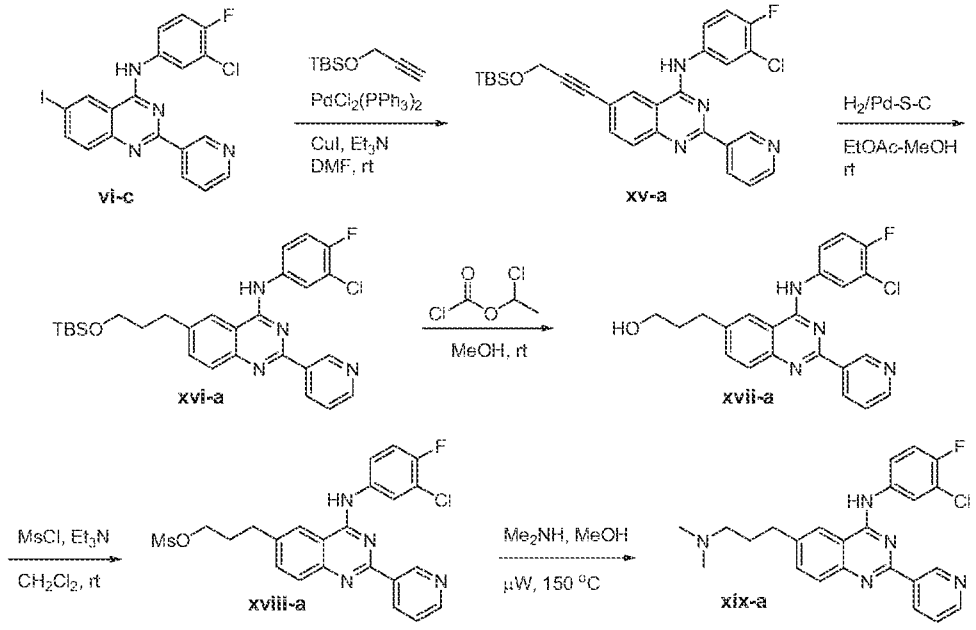
564		2 HCl	389.3824	1H-NMR (400 MHz, DMSO-d6): δ 13.08 (s, 1H), 9.40 (s, 1H), 8.86 (d, J = 8.1 Hz, 1H), 8.78 (s, 1H), 8.53 (d, J = 10.0 Hz, 1H), 8.46 (s, 1H), 8.03 (d, J = 8.7 Hz, 1H), 8.00 – 7.88 (m, 2H), 7.73 (t, J = 7.8 Hz, 1H), 7.66 (d, J = 10.3 Hz, 2H), 7.28 (t, J = 7.6 Hz, 1H), 3.99 (s, 3H).	DMSO	390.0 (M+1)	Method B (NH4CO3)	95	Method N, G1
565		2 HCl	401.4180	1H-NMR (400 MHz, CD3OD): δ 9.20 (s, 1H), 8.85 (s, 1H), 8.78 (s, 1H), 8.72 (d, J = 6.2 Hz, 1H), 8.02 (d, J = 9.1 Hz, 1H), 7.95 (d, J = 7.7 Hz, 1H), 7.77 – 7.67 (m, 3H), 7.39 (t, J = 7.6 Hz, 1H), 4.16 (s, 3H), 4.08 (s, 3H).	MeOD	402.1 (M+1)	Method B (NH4CO3)	95	Method N, G1

354

Scheme 8: General route for the synthesis of compounds with general formula xix



Scheme 9: Representative synthesis of compounds of formula xix (see Scheme 8)



Method O1: CuI/$Pd(PPh_3)_2Cl_2$/Et_3N/DMF/rt

O2: Propargyl bromide/CuI/$Pd(PPh_3)_2Cl_2$/Nucleophile/DMF/rt

O3: $Pd(OAc)_2$/ PPh_3/ TBAB/ piperdine/ THF-H_2O/ rt

Method O1: 6-(3-(tert-butyldimethylsilyloxy)prop-1-ynyl)-N-(3-chloro-4-fluorophenyl)-2-(pyridin-3-yl)quinazolin-4-amine (xv-a) A suspension of N-(3-chloro-4-fluorophenyl)-6-iodo-2-(pyridin-3-yl)quinazolin-4-amine **(synthesized as described in Scheme 1 and 4, substituting 5-iodo-2-nitrobenzoic acid for 2-nitro-5-propoxy-benzoic acid and 3-chloro-4-fluoroaniline for 2-aminobenzamide)** (1.00 g, 2.10 mmol), tert-butyldimethyl(2-propynyloxy)silane (0.85 ml, 4.20 mmol), copper(I) iodide (4.0 mg, 0.021 mmol), dichlorobis(triphenylphosphine) palladium (II) ($Pd(PPh_3)_2Cl_2$) (29 mg, 0.042 mmol), and triethylamine (1.17 ml, 8.39 mmol) in DMF (15 mL) was stirred overnight at room temperature under argon atmosphere. Water (30 mL) and ethyl acetate (30 mL) were added to the mixture. The resultant precipitate was removed by filtration. The filtrate was extracted with EtOAc (2 x 50 mL). The combined organic layer was washed with water (1 x 100 mL) and brine (1 x 100 mL) and was dried over Na_2SO_4. After filtration and evaporation, the crude product was obtained, which was purified by column chromatography on silica gel (eluted with hexane/ethyl acetate 6:1 to 1:3) to give 0.73 g of 6-(3-(tert-butyldimethylsilyloxy)prop-1-ynyl)-N-(3-chloro-4-fluorophenyl)-2-(pyridin-3-yl)quinazolin-4-amine as light brown solid (67 %). LCMS m/z = 519 (M +1) (Method D) (retention time = 3.22 min). ^{1}H NMR (300 MHz, DMSO) δ 9.99 (s, 1H), 9.35 (s, 1H), 8.62 – 8.44 (m, 3H), 8.11 (dd, J = 6.8, 2.6 Hz, 1H), 7.76 – 7.66 (m, 3H), 7.45 – 7.30 (m, 2H), 4.48 (s, 2H), 0.75 (s, 9H), 0.16 (s, 6H).

Method P: 6-(3-(tert-butyldimethylsilyloxy)propyl)-N-(3-chloro-4-fluorophenyl)-2-(pyridin-3-yl)quinazolin-4-amine (xvi-a) A suspension of 6-(3-(tert-butyldimethylsilyloxy)prop-1-ynyl)-N-(3-chloro-4-fluorophenyl)-2-(pyridin-3-yl)quinazolin-4-amine (0.20 g, 0.39 mmol) and 5 % Pd-S-C (40 mg) in EtOAc (5 mL) and MeOH (5 mL) was stirred overnight at room temperature under hydrogen atmosphere. The reaction mixture was filtered through Celite. The filtrate was

concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (eluted with hexane/ethyl acetate 6:1 to 2:3) to give 0.15 g of 6-(3-(tert-butyldimethylsilyloxy)propyl)-N-(3-chloro-4-fluorophenyl)-2-(pyridin-3-yl)quinazolin-4-amine as yellow solid (74 %). LCMS m/z = 523 (M +1) (Method D) (retention time = 3.35 min). ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.69 (dd, J = 2.2, 0.8 Hz, 1H), 8.79 – 8.65 (m, 2H), 8.07 (dd, J = 6.5, 2.7 Hz, 1H), 7.94 (d, J = 8.5 Hz, 1H), 7.76 – 7.61 (m, 3H), 7.47 – 7.37 (m, 2H), 7.31 – 7.18 (m, 1H), 3.68 (t, J = 6.1 Hz, 2H), 3.01 – 2.83 (m, 2H), 2.03 – 1.86 (m, 2H), 0.94 (s, 9H), 0.08 (s, 6H).

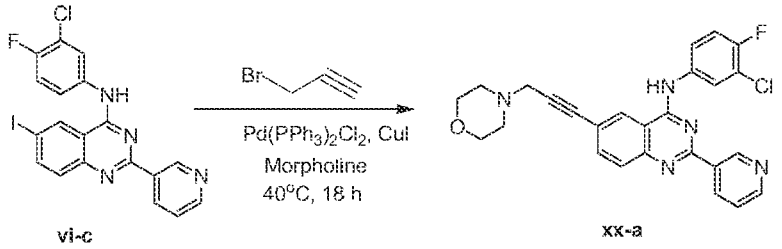
Method Q: 3-(4-(3-chloro-4-fluorophenylamino)-2-(pyridin-3-yl)quinazolin-6-yl)propan-1-ol (xvii-a) To a suspension of 6-(3-(tert-butyldimethylsilyloxy)propyl)-N-(3-chloro-4-fluorophenyl)-2-(pyridin-3-yl)quinazolin-4-amine (0.35 g, 0.67 mmol) in MeOH (10 mL) was added 1-chloroethyl chloroformate (7.2 µl, 0.067 mmol). The mixture was stirred overnight at room temperature. Methanol was removed *in vacuo*. Sat. $NaHCO_3$ aqueous (10 mL) and CH_2Cl_2 (10 mL) were added to the residue and stirred for a while. The resultant solid was collected by filtration and dried to give 0.25 g of 3-(4-(3-chloro-4-fluorophenylamino)-2-(pyridin-3-yl)quinazolin-6-yl)propan-1-ol as light yellow solid (91 %). MS m/z = 409 (M +1) (Method D) (retention time = 1.71 min). ^{1}H NMR (300 MHz, DMSO) δ 10.01 (s, 1H), 9.51 (s, 1H), 8.66 (m, 2H), 8.37 (s, 1H), 8.29 – 8.20 (m, 1H), 7.94 – 7.67 (m, 3H), 7.63 – 7.43 (m, 2H), 4.60 (t, J = 5.0 Hz, 1H), 3.56 – 3.35 (m, 2H), 2.94 – 2.69 (m, 2H), 2.15 – 1.56 (m, 2H).

Method R: 3-(4-(3-chloro-4-fluorophenylamino)-2-(pyridin-3-yl)quinazolin-6-yl)propyl methanesulfonate (xviii-a) To a suspension of 3-(4-(3-chloro-4-fluorophenylamino)-2-(pyridin-3-yl)quinazolin-6-yl)propan-1-ol (0.25 g, 0.61 mmol) and triethylamine (0.17 ml, 1.22 mmol) in CH_2Cl_2 (10 mL) was added methanesulfonyl chloride (0.057 ml, 0.73 mmol). The mixture was stirred at room temperature for 1 h. Water (10 mL) was added to the mixture and stirred for a while. The resultant precipitate was collected by filtration and washed with CH_2Cl_2 and dried to give 0.27 g of 3-(4-(3-chloro-4-fluorophenylamino)-2-(pyridin-3-yl)quinazolin-6-

yl)propyl methanesulfonate as pale yellow solid (91 %), which was used without further purification.

Method G4: N-(3-chloro-4-fluorophenyl)-6-(3-(dimethylamino)propyl)-2-(pyridin-3-yl)quinazolin-4-amine dihydrochloride (xviv-a) (This method is representative of method G4 and G5. These two methods can be implemented in a similar way except for substitution of the appropriate solvent and temperature) A solution of 3-(4-(3-chloro-4-fluorophenylamino)-2-(pyridin-3-yl)quinazolin-6-yl)propyl methanesulfonate (40 mg, 82 mmol) and 40 % Me_2NH aqueous (1 mL) in methanol (2 mL) was placed in a microwave reaction vial. The mixture was heated under microwave irradiation conditions at 150°C for 30 minutes after which the solvent was removed in vacuo. The crude product was obtained, which was purified by column chromatography on basic silica gel (eluted with ethyl acetate/methanol 1:0→5:1). The HCl salt generated by 4 M HCl in dioxane was crystallized from 2-propanol to give 10 mg of N-(3-chloro-4-fluorophenyl)-6-(3-(dimethylamino)propyl)-2-(pyridin-3-yl)quinazolin-4-amine dihydrochloride as pale brown powder (24 %). LCMS m/z = 436 (M +1) (Method C) (retention time = 1.68 min). ^{1}H NMR (300 MHz, DMSO) δ 10.59 (s, 1H), 10.18 (s, 1H), 9.51 (s, 1H), 8.98 – 8.76 (m, 2H), 8.65 (s, 1H), 8.26 (dd, J = 6.8, 2.6 Hz, 1H), 8.05 – 7.74 (m, 4H), 7.54 (t, J = 9.1 Hz, 1H), 3.19 – 3.03 (m, 2H), 2.97 – 2.83 (m, 2H), 2.78 (s, 3H), 2.77 (s, 3H), 2.16 (s, 2H).

Scheme 10: Method O2: Representative synthesis of compounds of formula xx



N-(3-chloro-4-fluorophenyl)-6-(3-morpholinoprop-1-ynyl)-2-(pyridin-3-yl) quinazolin-4-amine (xx-a) To a solution of N-(3-chloro-4-fluorophenyl)-6-iodo-2-(pyridin-3-yl)quinazolin-4-amine **(synthesized as described in Scheme 1 and 4, substituting 5-iodo-2-nitrobenzoic acid for 2-nitro-5-propoxy-benzoic acid and 3-**

chloro-4-fluoroaniline for 2-aminobenzamide) (2.19 g, 4.6 mmol, 1 eq.), $Pd(PPh_3)_2Cl_2$ (161 mg, 0.23 mmol, 0.05 eq.), CuI (87 mg, 0.46 mmol, 0.1 eq.) in morpholine (15 mL) was added 3-bromoprop-1-yne (814 mg, 6.9 mmol, 1.5 eq.) at 0 °C under Ar atmosphere, following a procedure from ***Tetrahedron*, 2007, 63, 10671-10683.** The mixture was stirred at 40 °C overnight. After cooling, the mixture was filtered and methanol (60 mL) was added to the filtrate to form a precipitate. The precipitate was collected and re-crystallized from ethyl acetate twice to afford 1.60 g of **xx-a** as yellow solid (yield 74%). LCMS m/z = 474.1 (M +1), 476.1 (M +3) (Method C) (retention time = 1.97 min).

The compounds in the following table were prepared in a manner analogous to that described in **Scheme 8** substituting with appropriate nucleophile.

Table 3:

Number	Product	Salt type	Molecular Mass	^{1}H-NMR	^{1}H-NMR Solvent	LCMS	Retention Time (Min)	LCMS Protocol	Purity percent	Method for Coupling
566			519.085	1H NMR (300 MHz, DMSO) δ 9.99 (s, 1H), 9.35 (s, 1H), 8.62 – 8.44 (m, 3H), 8.11 (dd, J = 6.8, 2.6 Hz, 1H), 7.76 – 7.66 (m, 3H), 7.45 – 7.30 (m, 2H), 4.48 (s, 2H), 0.75 (s, 9H), 0.00 (s, 6H).	DMSO	519 (M+1)	3.22	Method D	96	Method O1
567			523.117	1H NMR (300 MHz, CDCl3) δ 9.69 (dd, J = 2.2, 0.8 Hz, 1H), 8.79 – 8.65 (m, 2H), 8.07 (dd, J = 6.5, 2.7 Hz, 1H), 7.94 (d, J = 8.5 Hz, 1H), 7.76 – 7.61 (m, 3H), 7.47 – 7.37 (m, 2H), 7.31 – 7.18 (m, 1H), 3.68 (t, J = 6.1 Hz, 2H), 3.01 – 2.63 (m, 2H), 2.03 – 1.	CDCl3	523 (M+1)	3.35	Method D	100	Methods O1, P
568			408.856	1H NMR (300 MHz, DMSO) δ 10.01 (s, 1H), 9.51 (s, 1H), 8.66 (m, 2H), 8.37 (s, 1H), 8.29 – 8.20 (m, 1H), 7.94 – 7.67 (m, 3H), 7.63 – 7.43 (m, 2H), 4.60 (t, J = 5.0 Hz, 1H), 3.56 – 3.35 (m, 2H), 2.94 – 2.69 (m, 2H), 2.15 – 1.56 (m, 2H).	DMSO	409 (M+1)	1.71	Method D	100	Methods O1, P, Q
569		2 HCl	508.846	1H NMR (300 MHz, DMSO) δ 10.59 (s, 1H), 10.18 (s, 1H), 9.51 (s, 1H), 8.98 – 8.76 (m, 2H), 8.65 (s, 1H), 8.26 (dd, J = 6.8, 2.6 Hz, 1H), 8.05 – 7.74 (m, 4H), 7.54 (t, J = 9.1 Hz, 1H), 3.19 – 3.03 (m, 2H), 2.97 – 2.83 (m, 2H), 2.78 (s, 3H), 2.77 (s, 3H), 2.	DMSO	436 (M+1)	1.68	Method C	100	Method G4

570			409.841	1H NMR (300 MHz, CDCl3) δ 9.49 (d, J = 1.4 Hz, 1H), 8.73 – 8.51 (m, 2H), 8.14 (s, 1H), 8.01 (d, J = 8.6 Hz, 1H), 7.81 (dd, J = 8.6, 1.9 Hz, 1H), 7.51 – 7.13 (m, 4H), 3.77 (dd, J = 11.5, 6.2 Hz, 2H), 3.11 – 2.86 (m, 2H), 2.16 – 1.93 (m, 2H), 1.44 (t, J = 5	CDCl3	410 (M+1)	1.95	Method D	100	Methods O1, P, Q
571		2 HCl	550.882	1H NMR (300 MHz, DMSO) δ 10.83 – 10.37 (m, 2H), 9.51 (s, 1H), 8.97 – 8.74 (m, 2H), 8.62 (s, 1H), 8.27 (d, J = 4.2 Hz, 1H), 8.05 – 7.72 (m, 4H), 7.54 (t, J = 9.0 Hz, 1H), 3.96 (d, J = 12.7 Hz, 2H), 3.76 (t, J = 12.1 Hz, 2H), 3.47 (d, J = 12.0 Hz, 2H), 3.24	DMSO	478 (M+1)	2.01	Method C	100	Method G4
572			422.882	1H NMR (300 MHz, DMSO) δ 9.99 (s, 1H), 9.51 (s, 1H), 8.75 – 8.60 (m, 2H), 8.37 (s, 1H), 8.26 (dd, J = 6.9, 2.6 Hz, 1H), 7.99 – 7.86 (m, 1H), 7.88 – 7.73 (m, 2H), 7.60 – 7.46 (m, 2H), 3.39 (dd, J = 8.4, 4.1 Hz, 2H), 3.27 (s, 3H), 2.92 – 2.78 (m, 2H), 2.05	DMSO	423 (M+1)	2.09	Method D	100	Method G4
573		HCl	548.909	1H NMR (300 MHz, DMSO) δ 10.69 (s, 1H), 10.12 (s, 1H), 9.51 (s, 1H), 9.02 – 8.80 (m, 2H), 8.69 (s, 1H), 8.27 (dd, J = 6.9, 2.7 Hz, 1H), 8.08 – 7.78 (m, 4H), 7.54 (t, J = 9.1 Hz, 1H), 3.46 (d, J = 10.2 Hz, 2H), 3.17 – 3.00 (m, 2H), 2.99 – 2.75 (m, 4H), 2.3	DMSO	476 (M+1)	1.79	Method C	100	Method G4
574		HCl	500.395	1H NMR (300 MHz, DMSO) δ 10.68 (s, 1H), 9.49 (s, 1H), 9.12 – 8.99 (m, 1H), 8.94 (d, J = 3.9 Hz, 1H), 8.58 (d, J = 11.5 Hz, 1H), 8.17 (dd, J = 6.7, 2.6 Hz, 1H), 8.07 – 7.82 (m, 5H), 7.55 (t, J = 9.1 Hz, 1H), 3.43 – 3.29 (m, 2H), 3.08 – 2.65 (m, 5H), 2.09 –	DMSO	464 (M+1)	1.78	Method D	95	Method G4 followed by acylation with acetyl chloride/TEA/DCM, rt

361

575		HCl	600.39	1H NMR (300 MHz, DMSO) δ 11.79 (s, 1H), 10.81 (s, 1H), 9.50 (s, 1H), 8.98 (d, J = 8.2 Hz, 1H), 8.89 (d, J = 5.0 Hz, 1H), 8.75 (s, 1H), 8.27 (d, J = 4.8 Hz, 1H), 8.10 – 7.79 (m, 4H), 7.53 (t, J = 9.1 Hz, 1H), 5.18 – 3.09 (m, 10H), 3.01 – 2.69 (m, 5H), 2.37	DMSO	491 (M+1)	1.76	Method C	100	Method G4
576			473.93	1H NMR (300 MHz, DMSO) δ 10.17 (s, 1H), 9.52 (s, 1H), 8.70 (s, 1H), 8.66 (d, J = 8.1 Hz, 1H), 8.55 (d, J = 8.4 Hz, 1H), 8.27 (dd, J = 6.9, 2.6 Hz, 1H), 7.93 (s, 2H), 7.70 (d, J = 8.4 Hz, 1H), 7.61 – 7.51 (m, 2H), 3.67 – 3.61 (m, 6H), 2.61 – 2.55 (m, 4H).	DMSO	473.9 (M+1)	2.2	Method C	100	Method O1
577			435.92	1H NMR (300 MHz, DMSO) δ 10.06 (s, 1H), 9.54 (s, 1H), 8.77 – 8.63 (m, 2H), 8.52 (d, J = 8.4 Hz, 1H), 8.29 (d, J = 6.8 Hz, 1H), 7.93 (s, 1H), 7.79 (s, 1H), 7.64 – 7.51 (m, 3H), 3.00 (t, J = 8.2 Hz, 2H), 2.87 (t, J = 7.6 Hz, 2H), 2.72 (s, 6H), 2.14 – 1.99 (	DMSO	436.0 (M+1)	1.68	Method C	100	Methods O1, P
578			519.09	1H NMR (300 MHz, DMSO) δ 10.17 (s, 1H), 9.67 – 9.43 (m, 1H), 8.68 (s, 2H), 8.55 (d, J = 8.4 Hz, 1H), 8.28 (s, 1H), 7.89 (s, 2H), 7.68 (s, 1H), 7.56 (d, J = 9.1 Hz, 2H), 4.64 (s, 2H), 0.92 (s, 9H), 0.18 (s, 6H).	DMSO	518.8 (M+1)	3.18	Method C	100	Method O1

362

579			404.82	1H NMR (300 MHz, DMSO) δ 10.19 (s, 1H), 9.51 (s, 1H), 8.65 (d, J = 8.1 Hz, 2H), 8.54 (d, J = 8.4 Hz, 1H), 8.26 (s, 1H), 7.85 (s, 2H), 7.67 – 7.60 (m, 1H), 7.52 (d, J = 7.0 Hz, 2H), 5.48 (s, 1H), 4.39 (d, J = 5.8 Hz, 2H).	DMSO	404.9 (M+1)	2.05	Method C	100	Methods O1, Q
580			477.96	1H NMR (300 MHz, DMSO) δ 9.99 (s, 1H), 9.51 (s, 1H), 8.73 – 8.61 (m, 2H), 8.45 (d, J = 8.6 Hz, 1H), 8.28 (dd, J = 6.8, 2.5 Hz, 1H), 7.97 – 7.86 (m, 1H), 7.71 (s, 1H), 7.60 – 7.47 (m, 3H), 3.63 – 3.51 (m, 4H), 2.82 (t, J = 7.5 Hz, 2H), 2.42 – 2.25 (m, 6H),	DMSO	477.9 (M+1)	1.99	Method C	100	Methods O1, P
581			523.12	1H NMR (300 MHz, CDCl3) δ 9.67 (d, J = 1.3 Hz, 1H), 8.76 – 8.66 (m, 2H), 8.03 (dd, J = 6.5, 2.7 Hz, 1H), 7.82 – 7.74 (m, 2H), 7.64 (ddd, J = 8.9, 4.0, 2.7 Hz, 1H), 7.46 (s, 1H), 7.44 – 7.37 (m, 2H), 7.20 (t, J = 8.7 Hz, 1H), 3.67 (t, J = 6.1 Hz, 2H), 2.95	CDCl3	523.1 (M+1)	3.35	Method C	100	Methods O1, P
582			408.86	1H NMR (300 MHz, CD3OD) δ 9.50 (d, J = 1.3 Hz, 1H), 8.77 (d, J = 8.0 Hz, 1H), 8.62 (dd, J = 4.9, 1.6 Hz, 1H), 8.26 (d, J = 8.5 Hz, 1H), 8.18 (dd, J = 6.7, 2.6 Hz, 1H), 7.83 – 7.71 (m, 2H), 7.61 – 7.47 (m, 2H), 7.30 (t, J = 9.0 Hz, 1H), 3.65 (t, J = 6.4 Hz	CD3OD	409.0 (M+1)	1.99	Method C	100	Methods O1, P, Q

363

583			494.03	1H NMR (300 MHz, CD3OD) δ 9.50 – 9.46 (m, 1H), 8.77 – 8.70 (m, 1H), 8.61 (dd, J = 4.9, 1.6 Hz, 1H), 8.22 (d, J = 8.5 Hz, 1H), 8.17 (dd, J = 6.8, 2.6 Hz, 1H), 7.75 (ddd, J = 9.0, 4.2, 2.7 Hz, 1H), 7.70 (s, 1H), 7.54 (ddd, J = 8.0, 4.9, 0.8 Hz, 1H), 7.46 (d	CD3OD	494.0 (M+1)	2.29	Method C	91	Method G4
584			522	1H NMR (300 MHz, DMSO) δ 10.15 (s, 1H), 8.74 – 8.61 (m, 2H), 8.25 (d, J = 3.5 Hz, 1H), 7.96 – 7.80 (m, 4H), 7.59 – 7.46 (m, 2H), 3.79 (s, 2H), 3.18 (s, 4H), 3.06 (s, 4H).	DMSO	522.0 (M+1)	2.18	Method C	100	Method O2
585			526.06	1H NMR (300 MHz, DMSO) δ 9.99 (s, 1H), 9.52 (d, J = 2.0 Hz, 1H), 8.72 – 8.62 (m, 2H), 8.37 (s, 1H), 8.27 (dd, J = 6.9, 2.6 Hz, 1H), 7.96 – 7.88 (m, 1H), 7.83 (d, J = 2.6 Hz, 2H), 7.61 – 7.50 (m, 2H), 3.10 (s, J = 17.4 Hz, 6H), 2.95 – 2.80 (m, 8H), 2.58 –	DMSO	526.1 (M+1)	2.11	Method C	91	Methods O2, P
586		HCl	494.82	1H NMR (300 MHz, DMSO) δ 10.49 (s, 1H), 9.50 (s, 1H), 8.96 – 8.53 (m, 5H), 8.25 (dd, J = 6.9, 2.5 Hz, 1H), 8.05 – 7.73 (m, 4H), 7.54 (t, J = 9.1 Hz, 1H), 3.02 – 2.78 (m, 4H), 2.64 – 2.37 (m, 3H), 2.15 – 1.99 (m, 2H).	DMSO	422 (M+1)	1.64	Method B (Ammonium formate)	100	Method O2

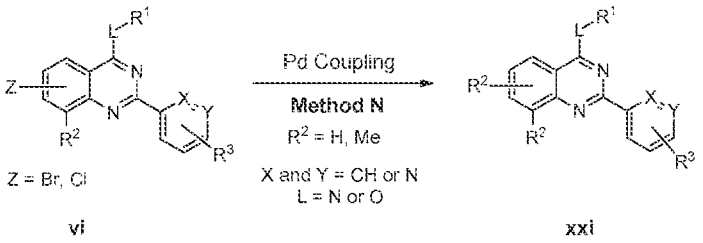
364

587		HCl	460.79	1H NMR (300 MHz, DMSO) δ 10.61 (s, 1H), 9.50 (s, 1H), 9.00 – 8.78 (m, 2H), 8.66 (s, 1H), 8.25 (dd, J = 6.8, 2.6 Hz, 1H), 8.13 – 7.75 (m, 7H), 7.54 (t, J = 9.1 Hz, 1H), 3.02 – 2.73 (m, 4H), 2.14 – 1.94 (m, 2H).	DMSO	408 (M+1)	1.60	Method B (Ammonium formate)	100	Method O2
588			431.89	1H NMR (300 MHz, DMSO) δ 10.18 (s, 1H), 8.65 (d, J = 6.6 Hz, 1H), 8.56 (d, J = 8.7 Hz, 1H), 8.23 (dd, J = 6.9, 2.4 Hz, 1H), 8.01 (s, 1H), 7.91 (dd, J = 7.0, 3.5 Hz, 1H), 7.73 (d, J = 8.5 Hz, 1H), 7.68 – 7.39 (m, 3H), 4.07 (s, 2H), 2.67 (s, 6H).	DMSO	431.9 (M+1)		Method C	99	Method O1
589			435.92	1H NMR (300 MHz, DMSO) δ 10.06 (s, 1H), 9.53 (s, 1H), 8.76 – 8.62 (m, 2H), 8.51 (d, J = 8.4 Hz, 1H), 8.28 (dd, J = 6.9, 2.5 Hz, 1H), 7.92 (dd, J = 4.5, 1.8 Hz, 1H), 7.79 (s, 1H), 7.65 – 7.49 (m, 3H), 3.08 – 2.95 (m, 2H), 2.86 (t, J = 7.6 Hz, 2H), 2.71 (s, J = 7.2 Hz, 6H), 2.05 (dt, J = 13.8, 7.1 Hz, 2H).	DMSO	436.0 (M+1)		Method C	99	Method O1, P
590			409.44	1H-NMR (300 MHz, DMSO): δ 13.19 (s, 1H), 9.11 (s, 1H), 8.88 (s, 1H), 8.53 (s, 1H), 8.29 (s, 1H), 8.06 (s, 1H), 7.94 (d, J = 10.6 Hz, 4H), 7.78 (s, 1H), 7.25 (s, 1H), 4.44 (s, 2H), 3.37 (s, 3H).	DMSO	410.5 (M+1)		Method C	95	Method O1

591			413.47		DMSO	414.5 (M+1)		Method C	95	Method O1, P

366

Scheme 11: General route for the synthesis of compounds with general formula xxi:



Method N1: $Pd(APhos)_2Cl_2$/ K_3PO_4 or Cs_2CO_3/ Boronic acid or ester/ Dioxane – H_2O, heat

Method N2: $Pd(PPh_3)_2Cl_2$/ K_2CO_3/ Boronic acid or ester/ DME-EtOH-H_2O / microwave, 120 °C

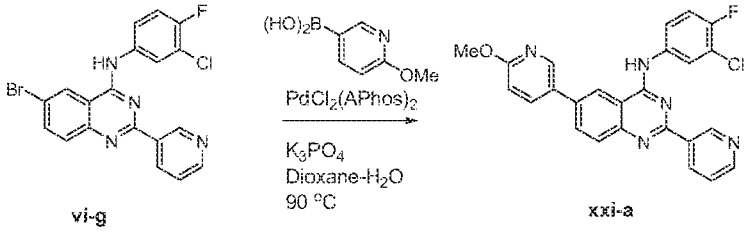
Method N3: $Pd(OAc)_2$/ Xphos/ Cs_2CO_3/ THF- H_2O, 80 °C

Method N4: $Pd(OAc)_2$/ Sphos/ K_2CO_3/ MeCN- H_2O, microwave, 120 °C

Method N5: $Pd(PPh_3)_4$/K_3PO_4/ Dioxane – H_2O, heat

Method N6: $Pd(dppf)Cl_2$-CH_2Cl_2/K_3PO_4/ Dioxane – H_2O, heat

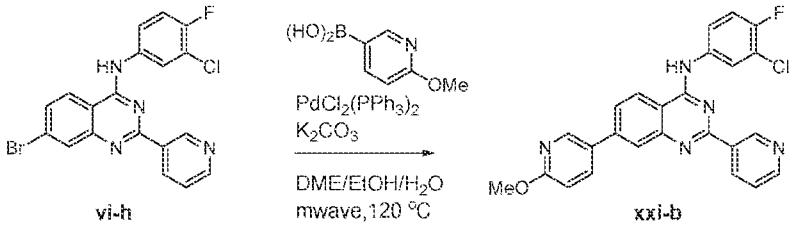
Scheme 12: Method N1: Representative synthesis of compounds of formula xxi (see Scheme 11).



N-(3-chloro-4-fluorophenyl)-6-(6-methoxypyridin-3-yl)-2-(pyridin-3-yl)quinazolin-4-amine (xxi-a) A 2.0 dram reaction vial was charged with 6-bromo-N-(3-chloro-4-fluorophenyl)-2-(pyridin-3-yl)quinazolin-4-amine (**synthesized as**

described in Scheme 1 and 4, substituting 5-bromo-2-nitrobenzoic acid for 2-nitro-5-propoxy-benzoic acid and 3-chloro-4-fluoroaniline for 2-aminobenzamide) (100 mg, 0.233 mmol, 1.0 equiv), 6-methoxypyridin-3-ylboronic acid (44.5 mg, 0.291 mmol, 1.25 equiv), $Pd(APhos)_2Cl_2$ (6.6 mg, 0.0093 mmol, 4 mol%) and potassium phosphate monohydrate (69 mg, 0.70 mmol, 3.0 equiv). The mixture was suspended in dioxane/water (9:1, 4 mL), and the reaction was heated at 90°C for 14 h. The reaction mixture was cooled to room temperature, diluted with water (15 mL) and the resultant precipitate was collected by filtration. The crude product was purified by stirring in methanol for 30 min at 60 °C to give the desired product as a pale yellow solid (58 mg, 54%) LCMS m/z = 458.1 (M+1) (Method C) (retention time = 2.56 min). ^{1}H NMR (300 MHz, DMSO) δ 10.12 (s, 1H), 9.53 (s, 1H), 8.82 (s, 1H), 8.70 (dd, *J* = 16.9, 5.4 Hz, 3H), 8.25 (d, *J* = 8.6 Hz, 3H), 8.01 – 7.87 (m, 2H), 7.57 (dd, *J* = 11.2, 6.0 Hz, 2H), 7.03 (d, *J* = 8.6 Hz, 1H), 3.94 (s, 3H).

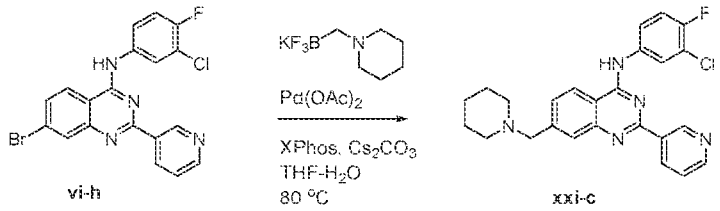
Scheme 13: Method N2: Representative synthesis of compounds of formula xxi (see Scheme 11)



N-(3-chloro-4-fluorophenyl)-7-(6-methoxypyridin-3-yl)-2-(pyridin-3-yl)quinazolin-4-amine (xxi-b) A microwave vial was charged with 7-bromo-N-(3-chloro-4-fluorophenyl)-2-(pyridin-3-yl)quinazolin-4-amine **(synthesized as described in Scheme 1 and 4, substituting 4-bromo-2-nitrobenzoic acid for 2-nitro-5-propoxy-benzoic acid and 3-chloro-4-fluoroaniline for 2-aminobenzamide)** (100 mg, 0.233 mmol), 6-methoxypyridin-3-ylboronic acid (44.5 mg, 0.291 mmol, 1.25 equiv), $Pd(PPh_3)_2Cl_2$ (8.1 mg, 5 mol%) and potassium carbonate (160.1 mg, 1.16 mmol, 5.0 equiv). The mixture was suspended in DME/water/ethanol (7:3:2, 4 mL), and the reaction was heated under microwave

irradiation conditions at 120°C for 10 minutes. The crude reaction mixture was diluted with water (10 mL) and then filtered. The solid residue was dissolved in methanol/THF (1:1, 5 mL) with heating and then filtered through Celite to remove the catalyst. The resulting filtrate was concentrated to afford the desired product as a tan solid (7.0 mg, 6.5%). LCMS m/z = 458.1 (M+1) (Method C) (retention time = 2.51 min). ^{1}H NMR (300 MHz, DMSO) δ 10.12 (s, 1H), 9.55 (s, 1H), 8.76 (d, J = 2.5 Hz, 1H), 8.72 – 8.65 (m, 2H), 8.62 (d, J = 8.6 Hz, 1H), 8.34 – 8.26 (m, 2H), 8.15 (d, J = 1.6 Hz, 1H), 8.02 (d, J = 8.7 Hz, 1H), 7.97 – 7.88 (m, 1H), 7.61 – 7.49 (m, 2H), 6.99 (d, J = 8.7 Hz, 1H), 3.94 (s, 3H).

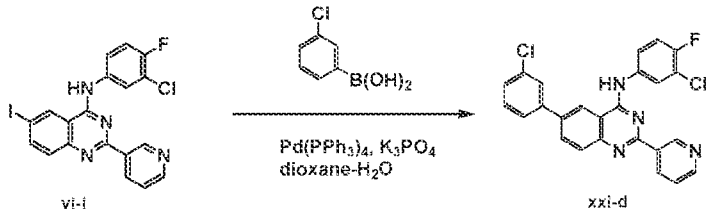
Scheme 14: Method N3: Representative synthesis of compounds of formula xxi (see Scheme 11). (This method is representative of method N4 except for substitution of the appropriate ligand, solvent and the use of microwave instead of heating)



N-(3-chloro-4-fluorophenyl)-7-(piperidin-1-ylmethyl)-2-(pyridin-3-yl)quinazolin-4-amine (xxi-c) A dry 15 mL sealed tube was charged with 7-bromo-N-(3-chloro-4-fluorophenyl)-2-(pyridin-3-yl)quinazolin-4-amine **(synthesized as described in Scheme 1 and 4, substituting 4-bromo-2-nitrobenzoic acid for 2-nitro-5-propoxy-benzoic acid and 3-chloro-4-fluoroaniline for 2-aminobenzamide)** (100 mg, 0.233mmol), potassium 1-trifluoroboratomethylpiperidine (52.5 mg, 0.256 mmol), cesium carbonate (227.5 mg, 0.698 mmol), $Pd(OAc)_2$ (1.6 mg, 3 mol%) and XPhos (6.7 mmol, 6 mol%) in THF/water (10:1, 3.3 mL). The reaction mixture was stirred at 80°C for 16 hours. The reaction mixture was filtered through a pad of Celite and solvent was removed *in vacuo*. The crude product was purified by ISCO (silica, 12 g column, 97% dichloromethane - 3% methanol – 0.1 % NH_4OH) to yield the desired

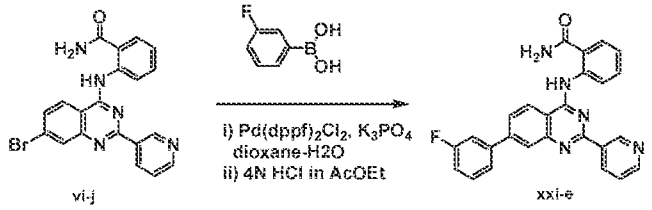
compound as a yellow solid (23.3 mg, 22%). LCMS m/z = 448.0 (M+1) (Method C) (retention time = 1.95 min). ^{1}H NMR (300 MHz, CD_3OD) δ 9.40 (d, J = 1.4 Hz, 1H), 8.70 – 8.62 (m, 1H), 8.56 (dd, J = 4.9, 1.6 Hz, 1H), 8.18 – 8.09 (m, 2H), 7.69 (ddd, J = 6.8, 4.1, 2.1 Hz, 2H), 7.54 – 7.45 (m, 2H), 7.23 (t, J = 9.0 Hz, 1H), 3.61 (s, 2H), 2.47 (s, 4H), 1.64 (dd, J = 13.9, 8.9 Hz, 5H), 1.49 (d, J = 4.1 Hz, 2H).

Scheme 15: Method N5: Representative synthesis of compounds of formula xxi (see Scheme 11)



N-(3-chloro-4-fluorophenyl)-6-(3-chlorophenyl)-2-(pyridin-3-yl)quinazolin-4-amine (xxi-d) A mixture of N-(3-chloro-4-fluorophenyl)-6-iodo-2-(pyridin-3-yl)quinazolin-4-amine (1.0 g, 2.10 mmol), 3-chlorophenylboronic acid (0.49 g, 3.13 mmol), $Pd(PPh_3)_4$ (0.24 g, 0.210 mmol), K_3PO_4 (1.34 g, 6.31 mmol) in dioxane (20 mL) and water (2.0 mL) was stirred under reflux for 2 h. Ethyl acetate (20 mL) was added to the cooled mixture and filtered. The filtered solid was recrystallized from DMF and water to give the title compound (0.50 g, 51.6 %). ^{1}H NMR (400 MHz, DMSO) δ 10.20 (s, 1H), 9.54 (s, 1H), 8.87 (s, 1H), 8.74 – 8.65 (m, 2H), 8.31 – 8.23 (m, 2H), 8.04 – 7.85 (m, 4H), 7.64 – 7.49 (m, 4H).

Scheme 16: Method N6: Representative synthesis of compounds of formula xxi (see Scheme 11)



2-(7-(3-fluorophenyl)-2-(pyridin-3-yl)quinazolin-4-ylamino)benzamide dihydrochloride (xxi-e) A mixture of 2-(7-bromo-2-(pyridin-3-yl)quinazolin-4-ylamino)benzamide (0.40 g, 0.952 mmol), 3-fluorophenylboronic acid (0.20g 1.43 mmol), $Pd(dppf)_2Cl_2$(77mg, 0.094mmol), K_3PO_4 (606 mg, 2.85 mmol) in dioxane (8 mL) and water (2 mL) was refluxed under argon atmosphere for 4 h and cooled. Ethyl acetate (10 mL) was added to the mixture and a precipitate formed and was filtered. The filtered solid was recrystallized from DMF and water to give the title compound as free form. The solid as free form was suspended in ethyl acetate (10 mL) and 4N HCl in ethyl acetate (0.71 mL) was added to the suspension. A precipitate formed and was subjected to sonication for 20 min, filtered and dried to give the title compound (0.24 g, 49.6 %). ^{1}H NMR (400 MHz, DMSO) δ 13.19 (s, 1H), 9.64 (s, 1H), 9.21 – 9.08 (m, 1H), 9.07 – 8.89 (m, 2H), 8.51 (s, 1H), 8.38 – 8.26 (m, 2H), 8.16 (d, J = 8.5 Hz, 1H), 8.07 – 7.87 (m, 3H), 7.83 – 7.70 (m, 3H), 7.62 (dd, J = 14.2, 7.7 Hz, 1H), 7.40 – 7.22 (m, 2H).

The compounds in the following table were prepared in a manner analogous to that described in **Scheme 11** substituting with appropriate boronic acid/ester or boronate salt, catalyst and solvent

Table 4:

PRODUCT	Salt type	Molecular Mass	^{1}H-NMR	^{1}H-NMR Solvent	LCMS	Retention Time (min)	LCMS Protocol	Purity percent	Method for Coupling
	2 HCl	536.401	^{1}H NMR (300 MHz, DMSO) δ 11.34 (s, 1H), 10.53 (s, 1H), 9.56 (s, 1H), 9.17 – 8.95 (m, 2H), 8.89 (d, *J* = 4.5 Hz, 1H), 8.19 (d, *J* = 8.8 Hz, 1H), 8.08 – 7.81 (m, 4H), 7.62 – 6.98 (m, 3H), 4.53 (s, 2H), 4.05 – 3.74 (m, 4H), 3.48 – 3.07 (m, 4H).	DMSO	464 (M+1)	2.01	Method C	100	Method N3
	HCl	515.406	^{1}H NMR (300 MHz, DMSO) δ 10.40 (s, 1H), 9.51 (s, 1H), 9.00 – 8.78 (m, 2H), 8.55 (s, 1H), 8.20 (d, *J* = 4.4 Hz, 1H), 8.03 – 7.75 (m, 4H), 7.54 (t, *J* = 9.1 Hz, 1H), 4.68 (s, 2H), 3.83 (d, *J* = 11.2 Hz, 2H), 3.44 – 3.18 (m, 4H), 1.98 – 1.78 (m, 1H), 1.62 (d, *J*	DMSO	479 (M+1)	2.08	Method D	97	Method N3
		446.920	^{1}H NMR (300 MHz, DMSO) δ 10.10 (s, 1H), 9.51 (s, 1H), 8.75 – 8.60 (m, 2H), 8.47 (s, 1H), 8.32 – 8.19 (m, 1H), 7.97 – 7.77 (m, 3H), 7.63 – 7.44 (m, 2H), 4.62 (s, 2H), 4.16 – 3.97 (m, 1H), 1.88 – 1.42 (m, 8H).	DMSO	449 (M+1)	2.62	Method D	92	Method N3
		457.89	^{1}H NMR (300 MHz, DMSO) δ 10.12 (s, 1H), 9.53 (s, 1H), 8.82 (s, 1H), 8.70 (dd, J = 16.9, 5.4 Hz, 3H), 8.25 (d, J = 8.6 Hz, 3H), 8.01 – 7.87 (m, 2H), 7.57 (dd, J = 11.2, 6.0 Hz, 2H), 7.03 (d, J = 8.6 Hz, 1H), 3.94 (s, 3H).	DMSO	458.2 (M+1)	2.56	Method C	100	Method N1

372

		449.91	^{1}H NMR (300 MHz, DMSO) δ 10.13 (s, 1H), 9.52 (s, 1H), 8.67 (d, J = 9.8 Hz, 2H), 8.47 (s, 1H), 8.34 – 8.20 (m, 1H), 8.02 – 7.84 (m, 3H), 7.54 (t, J = 9.2 Hz, 2H), 3.64 (d, J = 17.6 Hz, 6H), 2.43 (s, 4H).	DMSO	449.9 (M+1)	2.13	Method C	100	Method N3
		456.9		DMSO	456.0 (M+1)	2.64	Method C	100	Method N1
		445.88	^{1}H NMR (300 MHz, DMSO) δ 10.04 (s, 1H), 9.52 (s, 1H), 8.68 (t, J = 6.5 Hz, 2H), 8.51 (s, 1H), 8.22 (dd, J = 6.7, 2.4 Hz, 1H), 8.03 – 7.83 (m, 3H), 7.54 (dd, J = 11.9, 6.6 Hz, 2H), 2.50 (s, 3H), 2.33 (s, 3H).	DMSO	446 (M+1)	2.35	Method C	100	Method N1
		427.86	^{1}H NMR (300 MHz, DMSO) δ 10.10 (s, 1H), 9.51 (s, 1H), 9.13 (s, 1H), 8.86 (s, 1H), 8.66 (s, 3H), 8.24 (s, 3H), 7.94 (d, J = 8.7 Hz, 2H), 7.55 (dd, J = 16.7, 9.9 Hz, 3H).	DMSO	427.95 (M+1)	2.25	Method C	100	Method N1
		430.86	^{1}H NMR (300 MHz, DMSO) δ 9.98 (s, 1H), 9.51 (d, J = 1.6 Hz, 1H), 8.66 (dd, J = 11.7, 2.2 Hz, 3H), 8.38 – 8.20 (m, 2H), 8.20 – 8.02 (m, 2H), 8.02 – 7.80 (m, 2H), 7.71 – 7.42 (m, 2H), 3.93 (s, 3H).	DMSO	430.9 (M+1)	2.17	Method C	100	Method N1

		449.91	^{1}H NMR (300 MHz, DMSO) δ 9.99 (s, 1H), 9.52 (d, J = 1.3 Hz, 1H), 8.77 – 8.55 (m, 2H), 8.41 (s, 1H), 8.28 (dd, J = 6.9, 2.6 Hz, 1H), 8.03 – 7.77 (m, 3H), 7.65 – 7.44 (m, 2H), 3.34 (s, 8H), 3.15 – 2.90 (m, 5H), 2.90 – 2.64 (m, 5H).	DMSO	449.9 (M+1)	2.04	Method C	100	Method N1
		445.85	^{1}H NMR (300 MHz, DMSO) δ 10.09 (s, 1H), 9.50 (s, 1H), 8.88 – 8.74 (m, 2H), 8.66 (dd, J = 14.1, 5.5 Hz, 2H), 8.56 – 8.42 (m, 1H), 8.23 (dd, J = 10.0, 5.7 Hz, 2H), 7.98 – 7.85 (m, 2H), 7.62 – 7.46 (m, 2H), 7.45 – 7.36 (m, 1H).	DMSO	445.9 (M+1)	2.43	Method C	99	Method N1
		512.97	^{1}H NMR (300 MHz, DMSO) δ 10.05 (s, 1H), 9.51 (s, 1H), 8.70 (dd, J = 24.1, 7.0 Hz, 4H), 8.22 (dd, J = 14.3, 7.3 Hz, 2H), 8.10 (d, J = 7.9 Hz, 1H), 7.89 (d, J = 8.4 Hz, 2H), 7.53 (d, J = 7.4 Hz, 2H), 7.00 (d, J = 8.8 Hz, 1H), 3.74 (s, 4H), 3.55 (d, J = 4.7	DMSO	512.9 (M+1)	2.5	Method C	100	Method N1
		456.9	^{1}H NMR (300 MHz, DMSO) δ 10.16 (s, 1H), 9.53 (s, 1H), 8.81 (s, 1H), 8.73 – 8.60 (m, 2H), 8.30 – 8.20 (m, 2H), 7.99 – 7.89 (m, 2H), 7.55 (dd, J = 8.2, 4.7 Hz, 2H), 7.46 (t, J = 7.6 Hz, 3H), 7.10 – 6.96 (m, 1H), 3.88 (s, 3H).	DMSO	458.9 (M+2)	2.65	Method C	100	Method N1

374

		486.92	^{1}H NMR (300 MHz, DMSO) δ 10.16 (s, 1H), 9.54 (s, 1H), 8.79 (d, J = 9.7 Hz, 1H), 8.71 (s, 2H), 8.26 (d, J = 8.7 Hz, 1H), 7.95 (dd, J = 8.7, 3.7 Hz, 2H), 7.56 (dd, J = 11.7, 6.4 Hz, 1H), 7.43 (d, J = 15.2 Hz, 2H), 7.22 – 7.06 (m, 2H), 3.92 (s, 3H), 3.84 (s,	DMSO	486.9 (M+1)	2.48	Method C	100	Method N1
		486.92		DMSO	487.1 (M+1)	2.58	Method C	100	Method N1
		390.84		DMSO	390.9 (M+1)	2.48	Method C	100	Method N1
		539.99	^{1}H NMR (300 MHz, DMSO) δ 10.15 (s, 1H), 9.51 (s, 1H), 8.84 (s, 1H), 8.66 (dd, J = 9.7, 6.5 Hz, 2H), 8.29 – 8.19 (m, 2H), 7.92 (ddd, J = 8.9, 7.5, 4.6 Hz, 4H), 7.65 – 7.48 (m, 4H), 3.64 (s, 6H), 3.35 (s, 2H).	DMSO	539.9 (M+1)	2.23	Method C	100	Method N1

375

		526			526.16 (M+1)	2.55	Method C	94	Method N1
		471.91	^{1}H NMR (300 MHz, DMSO) δ 10.03 (s, 1H), 9.56 (d, J = 2.1 Hz, 1H), 8.77 – 8.66 (m, 3H), 8.64 (s, 1H), 8.24 (ddd, J = 8.7, 6.6, 2.6 Hz, 2H), 8.13 (s, 1H), 7.96 – 7.90 (m, 1H), 7.62 – 7.52 (m, 2H), 7.01 (d, J = 8.7 Hz, 1H), 3.94 (s, 3H), 2.78 (s, 3H).	$CDCl_3$	471.9 (M+1)	2.93	Method C	100	Method N1
		474.34	^{1}H NMR (300 MHz, DMSO) δ 10.09 (s, 1H), 9.53 (s, 1H), 8.77 (s, 1H), 8.67 (dd, J = 12.3, 4.1 Hz, 3H), 8.35 (d, J = 2.3 Hz, 1H), 8.27 – 8.13 (m, 2H), 8.02 – 7.88 (m, 2H), 7.72 (d, J = 8.8 Hz, 1H), 7.55 (dd, J = 7.7, 4.6 Hz, 1H), 7.00 (d, J = 8.6 Hz, 1H), 3.	DMSO	474.02 (M+1)	2.72	Method C	100	Method N1
		442.88		DMSO	443.1 (M+1)	2.37	Method C	100	Method N1

376

		465.91	^{1}H NMR (300 MHz, DMSO) δ 10.12 (s, 1H), 9.54 (s, 1H), 8.75 – 8.63 (m, 3H), 8.20 (dd, J = 8.2, 5.6 Hz, 2H), 8.09 (d, J = 8.5 Hz, 2H), 8.01 (d, J = 8.5 Hz, 2H), 7.88 (s, 1H), 7.55 (d, J = 9.1 Hz, 2H), 2.76 (s, 3H).	DMSO	466.1 (M+1)	2.78	Method C	100	Method N1
		457.89	^{1}H NMR (300 MHz, DMSO) d 10.18 (s, 1H), 9.51 (s, 1H), 8.92 (s, 1H), 8.67 (dd, J = 12.7, 5.8 Hz, 2H), 8.39 - 8.16 (m, 3H), 7.91 (dd, J = 14.8, 5.7 Hz, 2H), 7.65 - 7.45 (m, 3H), 7.35 (s, 1H), 3.94 (s, 3H).	DMSO	458.1 (M+1)	2.62	Method C	100	Method N1
		514.93	^{1}H NMR (300 MHz, DMSO) d 10.19 (s, 1H), 9.52 (s, 1H), 8.86 (s, 1H), 8.67 (dd, J = 10.1, 3.4 Hz, 2H), 8.28 (ddd, J = 9.4, 7.7, 2.1 Hz, 2H), 8.06 - 7.75 (m, 2H), 7.54 (dd, J = 9.0, 4.1 Hz, 4H), 3.99 (s, 3H), 3.82 (s, 3H)	DMSO	515.1 (M+1)	2.54	Method C	100	Method N1
		451.88	^{1}H NMR (300 MHz, DMSO) d 10.16 (s, 1H), 9.50 (s, 1H), 8.86 (s, 1H), 8.66 (dd, J = 15.2, 6.9 Hz, 2H), 8.35 - 8.16 (m, 2H), 8.15 - 7.82 (m, 6H), 7.55 (dd, J = 11.1, 6.0 Hz, 2H).	DMSO	452.0 (M+1)	2.61	Method C	96	Method N1

377

		436.47			437.2 (M+1)	2.08	Method C	95	Method N1
		421.45			422.2 (M+1)	1.8	Method C	100	Method N1
		449.91	^{1}H NMR (300 MHz, DMSO) δ 10.06 (s, 1H), 9.52 (d, *J* = 1.3 Hz, 1H), 8.73 – 8.64 (m, 2H), 8.51 (d, *J* = 6.5 Hz, 1H), 8.27 (dd, *J* = 6.9, 2.6 Hz, 1H), 7.96 – 7.86 (m, 1H), 7.82 (s, 1H), 7.64 (d, *J* = 8.4 Hz, 1H), 7.57 (t, *J* = 3.9 Hz, 1H), 7.52 (t, *J* = 9.1 Hz, 1H), 3.69 (s, 2H), 3.62 (s, 4H), 2.44 (s, 4H).	DMSO	449.9 (M+1)	2.13	Method C	100	Method N3
		457.89	^{1}H NMR (300 MHz, DMSO) δ 10.12 (s, 1H), 9.55 (s, 1H), 8.76 (d, *J* = 2.5 Hz, 1H), 8.72 – 8.65 (m, 2H), 8.62 (d, *J* = 8.6 Hz, 1H), 8.34 – 8.26 (m, 2H), 8.15 (d, *J* = 1.6 Hz, 1H), 8.02 (d, *J* = 8.7 Hz, 1H), 7.97 – 7.88 (m, 1H), 7.61 – 7.49 (m, 2H), 6.99 (d, *J* = 8.7 Hz, 1H), 3.94 (s, 3H).	DMSO	458.1 (M+1)	2.51	Method C	100	Method N2

378

		462.95	^{1}H NMR (300 MHz, CD_3OD) δ 9.40 (s, 1H), 8.66 (d, *J* = 8.0 Hz, 1H), 8.56 (s, 1H), 8.19 – 8.09 (m, 2H), 7.74 (s, 1H), 7.72 – 7.65 (m, 1H), 7.54 – 7.45 (m, 2H), 7.24 (t, *J* = 9.0 Hz, 1H), 3.68 (d, *J* = 8.0 Hz, 2H), 2.75 – 2.41 (m, 8H), 2.30 (s, 3H).	CD_3OD	463.0 (M+1)	1.71	Method C	100	Method N3
		433.91			434.0 (M+1)	1.73	Method C	100	Method N3
		435.92			436.0 (M+1)	1.84	Method C	100	Method N3
		430.865	^{1}H NMR (300 MHz, DMSO) δ 10.01 (s, 1H), 9.52 (d, *J* = 1.3 Hz, 1H), 8.72 – 8.60 (m, 2H), 8.49 (d, *J* = 8.6 Hz, 1H), 8.44 (s, 1H), 8.28 (dd, *J* = 6.9, 2.6 Hz, 1H), 8.15 (s, 1H), 8.03 (d, *J* = 1.5 Hz, 1H), 7.95 – 7.83 (m, 2H), 7.60 – 7.45 (m, 2H), 3.91 (s, 3H).	DMSO	431.0 (M+1)	2.12	Method C	100	Method N2

379

		465.97	^{1}H NMR (300 MHz, CD_3OD) δ 9.56 – 9.50 (m, 1H), 8.79 (dt, *J* = 8.1, 1.6 Hz, 1H), 8.63 (dd, *J* = 4.9, 1.7 Hz, 1H), 8.30 (s, 1H), 8.19 (dd, *J* = 6.7, 2.6 Hz, 1H), 7.91 (d, *J* = 1.1 Hz, 2H), 7.80 (ddd, *J* = 9.0, 4.2, 2.7 Hz, 1H), 7.56 (dd, *J* = 8.0, 4.9 Hz, 1H), 7.33 (t, *J* = 9.0 Hz, 1H), 3.75 (s, 2H), 2.84 – 2.66 (m, 8H).	CD_3OD	466.0 (M+1)	2.46	Method C	94	Method N3
		491.94	^{1}H NMR (300 MHz, DMSO) δ 10.00 (s, 1H), 9.52 (s, 1H), 8.73 – 8.63 (m, 2H), 8.42 (s, 1H), 8.26 (dd, *J* = 6.8, 2.6 Hz, 1H), 7.92 (ddd, *J* = 6.8, 4.2, 2.0 Hz, 1H), 7.85 (s, 2H), 7.60 – 7.50 (m, 2H), 3.56 – 3.43 (m, 9H), 3.07 (t, *J* = 7.6 Hz, 2H), 2.79 (t, *J* = 7.7 Hz, 2H).	DMSO	491.9 (M+1)	2	Method C	93	Method N1
		463.93	^{1}H NMR (300 MHz, DMSO) δ 9.99 (s, 1H), 9.54 (s, 1H), 8.67 (d, *J* = 5.3 Hz, 2H), 8.30 – 8.22 (m, 2H), 7.96 – 7.87 (m, 1H), 7.73 (s, 1H), 7.60 – 7.46 (m, 2H), 3.60 (s, 6H), 2.71 (s, 3H), 2.41 (s, 4H).	DMSO	464.0 (M+1)	2.52	Method C	100	Method N3
		419.43	^{1}H NMR (300 MHz, DMSO) δ 9.41 (d, *J* = 1.4 Hz, 1H), 9.15 (d, *J* = 1.7 Hz, 1H), 8.74 - 8.64 (m, 3H), 8.55 (dt, *J* = 7.9, 1.8 Hz, 1H), 8.42 (dd, *J* = 8.7, 2.0 Hz, 1H), 8.36 - 8.29 (m, 1H), 8.15 (d, *J* = 8.7 Hz, 1H), 7.90 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.61 (dd, *J* = 8.0, 4.8 Hz, 1H), 7.53 (dd, *J* = 7.9, 4.8 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 1H), 7.03 (t, *J* = 7.5 Hz, 1H), 6.93 (d, *J* = 7.7 Hz, 1H).	DMSO	420.1 (M+1)	2.12	Method C	99	Method N4

380

umber	Starting Material 1	Starting Material 2	Product	Salt type	^{1}H NMR	^{1}H NMR Solvent	Purity Percent	Method of Coupling
629					^{1}H NMR (400 MHz, DMSO) δ 10.20 (s, 1H), 9.54 (s, 1H), 8.87 (s, 1H), 8.74 – 8.65 (m, 2H), 8.31 – 8.23 (m, 2H), 8.04 – 7.85 (m, 4H), 7.64 – 7.49 (m, 4H).	DMSO	>98	N5
630					^{1}H NMR (400 MHz, DMSO) δ 10.20 (s, 1H), 9.54 (d, *J* = 1.4 Hz, 1H), 8.86 (s, 1H), 8.76 – 8.64 (m, 2H), 8.26 (dd, *J* = 6.8, 2.3 Hz, 2H), 8.03 – 7.89 (m, 4H), 7.70 – 7.52 (m, 4H).	DMSO	>98	N5
631					^{1}H NMR (400 MHz, DMSO) δ 10.20 (s, 1H), 9.54 (d, *J* = 1.4 Hz, 1H), 8.86 (s, 1H), 8.76 – 8.64 (m, 2H), 8.26 (dd, *J* = 6.8, 2.3 Hz, 2H), 8.03 – 7.89 (m, 4H), 7.70 – 7.52 (m, 4H).	DMSO	>98	N5
632					^{1}H NMR (400 MHz, DMSO) δ 10.22 – 10.11 (m, 1H), 9.54 (s, 1H), 8.86 – 8.77 (m, 1H), 8.74 – 8.65 (m, 2H), 8.30 – 8.17 (m, 2H), 8.01 – 7.90 (m, 2H), 7.74 – 7.66 (m, 2H), 7.60 – 7.51 (m, 2H), 7.51 – 7.42 (m, 1H), 7.28 (d, *J* = 7.5 Hz, 1H), 2.45 (s, 3H).	DMSO	>98	N5

633					^{1}H NMR (400 MHz, DMSO) δ 10.20 (s, 1H), 9.61 – 9.53 (m, 1H), 8.92 (s, 1H), 8.78 – 8.67 (m, 2H), 8.43 – 8.24 (m, 3H), 8.14 – 7.89 (m, 3H), 7.84 – 7.76 (m, 1H), 7.66 – 7.53 (m, 2H).	DMSO	>98	N5
634					^{1}H NMR (400 MHz, DMSO) δ 10.20 (s, 1H), 9.55 (d, *J* = 1.2 Hz, 1H), 8.89 (s, 1H), 8.75 – 8.67 (m, 2H), 8.35 – 8.22 (m, 2H), 8.00 (d, *J* = 8.7 Hz, 1H), 7.96 – 7.90 (m, 1H), 7.84 – 7.75 (m, 2H), 7.66 – 7.52 (m, 3H), 7.34 – 7.27 (m, 1H).	DMSO	>98	N5
635					^{1}H NMR (400 MHz, DMSO) δ 10.27 (s, 1H), 9.54 (d, *J* = 1.2 Hz, 1H), 8.94 (s, 1H), 8.77 – 8.66 (m, 3H), 8.40 – 8.21 (m, 4H), 7.99 (d, *J* = 8.9 Hz, 1H), 7.88 (t, *J* = 8.0 Hz, 2H), 7.61 – 7.50 (m, 2H).	DMSO	>98	N5
636					^{1}H NMR (400 MHz, DMSO) δ 10.13 (s, 1H), 9.56 (s, 1H), 8.77 – 8.68 (m, 2H), 8.65 (s, 1H), 8.27 (dd, *J* = 6.9, 2.6 Hz, 1H), 8.04 – 7.97 (m, 2H), 7.96 – 7.88 (m, 1H), 7.70 – 7.43 (m, 6H).	DMSO	>98	N5

382

637					^{1}H NMR (400 MHz, DMSO) δ 10.10 (s, 1H), 9.56 (s, 1H), 8.76 – 8.68 (m, 2H), 8.63 (s, 1H), 8.28 (dd, *J* = 6.7, 2.7 Hz, 1H), 8.05 (dd, *J* = 8.7, 1.8 Hz, 1H), 8.00 – 7.90 (m, 2H), 7.70 – 7.43 (m, 4H), 7.21 (d, *J* = 8.1 Hz, 1H), 7.14 (t, *J* = 7.4 Hz, 1H), 3.82 (s, 3H).	DMSO	>98	N5
638					^{1}H NMR (400 MHz, DMSO) δ 10.16 (s, 1H), 9.54 (s, 1H), 8.81 (s, 1H), 8.74 – 8.64 (m, 2H), 8.30 – 8.17 (m, 2H), 8.01 – 7.87 (m, 4H), 7.61 – 7.51 (m, 2H), 7.42 (t, *J* = 8.8 Hz, 2H).	DMSO	>98	N5
639					1H NMR (400 MHz, DMSO) δ 10.21 (s, 1H), 9.57 (s, 1H), 8.80 (d, J = 1.8 Hz, 1H), 8.76 – 8.69 (m, 2H), 8.27 (dd, J = 6.9, 2.6 Hz, 1H), 8.14 (dd, J = 8.6, 1.8 Hz, 1H), 8.10 – 8.02 (m, 2H), 7.97 – 7.88 (m, 2H), 7.83 (d, J = 6.8 Hz, 1H), 7.70 (td, J = 7.6, 1.2 Hz, 1H), 7.63 – 7.52 (m, 2H).	DMSO	>98	N5
640					^{1}H NMR (400 MHz, DMSO) δ 10.12 (s, 1H), 9.55 (s, 1H), 8.77 – 8.66 (m, 2H), 8.62 (s, 1H), 8.25 (dd, *J* = 6.8, 2.3 Hz, 1H), 8.16 (d, *J* = 8.3 Hz, 1H), 7.99 – 7.80 (m, 4H), 7.80 – 7.71 (m, 2H), 7.61 – 7.49 (m, 2H).	DMSO	>98	N5

383

641					1H NMR (400 MHz, DMSO) δ 9.57 (s, 1H), 8.85-8.55 (m, 3H), 8.20-7.95 (m, 3H), 7.85-7.20 (m, 7H)	DMSO	>98	N5
642					^{1}H NMR (400 MHz, DMSO) δ 10.19 (s, 1H), 9.55 (d, J = 1.2 Hz, 1H), 8.83 (s, 1H), 8.74 – 8.66 (m, 2H), 8.32 – 8.23 (m, 2H), 8.02 – 7.89 (m, 2H), 7.61 – 7.53 (m, 2H), 7.05 (d, J = 2.2 Hz, 2H), 6.62 (t, J = 2.1 Hz, 1H), 3.88 (s, 6H).	DMSO	>98	N5
643					^{1}H NMR (400 MHz, DMSO) δ 10.18 (s, 1H), 9.55 (d, J = 2.0 Hz, 1H), 8.81 (d, J = 1.7 Hz, 1H), 8.74 – 8.65 (m, 2H), 8.31 – 8.20 (m, 2H), 8.04 – 7.88 (m, 2H), 7.65 – 7.53 (m, 2H), 7.42 – 7.34 (m, 1H), 7.23 – 7.09 (m, 2H), 6.83 (dd, J = 8.3, 1.9 Hz, 1H), 3.02 (s, 6H).	DMSO	>98	N5
644					1H NMR (400 MHz, DMSO) δ 10.14 (s, 1H), 9.55 (s, 1H), 8.77 – 8.68 (m, 2H), 8.65 (d, J = 1.5 Hz, 1H), 8.28 (dd, J = 6.9, 2.6 Hz, 1H), 8.05 (dd, J = 8.6, 1.7 Hz, 1H), 8.01 – 7.90 (m, 2H), 7.60 – 7.51 (m, 2H), 7.29 – 7.21 (m, 1H), 7.18 (dd, J = 8.3, 1.6 Hz, 1H), 7.12 (dd, J = 7.6, 1.6 Hz, 1H), 3.89 (s, 3H), 3.58 (s, 3H).	DMSO	>98	N5

384

645					1H NMR (400 MHz, DMSO) δ 10.09 (s, 1H), 9.56 (s, 1H), 8.74 – 8.67 (m, 2H), 8.64 (s, 1H), 8.28 (dd, J = 6.9, 2.6 Hz, 1H), 8.06 (dd, J = 8.6, 1.7 Hz, 1H), 7.98 – 7.89 (m, 2H), 7.62 – 7.51 (m, 2H), 7.14 (d, J = 9.0 Hz, 1H), 7.09 (d, J = 3.1 Hz, 1H), 7.02 (dd, J = 8.9, 3.1 Hz, 1H), 3.81 (s, 3H), 3.76 (s, 3H).	DMSO	>98	N5
646					1H NMR (400 MHz, DMSO) δ 9.99 (s, 1H), 9.56 (d, J = 0.9 Hz, 1H), 8.71 (dd, J = 7.1, 1.6 Hz, 2H), 8.46 (d, J = 1.5 Hz, 1H), 8.29 (dd, J = 6.9, 2.6 Hz, 1H), 8.00 – 7.87 (m, 2H), 7.73 (dd, J = 8.5, 1.7 Hz, 1H), 7.63 – 7.47 (m, 2H), 7.41 (t, J = 8.4 Hz, 1H), 6.84 (d, J = 8.5 Hz, 2H), 3.77 – 3.66 (m, 6H).	DMSO	>98	N5
647					^{1}H NMR (400 MHz, DMSO) δ 10.06 – 9.96 (m, 1H), 9.52 (s, 1H), 8.75 – 8.62 (m, 3H), 8.40 – 8.33 (m, 1H), 8.28 – 8.22 (m, 1H), 8.22 – 8.14 (m, 1H), 7.97 – 7.85 (m, 3H), 7.64 – 7.49 (m, 2H), 7.16 (s, 1H).	DMSO	>98	N5
648					^{1}H NMR (400 MHz, DMSO) δ 10.10 (s, 1H), 9.54 (s, 1H), 8.85 (s, 1H), 8.77 – 8.65 (m, 2H), 8.32 (d, *J* = 8.7 Hz, 1H), 8.26 (dd, *J* = 6.8, 2.6 Hz, 1H), 8.12 (s, 1H), 7.94 (d, *J* = 8.7 Hz, 2H), 7.86 – 7.76 (m, 2H), 7.64 – 7.54 (m, 2H).	DMSO	>98	N5

385

649					1H NMR (400 MHz, DMSO) δ 10.20 (s, 1H), 9.53 (s, 1H), 8.78 (s, 1H), 8.71 – 8.64 (m, 2H), 8.26 – 8.19 (m, 2H), 7.95 – 7.90 (m, 2H), 7.77 – 7.69 (m, 2H), 7.60 – 7.53 (m, 2H), 7.26 (t, *J* = 3.7 Hz, 1H).	DMSO	>98	N5
650					^{1}H NMR (400 MHz, DMSO) δ 10.12 (s, 1H), 9.55 (d, *J* = 2.2 Hz, 1H), 8.75 – 8.67 (m, 3H), 8.33 – 8.23 (m, 2H), 8.13 (dd, *J* = 8.7, 1.8 Hz, 1H), 8.00 – 7.90 (m, 3H), 7.63 – 7.51 (m, 2H), 7.22 (dd, *J* = 7.3, 5.0 Hz, 1H), 3.95 (s, 3H).	DMSO	>98	N5
651					^{1}H NMR (400 MHz, DMSO) δ 10.22 (s, 1H), 9.53 (s, 1H), 8.97 (s, 1H), 8.75 (d, *J* = 5.5 Hz, 2H), 8.73 – 8.64 (m, 2H), 8.38 – 8.30 (m, 1H), 8.24 (d, *J* = 6.8 Hz, 1H), 8.05 – 7.97 (m, 1H), 7.97 – 7.88 (m, 3H), 7.63 – 7.51 (m, 2H).	DMSO	>98	N5
652					1H NMR (400 MHz, DMSO) δ 10.05 (s, 1H), 9.50 (s, 1H), 9.33 (s, 2H), 9.26 (s, 1H), 8.90 (s, 1H), 8.69 (d, J = 3.6 Hz, 1H), 8.64 (d, J = 8.0 Hz, 1H), 8.33 (d, J = 8.6 Hz, 1H), 8.22 (dd, J = 6.7, 2.0 Hz, 1H), 7.96 (d, J = 8.7 Hz, 1H), 7.93 – 7.86 (m, 1H), 7.61 – 7.48 (m, 2H).	DMSO	>98	N5

386

653					^{1}H NMR (400 MHz, DMSO) δ 10.10 (s, 1H), 9.55 (d, *J* = 1.2 Hz, 1H), 8.77 – 8.67 (m, 2H), 8.61 (s, 1H), 8.26 (dd, *J* = 6.9, 2.6 Hz, 1H), 8.12 (dd, *J* = 8.7, 1.8 Hz, 1H), 8.01 – 7.89 (m, 3H), 7.62 – 7.51 (m, 2H), 4.02 (s, 3H), 4.00 (s, 3H).	DMSO	>98	N5
654					^{1}H NMR (400 MHz, DMSO) δ 10.09 (s, 1H), 9.56 (s, 1H), 8.77 – 8.68 (m, 2H), 8.65 (d, *J* = 1.6 Hz, 1H), 8.30 (dd, *J* = 6.9, 2.6 Hz, 1H), 8.17 (dd, *J* = 8.7, 1.7 Hz, 1H), 7.99 – 7.88 (m, 2H), 7.61 – 7.50 (m, 2H), 7.42 – 7.33 (m, 2H), 7.21 – 7.08 (m, 2H), 2.53 (s, 6H).	DMSO	>98	N5
655					^{1}H NMR (400 MHz, DMSO) δ 10.08 (s, 1H), 9.55 (s, 1H), 8.74 – 8.66 (m, 2H), 8.63 (s, 1H), 8.26 (dd, *J* = 6.8, 2.5 Hz, 1H), 8.12 (d, *J* = 8.7 Hz, 1H), 7.97 – 7.88 (m, 3H), 7.62 – 7.51 (m, 2H), 6.61 (d, *J* = 8.1 Hz, 1H), 3.97 (s, 3H), 3.96 (s, 3H).	DMSO	>98	N5
656					^{1}H NMR (400 MHz, DMSO) δ 10.21 (s, 1H), 9.54 (d, *J* = 2.0 Hz, 1H), 8.91 (s, 1H), 8.76 – 8.65 (m, 2H), 8.31 (d, *J* = 8.8 Hz, 1H), 8.26 (dd, *J* = 6.8, 2.6 Hz, 1H), 8.15 – 7.89 (m, 7H), 7.61 – 7.52 (m, 2H), 7.46 (s, 1H).	DMSO	>98	N5

387

657					^{1}H NMR (400 MHz, DMSO) δ 10.21 (s, 1H), 9.54 (d, *J* = 2.0 Hz, 1H), 8.91 (s, 1H), 8.76 – 8.65 (m, 2H), 8.31 (d, *J* = 8.8 Hz, 1H), 8.26 (dd, *J* = 6.8, 2.6 Hz, 1H), 8.15 – 7.89 (m, 7H), 7.61 – 7.52 (m, 2H), 7.46 (s, 1H).	DMSO	>98	N5
658					^{1}H NMR (400 MHz, DMSO) δ 10.20 (s, 1H), 9.54 (s, 1H), 8.88 (s, 1H), 8.79 – 8.61 (m, 2H), 8.34 – 8.22 (m, 2H), 8.05 – 7.84 (m, 4H), 7.72 (t, *J* = 8.0 Hz, 1H), 7.65 – 7.53 (m, 2H), 7.47 (d, *J* = 8.4 Hz, 1H).	DMSO	>98	N5
659					1H NMR (400 MHz, DMSO) δ 10.06 (s, 1H), 9.53 (s, 1H), 8.75 (s, 1H), 8.75 – 8.66 (m, 3H), 8.28 – 8.21 (m, 1H), 8.20 (dd, *J* = 7.7, 1.8 Hz, 1H), 8.06 (dd, *J* = 8.9, 2.5 Hz, 1H), 7.96 – 7.90 (m, 2H), 7.58 – 7.54 (m, 2H), 6.81 (d, *J* = 8.9 Hz, 1H), 3.11 (s, 6H).	DMSO	>98	N5
660					^{1}H NMR (400 MHz, DMSO) δ 10.15 (s, 1H), 9.54 (s, 1H), 8.91 (s, 1H), 8.76 (s, 1H), 8.74 – 8.66 (m, 2H), 8.39 (d, *J* = 2.7 Hz, 1H), 8.37 – 8.30 (m, 1H), 8.26 (dd, *J* = 6.8, 2.6 Hz, 1H), 8.03 – 7.97 (m, 1H), 7.97 – 7.90 (m, 1H), 7.85 (d, *J* = 1.9 Hz, 1H), 7.62– 7.52 (m, 2H), 3.98 (s, 3H).	DMSO	>98	N5

388

661					^{1}H NMR (400 MHz, DMSO) δ 10.06 (s, 1H), 9.52 (d, *J* = 1.3 Hz, 1H), 8.76 (d, *J* = 19.6 Hz, 1H), 8.73 – 8.61 (m, 3H), 8.29 – 8.16 (m, 3H), 7.99 – 7.87 (m, 2H), 7.61 – 7.51 (m, 2H), 6.98 (d, *J* = 8.6 Hz, 1H), 4.39 (q, *J* = 7.0 Hz, 2H), 1.37 (t, *J* = 7.0 Hz, 3H).	DMSO	>98	N5
662					^{1}H NMR (400 MHz, DMSO) δ 10.11 (s, 1H), 9.53 (dd, *J* = 2.1, 0.7 Hz, 1H), 8.75 (d, *J* = 1.9 Hz, 1H), 8.73 – 8.64 (m, 2H), 8.25 (dd, *J* = 6.9, 2.6 Hz, 1H), 8.19 (dd, *J* = 8.7, 1.9 Hz, 1H), 7.97 – 7.89 (m, 2H), 7.61 – 7.50 (m, 3H), 7.41 (dd, *J* = 8.1, 1.9 Hz, 1H), 7.11 (d, J = 8.1 Hz, 1H), 6.13 (s, 2H).	DMSO	>98	N5
663					^{1}H NMR (400 MHz, DMSO) δ 10.19 (s, 1H), 9.54 (s, 1H), 8.85 (s, 1H), 8.76 – 8.66 (m, 2H), 8.33 – 8.22 (m, 2H), 8.00 – 7.89 (m, 2H), 7.62 – 7.52 (m, 3H), 7.43 (s, 1H), 7.14 (s, 1H), 3.91 (s, 3H).	DMSO	>98	N5
664					^{1}H NMR (400 MHz, DMSO) δ 10.16 (s, 1H), 9.52 (d, *J* = 1.3 Hz, 1H), 8.89 – 8.81 (m, 1H), 8.73 – 8.64 (m, 2H), 8.37 – 8.28 (m, 1H), 8.28 – 8.21 (m, 1H), 8.01 – 7.86 (m, 2H), 7.81 – 7.69 (m, 2H), 7.60 – 7.51 (m, 2H), 7.33 (s, 1H), 3.97 (s, 3H).	DMSO	>98	N5

389

665					1H NMR (400 MHz, DMSO) δ 10.19 (s, 1H), 9.53 (d, J = 1.9 Hz, 1H), 8.89 (s, 1H), 8.73 – 8.61 (m, 2H), 8.57 (d, J = 4.5 Hz, 1H), 8.34 – 8.18 (m, 2H), 8.09 – 7.86 (m, 5H), 7.62 – 7.49 (m, 2H), 2.88 – 2.80 (m, 4H).	DMSO	>98	N5
666				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.57 (s, 1H), 9.52 (d, *J* = 1.6 Hz, 1H), 9.21 (s, 2H), 9.08 – 9.02 (m, 1H), 9.02 – 8.96 (m, 1H), 8.89 (dd, *J* = 5.2, 1.5 Hz, 1H), 8.39 – 8.30 (m, 1H), 8.25 – 8.18 (m, 1H), 8.07 – 7.87 (m, 3H), 7.56 (t, *J* = 9.1 Hz, 1H).	DMSO	>98	N5
667				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.78 (s, 1H), 9.53 (s, 1H), 9.16 – 9.02 (m, 2H), 8.99 – 8.88 (m, 1H), 8.66 – 8.55 (m, 1H), 8.38 (d, *J* = 8.2 Hz, 1H), 8.20 (d, *J* = 5.0 Hz, 1H), 8.04 (dt, *J* = 27.3, 13.6 Hz, 7H), 7.57 (t, *J* = 8.8 Hz, 1H), 2.84 (d, *J* = 3.8 Hz, 3H).	DMSO	>98	N5
668				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.49 (s, 1H), 9.53 (d, *J* = 1.5 Hz, 1H), 8.99 – 8.83 (m, 3H), 8.34 – 8.25 (m, 1H), 8.21 (dd, *J* = 6.8, 2.6 Hz, 1H), 8.03 (d, *J* = 8.7 Hz, 1H), 7.98 – 7.91 (m, 1H), 7.86 (dd, *J* = 7.8, 5.2 Hz, 1H), 7.78 – 7.70 (m, 2H), 7.57 (t, *J* = 9.1 Hz, 1H), 7.47 (t, J = 7.6 Hz, 1H), 7.29 (d, J = 7.5 Hz, 1H), 2.45 (s, 6H).	DMSO	>98	N5

390

669				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.22 (s, 1H), 9.55 (d, *J* = 1.4 Hz, 1H), 8.81 – 8.70 (m, 3H), 8.25 (dd, *J* = 6.8, 2.6 Hz, 1H), 8.13 – 8.05 (m, 1H), 7.99 (d, *J* = 8.7 Hz, 1H), 7.97 – 7.89 (m, 1H), 7.64 (dd, *J* = 7.9, 4.9 Hz, 1H), 7.61 – 7.49 (m, 2H), 7.37 – 7.26 (m, 2H), 2.41 (s, 3H).	DMSO	>98	N5
670				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.77 (s, 1H), 9.52 (d, *J* = 1.6 Hz, 1H), 9.09 – 8.95 (m, 2H), 8.90 (dd, *J* = 5.2, 1.5 Hz, 1H), 8.41 – 8.29 (m, 1H), 8.23 (dd, *J* = 6.8, 2.6 Hz, 1H), 8.05 (d, *J* = 8.7 Hz, 1H), 8.01 – 7.88 (m, 2H), 7.56 (t, *J* = 9.1 Hz, 1H), 7.50 – 7.38 (m, 2H), 7.32 (d, J = 8.2 Hz, 1H), 3.97 (s, 3H), 2.23 (s, 3H).	DMSO	>98	N5
671				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.77 (s, 1H), 9.52 (d, *J* = 1.6 Hz, 1H), 9.09 – 8.95 (m, 2H), 8.90 (dd, *J* = 5.2, 1.5 Hz, 1H), 8.41 – 8.29 (m, 1H), 8.23 (dd, *J* = 6.8, 2.6 Hz, 1H), 8.05 (d, *J* = 8.7 Hz, 1H), 8.01 – 7.88 (m, 2H), 7.56 (t, *J* = 9.1 Hz, 1H), 7.50 – 7.38 (m, 2H), 7.32 (d, J = 8.2 Hz, 1H), 3.97 (s, 3H), 2.23 (s, 3H).	DMSO	>98	N5
672				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.67 (s, 1H), 9.47 (d, *J* = 1.6 Hz, 1H), 9.04 – 8.94 (m, 2H), 8.89 (dd, *J* = 5.3, 1.5 Hz, 1H), 8.26 (dd, *J* = 8.8, 1.9 Hz, 1H), 8.18 (dd, *J* = 6.8, 2.6 Hz, 1H), 8.09 – 8.00 (m, 1H), 8.00 – 7.87 (m, 3H), 7.86 – 7.77 (m, 1H), 7.68 – 7..57 (m, 1H), 7.53 (t, J = 9.1 Hz, 1H).	DMSO	>98	N5

391

673				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.82 (s, 1H), 9.53 (s, 1H), 9.17 – 9.04 (m, 1H), 9.04 – 8.93 (m, 2H), 8.34 (dd, *J* = 8.7, 1.7 Hz, 1H), 8.18 (dd, *J* = 6.8, 2.6 Hz, 1H), 8.08 (d, *J* = 8.6 Hz, 1H), 8.05 – 7.89 (m, 2H), 7.57 (t, *J* = 9.0 Hz, 1H), 7.53 – 7.44 (m, 3H), 7.09 – 6.98 (m, 1H), 4.82 (dt, J = 11.7, 5.9 Hz, 1H), 1.33 (d, J = 6.0 Hz, 6H).	DMSO	>98	N5
674				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.60 (s, 1H), 9.50 (d, *J* = 1.7 Hz, 1H), 9.11 – 9.02 (m, 1H), 8.99 – 8.91 (m, 1H), 8.76 (d, *J* = 8.8 Hz, 1H), 8.25 (d, *J* = 1.4 Hz, 1H), 8.19 (dd, *J* = 6.8, 2.6 Hz, 1H), 8.10 – 7.92 (m, 4H), 7.82 – 7.72 (m, 1H), 7.65 – 7.56 (m, 1H), 7.52 (t, *J* = 9.1 Hz, 1H).	DMSO	>98	N5
675				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.51 (s, 1H), 9.51 (d, *J* = 1.7 Hz, 1H), 9.07 – 9.00 (m, 1H), 8.93 (dd, *J* = 5.3, 1.4 Hz, 1H), 8.75 (d, *J* = 8.8 Hz, 1H), 8.28 (d, *J* = 1.7 Hz, 1H), 8.21 (dd, *J* = 6.8, 2.6 Hz, 1H), 8.10 (dd, *J* = 8.7, 1.9 Hz, 1H), 8.02 – 7.93 (m, 2H), 7.74 – 7.65 (m, 2H), 7.52 (t, *J* = 9.1 Hz, 1H), 7.40 – 7.31 (m, 1H).	DMSO	>98	N5
676				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.63 (s, 1H), 9.54 (d, *J* = 1.7 Hz, 1H), 9.10 (d, *J* = 8.1 Hz, 1H), 8.95 (dd, *J* = 5.3, 1.4 Hz, 1H), 8.81 (d, *J* = 8.7 Hz, 1H), 8.26 – 8.14 (m, 2H), 8.08 – 7.91 (m, 3H), 7.75 – 7.64 (m, 1H), 7.51 (ddd, *J* = 14.7, 14.2, 6.9 Hz, 2H), 7.44 – 7.34 (m, 1H).	DMSO	>98	N5

392

677				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.52 (s, 1H), 9.60 – 9.49 (m, 1H), 9.37 – 9.31 (m, 1H), 8.99 (d, *J* = 8.3 Hz, 1H), 8.95 – 8.81 (m, 3H), 8.75 (d, *J* = 8.3 Hz, 1H), 8.40 (d, *J* = 1.7 Hz, 1H), 8.30 – 8.18 (m, 2H), 8.04 – 7.87 (m, 3H), 7.56 (t, *J* = 9.1 Hz, 1H).	DMSO	>98	N5
678				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.42 (s, 1H), 9.50 (d, *J* = 1.6 Hz, 1H), 9.38 (s, 2H), 9.30 (s, 1H), 9.00 – 8.92 (m, 1H), 8.92 – 8.86 (m, 1H), 8.76 (d, *J* = 8.7 Hz, 1H), 8.34 (d, *J* = 1.7 Hz, 1H), 8.23 (dd, *J* = 6.8, 2.6 Hz, 1H), 8.15 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.99 – 7.85 (m, 2H), 7.52 (t, *J* = 9.1 Hz, 1H).	DMSO	>98	N5
679				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.47 (s, 1H), 9.58 – 9.49 (m, 1H), 9.21 (s, 2H), 9.09 – 8.98 (m, 1H), 8.92 (d, *J* = 3.8 Hz, 1H), 8.77 (d, *J* = 8.8 Hz, 1H), 8.32 (d, *J* = 1.8 Hz, 1H), 8.27 – 8.20 (m, 1H), 8.15 (dd, *J* = 8.7, 1.8 Hz, 1H), 8.03 – 7.89 (m, 2H), 7.55 (t, *J* = 9.1 Hz, 1H), 4.02 (s, 3H).	DMSO	>98	N5
680					^{1}H NMR (400 MHz, DMSO) δ 10.09 (s, 1H), 9.56 (d, *J* = 1.3 Hz, 1H), 8.75 – 8.67 (m, 2H), 8.60 (d, *J* = 8.7 Hz, 1H), 8.32 (dd, *J* = 6.9, 2.6 Hz, 1H), 8.10 (d, *J* = 1.6 Hz, 1H), 8.03 – 7.87 (m, 4H), 7.60 – 7.50 (m, 2H), 7.12 (d, *J* = 8.8 Hz, 2H), 3.85 (s, 3H).	DMSO	>98	N5

393

681					^{1}H NMR (400 MHz, DMSO) δ 10.05 (s, 1H), 9.55 – 9.46 (m, 1H), 8.69 – 8.60 (m, 2H), 8.56 (d, *J* = 8.7 Hz, 1H), 8.25 (dd, *J* = 6.9, 2.6 Hz, 1H), 8.10 (d, *J* = 1.8 Hz, 1H), 7.96 (dd, *J* = 8.7, 1.9 Hz, 1H), 7.91 – 7.85 (m, 1H), 7.55 – 7.35 (m, 5H), 7.03 – 6.95 (m, 1H), 3.83 (s, 3H).	DMSO	>98	N5
682					^{1}H NMR (400 MHz, DMSO) δ 10.09 (s, 1H), 9.55 (d, *J* = 1.9 Hz, 1H), 8.74 – 8.67 (m, 2H), 8.57 (d, *J* = 8.7 Hz, 1H), 8.32 (dd, *J* = 6.9, 2.6 Hz, 1H), 8.00 – 7.91 (m, 2H), 7.80 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.60 – 7.41 (m, 4H), 7.21 (d, *J* = 7.8 Hz, 1H), 7.12 (td, *J* = 7.4, 0.9 Hz, 1H), 3.84 (s, 3H).	DMSO	>98	N5
683					^{1}H NMR (400 MHz, DMSO) δ 10.10 (s, 1H), 9.55 (s, 1H), 8.74 – 8.65 (m, 2H), 8.56 (d, *J* = 8.6 Hz, 1H), 8.35 – 8.26 (m, 1H), 7.99 – 7.89 (m, 2H), 7.81 (s, 1H), 7.70 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.63 – 7.47 (m, 6H), 7.40 (s, 1H).	DMSO	>98	N5
684					^{1}H NMR (400 MHz, DMSO) δ 10.16 (s, 1H), 9.61 – 9.53 (m, 1H), 8.76 – 8.62 (m, 3H), 8.35 – 8.28 (m, 1H), 8.24 (d, *J* = 1.8 Hz, 1H), 8.16 – 7.99 (m, 6H), 7.99 – 7.92 (m, 1H), 7.63 – 7.51 (m, 2H), 7.45 (s, 1H).	DMSO	>98	N5

394

685					^{1}H NMR (400 MHz, DMSO) δ 10.21 (s, 1H), 9.55 (d, *J* = 1.5 Hz, 1H), 8.78 – 8.62 (m, 3H), 8.31 (dd, *J* = 6.9, 2.6 Hz, 1H), 8.15 – 8.00 (m, 2H), 8.00 – 7.80 (m, 5H), 7.74 – 7.65 (m, 1H), 7.64 – 7.51 (m, 2H).	DMSO	>98	N5
686					^{1}H NMR (400 MHz, DMSO) δ 10.18 (s, 1H), 9.60 – 9.55 (m, 1H), 8.77 – 8.65 (m, 2H), 8.46 (s, 1H), 8.37 – 8.28 (m, 2H), 8.17 – 8.10 (m, 1H), 7.99 – 7.93 (m, 2H), 7.81 – 7.72 (m, 2H), 7.62 – 7.50 (m, 3H).	DMSO	>98	N5
687					^{1}H NMR (400 MHz, DMSO) δ 10.18 (s, 1H), 9.56 (d, *J* = 2.2 Hz, 1H), 8.75 – 8.61 (m, 3H), 8.32 (dd, *J* = 6.8, 2.6 Hz, 1H), 8.07 (s, 1H), 7.99 – 7.91 (m, 1H), 7.91 – 7.85 (m, 1H), 7.82 – 7.75 (m, 1H), 7.61 – 7.50 (m, 3H), 7.47 – 7.36 (m, 2H).	DMSO	>98	N5
688					^{1}H NMR (400 MHz, DMSO) δ 10.14 (s, 1H), 9.60 – 9.53 (m, 1H), 8.74 – 8.61 (m, 3H), 8.31 (dd, *J* = 6.9, 2.6 Hz, 1H), 8.20 (d, *J* = 1.8 Hz, 1H), 8.06 (dd, *J* = 8.7, 1.9 Hz, 1H), 7.99 – 7.90 (m, 1H), 7.86 – 7.77 (m, 2H), 7.65 – 7.48 (m, 3H), 7.37 – 7.26 (m, 1H).	DMSO	>98	N5

395

689					^{1}H NMR (400 MHz, DMSO) δ 10.13 (s, 1H), 9.56 (d, J = 1.5 Hz, 1H), 8.75 – 8.60 (m, 3H), 8.31 (dd, J = 6.9, 2.6 Hz, 1H), 8.15 (d, J = 1.7 Hz, 1H), 8.07 – 7.88 (m, 4H), 7.65 – 7.49 (m, 2H), 7.39 (t, J = 8.8 Hz, 2H).	DMSO	>98	N5
690					^{1}H NMR (400 MHz, DMSO) δ 10.14 (s, 1H), 9.54 (d, J = 1.6 Hz, 1H), 8.76 – 8.60 (m, 3H), 8.34 – 8.25 (m, 1H), 8.21 (d, J = 1.7 Hz, 1H), 8.13 (d, J = 8.4 Hz, 2H), 8.10 – 7.97 (m, 3H), 7.97 – 7.87 (m, 1H), 7.62 – 7.45 (m, 2H).	DMSO	>98	N5
691				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.45 (s, 1H), 9.54 (d, J = 1.6 Hz, 1H), 8.99 – 8.91 (m, 1H), 8.91 – 8.83 (m, 1H), 8.75 (d, J = 8.8 Hz, 1H), 8.42 (s, 1H), 8.31 (t, J = 3.2 Hz, 1H), 8.29 – 8.22 (m, 2H), 8.13 (dd, J = 8.7, 1.8 Hz, 1H), 8.08 (d, J = 7.8 Hz, 1H), 8.03 – 7.92 (m, 2H), 7.86 (dd, J = 8.0, 5.2 Hz, 1H), 7.65 (t, J = 7.7 Hz, 1H), 7.59 – 7.46 (m, 2H).	DMSO	>98	N5
692				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.38 (s, 1H), 9.56 (d, J = 1.5 Hz, 1H), 8.93 (d, J = 8.2 Hz, 1H), 8.85 (dd, J = 5.1, 1.5 Hz, 1H), 8.71 (d, J = 8.8 Hz, 1H), 8.27 (dd, J = 6.8, 2.6 Hz, 1H), 8.21 (d, J = 1.7 Hz, 1H), 8.10 (dd, J = 8.7, 1.8 Hz, 1H), 8.01 – 7.90 (m, 3H), 7.83 (dd, J = 7.8, 5.0 Hz, 1H), 7.64 – 7.46 (m, 4H).	DMSO	>98	N5

396

693				3 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.91 (s, 1H), 9.52 (d, J = 1.5 Hz, 1H), 9.14 (d, J = 8.1 Hz, 1H), 9.00 (dd, J = 5.4, 1.2 Hz, 1H), 8.91 (d, J = 8.8 Hz, 1H), 8.34 (d, J = 5.1 Hz, 1H), 8.20 (dd, J = 6.8, 2.6 Hz, 1H), 8.14 – 8.04 (m, 2H), 8.04 – 7.89 (m, 2H), 7.75 – 7.48 (m, 4H), 3.18 (s, 6H).	DMSO	>98	N5
694				3 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.99 (s, 1H), 9.52 (d, J = 1.7 Hz, 1H), 9.08 (d, J = 8.0 Hz, 1H), 8.97 (dd, J = 5.3, 1.4 Hz, 1H), 8.80 (d, J = 8.8 Hz, 1H), 8.33 (d, J = 2.3 Hz, 1H), 8.18 (dd, J = 6.8, 2.6 Hz, 1H), 8.10 (dd, J = 8.8, 1.8 Hz, 1H), 8.04 – 7.91 (m, 2H), 7.85 (d, J = 8.7 Hz, 2H), 7.56 (t, J = 9.1 Hz, 1H), 7.09 (s, 2H), 3.05 (s, 6H).	DMSO	>98	N5
695				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.67 (s, 1H), 9.53 (d, J = 1.7 Hz, 1H), 9.07 (d, J = 8.2 Hz, 1H), 8.95 (dd, J = 5.3, 1.4 Hz, 1H), 8.78 (d, J = 8.7 Hz, 1H), 8.26 (s, 1H), 8.21 (dd, J = 6.8, 2.6 Hz, 1H), 8.09 (dd, J = 8.7, 1.8 Hz, 1H), 8.04 – 7.92 (m, 2H), 7.79 – 7.67 (m, 2H), 7.55 (t, J = 9.1 Hz, 1H), 7.46 (t, J = 7.6 Hz, 1H), 7.32 (d, J = 7.5 Hz, 1H), 2.45 (s, 3H).	DMSO	>98	N5
696				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.48 (s, 1H), 9.54 (d, J = 1.5 Hz, 1H), 8.93 – 8.84 (m, 1H), 8.71 (d, J = 8.8 Hz, 1H), 8.30 – 8.16 (m, 2H), 8.08 (dd, J = 8.7, 1.8 Hz, 1H), 8.01 – 7.78 (m, 4H), 7.55 (t, J = 9.1 Hz, 1H), 7.39 (d, J = 7.9 Hz, 2H), 2.40 (s, 3H).	DMSO	>98	N5

397

697				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.68 (s, 1H), 9.52 (s, 1H), 9.08 (d, *J* = 8.1 Hz, 1H), 8.95 (d, *J* = 4.7 Hz, 1H), 8.82 (d, *J* = 8.7 Hz, 1H), 8.25 – 8.12 (m, 2H), 8.06 – 7.88 (m, 3H), 7.63 – 7.48 (m, 3H), 7.47 – 7.35 (m, 1H).	DMSO	>98	N5
698				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.47 (s, 1H), 9.53 (d, *J* = 1.6 Hz, 1H), 9.01 – 8.92 (m, 1H), 8.87 (dd, *J* = 5.1, 1.4 Hz, 1H), 8.73 (d, *J* = 8.7 Hz, 1H), 8.24 (dd, *J* = 6.8, 2.6 Hz, 1H), 8.09 (s, 1H), 7.99 – 7.78 (m, 4H), 7.59 – 7.42 (m, 2H), 7.37 – 7.25 (m, 1H).	DMSO	>98	N5
699				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 13.12 (s, 1H), 9.59 (s, 1H), 9.10 (d, *J* = 8.1 Hz, 1H), 9.00 – 8.86 (m, 2H), 8.50 (s, 1H), 8.22 – 8.07 (m, 2H), 8.03 – 7.86 (m, 4H), 7.72 (t, *J* = 7.9 Hz, 1H), 7.28 (t, *J* = 7.1 Hz, 1H).	DMSO	>98	Scheme 4 synthesis using method N6 coupling
700				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 13.19 (s, 1H), 9.64 (s, 1H), 9.21 – 9.08 (m, 1H), 9.07 – 8.89 (m, 2H), 8.51 (s, 1H), 8.38 – 8.26 (m, 2H), 8.16 (d, *J* = 8.5 Hz, 1H), 8.07 – 7.87 (m, 3H), 7.83 – 7.70 (m, 3H), 7.62 (dd, *J* = 14.2, 7.7 Hz, 1H), 7.40 – 7.22 (m, 2H).	DMSO	>98	N6

398

701				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 13.17 (s, 1H), 9.65 (s, 1H), 9.13 – 8.99 (m, 2H), 8.89 (d, *J* = 5.1 Hz, 1H), 8.50 (s, 1H), 8.31 (d, *J* = 8.7 Hz, 1H), 8.21 (d, *J* = 1.8 Hz, 1H), 8.11 (dd, *J* = 8.6, 1.9 Hz, 1H), 8.05 – 7.84 (m, 5H), 7.81 – 7.67 (m, 1H), 7.46 – 7.34 (m, 2H), 7.27 (dd, *J* = 11.8, 4.5 Hz, 1H).	DMSO	>98	N6
702				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 13.19 (s, 1H), 9.66 (d, *J* = 1.8 Hz, 1H), 9.20 (d, *J* = 7.5 Hz, 1H), 9.04 – 8.89 (m, 2H), 8.50 (s, 1H), 8.35 (d, *J* = 8.7 Hz, 1H), 8.17 (s, 1H), 8.11 – 7.86 (m, 4H), 7.86 – 7.68 (m, 2H), 7.65 – 7.52 (m, 1H), 7.52 – 7.39 (m, 2H), 7.39 – 7.23 (m, 1H).	DMSO	>98	N6
703				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 13.17 (s, 1H), 9.62 (d, *J* = 1.6 Hz, 1H), 9.18 (d, *J* = 8.2 Hz, 1H), 9.03 – 8.91 (m, 2H), 8.51 (s, 1H), 8.34 – 8.20 (m, 2H), 8.16 – 7.86 (m, 5H), 7.84 – 7.68 (m, 2H), 7.68 – 7.54 (m, 1H), 7.35 – 7.19 (m, 1H).	DMSO	>98	N6
704				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 13.19 (s, 1H), 9.61 (d, *J* = 1.8 Hz, 1H), 9.32 – 9.22 (m, 1H), 9.02 (dd, *J* = 5.5, 1.2 Hz, 1H), 8.88 (d, *J* = 7.8 Hz, 1H), 8.75 (s, 1H), 8.53 (s, 1H), 8.28 (d, *J* = 8.7 Hz, 1H), 8.16 – 8.07 (m, 2H), 8.01 – 7.88 (m, 3H), 7.85 – 7.76 (m, 1H), 7.76 – 7.65 (m, 1H), 7.54 – 7.42 (m, 1H), 7.37 – 7.19 (m, 2H).	DMSO	>98	N6

399

705				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 13.20 (s, 1H), 9.63 (s, 1H), 9.26 (d, *J* = 8.1 Hz, 1H), 9.01 (d, *J* = 5.0 Hz, 1H), 8.91 (d, *J* = 8.3 Hz, 1H), 8.52 (s, 1H), 8.33 (d, *J* = 8.7 Hz, 1H), 8.21 – 8.06 (m, 2H), 8.06 – 7.87 (m, 3H), 7.72 (t, *J* = 7.7 Hz, 1H), 7.66 – 7.52 (m, 2H), 7.49 – 7.35 (m, 1H), 7.29 (t, *J* = 7.5 Hz, 1H).	DMSO	>98	N6
706				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 9.64 (d, *J* = 1.7 Hz, 1H), 9.25 (d, *J* = 8.2 Hz, 1H), 9.05 – 8.89 (m, 2H), 8.67 – 8.45 (m, 1H), 8.34 (d, *J* = 8.7 Hz, 1H), 8.19 (s, 1H), 8.09 (dd, *J* = 8.0, 5.5 Hz, 1H), 8.04 – 7.88 (m, 3H), 7.79 – 7.62 (m, 2H), 7.56 – 7.35 (m, 2H), 7.35 – 7.23 (m, 1H).	DMSO	>98	N6
707				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 13.18 (s, 1H), 9.62 (d, *J* = 1.6 Hz, 1H), 9.16 (d, *J* = 8.1 Hz, 1H), 9.08 – 8.88 (m, 2H), 8.51 (s, 1H), 8.37 – 8.23 (m, 2H), 8.19 – 8.09 (m, 1H), 8.09 – 7.88 (m, 3H), 7.83 – 7.63 (m, 3H), 7.43 – 7.32 (m, 1H), 7.32 – 7.21 (m, 1H).	DMSO	>98	N6
708				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.52 (s, 1H), 9.56 (d, *J* = 1.6 Hz, 1H), 9.04 (d, *J* = 7.8 Hz, 1H), 8.92 (d, *J* = 4.8 Hz, 1H), 8.78 (d, *J* = 8.8 Hz, 1H), 8.24 (d, *J* = 1.7 Hz, 1H), 8.13 – 8.08 (m, 2H), 8.08 – 7.98 (m, 3H), 7.98 – 7.88 (m, 1H), 7.63 (t, *J* = 8.2 Hz, 1H), 7.42 (t, *J* = 8.8 Hz, 2H), 7.28 – 7.15 (m, 1H).	DMSO	>98	N6/F5 followed by G1

400

709				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.60 (s, 1H), 9.56 (s, 1H), 9.07 (d, *J* = 7.9 Hz, 1H), 8.93 (d, *J* = 4.3 Hz, 1H), 8.77 (d, *J* = 8.7 Hz, 1H), 8.41 (s, 1H), 8.37 – 8.27 (m, 1H), 8.24 (d, *J* = 1.7 Hz, 1H), 8.11 (dd, *J* = 8.7, 1.8 Hz, 1H), 8.08 – 7.94 (m, 3H), 7.79 – 7.65 (m, 2H), 7.41 (t, *J* = 8.8 Hz, 2H).	DMSO	>98	N6/F5 followed by G1
710					1H NMR (DMSO-d6) ppm 3.81(s, 3H), 3.88 (s, 3H), 7.11-7.71 (m, 9H), 7.91 (d, 1H, *J* = 8.7 Hz), 8.23 (d, 1H, J = 8.7 Hz), 8.53-8.64 (m, 2H), 8.87 (d, 1H, J = 1.5 Hz), 9.37 (d, 1H, J = 1.5 Hz), 9.83 (s, 1H)	DMSO	>98	N6/F5 followed by G1
711					1H NMR (DMSO-d6) ppm 3.89 (s, 3H), 7.04 (d, 1H, *J* = 4.1 Hz), 7.48-7.57 (m, 5H), 7.98 (dd, 1H, J = 7.1, 1.7 Hz), 8.26-8.29 (m, 3H), 8.27 (dd, 1H, J = 7.1, 8.7 Hz), 8.78-9.53 (m, 3H), 9.54 (s, 1H), 10.37 (s, 1H)	DMSO	>98	N6/F5 followed by G1
712					1H NMR (DMSO-d6) ppm 3.89 (s, 3H), 7.05 (d, 1H, *J* = 4.1 Hz), 7.48-7.57 (m, 4H), 7.88 (dd, 1H, J = 7.1, 1.7 Hz), 8.25-8.29 (m, 3H), 8.37 (dd, 1H, J = 7.1, 8.7 Hz), 8.78-9.53 (m, 3H), 9.54 (s, 1H), 10.37 (s, 1H)	DMSO	>98	N6/F5 followed by G1

401

713					1H NMR (DMSO-d6) ppm 3.88 (s, 3H), 7.05-7.51 (m, 9H), 7.95 (d, 1H, *J* = 8.7 Hz), 8.26 (d, 1H, J = 8.7 Hz), 8.54-8.88 (m, 3H), 9.38 (s, 1H), 10.19 (s, 1H)	DMSO	>98	N6/F5 followed by G1
714					1H NMR (DMSO-d6) ppm 3.89 (s, 3H), 7.04-7.06 (m, 2H), 7.46-7.76 (m, 8H), 7.95 (d, 2H, *J* = 8.6 Hz), 8.24 (d, 1H, *J* = 1.7 Hz), 8.69-8.87 (m, 3H), 9.56 (s, 1H), 10.18 (s, 1H)	DMSO	>98	N6/F5 followed by G1
715					1H NMR (DMSO-d6) ppm 3.84 (s, 3H), 3.89 (s, 3H), 6.81-7.56 (m, 2H), 7.40-7.70 (m, 7H), 7.95 (d, 1H, *J* = 8.5 Hz), 8.23 (d, 1H, *J* = 1.5 Hz), 8.69-8.89 (m, 3H), 9.58 (s, 1H), 10.06 (s, 1H)	DMSO	>98	N6/F5 followed by G1
716					1H NMR (DMSO-d6) ppm 3.88 (s, 3H), 7.03-7.06 (m, 1H), 7.50-8.39 (m, 10H), 8.86-8.98 (m, 3H), 9.58 (s, 1H), 10.06 (s, 1H)	DMSO	>98	N6/F5 followed by G1
717					1H NMR (DMSO-d6) ppm 3.89 (s, 3H), 7.02-7.07 (m, 2H), 7.31 (s, 1H), 7.47-7.56 (m, 5H), 7.81-8.26 (m, 4H), 8.26-8.90 (m, 3H), 9.57 (s, 1H), 10.27 (s, 1H)	DMSO	>98	N6/F5 followed by G1

718					1H NMR (DMSO-d6) ppm 3.87 (s, 3H), 7.03-7.50 (m, 8H), 7.98 (d, 1H, *J* = 8.7 Hz), 8.30 (d, 1H, J = 8.7 Hz), 8.48-8.91 (m, 3H), 9.30 (s, 1H), 10.19 (s, 1H)	DMSO	>98	N6/F5 followed by G1
719					1H NMR (DMSO-d6) ppm 3.88 (s, 3H), 7.03-7.54 (m, 8H), 7.97 (d, 1H, *J* = 8.7 Hz), 8.28 (d, 1H, J = 8.7 Hz), 8.56-8.86 (m, 3H), 9.40 (s, 1H), 10.23 (s, 1H)	DMSO	>98	N6/F5 followed by G1
720					1H NMR (DMSO-d6) ppm 3.88 (s, 3H), 7.03-7.52 (m, 8H), 7.95 (d, 1H, *J* = 8.7 Hz), 8.26 (d, 1H, J = 8.7 Hz), 8.52-8.85 (m, 3H), 9.38 (s, 1H), 10.17 (s, 1H)	DMSO	>98	N6/F5 followed by G1
721					1H NMR (DMSO-d6) ppm 3.87 (s, 3H), 7.05-7.54 (m, 8H), 8.00 (d, 1H, *J* = 8.7 Hz), 8.27 (d, 1H, J = 8.7 Hz), 8.55-8.87 (m, 3H), 9.38 (s, 1H), 10.34 (s, 1H)	DMSO	>98	N6/F5 followed by G1
722					1H NMR (DMSO-d6) ppm 3.89 (s, 3H), 7.05-7.53 (m, 7H), 7.93 (s, 1H), 7.96 (d, 1H, *J* = 8.7 Hz), 8.16 (s, 1H), 8.26 (d, 1H, J = 8.7 Hz), 8.74-8.89 (m, 3H), 9.55 (s, 1H), 10.27 (s, 1H)	DMSO	>98	N6/F5 followed by G1

403

723					1H NMR (DMSO-d6) ppm 3.88 (s, 3H), 7.03-7.54 (m, 7H), 7.92 (s, 1H), 7.97 (d, 1H, *J* = 8.7 Hz), 8.28 (d, 1H, J = 8.7 Hz), 8.56-8.85 (m, 3H), 9.40 (s, 1H), 10.25 (s, 1H)	DMSO	>98	N6/F5 followed by G1
724					1H NMR (DMSO-d6) ppm 3.88 (s, 3H), 7.03-7.74 (m, 8H), 7.98 (d, 1H, *J* = 8.7 Hz), 8.27 (d, 1H, J = 8.7 Hz), 8.52-8.87 (m, 3H), 9.32 (s, 1H), 10.22 (s, 1H)	DMSO	>98	N6/F5 followed by G1
725					1H NMR (DMSO-d6) ppm 3.89 (s, 3H), 7.05-7.71 (m, 8H), 7.99 (d, 1H, *J* = 8.6 Hz), 8.30 (d, 1H, J = 8.7 Hz), 8.67-8.92 (m, 3H), 9.37 (s, 1H), 10.52 (s, 1H)	DMSO	>98	N6/F5 followed by G1
726					1H NMR (DMSO-d6) ppm 3.89 (s, 3H), 7.03-7.71 (m, 9H), 7.99 (d, 1H, *J* = 8.7 Hz), 8.29 (d, 1H, J = 8.7 Hz), 8.67-8.92 (m, 3H), 9.37 (s, 1H), 10.52 (s, 1H)	DMSO	>98	N6/F5 followed by G1

404

727					1H NMR (DMSO-d6 at 70 °C) ppm 3.89 (s, 3H), 7.02-7.52 (m, 8H), 7.90 (d, 1H, J = 8.5 Hz), 7.93 (s, 1H), 7.99 (d, 1H, J = 8.6 Hz), 8.22 (s, 1H), 8.74-8.91 (m, 3H), 9.52 (s, 1H), 10.23 (s, 1H)	DMSO	>98	N6/F5 followed by G1
728					^{1}H NMR (DMSO-d_6) ppm 2.50 (s, 3H), 3.89 (s, 3H), 7.06 (s, 1H), 7.49-7.85 (m, 9H), 8.01-8.96 (m, 4H), 9.58 (s, 1H), 10.50 (s, 1H)	DMSO	>98	N6/F5 followed by G1
729					^{1}H NMR (DMSO-d_6) ppm 3.89 (s, 3H), 7.04 (br s, 1H), 7.22 (s, 1H), 7.49-8.30 (m, 9H), 8.77-8.91 (m, 3H), 9.55 (s, 1H), 10.37 (s, 1H)	DMSO	>98	N6/F5 followed by G1
730					^{1}H NMR (DMSO-d_6) ppm 3.89 (s, 3H), 7.04 (s, 1H), 7.49-8.32 (m, 9H), 8.91-9.04 (m, 3H), 9.54 (s, 1H), 10.63 (s, 1H)	DMSO	>98	N6/F5 followed by G1
731					^{1}H NMR (DMSO-d_6) ppm 3.87 (s, 3H), 7.03 (s, 1H), 7.44-8.25 (m, 9H), 8.71-8.84 (m, 3H), 9.52 (s, 1H), 10.23 (s, 1H)	DMSO	>98	N6/F5 followed by G1

732					^{1}H NMR (400 MHz, DMSO) δ 12.02 (s, 1H), 10.53 (s, 1H), 9.49 (s, 1H), 9.02 – 8.72 (m, 3H), 8.30 (dd, *J* = 8.7, 1.6 Hz, 1H), 8.05 (dd, *J* = 32.2, 5.3 Hz, 2H), 7.81 – 7.72 (m, 2H), 7.49 (dd, *J* = 8.0, 5.4 Hz, 3H), 7.25 (t, *J* = 9.2 Hz, 1H), 7.11 – 6.98 (m, 1H), 3.89 (s, 3H).	DMSO	>98	N6/F5 followed by G1
733					^{1}H NMR (400 MHz, DMSO) δ 10.54 (s, 1H), 9.43 (s, 1H), 8.86 (d, *J* = 1.8 Hz, 1H), 8.64 (dd, *J* = 21.1, 5.9 Hz, 2H), 8.31 (dd, *J* = 8.7, 1.9 Hz, 1H), 8.01 (d, *J* = 8.7 Hz, 1H), 7.59 – 7.45 (m, 4H), 7.42 – 7.30 (m, 3H), 7.09 – 6.98 (m, 1H), 3.89 (s, 3H).	DMSO	>98	N6/F5 followed by G1
734					^{1}H NMR (400 MHz, DMSO) δ 13.18 (s, 1H), 10.57 (s, 1H), 9.48 (s, 1H), 8.98 (d, *J* =1.3 Hz, 1H), 8.78 (t, *J* =7.1 Hz, 2H), 8.30 (dd, *J* = 8.7, 1.7 Hz, 1H), 8.18 (d, *J* =8.4 Hz, 2H), 8.01 (d, *J*=8.7 Hz, 1H), 7.83 (dd, *J*=8.9, 1.8 Hz, 1H), 7.74 – 7.62 (m, 2H), 7.56 – 7.43 (m, 2H), 7.09 – 7.01 (m, 1H), 3.90 (s, 3H).	DMSO	>98	N6/F5 followed by G1
735					^{1}H NMR (400 MHz, DMSO) δ 11.16 (s, 1H), 10.11 (s, 1H), 9.51 (d, *J* = 1.2 Hz, 1H), 8.91 (d, *J* = 1.7 Hz, 1H), 8.71 – 8.58 (m, 2H), 8.23 (dd, *J* = 8.7, 1.9 Hz, 1H), 7.95 (dd, *J* = 23.9, 5.2 Hz, 2H), 7.60 – 7.34 (m, 5H), 7.06 – 6.98 (m, 1H), 6.06 (s, 2H), 3.89 (s, 3H).	DMSO	>98	N6/F5 followed by G1

406

736					^{1}H NMR (400 MHz, DMSO) δ 10.78 (s, 1H), 10.65 (s, 1H), 10.08 (s, 1H), 9.55 (d, *J* = 2.0 Hz, 1H), 8.88 (d, *J* = 1.8 Hz, 1H), 8.76 – 8.66 (m, 2H), 8.24 (dd, *J* = 8.7, 1.9 Hz, 1H), 7.94 (d, *J*8.7 Hz, 1H), 7.65 (d, *J* = 1.9 Hz, 1H), 7.58 (dd, *J* =7.7, 5.1 Hz, 1H), 7.49 (dt, *J*=4.7, 3.1 Hz, 3H), 7.41 (dd, *J*=8.4, 2.0 Hz, 1H), 7.08 – 6.99 (m, 3H), 3.88 (s, 3H).	DMSO	>98	N6/F5 followed by G1
737				HCl	^{1}H NMR (400 MHz, DMSO) δ 9.93 (s, 1H), 9.40 (s, 1H), 8.86 (d, *J* = 1.7 Hz, 1H), 8.64 (dd, *J* = 28.9, 5.8 Hz, 2H), 8.27 (dd, *J* = 8.7, 1.9 Hz, 1H), 7.96 (d, *J* = 8.7 Hz, 1H), 7.87 (d, *J* = 2.6 Hz, 1H), 7.61 – 7.45 (m, 5H), 7.38 (dd, *J* = 8.8, 2.6 Hz, 1H), 7.24 (d, *J* = 8.9 Hz, 1H), 7.09 – 6.98 (m, 1H), 3.89 (d, *J* = 2.9 Hz, 1H), 3.83 (s, 3H).	DMSO	>98	N6/F5 followed by G1
738					^{1}H NMR (400 MHz, DMSO) δ 10.19 (s, 1H), 9.56 (s, 1H), 8.88 (d, *J* = 1.7 Hz, 1H), 8.75 (t, *J* = 7.2 Hz, 2H), 8.27 (dd, *J* = 8.6, 1.4 Hz, 1H), 8.14 (d, *J* = 1.6 Hz, 1H), 7.97 (d, *J* = 8.7 Hz, 1H), 7.84 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.63 (dd, *J* = 7.7, 4.9 Hz, 1H), 7.48 (dd, *J* = 11.4, 4.0 Hz, 4H), 7.10 – 6.98 (m, 1H), 3.89 (s, 3H), 3.83 (s, 3H).	DMSO	>98	N6/F5 followed by G1
739					^{1}H NMR (400 MHz, DMSO) δ 10.07 (s, 1H), 9.55 (s, 1H), 8.85 (s, 1H), 8.70 (d, *J* = 5.5 Hz, 2H), 8.24 (dd, *J* = 8.7, 1.5 Hz, 1H), 8.10 (d, *J* = 2.4 Hz, 1H), 7.99 – 7.83 (m, 2H), 7.60 – 7.40 (m, 4H), 7.30 (d, *J* = 9.0 Hz, 1H), 7.04 (dd, *J* = 7.1, 4.4 Hz, 1H), 3.90 (s, 3H), 2.29 (s, 3H).	DMSO	>98	N6/F5 followed by G1

407

740					^{1}H NMR (400 MHz, DMSO) δ 10.05 (s, 1H), 9.60 (s, 1H), 8.89 (d, *J* = 1.8 Hz, 1H), 8.71 (dd, *J* = 12.8, 6.3 Hz, 2H), 8.24 (dd, *J* = 8.7, 1.9 Hz, 1H), 7.95 (d, *J* = 8.7 Hz, 1H), 7.68 (d, *J* = 1.7 Hz, 1H), 7.61 – 7.45 (m, 5H), 7.44 – 7.37 (m, 1H), 7.24 (d, *J* = 8.0 Hz, 1H), 3.89 (s, 3H), 3.65 (s, 3H).	DMSO	>98	N6/F5 followed by G1
741					^{1}H NMR (400 MHz, DMSO) δ 10.04 (s, 1H), 9.60 (s, 1H), 8.89 (d, *J* = 1.7 Hz, 1H), 8.71 (dd, *J* = 12.7, 6.3 Hz, 2H), 8.24 (dd, *J* = 8.7, 1.9 Hz, 1H), 7.95 (d, *J* = 8.7 Hz, 1H), 7.68 (d, *J* = 1.7 Hz, 1H), 7.59 – 7.45 (m, 4H), 7.44 – 7.37 (m, 1H), 7.25 (t, *J* = 6.7 Hz, 1H), 7.07 – 6.98 (m, 1H), 3.89 (s, 6H), 2.19 (s, 3H).	DMSO	>98	N6/F5 followed by G1
742					^{1}H NMR (400 MHz, DMSO) δ 9.73 (s, 1H), 9.37 (s, 1H), 8.86 (d, *J* = 1.6 Hz, 1H), 8.63 (d, *J* = 3.4 Hz, 1H), 8.54 (d, *J* = 8.0 Hz, 1H), 8.23 (dd, *J* = 8.7, 1.8 Hz, 1H), 7.91 (d, *J* = 8.7 Hz, 1H), 7.55 – 7.42 (m, 5H), 7.05 – 6.98 (m, 1H), 6.77 (d, *J* = 2.6 Hz, 1H), 6.68 (dd, *J* = 8.6, 2.6 Hz, 1H), 3.89 (s, 3H), 3.85 (s, 3H), 3.79 (s, 3H).	DMSO	>98	N6/F5 followed by G1
743					^{1}H NMR (400 MHz, DMSO) δ 10.25 (s, 1H), 9.56 (s, 1H), 8.84 (d, *J* = 1.7 Hz, 1H), 8.71 (d, *J* = 9.1 Hz, 1H), 8.27 (dd, *J* = 8.7, 1.8 Hz, 1H), 7.99 (d, *J* = 8.7 Hz, 1H), 7.86 – 7.77 (m, 2H), 7.65 – 7.56 (m, 1H), 7.52 – 7.44 (m, 4H), 7.09 – 6.99 (m, 2H), 3.89 (s, 3H).	DMSO	>98	N6/F5 followed by G1

408

744					^{1}H NMR (400 MHz, DMSO) δ 10.42 (s, 1H), 9.55 (s, 1H), 8.87 (d, *J* = 26.7 Hz, 3H), 8.31 (dd, *J* = 8.7, 1.7 Hz, 2H), 8.17 (d, *J* = 1.7 Hz, 2H), 8.02 (d, *J* = 8.7 Hz, 1H), 7.81 (s, 1H), 7.54 – 7.39 (m, 3H), 7.11 – 6.98 (m, 1H), 3.89 (s, 3H).	DMSO	>98	N6/F5 followed by G1
745					^{1}H NMR (400 MHz, DMSO) δ 14.27 (s, 1H), 9.79 (s, 1H), 9.32 (d, *J* = 8.4 Hz, 1H), 8.98 (d, *J* = 5.2 Hz, 1H), 8.34 (dd, *J* = 8.7, 1.8 Hz, 1H), 8.29 – 8.19 (m, 2H), 8.07 (dd, *J* = 14.6, 8.3 Hz, 2H), 7.93 (s, 1H), 7.64 (d, *J* = 5.9 Hz, 1H), 7.52 (t, *J* = 7.9 Hz, 1H), 7.39 (dd, *J* = 8.9, 4.9 Hz, 2H), 7.23 (d, *J* = 5.8 Hz, 1H), 7.08 (dd, *J* = 8.2, 1.8 Hz, 1H), 3.86 (s, 3H).	DMSO	>98	N6/F5 followed by G1
746				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 11.10 (s, 1H), 9.36 (s, 1H), 9.11 (s, 1H), 9.00 (dd, *J* = 23.2, 6.7 Hz, 2H), 8.41 (d, *J* = 9.1 Hz, 1H), 8.16 (d, *J* = 8.7 Hz, 1H), 8.05 (dd, *J* = 7.9, 5.5 Hz, 1H), 7.80 – 7.65 (m, 2H), 7.59 – 7.44 (m, 3H), 7.41 – 7.32 (m, 1H), 7.06 (d, *J* = 8.0 Hz, 1H), 3.90 (s, 3H).	DMSO		N6/F5 followed by G1
747					^{1}H NMR (400 MHz, DMSO) δ 12.92 (d, *J* = 17.9 Hz, 1H), 9.64 (s, 1H), 9.09 (d, *J* = 7.9 Hz, 1H), 8.92 (d, *J* = 4.9 Hz, 1H), 8.52 (d, *J* = 5.4 Hz, 1H), 8.38 (s, 1H), 8.30 (dd, *J* = 8.7, 1.7 Hz, 1H), 8.04 (d, *J* = 8.7 Hz, 1H), 7.98 – 7.84 (m, 3H), 7.50 (t, *J* = 7.9 Hz, 1H), 7.39 (dd, *J* = 8.1, 5.0 Hz, 2H), 7.06 (dd, *J* = 8.2, 1.8 Hz, 2H), 3.89 (s, 3H).	DMSO	>98	N6/F5 followed by G1

409

umber	Starting Material 1	Starting Material 2	Product	Salt type	^{1}H NMR	^{1}H NMR Solvent	Purity percent	Method of Coupling	LCMS	LCMS Method
748				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.71 (s, 1H), 9.56 (s, 1H), 9.45 (s, 2H), 9.29 (s, 1H), 9.22 (s, 1H), 9.13 (d, *J* = 7.6 Hz, 1H), 8.96 (d, *J* = 4.3 Hz, 1H), 8.47 (d, *J* = 8.4 Hz, 1H), 8.16 – 8.08 (m, 2H), 8.07 – 7.99 (m, 1H), 7.75 (s, 1H), 7.59 (dd, *J* = 19.3, 9.0 Hz, 1H).	DMSO	>98	Method N6		
749					^{1}H NMR (400 MHz, DMSO) δ 10.12 (s, 1H), 9.55 (d, *J* = 1.4 Hz, 1H), 8.74 – 8.66 (m, 3H), 8.28 (d, *J* = 4.9 Hz, 1H), 8.17 – 8.08 (m, 2H), 7.98 – 7.91 (m, 2H), 7.73 (d, *J* = 9.1 Hz, 1H), 7.61 – 7.51 (m, 2H), 7.22 (dd, *J* = 7.3, 5.0 Hz, 1H), 3.95 (s, 3H).	DMSO	>98	Method N6		
750				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.92 (s, 1H), 9.55 (d, *J* = 1.5 Hz, 1H), 9.33 (s, 1H), 9.10 – 8.99 (m, 2H), 8.93 (d, *J* = 5.2 Hz, 1H), 8.54 (d, *J* = 2.5 Hz, 1H), 8.46 (dd, *J* = 8.8, 1.8 Hz, 1H), 8.33 (s, 1H), 8.18 (ddd, *J* = 13.0, 7.4, 2.4 Hz, 1H), 8.08 (d, *J* = 8.7 Hz, 1H), 8.01 – 7.93 (m, 1H), 7.84 (d, *J* = 9.0 Hz, 1H), 7.57 (dd, *J* = 19.7, 9.1 Hz, 1H), 4.03 (s, 3H).	DMSO	>98	Method N6		

751				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.57 (s, 1H), 9.53 (d, *J* = 1.7 Hz, 1H), 9.00 (dd, *J* = 14.9, 4.8 Hz, 2H), 8.90 (dd, *J* = 5.1, 1.4 Hz, 1H), 8.78 (d, *J* = 2.1 Hz, 1H), 8.31 (dt, *J* = 8.7, 2.2 Hz, 2H), 8.11 (ddd, *J* = 12.9, 7.5, 2.5 Hz, 1H), 8.03 (d, *J* = 8.7 Hz, 1H), 7.93 (dd, *J* = 8.0, 5.1 Hz, 1H), 7.75 (dd, *J* = 6.0, 2.9 Hz, 1H), 7.63 – 7.51 (m, 1H), 7.03 (d, *J* = 8.6 Hz, 1H), 3.94 (d, *J* = 8.4 Hz, 3H).	DMSO	>98	Method N6		
752					^{1}H NMR (400 MHz, DMSO) δ 10.05 (s, 1H), 9.52 (s, 1H), 9.14 (d, *J* = 5.6 Hz, 2H), 8.84 (s, 1H), 8.68 (dd, *J* = 14.0, 6.4 Hz, 2H), 8.28 (dd, *J* = 8.7, 1.7 Hz, 1H), 8.17 – 8.06 (m, 1H), 7.96 (d, *J* = 8.7 Hz, 1H), 7.70 (d, *J* = 9.0 Hz, 1H), 7.62 – 7.50 (m, 2H), 4.02 (s, 3H).	DMSO	>98	Method N6		
753					^{1}H NMR (400 MHz, DMSO) δ 10.17 (s, 1H), 9.54 (d, *J* = 1.5 Hz, 1H), 9.16 (d, *J* = 1.9 Hz, 1H), 8.93 (d, *J* = 1.7 Hz, 1H), 8.74 – 8.60 (m, 3H), 8.35 – 8.26 (m, 2H), 8.19 – 8.07 (m, 1H), 8.01 (d, *J* = 8.7 Hz, 1H), 7.77 – 7.69 (m, 1H), 7.64 – 7.51 (m, 3H).	DMSO	>98	Method N6		
754					^{1}H NMR (400 MHz, DMSO) δ 10.12 (s, 1H), 9.53 (d, *J* = 1.4 Hz, 1H), 8.79 – 8.62 (m, 3H), 8.24 – 8.06 (m, 2H), 7.94 (t, *J* = 7.7 Hz, 1H), 7.73 (dd, *J* = 6.2, 2.9 Hz, 1H), 7.56 (ddd, *J* = 15.3, 10.1, 4.8 Hz, 3H), 7.41 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.11 (d, *J* = 8.1 Hz, 1H), 6.13 (s, 2H).	DMSO	>98	Method N6		

411

755				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 11.36 (s, 1H), 9.73 (d, *J* = 1.7 Hz, 1H), 9.52 (d, *J* = 1.8 Hz, 1H), 9.13 – 9.02 (m, 3H), 8.96 (dd, *J* = 5.4, 1.4 Hz, 1H), 8.79 (d, *J* = 6.9 Hz, 2H), 8.56 (dd, *J* = 8.9, 1.9 Hz, 1H), 8.19 (ddd, *J* = 13.0, 7.5, 2.5 Hz, 1H), 8.09 (d, *J* = 8.6 Hz, 1H), 8.02 (dd, *J* = 8.0, 5.4 Hz, 1H), 7.90 (dt, *J* = 9.0, 2.8 Hz, 1H), 7.62 – 7.50 (m, 1H).	DMSO	>98	Method N6		
756					^{1}H NMR (400 MHz, DMSO) δ 10.19 (s, 1H), 9.55 (d, *J* = 1.4 Hz, 1H), 8.86 (d, *J* = 1.7 Hz, 1H), 8.69 (dd, *J* = 8.8, 2.9 Hz, 2H), 8.25 (dd, *J* = 8.7, 1.8 Hz, 1H), 8.18 – 8.07 (m, 1H), 7.99 (d, *J* = 8.7 Hz, 1H), 7.92 (d, *J* = 7.2 Hz, 2H), 7.78 – 7.68 (m, 1H), 7.62 – 7.53 (m, 4H), 7.47 (t, *J* = 7.4 Hz, 1H)	DMSO	>98	Method N6		
757				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.84 (s, 1H), 9.55 (s, 1H), 9.19 – 9.05 (m, 2H), 8.95 (d, *J* = 4.1 Hz, 1H), 8.53 (s, 1H), 8.41 (dd, *J* = 8.7, 1.7 Hz, 1H), 8.28 (s, 1H), 8.16 – 8.07 (m, 3H), 8.05 – 7.92 (m, 2H), 7.79 (d, *J* = 9.1 Hz, 1H), 7.70 – 7.46 (m, 3H).	DMSO	>98	Method N6		
758				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.78 (s, 1H), 9.55 (d, *J* = 1.8 Hz, 1H), 9.12 (d, *J* = 8.6 Hz, 2H), 8.96 (dd, *J* = 5.4, 1.4 Hz, 1H), 8.40 (dd, *J* = 8.8, 1.8 Hz, 1H), 8.16 – 7.96 (m, 8H), 7.79 – 7.71 (m, 1H), 7.64 – 7.53 (m, 1H), 7.47 (s, 1H).	DMSO	>98	Method N6		

412

759				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.41 (s, 1H), 9.56 (s, 1H), 8.98 – 8.77 (m, 3H), 8.23 – 8.02 (m, 4H), 7.99 – 7.65 (m, 5H), 7.56 (dd, *J* = 19.1, 9.4 Hz, 1H).	DMSO	>98	Method N6		
760				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.51 (s, 1H), 9.55 (d, *J* = 1.6 Hz, 1H), 9.04 (d, *J* = 8.1 Hz, 1H), 8.95 – 8.84 (m, 2H), 8.21 – 8.02 (m, 3H), 7.93 (dt, *J* = 10.6, 5.3 Hz, 1H), 7.77 – 7.68 (m, 1H), 7.63 – 7.51 (m, 3H), 7.49 – 7.38 (m, 1H).	DMSO	>98	Method N6		
761				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.51 (s, 1H), 9.55 (d, *J* = 1.5 Hz, 1H), 9.03 (d, *J* = 8.2 Hz, 1H), 8.91 (dd, *J* = 5.3, 1.5 Hz, 1H), 8.82 (s, 1H), 8.16 – 8.00 (m, 3H), 7.94 (dd, *J* = 8.0, 5.2 Hz, 1H), 7.87 – 7.78 (m, 1H), 7.75 – 7.66 (m, 1H), 7.61 – 7.44 (m, 2H), 7.39 – 7.28 (m, 1H).	DMSO	>98	Method N6		
762				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.75 (s, 1H), 9.53 (d, *J* = 1.7 Hz, 1H), 9.07 (dd, *J* = 23.2, 4.9 Hz, 2H), 8.95 (dd, *J* = 5.3, 1.4 Hz, 1H), 8.36 (dd, *J* = 8.6, 1.9 Hz, 1H), 8.15 – 7.96 (m, 3H), 7.76 (dd, *J* = 9.0, 4.1 Hz, 1H), 7.64 – 7.50 (m, 1H), 7.41 (dt, *J* = 12.9, 1.6 Hz, 2H), 6.99 – 6.90 (m, 1H), 3.90 (s, 3H).	DMSO	>98	Method N6		

763				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.54 (s, 1H), 9.55 (s, 1H), 9.05 (d, *J* = 8.2 Hz, 1H), 8.92 (d, *J* = 4.6 Hz, 1H), 8.84 (s, 1H), 8.17 – 8.02 (m, 3H), 7.96 (dd, *J* = 7.9, 5.4 Hz, 1H), 7.72 (d, *J* = 9.0 Hz, 1H), 7.56 (dd, *J* = 19.6, 9.1 Hz, 1H), 7.39 – 7.21 (m, 3H), 3.89 (s, 3H).	DMSO	>98	Method N6		
764				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.68 (s, 1H), 9.51 (d, *J* = 1.3 Hz, 1H), 9.04 (d, *J* = 8.1 Hz, 1H), 8.97 – 8.87 (m, 2H), 8.51 (s, 1H), 8.32 – 8.22 (m, 2H), 8.16 – 8.05 (m, 2H), 8.00 – 7.90 (m, 2H), 7.80 – 7.73 (m, 1H), 7.65 (t, *J* = 7.8 Hz, 1H), 7.60 – 7.47 (m, 2H).	DMSO	>98	Method N6		
765				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.43 (s, 1H), 9.46 (d, *J* = 1.3 Hz, 1H), 9.01 (d, *J* = 8.1 Hz, 1H), 8.91 (d, 1H), 8.63 (s, 1H), 8.13 – 7.91 (m, 3H), 7.73 – 7.66 (m, 1H), 7.59 – 7.49 (m, 2H), 7.44 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.07 (d, *J* = 8.1 Hz, 1H), 6.12 (s, 2H).	DMSO	>98	Method N6		
766					^{1}H NMR (400 MHz, DMSO) δ 10.33 (s, 1H), 9.52 (s, 1H), 8.83 (s, 1H), 8.70 (d, *J* = 6.3 Hz, 2H), 8.32 (d, *J* = 8.6 Hz, 2H), 8.13 – 8.03 (m, 1H), 7.70 (d, *J* = 7.3 Hz, 1H), 7.58 (dd, *J* = 7.3, 5.7 Hz, 3H), 7.42 (s, 1H), 3.95 (s, 3H).	DMSO	>98	Method N6		

767				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.71 (s, 1H), 9.52 – 9.41 (m, 3H), 9.26 (s, 1H), 9.11 – 9.02 (m, 2H), 8.96 (d, *J* = 5.4 Hz, 1H), 8.37 (d, *J* = 11.6 Hz, 1H), 8.14 – 7.99 (m, 2H), 7.80 – 7.71 (m, 1H), 7.55 (d, *J* = 9.1 Hz, 1H).	DMSO	>98	Method N6		
768				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.53 (s, 1H), 9.51 (d, *J* = 1.6 Hz, 1H), 9.07 – 9.00 (m, 1H), 8.91 (dd, *J* = 5.3, 1.5 Hz, 1H), 8.79 (s, 1H), 8.20 (dd, *J* = 11.9, 1.6 Hz, 1H), 8.13 – 8.03 (m, 1H), 8.00 – 7.91 (m, 3H), 7.76 – 7.68 (m, 1H), 7.62 – 7.44 (m, 4H).	DMSO	>98	Method N6		
769				3 HCl	^{1}H NMR (400 MHz, DMSO) δ 11.13 (s, 1H), 9.64 (d, *J* = 1.7 Hz, 1H), 9.47 (d, *J* = 1.5 Hz, 1H), 9.38 (s, 1H), 9.09 (t, *J* = 7.3 Hz, 2H), 9.01 – 8.94 (m, 1H), 8.91 – 8.83 (m, 1H), 8.39 (dd, *J* = 11.6, 1.3 Hz, 1H), 8.22 – 8.13 (m, 1H), 8.11 – 7.98 (m, 2H), 7.93 – 7.84 (m, 1H), 7.53 (dd, *J* = 19.7, 9.2 Hz, 1H).	DMSO	>98	Method N6		
770				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.69 (s, 1H), 9.55 (d, *J* = 1.7 Hz, 1H), 9.12 (d, *J* = 8.2 Hz, 1H), 8.97 (dd, *J* = 5.4, 1.4 Hz, 1H), 8.81 (d, *J* = 8.7 Hz, 1H), 8.30 (d, *J* = 1.3 Hz, 1H), 8.15 – 7.99 (m, 3H), 7.96 – 7.88 (m, 2H), 7.81 – 7.72 (m, 1H), 7.63 – 7.47 (m, 4H).	DMSO	>98	Method N6		

415

771				3 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.89 (s, 1H), 9.54 – 9.45 (m, 2H), 9.17 (t, *J* = 8.6 Hz, 1H), 9.10 – 8.93 (m, 4H), 8.48 (d, *J* = 1.5 Hz, 1H), 8.25 – 8.06 (m, 4H), 7.69 – 7.79 (m, 1H), 7.53 (dd, *J* = 19.6, 9.2 Hz, 1H).	DMSO	>98	Method N6		
772				3 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.67 (s, 1H), 9.54 (d, *J* = 1.7 Hz, 1H), 9.40 (s, 2H), 9.31 (s, 1H), 9.20 (d, *J* = 8.2 Hz, 1H), 9.02 (d, *J* = 4.3 Hz, 1H), 8.89 (d, *J* = 8.7 Hz, 1H), 8.43 (s, 1H), 8.22 (dd, *J* = 8.7, 1.9 Hz, 1H), 8.17 – 8.06 (m, 2H), 7.82 – 7.74 (m, 1H), 7.56 (dd, *J* = 19.7, 9.2 Hz, 1H).	DMSO	>98	Method N6		
773				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.81 (s, 1H), 9.56 (s, 1H), 9.11 (d, *J* = 8.2 Hz, 1H), 8.94 (dd, *J* = 17.5, 6.7 Hz, 2H), 8.42 (d, *J* = 11.9 Hz, 2H), 8.28 (s, 1H), 8.22 – 7.94 (m, 5H), 7.81 (d, *J* = 8.8 Hz, 1H), 7.71 – 7.46 (m, 3H).	DMSO	>98	Method N6		
774				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.32 (s, 1H), 9.54 (s, 1H), 8.95 – 8.76 (m, 2H), 8.65 (d, *J* = 8.8 Hz, 1H), 8.19 – 8.09 (m, 2H), 8.02 (d, *J* = 8.7, 1H), 7.85 – 7.69 (m, 2H), 7.62 – 7.37 (m, 3H), 7.09 (d, *J* = 7.0 Hz, 1H), 6.13 (s, 2H)	DMSO	>98	Method N6		

416

775				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.59 (s, 1H), 9.56 (d, *J* = 1.7 Hz, 1H), 9.11 (d, *J* = 8.1 Hz, 1H), 9.01 – 8.88 (m, 1H), 8.79 (d, *J* = 8.7 Hz, 1H), 8.18 – 8.06 (m, 2H), 8.05 – 7.91 (m, 2H), 7.82 – 7.72 (m, 2H), 7.61 – 7.52 (m, 2H), 7.46 – 7.37 (m, 2H).	DMSO	>98	Method N6		
776				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.46 (s, 1H), 9.53 (d, *J* = 1.6 Hz, 1H), 9.04 (dt, *J* = 8.1, 1.6 Hz, 1H), 8.91 (dd, *J* = 5.2, 1.4 Hz, 1H), 8.73 (d, *J* = 8.7 Hz, 1H), 8.24 (d, *J* = 1.8 Hz, 1H), 8.15 – 8.04 (m, 2H), 7.96 (dd, *J* = 8.0, 5.3 Hz, 1H), 7.84 – 7.70 (m, 2H), 7.65 – 7.48 (m, 2H), 7.39 – 7.25 (m, 1H).	DMSO	>98	Method N6		
777				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.62 (s, 1H), 9.55 (d, *J* = 1.7 Hz, 1H), 9.12 (d, *J* = 8.1 Hz, 1H), 8.96 (dd, *J* = 5.3, 1.3 Hz, 1H), 8.76 (d, *J* = 8.7 Hz, 1H), 8.25 (d, *J* = 1.7 Hz, 1H), 8.16 – 7.91 (m, 6H), 7.81 – 7.69 (m, 1H), 7.56 (dd, *J* = 19.7, 9.1 Hz, 1H), 7.41 (t, *J* = 8.8 Hz, 1H).	DMSO	>98	Method N6		
778				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.65 (s, 1H), 9.55 (d, *J* = 1.7 Hz, 1H), 9.14 (d, *J* = 8.1 Hz, 1H), 8.97 (dd, *J* = 5.4, 1.3 Hz, 1H), 8.81 (d, *J* = 8.7 Hz, 1H), 8.20 – 8.00 (m, 3H), 7.96 – 7.71 (m, 3H), 7.63 – 7.42 (m, 2H), 7.38 – 7.25 (m, 1H).	DMSO	>98	Method N6		

417

779				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.40 (s, 1H), 9.54 (d, *J* = 1.6 Hz, 1H), 9.00 (d, *J* = 8.1 Hz, 1H), 8.90 (dd, *J* = 5.2, 1.4 Hz, 1H), 8.71 (d, *J* = 8.7 Hz, 1H), 8.23 (d, *J* = 1.8 Hz, 1H), 8.17 – 8.01 (m, 3H), 7.93 (dd, *J* = 8.0, 5.2 Hz, 1H), 7.84 – 7.71 (m, 2H), 7.69 – 7.49 (m, 2H).	DMSO	>98	Method N6		
780				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.78 (s, 1H), 9.54 (d, *J* = 1.6 Hz, 1H), 9.19 (d, *J* = 8.1 Hz, 1H), 9.06 – 8.96 (m, 1H), 8.87 (d, *J* = 8.7 Hz, 1H), 8.22 – 8.04 (m, 3H), 7.93 (t, *J* = 10.1 Hz, 1H), 7.78 (dd, *J* = 6.1, 2.9 Hz, 1H), 7.64 – 7.49 (m, 3H), 7.47 – 7.35 (m, 1H).	DMSO	>98	Method N6		
781				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.47 (s, 1H), 9.53 (d, *J* = 1.7 Hz, 1H), 9.08 (d, *J* = 8.1 Hz, 1H), 8.94 (dd, *J* = 5.3, 1.3 Hz, 1H), 8.74 (d, *J* = 8.8 Hz, 1H), 8.29 (d, *J* = 1.8 Hz, 1H), 8.17 – 7.95 (m, 3H), 7.80 – 7.65 (m, 3H), 7.61 – 7.48 (m, 1H), 7.42 – 7.30 (m, 1H).	DMSO	>98	Method N6		
782				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 13.20 (s, 1H), 9.63 (s, 1H), 9.20 (d, *J* = 8.1 Hz, 1H), 8.97 (dd, *J* = 5.3, 1.3 Hz, 1H), 8.89 (d, *J* = 8.3 Hz, 1H), 8.56 (d, *J* = 1.6 Hz, 1H), 8.46 (s, 1H), 8.31 (dd, *J* = 8.7, 1.8 Hz, 1H), 8.13 – 7.92 (m, 4H), 7.90 – 7.83 (m, 2H), 7.77 – 7.70 (m, 1H), 7.59 (dd, *J* = 10.4, 4.8 Hz, 2H), 7.53 – 7.46 (m, 2H), 7.34 – 7.25 (m, 1H).	DMSO	>98	Method N6		

418

783				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 13.22 (s, 1H), 9.65 (s, 1H), 9.19 (d, *J* = 8.1 Hz, 1H), 9.00 – 8.91 (m, 2H), 8.44 (d, *J* = 12.8 Hz, 2H), 8.18 – 7.89 (m, 5H), 7.84 – 7.70 (m, 2H), 7.56 – 7.45 (m, 1H), 7.38 – 7.23 (m, 2H).	DMSO	>98	Method N6		
784				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 13.15 (s, 1H), 9.65 (s, 1H), 9.38 – 9.27 (m, 3H), 9.17 (d, *J* = 9.2 Hz, 1H), 8.92 (dd, *J* = 25.3, 6.7 Hz, 2H), 8.68 (s, 1H), 8.45 (d, *J* = 8.9 Hz, 2H), 8.12 (d, *J* = 9.8 Hz, 1H), 8.04 – 7.92 (m, 3H), 7.74 (t, *J* = 7.6 Hz, 1H), 7.30 (t, *J* = 8.1 Hz, 1H).	DMSO	>98	Method N6		
785				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 13.10 (s, 1H), 9.63 (s, 1H), 9.16 (d, *J* = 8.0 Hz, 1H), 8.96 (dd, *J* = 5.3, 1.3 Hz, 1H), 8.87 (d, *J* = 8.1 Hz, 1H), 8.46 (d, *J* = 21.1 Hz, 2H), 8.27 (dd, *J* = 8.7, 1.8 Hz, 1H), 8.09 – 7.89 (m, 4H), 7.74 (t, *J* = 7.1 Hz, 1H), 7.46 (d, *J* = 1.8 Hz, 1H), 7.38 (dd, *J* = 8.1, 1.9 Hz, 1H), 7.30 (t, *J* = 7.2 Hz, 1H), 7.12 (d, *J* = 8.1 Hz, 1H), 6.12 (s, 2H).	DMSO	>98	Method N6		
786				2 HCl	1H NMR (DMSO-d6) ppm 9.79 (d, J = 1.56 Hz, 1H), 9.26 (brd, J = 7.2 Hz, 1H), 9.00-8.90 (brm, 2H), 8.18 (d, J = 8.64 Hz, 1H), 8.11 (d, J = 8.64 Hz, 1H), 8.01(brt, J = 6.28 Hz, 1H), 7.86-7.80 (brm, 1H), 7.72 (d, J = 3.96 Hz, 1H), 7.53- 7.46 (m, 2H), 7.37-7.32 (brm, 1H) . The 1H of 2HCl and NH-were not observed.	DMSO	>98	N6 using Na_2CO_3 instead of K_3PO_4		

787					1H NMR (DMSO-d6) ppm 12.63 (brs, 1H), 9.80 (d, J = 1.64 Hz, 1H), 9.05- 8.91 (brm, 2H), 8.76 (brd, J = 4.6 Hz, 1H), 8.10 (brd, J = 8.64 Hz, 1H), 8.02 (d, J = 8.64 Hz, 1H), 7.86-7.80 (brm, 1H), 7.66-7.62 (brm, 1H), 7.51-7.45 (brm, 1H), 7.34-7.30 (brm, 1H), 6.94 (brs, 1H), 2.35 (brs, 3H).	DMSO	>98	N6 using Na_2CO_3 instead of K_3PO_4		
788					1H NMR (300 MHz, CD3OD) δ 9.40 (s, 1H), 8.65 (d, J = 8.0 Hz, 1H), 8.56 (d, J = 3.2 Hz, 1H), 8.18 – 8.08 (m, 2H), 7.76 – 7.65 (m, 2H), 7.54 – 7.44 (m, 2H), 7.23 (t, J = 9.0 Hz, 1H), 3.66 (s, J = 8.0 Hz, 2H), 2.55 (s, J = 20.6 Hz, 8H), 2.30 (s, 3H).	CD3OD	99	Method N3	463.0 (M+1)	Method C
789					-		99	Method N3	434.0 (M+1)	Method C
790					-		99	Method N3	436.0 (M+1)	Method C

420

791					^{1}H-NMR (400 MHz, DMSO-d_6): δ 12.20 (s, 1H), 9.64 (s, 1H), 9.58 (s, 1H), 8.73 (d, *J* = 5.5 Hz, 2H), 8.60 (s, 1H), 8.53 (dd, *J* = 7.2, 1.5 Hz, 1H), 8.28 – 8.25 (m, 1H), 7.99 (d, *J* = 8.7 Hz, 1H), 7.61 – 7.58 (m, 1H), 7.50 (t, *J* = 4.5 Hz, 3H), 7.30 (d, *J* = 5.8 Hz, 1H), 7.06 (dd, *J* = 7.4, 4.1 Hz, 1H), 6.49 (t, *J* = 6.9 Hz, 1H), 3.91 (s, 3H).	DMSO	95	Method N1	422.2 (M+1)	Method B (NH4HCO3)
792				HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 13.42 (s, 1H), 8.99 (d, *J* = 8.0 Hz, 1H), 8.64 (td, *J* = 7.6, 2.0 Hz, 1H), 8.51 (s, 1H), 8.44 (d, *J* = 4.4 Hz, 1H), 8.01 – 7.95 (m, 3H), 7.68 – 7.58 (m, 4H), 7.24 (t, *J* = 7.8 Hz, 1H), 4.26 (q, *J* = 2.8 Hz, 2H), 1.47 (t, *J* = 2.8 Hz, 3H).	DMSO	95	Method N1	404.0 (M+1)	Method B (NH4HCO3)
793				HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.31 (s, 1H), 9.13 (d, *J* = 2.0 Hz, 1H), 8.83 (td, *J* = 8.4, 2.4 Hz, 1H), 8.09 (d, *J* = 1.2 Hz, 2H), 7.93 (d, *J* = 8.4 Hz, 2H), 7.66 – 7.60 (m, 2H), 7.36 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.22 (d, *J* = 8.0 Hz, 1H), 4.28 (q, *J* = 6.8 Hz, 2H), 1.47 (t, *J* = 6.8 Hz, 3H).	DMSO	95	Method N1	445.0 (M+1)	Method B (NH4HCO3)
794				2HCl		DMSO	95	Method N1	382.5 (M+1)	Method C

421

795				3HCl	1H-NMR (300 MHz, DMSO): δ 13.10 (s, 1H), 9.61 (s, 1H), 9.12 (d, *J* = 9.8 Hz, 1H), 8.93 (s, 1H), 8.83 (d, *J* = 15.2 Hz, 2H), 8.66 (s, 1H), 8.58 – 8.36 (m, 3H), 8.08 (d, *J* = 11.6 Hz, 2H), 7.96 (d, *J* = 9.2 Hz, 3H), 7.73 (s, 1H), 7.29 (t, *J* = 8.7 Hz, 1H), 4.02 (s, 3H).	DMSO	95	Method N1	449.4 (M+1)	Method C
796				3HCl	1H-NMR (300 MHz, DMSO): δ 12.79 (s, 1H), 9.54 (d, *J* = 1.6 Hz, 1H), 9.18 (d, *J* = 6.2 Hz, 1H), 9.08 (d, *J* = 6.7 Hz, 2H), 9.05 – 8.96 (m, 2H), 8.63 – 8.46 (m, 4H), 8.39 (s, 1H), 8.08 (dd, *J* = 11.6, 8.5 Hz, 2H), 7.92 (d, *J* = 6.7 Hz, 1H), 7.77 (s, 1H), 7.68 (t, *J* = 7.1 Hz, 1H), 7.32 (t, *J* = 7.2 Hz, 1H).	DMSO	95	Method N1	419.1 (M+1)	Method C
797				3HCl	1H-NMR (300 MHz, DMSO): δ 12.81 (s, 1H), 9.54 (s, 1H), 9.45 (s, 1H), 9.23 (d, *J* = 8.2 Hz, 1H), 9.08 – 8.93 (m, 3H), 8.83 (s, 1H), 8.52 (d, *J* = 8.2 Hz, 1H), 8.47 – 8.34 (m, 2H), 8.14 (ddd, *J* = 12.9, 8.1, 4.9 Hz,3H), 7.92 (d, *J* = 6.6 Hz, 1H), 7.79 (s, 1H), 7.68 (t, *J* = 7.2 Hz, 1H), 7.32 (t, *J* = 7.2 Hz, 1H).	DMSO	95	Method N1	419.1 (M+1)	Method C
798				2HCl	1H-NMR (300 MHz, DMSO): δ 13.20 (s, 1H), 9.62 (s, 1H), 9.13 (d, *J* = 8.1 Hz, 1H), 8.94 (d, *J* = 3.5 Hz, 2H), 8.55 (s, 1H), 8.48 (s, 1H), 8.31 (d, *J* = 8.7 Hz, 1H), 8.06 (d, *J* = 8.7 Hz, 1H), 7.96 (s, 3H), 7.74 (s, 1H), 7.55 – 7.40 (m, 3H), 7.29 (s, 1H), 7.06 (d, *J* = 7.4 Hz, 1H), 3.90 (s, 3H)	DMSO	95	Method N1	448.1 (M+1)	Method C

422

799					1H-NMR (300 MHz, DMSO): δ 13.13 (s, 1H), 9.60 (d, *J* = 1.4 Hz, 1H), 9.12 (d, *J* = 7.8 Hz, 1H), 8.73 (dd, *J* = 9.7, 6.4 Hz, 2H), 8.52 (s, 1H), 8.35 (s, 1H), 8.28 (s, 1H), 8.14 (d, *J* = 8.7 Hz, 1H), 8.08 – 7.88 (m, 4H), 7.76 (d, *J* = 7.2 Hz, 1H), 7.59 (dd, *J* = 7.4, 4.8 Hz, 1H), 7.23 (t, *J* = 7.1 Hz, 1H), 3.94 (s, 3H).	DMSO	95	Method N1	422.2 (M+1)	Method C
800					^{1}H NMR (400 MHz, DMSO) δ 10.08 (s, 1H), 9.59 – 9.49 (m, 1H), 8.79 – 8.63 (m, 3H), 8.55 (d, *J* = 2.1 Hz, 1H), 8.27 (dd, *J* = 6.9, 2.6 Hz, 1H), 8.18 (dd, *J* = 8.7, 1.9 Hz, 1H), 8.02 – 7.90 (m, 3H), 7.63 – 7.51 (m, 2H), 6.62 (d, *J* = 8.6 Hz, 1H), 6.24 (s, 2H).	DMSO	>98	N5		
801				MsOH	1H NMR (DMSO-d6) ppm 9.78 (brs, 1H), 9.20-8.80 (br, 3H), 8.14 (brd, J = 8.64Hz, 1H), 8.04 (d, J = 8.64Hz, 1H), 7.83 'brm, 2H), 7.52-7.47 (m,1H), 7.35-7.31(m, 1H), 7.00 (brs, 1H), 2.36 (brs, 3H), 2.30 (brs, 3H). The 1H of MsOH and NH were not observed.	DMSO	>98	N6 using Na_2CO_3 instead of K_3PO_4		

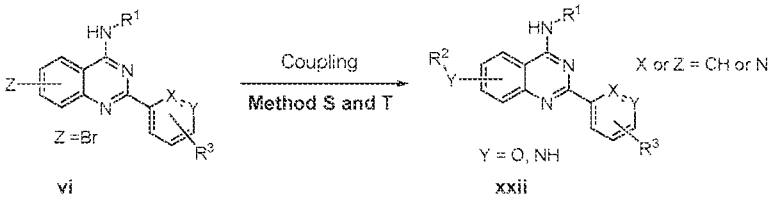
423

Number	PRODUCT	Salt type	Molecular Mass	^{1}H-NMR	^{1}H-NMR Solvent	LCMS	LCMS Protocol	Purity percent	Method for Coupling
802			494.87	^{1}H-NMR (400 MHz, DMSO-d_6): δ10.18 (s, 1H), 9.21 (d, J = 1.8 Hz, 1H), 8.65 – 8.60 (m, 2H), 8.34 – 8.24 (m, 2H), 7.96 – 7.90 (m, 2H), 7.85 – 7.68 (m, 4H), 7.56 (t, J = 9.0 Hz, 1H), 7.51 – 7.44 (m, 2H).	DMSO	495.0, 497.0 (M+1)	Method B (NH4HCO3)	95	Method N1
803			458.89	^{1}H-NMR (400 MHz, DMSO-d_6): δ10.14 (s, 1H), 9.44 (s, 1H), 8.73 – 8.63 (m, 1H), 8.55 (t, J = 6.6 Hz, 2H), 8.27 (d, J = 4.6 Hz, 1H), 7.96 (d, J = 6.8 Hz, 2H), 7.76 – 7.64 (m, 3H), 7.58 – 7.52 (m, 2H), 7.31 (t, J = 9.2 Hz, 1H), 2.37 (s, 3H).	DMSO	459.0, 461.0 (M+1)	Method B (NH4HCO4)	95	Method N1
804			427.86	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.19 (s, 1H), 9.42 (d, J = 1.5 Hz, 1H), 8.74 (d, J = 5.6 Hz, 2H), 8.69 – 8.63 (m, 2H), 8.52 (d, J = 8.0 Hz, 1H), 8.28 (dd, J = 6.8, 2.6 Hz, 1H), 8.05 (d, J = 7.2 Hz, 1H), 7.96 – 7.91 (m, 1H), 7.80 (dd, J = 14.6, 6.8 Hz, 3H), 7.59 – 7.52 (m, 2H).	DMSO	428.0, 430.0 (M+1) 214.6 (M/2+1)	Method A (TFA)	95	Method N1

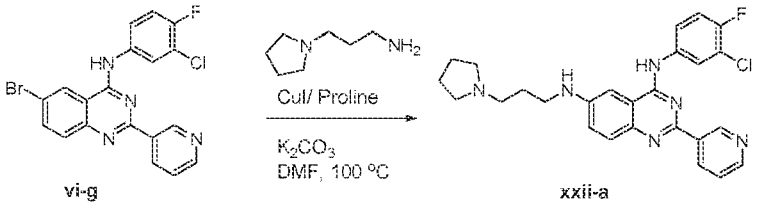
805			426.87	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.13 (s, 1H), 9.43 (d, *J* = 1.6 Hz, 1H), 8.66 (dd, *J* = 4.7, 1.6 Hz, 1H), 8.59 – 8.56 (m, 1H), 8.52 (td, *J* = 7.9, 1.8 Hz, 1H), 8.30 (dd, *J* = 6.84, 2.60Hz, 1H), 7.99 – 7.92 (m, 2H), 7.82 – 7.73 (m, 3H), 7.58 – 7.51 (m, 4H), 7.46 (t, *J* = 7.4 Hz, 1H).	DMSO	427.1, 429.1 (M+1)	Method A (TFA)	95	Method N1
806			456.9	^{1}H-NMR (400 MHz, DMSO-d6): δ 10.13 (s, 1H), 9.45 (s, 1H), 8.67 (dd, *J* = 4.7, 1.7 Hz, 1H), 8.62 – 8.49 (m, 2H), 8.29 (dd, *J* = 6.8, 2.6 Hz, 1H), 8.03 – 7.68 (m, 2H), 7.81 – 7.68 (m, 1H), 7.62 – 7.49 (m, 2H), 7.48 – 7.30 (m, 3H), 7.04 (dd, *J* = 7.8, 2.1 Hz, 1H), 3.87 – 3.81 (m, 3H).	DMSO	457.1, 459.1 (M+1)	Method A (TFA)	95	Method N1
807			456.9	^{1}H-NMR (400 MHz, DMSO-d6): δ10.10 (s, 1H), 9.31 (d, *J* = 1.6 Hz, 1H), 8.63 (dd, *J* = 4.8, 1.7 Hz, 1H), 8.61 – 8.52 (m, 1H), 8.41 (td, *J* = 8.0, 1.9 Hz, 1H), 8.30 (dd, J = 6.9, 2.6 Hz, 1H), 7.97 – 7.92 (m, 1H), 7.83 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.78 – 7.66 (m, 1H), 7.62 – 7.40 (m, 3H), 7.36 (dd, *J* = 7.4, 1.7 Hz, 1H), 7.19 (d, *J* = 8.1 Hz, 1H), 7.10 (t, *J* = 7.4 Hz, 1H), 3.66 (s, 3H).	DMSO	457.1, 459.1 (M+2)	Method B (NH4HCO3)	95	Method N1

425

Scheme 20: General route for the synthesis of compounds with general formula xxii



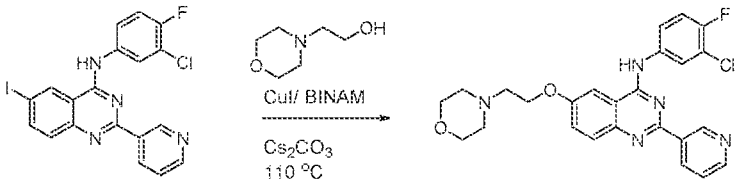
Scheme 21: Representative synthesis of compounds of formula xxii (see Scheme 20)



Method S: N^4-(3-chloro-4-fluorophenyl)-2-(pyridin-3-yl)-N^6-(3-(pyrrolidin-1-yl)propyl)quinazoline-4,6-diamine (xxii-a) A 2.0 dram reaction vial was charged with 6-bromo-N-(3-chloro-4-fluorophenyl)-2-(pyridin-3-yl)quinazolin-4-amine **(synthesized as described in Scheme 1 and 4, substituting 5-bromo-2-nitrobenzoic acid for 2-nitro-5-propoxy-benzoic acid and 3-chloro-4-fluoroaniline for 2-aminobenzamide)** (100 mg, 0.233 mmol, 1.0 equiv), 3-(pyrrolidin-1-yl)propan-1-amine (40 mg, 0.345 mmol, 1.5 equiv), copper(I) iodide (4.4 mg, 0.023 mmol, 0.1 equiv), *L*-proline (5.3 mg, 0.046 mmol, 0.2 equiv), and potassium carbonate (96 mg, 0.69 mmol, 3.0 equiv) in DMF (3 mL). The reaction mixture was heated at 100 °C overnight. After cooling, water was added to the reaction mixture, and the resultant precipitate was collected by filtration. The crude product was purified via prep-TLC (silica, 2000 micron plate, 95% dichloromethane - 5% methanol – 0.1 % NH_4OH) to yield the desired compound as a brown solid (17.2 mg, 15%). LCMS m/z = 477.4 (M+1) (Method C) (retention time = 1.68 min). ^1H NMR (300 MHz, DMSO) δ 9.68 (s, 1H), 9.46 (s, 1H), 8.59 (d, *J* = 9.4 Hz, 2H), 8.25 (dd, *J* = 6.8, 2.6 Hz, 1H), 7.93 (dd, *J* = 8.3, 3.5 Hz, 1H), 7.69 – 7.59 (m, 1H), 7.52 (dd,

J = 11.0, 7.1 Hz, 2H), 7.36 – 7.19 (m, 2H), 6.41 (s, 1H), 3.34 (m, 2H), 2.69 (m, 6H), 2.02 – 1.82 (m, 2H), 1.75 (bs, 4H).

Scheme 22: Representative synthesis of compounds of formula xxii (see Scheme 20)



Method T: N-(3-chloro-4-fluorophenyl)-6-(2-morpholinoethoxy)-2-(pyridin-3-yl)quinazolin-4-amine (xxii-b) A 2.5 dram reaction vial was charged with N-(3-chloro-4-fluorophenyl)-6-iodo-2-(pyridin-3-yl)quinazolin-4-amine (0.250 g, 0.524 mmol), 2-morpholinoethanol (1 ml, 8.17 mmol) as solvent, copper(I) iodide (0.020 g, 0.105 mmol), racemic-2,2'-diamino-1,1'-binaphthyl (0.030 g, 0.105 mmol), and cesium carbonate (0.513 g, 1.573 mmol). The reaction mixture was heated at 110 °C overnight. After cooling, water was added to the reaction mixture, and the resultant precipitate was collected by filtration. The solid residue was purified via ISCO (silica, 12 g column, 95% dichloromethane - 5% methanol – 0.1 % NH_4OH) to yield the desired compound as a brown solid. The solid was further washed with a mixture of water and saturated $NaHCO_3$ solution and dried. The product off the column was further purified by prep TLC (silica gel, 1000 micron, 95% dichloromethane - 5% methanol – 0.1 % NH_4OH) to afford the desired product as a light brown solid (21.2 mg, 8%). LCMS m/z = 480.0 (M+1) (Method C) (retention time = 2.09 min). ^1H NMR (300 MHz, DMSO) δ 9.81 (s, 1H), 9.47 (d, J = 1.8 Hz, 1H), 8.66 – 8.57 (m, 2H), 8.21 (dd, J = 6.8, 2.6 Hz, 1H), 7.92 (d, J = 2.5 Hz, 1H), 7.87 (ddd, J = 8.9, 4.3, 2.7 Hz, 1H), 7.81 (d, J = 9.1 Hz, 1H), 7.57 – 7.47 (m, 3H), 4.25 (t, J = 5.8 Hz, 2H), 3.64 – 3.55 (m, 4H), 2.78 (t, J = 5.7 Hz, 2H), 2.55 – 2.49 (m, 4H).

The compounds in the following table were prepared in a manner analogous to that described in **Scheme 20** substituting with appropriate amine or alcohol

Table 5:

Number	Product	Salt type	Molecular Mass	^{1}H-NMR	^{1}H-NMR Solvent	LCMS	Retention Time (min.)	LCMS Protocol	Purity Percent	Method for Coupling
808			476.98	1H NMR (300 MHz, DMSO) δ 9.68 (s, 1H), 9.46 (s, 1H), 8.59 (d, J = 9.4 Hz, 2H), 8.25 (dd, J = 6.8, 2.6 Hz, 1H), 7.93 (dd, J = 8.3, 3.5 Hz, 1H), 7.69 – 7.59 (m, 1H), 7.52 (dd, J = 11.0, 7.1 Hz, 2H), 7.36 – 7.19 (m, 2H), 6.41 (s, 1H), 3.34 (m, 2H), 2.69 (m,	DMSO	477.4 (M+1)	1.68	Method C	95	Method S
809			492.96	1H NMR (300 MHz, DMSO) δ 9.63 (s, 1H), 9.46 (s, 1H), 8.60 (td, J = 4.2, 2.4 Hz, 2H), 8.23 (dd, J = 6.8, 2.6 Hz, 1H), 7.90 (ddd, J = 8.9, 4.2, 2.6 Hz, 1H), 7.65 (d, J = 9.0 Hz, 1H), 7.57 – 7.45 (m, 2H), 7.32 (dd, J = 9.1, 2.2 Hz, 1H), 7.20 (s, 1H), 6.38 (s	DMSO	493 (M+1)	1.97	Method C	100	Method S
810			423.87	1H NMR (300 MHz, DMSO) δ 9.60 (s, 1H), 9.46 (s, 1H), 8.60 (dd, J = 9.1, 3.1 Hz, 2H), 8.22 (dd, J = 6.9, 2.5 Hz, 1H), 7.89 (ddd, J = 9.0, 4.3, 2.7 Hz, 1H), 7.64 (d, J = 9.0 Hz, 1H), 7.58 – 7.46 (m, 2H), 7.37 (dd, J = 9.1, 2.2 Hz, 1H), 7.25 (s, 1H), 6.40 (t	DMSO	423.9 (M+1)	2.16	Method C	100	Method S
811			463.93	1H NMR (300 MHz, DMSO) δ 9.62 (s, 1H), 9.49 (d, J = 1.7 Hz, 1H), 8.70 – 8.59 (m, 2H), 8.27 (dd, J = 6.9, 2.5 Hz, 1H), 8.19 (dd, J = 9.0, 5.0 Hz, 1H), 7.91 – 7.82 (m, 1H), 7.57 – 7.43 (m, 2H), 7.01 (dd, J = 9.0, 2.1 Hz, 1H), 6.77 (t, J = 5.3 Hz, 1H), 6.72	DMSO	464.0 (M+1)	2.19	Method C	100	Method S

429

812			449.91	1H NMR (300 MHz, DMSO) δ 9.65 (s, 1H), 9.49 (d, J = 2.1 Hz, 1H), 8.69 – 8.59 (m, 2H), 8.27 (dd, J = 6.9, 2.6 Hz, 1H), 8.20 (d, J = 9.0 Hz, 1H), 7.87 (ddd, J = 9.0, 4.3, 2.7 Hz, 1H), 7.56 – 7.43 (m, 2H), 7.00 (dd, J = 9.1, 2.2 Hz, 1H), 6.79 (d, J = 2.1 Hz,	DMSO	449.9 (M+1)	2.12	Method C	100	Method S
813			409.84	1H NMR (300 MHz, DMSO) δ 9.71 (s, 1H), 9.46 (s, 1H), 8.66 – 8.55 (m, 2H), 8.24 (d, J = 4.3 Hz, 1H), 7.96 – 7.87 (m, 1H), 7.64 (d, J = 9.1 Hz, 1H), 7.56 – 7.46 (m, 3H), 7.36 (d, J = 9.0 Hz, 1H), 7.28 (s, 1H), 6.38 (s, 1H), 4.96 (s, 1H), 3.69 (s, 2H), 3.42	DMSO	409.9 (M+1)	1.86	Method C	100	Method S
814			463.93	1H NMR (300 MHz, DMSO) δ 9.59 (s, 1H), 9.45 (d, J = 1.2 Hz, 1H), 8.60 (dd, J = 7.4, 5.7 Hz, 2H), 8.23 (dd, J = 6.8, 2.5 Hz, 1H), 7.90 (dd, J = 9.0, 2.7 Hz, 1H), 7.64 (d, J = 9.0 Hz, 1H), 7.57 – 7.46 (m, 2H), 7.36 (d, J = 9.1 Hz, 1H), 7.19 (s, 1H), 6.38 (s	DMSO	464.0 (M+1)	2.19	Method C	95	Method S
815			479.93	1H NMR (300 MHz, DMSO) δ 9.81 (s, 1H), 9.47 (d, J = 1.8 Hz, 1H), 8.66 – 8.57 (m, 2H), 8.21 (dd, J = 6.8, 2.6 Hz, 1H), 7.92 (d, J = 2.5 Hz, 1H), 7.87 (ddd, J = 8.9, 4.3, 2.7 Hz, 1H), 7.81 (d, J = 9.1 Hz, 1H), 7.57 – 7.47 (m, 3H), 4.25 (t, J = 5.8 Hz, 2H),	DMSO	480.0 (M+1)	2.09	Method C	91	Method T

430

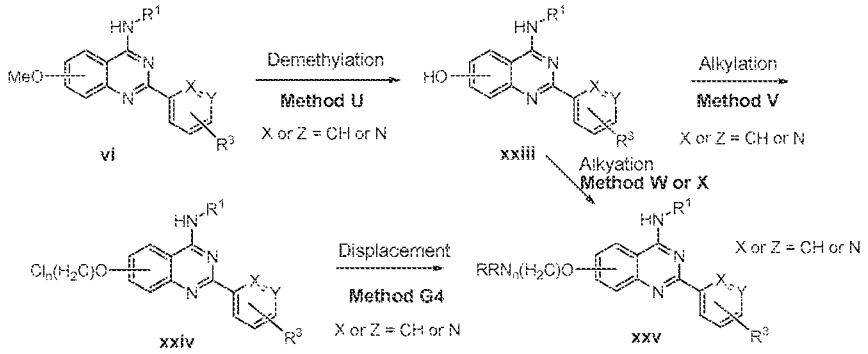
816			423.87	1H NMR (300 MHz, DMSO) δ 9.60 (s, 1H), 9.47 (s, 1H), 8.67 – 8.55 (m, 2H), 8.23 (dd, J = 6.9, 2.5 Hz, 1H), 7.90 (ddd, J = 9.0, 4.3, 2.7 Hz, 1H), 7.65 (d, J = 9.0 Hz, 1H), 7.56 – 7.47 (m, 2H), 7.37 (dd, J = 9.1, 2.2 Hz, 1H), 7.25 (d, J = 1.3 Hz, 1H), 6.41 (t, J = 5.6 Hz, 1H), 3.63 (t, J = 5.7 Hz, 2H), 3.48 – 3.35 (m, 5H).	DMSO	423.9 (M+1)		Method C	99	Method S
817			437.9	1H NMR (300 MHz, DMSO) δ 9.63 (s, 1H), 9.47 (s, 1H), 8.66 – 8.55 (m, 2H), 8.23 (dd, J = 6.9, 2.5 Hz, 1H), 7.90 (ddd, J = 8.8, 4.3, 2.5 Hz, 1H), 7.65 (d, J = 9.0 Hz, 1H), 7.58 – 7.45 (m, 2H), 7.32 (dd, J = 9.0, 1.8 Hz, 1H), 7.21 (s, 1H), 6.34 (t, J = 5.0 Hz, 1H), 3.50 (t, J = 6.1 Hz, 2H), 3.31 – 3.20 (m, 5H), 1.92 (p, J = 6.5 Hz, 2H).	DMSO	438.1 (M+1)		Method C	99	Method S
818			449.91	1H NMR (300 MHz, DMSO) δ 9.61 (s, 1H), 9.46 (d, J = 2.1 Hz, 1H), 8.65 – 8.56 (m, 2H), 8.23 (dd, J = 6.9, 2.6 Hz, 1H), 7.90 (ddd, J = 8.9, 4.2, 2.6 Hz, 1H), 7.64 (d, J = 9.0 Hz, 1H), 7.58 – 7.47 (m, 2H), 7.40 (dd, J = 8.9, 2.2 Hz, 1H), 7.26 (d, J = 1.7 Hz, 1H), 6.39 (t, J = 5.7 Hz, 1H), 4.12 (t, J = 6.2 Hz, 1H), 3.85 (dd, J = 14.2, 7.2 Hz, 1H), 3.70 (dd, J = 14.2, 7.7 Hz, 1H), 3.34 – 3.25 (m, 5H), 2.15 – 1.99 (m, 1H), 1.97 – 1.80 (m, 3H), 1.74 – 1.58 (m, 2H).	DMSO	449.9 (M+1)		Method C	94	Method S

431

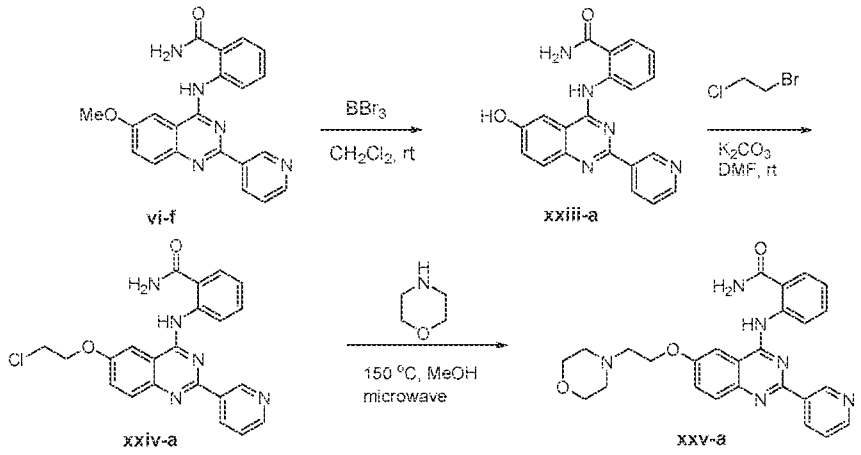
819				1H-NMR (300 MHz, DMSO): δ 10.04 (s, 1H), 9.48 (s, 1H), 8.67 (s, 2H), 8.43 – 8.31 (m, 1H), 8.14 – 8.01 (m, 1H), 7.72 (d, J = 9.0 Hz, 1H), 7.65 (s, 1H), 7.54 (dd, J = 9.7 Hz, 2H), 7.35 (d, J = 9.0 Hz, 1H), 6.77 (s, 1H), 3.67 (broad doublet, 4H), 3.41 (bs, 2H), 3.08 (d, J = 4.7 Hz, 2H), 2.03 (bs, 2H), 1.91 (bs, 2H).	DMSO	463.9 (M+1)		Method C	95	Method S

432

Scheme 23: General route for the synthesis of compounds with general formula xxv



Scheme 24: Representative synthesis of compounds of formula xxv (see Scheme 23)



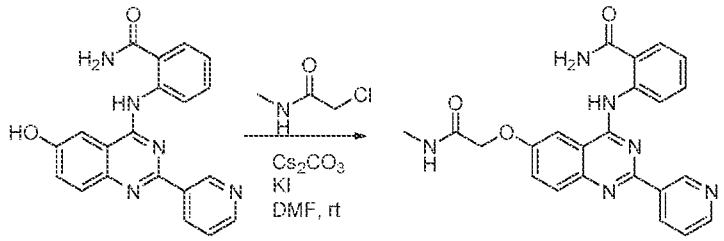
Method U: 2-(6-hydroxy-2-(pyridin-3-yl)quinazolin-4-ylamino)benzamide (xxiii-a) To a suspension of 2-(6-methoxy -2-(pyridin-3-yl)quinazolin-4-ylamino)benzamide **(synthesized as described in Scheme 1 and 4, substituting 5-methoxy-2-nitrobenzoic acid for 2-nitro-5-propoxy-benzoic acid)** (371 mg, 1.0 mmol) in CH_2Cl_2 (4.5 mL) was slowly added boron tribromide, 1M solution in dichloromethane (4.5 ml, 4.5 mmol) at 0 °C. The reaction mixture was stirred overnight at room temperature after which it was carefully poured into a vigorously stirring mixture of ice and saturated solution of aqueous $NaHCO_3$. The resultant solid was collected by filtration, dried and then stirred in a saturated solution of aqueous NH_4Cl for 1 h after

which the suspension was filtered to give the desired product as a yellowish tan solid (262 mg, 73%). LCMS m/z = 357.9 (M +1) (Method C) (retention time = 1.68 min). ^{1}H NMR (300 MHz, DMSO) δ 12.80 (s, 1H), 10.50 (s, 1H), 9.57 (s, 1H), 9.15 (d, *J* = 8.5 Hz, 1H), 8.70 (t, *J* = 7.3 Hz, 2H), 8.50 (s, 1H), 8.08 – 7.79 (m, 3H), 7.73 (t, *J* = 7.5 Hz, 1H), 7.57 (dd, *J* = 7.6, 4.8 Hz, 1H), 7.46 (d, *J* = 8.5 Hz, 2H), 7.19 (t, *J* = 7.6 Hz, 1H).

Method V: 2-(6-(2-chloroethoxy)-2-(pyridin-3-yl)quinazolin-4-ylamino)benzamide (xxiv-a) The suspension of 2-(6-hydroxy-2-(pyridin-3-yl)quinazolin-4-ylamino)benzamide (50 mg, 0.14 mmol), 1-bromo-2-chloroethane (0.015 ml, 0.15 mmol), and potassium carbonate (23 mg, 0.17mmol) in DMF (5 mL) was stirred for 3 days at room temperature. Water (10 mL) was added to the mixture and extracted with ethyl acetate (2 x 10 mL). The combined organic layer was washed with water (1 x 20 mL) and brine (1 x 20 mL) and was dried over $MgSO_4$. After filtration and evaporation, the crude product was obtained, which was washed with hexane and dried to give 48 mg of 2-(6-(2-chloroethoxy)-2-(pyridin-3-yl)quinazolin-4-ylamino)benzamide as light brown solid (79 %).

Method G4: 2-(6-(2-morpholinoethoxy)-2-(pyridin-3-yl)quinazolin-4-ylamino)benzamide (xxv-a) 2-(6-(2-morpholinoethoxy)-2-(pyridin-3-yl)quinazolin-4-ylamino)benzamide was prepared from 2-(6-(3-chloroethoxy)-2-(pyridin-3-yl)quinazolin-4-ylamino)benzamide and morpholine in a manner analogous to that described for N-(3-chloro-4-fluorophenyl)-6-(3-(dimethylamino)propyl)-2-(pyridin-3-yl)quinazolin-4-amine dihydrochloride in Scheme 9 using **Method G4** to give 50 mg of 2-(6-(2-morpholinoethoxy)-2-(pyridin-3-yl)quinazolin-4-ylamino)benzamide as light yellow solid. LCMS m/z = 485 (M +1) (Method C) (retention time = 1.71 min). ^{1}H NMR (300 MHz, DMSO) δ 9.57 (s, 1H), 9.12 (d, J = 8.5 Hz, 1H), 8.78 – 8.63 (m, 2H), 8.48 (s, 1H), 8.02 – 7.93 (m, 2H), 7.88 (d, J = 9.0 Hz, 1H), 7.73 (t, J = 8.0 Hz, 1H), 7.63 – 7.49 (m, 3H), 7.20 (t, J = 7.6 Hz, 1H), 4.29 – 4.16 (m, 2H), 3.65 – 3.51 (m, 4H), 3.44 – 3.21 (m, 2H), 2.45 – 2.31 (m, 4H), 2.06 – 1.91 (m, 2H).

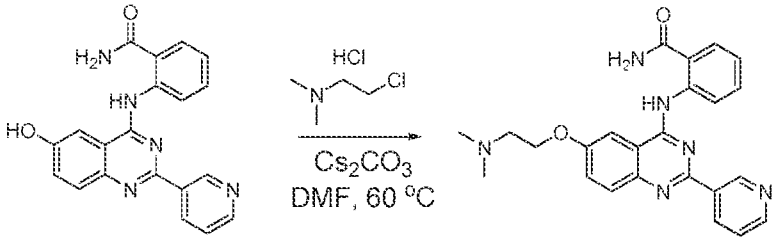
Scheme 25: Representative synthesis of compounds of formula xxv-b (see Scheme 23)



xxiii-a xxv-b

Method W: 2-(6-(2-(methylamino)-2-oxoethoxy)-2-(pyridin-3-yl)quinazolin-4-ylamino)benzamide The suspension of 2-(6-hydroxy-2-(pyridin-3-yl)quinazolin-4-ylamino)benzamide **(synthesized as described in Scheme 24)** (0.20 g, 0.56 mmol), 2-chloro-N-methylacetamide (90 mg, 0.80 mmol), cesium carbonate (0.37 g, 1.12 mmol) and potassium iodide (0.19 g, 1.12 mmol) in DMF (10 mL) was stirred for 4 days at room temperature. Water (20 mL) was added to the mixture. The resultant solid was collected by filtration. The obtained solid was washed with CH_2Cl_2-THF (1:1) solution and dried to give 0.11 g of 2-(6-(2-(methylamino)-2-oxoethoxy)-2-(pyridin-3-yl)quinazolin-4-ylamino)benzamide as pale brown solid (46 %). LCMS m/z = 429 (M +1) (Method C) (retention time = 1.65 min). ^{1}H NMR (300 MHz, DMSO) δ 9.58 (s, 1H), 9.12 (d, J = 8.4 Hz, 1H), 8.82 – 8.64 (m, 2H), 8.48 (s, 1H), 8.32 – 8.17 (m, 1H), 8.10 – 7.87 (m, 3H), 7.81 – 7.49 (m, 4H), 7.21 (t, J = 7.5 Hz, 1H), 4.66 (s, 2H), 2.71 (d, J = 4.5 Hz, 3H).

Scheme 26: Representative synthesis of compounds of formula xxv-c (see Scheme 23)



xxiii-a xxv-c

Method X: 2-(6-(2-(dimethylamino)ethoxy-2-(pyridin-3-yl)quinazolin-4-ylamino)benzamide A suspension of 2-(6-hydroxy-2-(pyridin-3-yl)quinazolin-4-ylamino)benzamide **(synthesized as described in Scheme 24)** (25 mg, 0.07 mmol), 2-chloro-*N,N*-dimethylethylamine hydrochloride (20 mg, 0.14 mmol) and cesium carbonate (68.4 mg, 0.21 mmol) in DMF (1 mL) was stirred at 60 °C overnight. The reaction mixture was cooled to room temperature, diluted with water (5 mL) and extracted with dichloromethane (3 X 5 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo*. The crude product was purified by prep-TLC (silica, 2000 micron plate, 95% dichloromethane - 5% methanol – 0.1 % NH_4OH) to yield the desired compound as a brown solid (12.6 mg, 40%). LCMS m/z = 428.9 (M+1) (Method C) (retention time = 1.41 min). ^{1}H NMR (300 MHz, DMSO) δ 12.99 (s, 1H), 9.59 (d, *J* = 1.3 Hz, 1H), 9.12 (d, *J* = 8.4 Hz, 1H), 8.81 – 8.66 (m, 2H), 8.52 (s, 1H), 8.06 – 7.88 (m, 3H), 7.80 – 7.53 (m, 4H), 7.22 (t, *J* = 7.6 Hz, 1H), 4.46 (s, 2H), 3.35 (s, 2H), 2.69 (s, 6H).

The compounds in the following table were prepared in a manner analogous to that described in **Scheme 23** substituting with appropriate nucleophile.

Table 6:

Number	Product	Salt type	Molecular Mass	^{1}H-NMR	^{1}H-NMR Solvent	LCMS	Retention Time (min.)	LCMS Protocol	Purity Percent	Method for Coupling
820			484 550	1H NMR (300 MHz, DMSO) δ 9.57 (s, 1H), 9.12 (d, J = 8.5 Hz, 1H), 8.78 – 8.63 (m, 2H), 8.48 (s, 1H), 8.02 – 7.93 (m, 2H), 7.88 (d, J = 9.0 Hz, 1H), 7.73 (t, J = 8.0 Hz, 1H), 7.63 – 7.49 (m, 3H), 7.20 (t, J = 7.6 Hz, 1H), 4.29 – 4.16 (m, 2H), 3.65 – 3.51 (m	DMSO	485 (M+1)	1.71	Method C	100	Methods V, G4
821			470.523	1H NMR (300 MHz, DMSO) δ 9.56 (s, 1H), 9.24 – 9.08 (m, 1H), 8.82 – 8.61 (m, 2H), 8.49 (s, 1H), 8.09 – 7.84 (m, 3H), 7.73 (t, J = 7.8 Hz, 1H), 7.67 – 7.47 (m, 3H), 7.19 (t, J = 7.5 Hz, 1H), 4.29 – 4.09 (m, 2H), 3.63 – 3.42 (m, 2H), 3.07 – 2.77 (m, 3H), 2.2	DMSO	471 (M+1)	1.75	Method C	100	Methods V, G4 followed by acylation with acetyl chloride/TEA in DCM at rt.
822			442 470	1H NMR (300 MHz, DMSO) δ 9.58 (s, 1H), 9.16 (d, J = 8.4 Hz, 1H), 8.82 – 8.60 (m, 2H), 8.49 (s, 1H), 8.05 – 7.80 (m, 3H), 7.79 – 7.68 (m, 1H), 7.67 – 7.51 (m, 2H), 7.43 (s, 1H), 7.29 – 7.12 (m, 1H), 5.03 (s, 2H), 3.10 (s, 3H), 2.89 (s, 3H).	DMSO	443 (M+1)	1.63	Method C	100	Method W

437

823		HCl	561.94	1H NMR (300 MHz, DMSO) δ 10.51 (s, 1H), 9.49 (s, 1H), 8.95 (d, J = 6.6 Hz, 1H), 8.65 (d, J = 5.0 Hz, 1H), 8.26 (s, 1H), 8.10 (s, 1H), 8.03 – 7.80 (m, 3H), 7.73 – 7.51 (m, 2H), 7.19 (d, J = 7.4 Hz, 1H), 5.12 (s, 2H), 3.75 – 3.36 (m, 8H).	DMSO	526 (M+1)	2.02	Method C	100	Method W
824		HCl	598.44	1H NMR (300 MHz, DMSO) δ 10.98 (s, 1H), 10.59 (s, 1H), 9.50 (s, 1H), 8.96 (d, J = 8.1 Hz, 1H), 8.86 (d, J = 5.1 Hz, 1H), 8.31 (s, 1H), 8.10 (s, 1H), 8.07 – 7.93 (m, 2H), 7.92 – 7.80 (m, 1H), 7.71 – 7.54 (m, 2H), 7.21 (d, J = 8.0 Hz, 1H), 4.47 – 4.23 (m, 2	DMSO	526 (M+1)	2.25	Method C	100	Methods V, G4
825			469.42	1H NMR (300 MHz, DMSO) δ 9.95 (s, 1H), 9.51 (s, 1H), 8.76 – 8.56 (m, 2H), 8.26 – 8.08 (m, 2H), 8.01 (s, 1H), 7.95 – 7.81 (m, 2H), 7.70 – 7.56 (m, 2H), 7.52 (dd, J = 7.9, 4.9 Hz, 1H), 7.17 (d, J = 8.3 Hz, 1H), 4.69 (s, 2H), 2.71 (d, J = 4.5 Hz, 3H).	DMSO	470 (M+1)	2.04	Method C	100	Method W
826			483.44	1H NMR (300 MHz, DMSO) δ 9.92 (s, 1H), 9.51 (s, 1H), 8.74 – 8.57 (m, 2H), 8.17 (s, 1H), 8.01 (d, J = 2.5 Hz, 1H), 7.96 – 7.83 (m, 2H), 7.70 – 7.46 (m, 3H), 7.16 (d, J = 7.0 Hz, 1H), 5.03 (s, 2H), 3.06 (s, 3H), 2.88 (s, 3H).	DMSO	484 (M+1)	1.71	Method D	100	Method W

438

827		HCl	564.91	1H NMR (300 MHz, DMSO) δ 10.59 (s, 1H), 9.99 (s, 1H), 9.49 (s, 1H), 8.97 (d, J = 7.7 Hz, 1H), 8.87 (d, J = 5.3 Hz, 1H), 8.33 – 8.18 (m, 2H), 8.04 – 7.83 (m, 3H), 7.68 – 7.47 (m, 2H), 4.41 – 4.27 (m, 2H), 3.55 – 3.43 (m, 2H), 3.34 – 3.20 (m, 2H), 3.03 – 2.	DMSO	492 (M+1)	1.81	Method C	100	Methods V, G4
828			437.85	1H NMR (300 MHz, DMSO) δ 9.87 (s, 1H), 9.49 (s, 1H), 8.76 – 8.53 (m, 2H), 8.32 – 8.08 (m, 2H), 8.01 – 7.77 (m, 3H), 7.69 – 7.43 (m, 3H), 4.67 (s, 2H), 2.71 (d, J = 4.6 Hz, 3H).	DMSO	438 (M+1)	1.65	Method D	100	Method W
829			493.92	1H NMR (300 MHz, DMSO) δ 9.86 (s, 1H), 9.50 (s, 1H), 8.76 – 8.57 (m, 2H), 8.27 (d, J = 7.0 Hz, 1H), 8.05 – 7.80 (m, 3H), 7.69 – 7.45 (m, 3H), 5.04 (s, 2H), 3.78 – 3.41 (m, 8H).	DMSO	494 (M+1)	1.98	Method C	98	Method W
830			479.93	1H NMR (300 MHz, DMSO) δ 9.85 (s, 1H), 9.50 (s, 1H), 8.76 – 8.53 (m, 2H), 8.26 (dd, J = 6.9, 2.5 Hz, 1H), 8.08 – 7.76 (m, 3H), 7.71 – 7.41 (m, 3H), 4.98 (s, 2H), 3.52 – 3.09 (m, 4H), 1.37 – 0.88 (m, 6H).	DMSO	480 (M+1)	2.20	Method C	100	Method W

439

831		HCl	580.91	1H NMR (300 MHz, DMSO) δ 10.71 (s, 2H), 9.48 (s, 1H), 9.10 – 8.95 (m, 1H), 8.94 – 8.79 (m, 1H), 8.36 – 8.27 (m, 1H), 8.26 – 8.16 (m, 1H), 8.07 – 7.83 (m, 3H), 7.68 – 7.46 (m, 2H), 4.39 – 4.18 (m, 2H), 4.05 – 3.89 (m, 2H), 3.79 (t, J = 11.9 Hz, 2H), 3.53 –	DMSO	508 (M+1)	2.14	Method C	100	Methods V, G4
832			451.88	1H NMR (300 MHz, DMSO) δ 9.85 (s, 1H), 9.50 (s, 1H), 8.71 – 8.58 (m, 2H), 8.25 (dd, J = 6.8, 2.5 Hz, 1H), 8.01 – 7.60 (m, 3H), 7.66 – 7.45 (m, 3H), 5.02 (s, 2H), 3.06 (s, 3H), 2.88 (s, 3H).	DMSO	452 (M+1)	1.99	Method C	100	Method W
833		HCl	566.88	1H NMR (300 MHz, DMSO) δ 11.18 (s, 1H), 10.93 (s, 1H), 9.48 (s, 1H), 9.08 (d, J = 8.4 Hz, 1H), 8.94 (d, J = 5.0 Hz, 1H), 8.42 (s, 1H), 8.23 (dd, J = 6.8, 2.5 Hz, 1H), 8.12 – 7.89 (m, 3H), 7.63 (d, J = 9.1 Hz, 1H), 7.54 (t, J = 9.1 Hz, 1H), 4.45 – 4.26 (m,	DMSO	494 (M+1)	2.10	Method C	100	Methods V, G4

440

834			366.78	1H NMR (300 MHz, DMSO) δ 9.98 – 9.59 (m, 1H), 9.53 – 9.41 (m, 1H), 8.71 – 8.48 (m, 2H), 8.31 (dd, J = 6.9, 2.5 Hz, 1H), 8.01 – 7.85 (m, 1H), 7.83 – 7.66 (m, 2H), 7.59 – 7.35 (m, 3H).	DMSO	367 (M+1)	1.69	Method D	100	Method U
835			428.44	1H NMR (300 MHz, DMSO) δ 9.58 (s, 1H), 9.12 (d, J = 8.4 Hz, 1H), 8.82 – 8.64 (m, 2H), 8.48 (s, 1H), 8.32 – 8.17 (m, 1H), 8.10 – 7.87 (m, 3H), 7.81 – 7.49 (m, 4H), 7.21 (t, J = 7.5 Hz, 1H), 4.66 (s, 2H), 2.71 (d, J = 4.5 Hz, 3H).	DMSO	429 (M+1)	1.65	Method C	100	Method W
836			484.51	1H NMR (300 MHz, DMSO) δ 9.58 (s, 1H), 9.13 (d, J = 8.3 Hz, 1H), 8.78 – 8.64 (m, 2H), 8.50 (s, 1H), 8.02 – 7.80 (m, 3H), 7.73 (t, J = 7.9 Hz, 1H), 7.68 – 7.53 (m, 2H), 7.49 (s, 1H), 7.20 (t, J = 7.5 Hz, 1H), 5.07 (s, 2H), 3.79 – 3.40 (m, 8H).	DMSO	485 (M+1)	1.72	Method C	91	Method W

441

837			442.47	1H NMR (300 MHz, DMSO) δ 9.59 (s, 1H), 9.12 (d, J = 8.4 Hz, 1H), 8.78 – 8.63 (m, 1H), 8.49 (s, 1H), 8.29 (s, 1H), 8.11 – 7.88 (m, 2H), 7.79 – 7.47 (m, 4H), 7.26 – 7.14 (m, 1H), 4.56 (s, 2H), 3.27 – 3.06 (m, 2H), 1.16 – 0.93 (m, 3H).	DMSO	443 (M+1)	1.69	Method C	100	Method W
838			357.37	1H NMR (300 MHz, DMSO) δ 12.80 (s, 1H), 10.50 (s, 1H), 9.57 (s, 1H), 9.15 (d, J = 8.5 Hz, 1H), 8.70 (t, J = 7.3 Hz, 2H), 8.50 (s, 1H), 8.06 – 7.79 (m, 3H), 7.73 (t, J = 7.5 Hz, 1H), 7.57 (dd, J = 7.6, 4.8 Hz, 1H), 7.46 (d, J = 8.5 Hz, 2H), 7.19 (t, J = 7.6 Hz, 1H).	DMSO	357.9 (M+1)	1.68	Method C	100	Method U
839		2HCl	443.86	1H NMR (300 MHz, DMSO) δ 10.57 (s, 1H), 9.49 (s, 1H), 8.97 (d, J = 8.2 Hz, 1H), 8.89 (s, 1H), 8.81 (s, 1H), 8.16 (ddd, J = 12.2, 10.9, 5.2 Hz, 3H), 8.05 (d, J = 2.3 Hz, 1H), 8.00 – 7.86 (m, 3H), 7.55 (t, J = 9.1 Hz, 1H), 6.55 (d, J = 9.5 Hz, 1H).	DMSO	443.9 (M+1)	1.87	Method C	100	Method U

442

840		2HCl	457.89	1H NMR (300 MHz, DMSO) δ 10.27 (s, 1H), 9.47 (s, 1H), 9.09 (d, J = 8.1 Hz, 1H), 8.91 (d, J = 4.4 Hz, 1H), 8.56 (s, 1H), 8.18 – 8.08 (m, 2H), 8.01 (d, J = 6.3 Hz, 3H), 7.96 – 7.89 (m, 1H), 7.49 (t, J = 9.1 Hz, 1H), 6.52 (d, J = 9.6 Hz, 1H), 2.71 (s, 3H).	DMSO	458.0 (M+1)	2.12	Method D	100	Method U
841			448.48	1H NMR (300 MHz, DMSO) δ 13.08 (s, 1H), 9.59 (s , 1H), 9.16 (d , J = 8.4 Hz, 1H), 8.88 – 8.44 (m, 5H), 8.12 – 7.85 (m, 4H), 7.73 (q, J = 8.7 Hz, 3H), 7.58 (dd , J = 7.9, 4.8 Hz, 1H), 7.49 (dd , J = 7.8, 4.8 Hz, 1H), 7.21 (t, J = 7.6 Hz, 1H), 5.36 (s, 2H).	DMSO	449.2 (M+1)	1.93	Method C	96	Method X
842			448.48	1H NMR (300 MHz, DMSO) δ 13.00 (s, 1H), 9.57 (s, 1H), 9.12 (d, J = 8.4 Hz, 1H), 8.76 – 8.60 (m, 4H), 8.50 (s, 1H), 8.03 – 7.89 (m, 3H), 7.68 (dd, J = 15.6, 5.2 Hz, 3H), 7.57 (t, J = 4.6 Hz, 3H), 7.19 (t, J = 7.6 Hz, 1H), 5.37 (s, 2H).	DMSO	449.1 (M+1)	1.89	Method C	100	Method X
843			425.48	1H NMR (300 MHz, DMSO) δ 12.95 (s, 1H), 9.56 (s, 1H), 9.10 (d, J = 8.4 Hz, 1H), 8.75 – 8.64 (m, 2H), 8.46 (s, 1H), 7.98 – 7.91 (m, 2H), 7.85 (dd, J = 9.0, 0.8 Hz, 1H), 7.71 (t, J = 7.9 Hz, 1H), 7.61 – 7.48 (m, 3H), 7.16 (t, J = 7.6 Hz, 1H), 4.12 (d, J = 6.6 Hz, 2H), 2.84 (dd, J = 14.3, 7.4 Hz, 1H), 2.18 – 2.05 (m, 2H), 1.97 – 1.84 (m, 5H).	DMSO	426.2 (M+1)	2.46	Method C	100	Method X

443

844			457.89	1H-NMR (400 MHz, DMSO-d6): δ 9.95 (s, 1H), 9.54 (d, J = 1.6 Hz, 1H), 8.82 (d, J = 1.7 Hz, 1H), 8.76 – 8.59 (m, 3H), 8.29 (dd, J = 6.8, 2.6 Hz, 1H), 8.16 (d, J = 2.5 Hz, 1H), 8.06 – 7.86 (m, 3H), 7.69 (dd, J = 9.1, 2.5 Hz, 1H), 7.64 – 7.47 (m, 3H), 5.37 (s, 2H).	DMSO	458.1, 460.1 (M+1) 229.6, 230.3 (M/2+1)		Method A	95	Method X
845			487.91	1H-NMR (400 MHz, DMSO-d6): δ 9.74 (s, 1H), 9.34 (s, 1H), 8.57 – 8.41 (m, 2H), 8.22 (d, J = 2.2 Hz, 1H), 8.10 (dd, J = 6.8, 2.6 Hz, 1H), 7.95 (d, J = 2.5 Hz, 1H), 7.80 – 7.63 (m, 3H), 7.53 – 7.30 (m, 3H), 6.82 – 6.68 (m, 1H), 5.07 (s, 2H), 3.71 (s, 3H).	DMSO	488.1, 490.1 (M+1) 244.6, 245.4 (M/2+1)		Method A	95	Method X

444

lumber	Starting Material R[1]	Starting Material R[2]	Product	Salt Type	^{1}H NMR	^{1}H NMR Solvent	Purity percent	Method of Coupling
846				HCl	1H NMR (400 MHz, DMSO) δ 9.31 (d, J = 1.7 Hz, 1H), 8.83 – 8.76 (m, 1H), 8.76 – 8.67 (m, 1H), 8.07 (d, J = 9.2 Hz, 1H), 7.86 (dd, J = 6.3, 2.8 Hz, 1H), 7.83 – 7.73 (m, 2H), 7.70 (d, J = 2.8 Hz, 1H), 7.68 – 7.61 (m, 1H), 7.60 – 7.52 (m, 1H), 5.12 (s, 2H), 3.05 (s, 3H), 2.88 (s, 3H).	DMSO	>98	Method X using K_2CO_3 instead of Cs_2CO_3
847					1H NMR (400 MHz, DMSO) δ 9.28 (dd, J = 2.2, 0.8 Hz, 1H), 8.66 (dd, J = 4.8, 1.7 Hz, 1H), 8.50 – 8.44 (m, 1H), 8.04 (d, J = 9.2 Hz, 1H), 7.92 (d, J = 2.7 Hz, 1H), 7.85 (d, J = 8.8 Hz, 1H), 7.75 (dd, J = 9.2, 2.9 Hz, 1H), 7.67 (d, J = 2.8 Hz, 1H), 7.56 (dd, J = 8.8, 2.7 Hz, 1H), 7.52 (ddd, J = 8.0, 4.8, 0.8 Hz, 1H), 5.10 (s, 2H), 3.05 (s, 3H), 2.88 (s, 3H).	DMSO	>98	Method X using K_2CO_3 instead of Cs_2CO_3
848					^{1}H NMR (400 MHz, $CDCl_3$) δ 9.45 (dd, *J* = 2.1, 0.8 Hz, 1H), 8.61 (dd, *J* = 4.8, 1.7 Hz, 1H), 8.59 – 8.53 (m, 1H), 8.01 (dd, *J* = 8.7, 0.8 Hz, 1H), 7.72 – 7.62 (m, 2H), 7.56 – 7.47 (m, 2H), 7.39 – 7.29 (m, 4H), 4.90 (s, 2H), 3.15 (s, 3H), 3.04 (s, 3H).	CDCl3	>98	Method X using K_2CO_3 instead of Cs_2CO_3
849				2 HCl	1H NMR (300 MHz, DMSO) δ 13.01 – 11.72 (m, 1H), 9.70 (s, 1H), 9.40 – 9.30 (m, 1H), 8.99 (d, J = 4.5 Hz, 1H), 8.23 (d, J = 2.6 Hz, 1H), 8.12 (dd, J = 8.1, 5.5 Hz, 1H), 8.06 – 7.98 (m, 2H), 7.92 (d, J = 9.1 Hz, 1H), 7.84 (d, J = 4.9 Hz, 1H), 7.63 (dd, J = 9.1, 2.6 Hz, 1H), 7.56 – 7.49 (m, 2H), 5.05 (s, 3H), 3.11 (s, 3H), 2.92 (s, 3H).	DMSO	>98	W

445

850				2 HCl	1H NMR (300 MHz, DMSO) δ 9.74 (d, J = 1.8 Hz, 1H), 9.47 – 9.36 (m, 1H), 9.01 (dd, J = 5.5, 1.2 Hz, 1H), 8.28 (d, J = 2.6 Hz, 1H), 8.16 (dd, J = 8.2, 5.5 Hz, 1H), 8.06 – 7.93 (m, 3H), 7.81 (s, 1H), 7.66 (dd, J = 9.1, 2.6 Hz, 1H), 7.54 – 7.44 (m, 2H), 7.42 – 7.33 (m, 1H), 5.07 (s, 2H), 3.11 (s, 3H), 2.91 (s, 3H).	DMSO	>98	W
851				2 HCl	1H NMR (300 MHz, DMSO) δ 12.67 (s, 1H), 9.31 – 9.25 (m, 1H), 8.73 (dd, J = 4.8, 1.6 Hz, 1H), 8.52 – 8.42 (m, 1H), 7.74 (d, J = 8.9 Hz, 1H), 7.66 (d, J = 2.9 Hz, 1H), 7.61 – 7.47 (m, 4H), 7.45 – 7.31 (m, 3H), 5.27 (s, 2H), 3.30 (s, 3H).	DMSO	>98	W
852				3 HCl	1H NMR (300 MHz, DMSO) δ 9.56 (d, J = 1.8 Hz, 1H), 9.25 (d, J = 8.2 Hz, 1H), 9.08 – 8.98 (m, 1H), 8.81 (d, J = 4.5 Hz, 1H), 8.31 (td, J = 7.8, 1.6 Hz, 1H), 8.20 – 8.08 (m, 1H), 7.95 (d, J = 7.9 Hz, 1H), 7.88 – 7.63 (m, 4H), 7.47 (d, J = 2.1 Hz, 1H), 7.30 (dd, J = 8.6, 2.2 Hz, 1H), 5.60 (s, 2H), 4.63 (t, J = 7.8 Hz, 2H), 3.25 (t, J = 7.7 Hz, 2H).	DMSO	>98	W
853				3 HCl	1H NMR (300 MHz, DMSO) δ 9.56 (d, J = 1.8 Hz, 1H), 9.22 (d, J = 8.3 Hz, 1H), 9.00 (dd, J = 5.5, 1.3 Hz, 1H), 8.80 (d, J = 4.4 Hz, 1H), 8.29 (td, J = 7.8, 1.6 Hz, 1H), 8.21 – 8.05 (m, 2H), 8.00 – 7.66 (m, 5H), 7.29 (dd, J = 8.4, 2.6 Hz, 1H), 7.12 (td, J = 9.0, 2.8 Hz, 1H), 5.59 (s, 2H), 4.66 (t, J = 7.8 Hz, 2H), 3.25 (t, J = 7.6 Hz, 2H).	DMSO	>98	W
854				2 HCl	1H NMR (300 MHz, DMSO) δ 9.55 (d, J = 1.8 Hz, 1H), 9.30 – 9.18 (m, 1H), 9.00 (dd, J = 5.5, 1.3 Hz, 1H), 8.18 – 8.02 (m, 2H), 7.87 (dd, J = 8.8, 4.8 Hz, 1H), 7.71 (dd, J = 9.2, 2.7 Hz, 1H), 7.49 (d, J = 2.7 Hz, 1H), 7.29 (dd, J = 8.4, 2.6 Hz, 1H), 7.13 (td, J = 9.1, 2.8 Hz, 1H), 5.05 (s, 2H), 4.63 (d, J = 7.7 Hz, 2H), 3.25 (t, J = 7.5 Hz, 2H), 3.02 (s, 3H), 2.86 (s, 3H).	DMSO	>98	W

446

855				2 HCl	1H NMR (300 MHz, DMSO) δ 9.55 (d, J = 1.7 Hz, 1H), 9.15 (d, J = 8.2 Hz, 1H), 8.99 – 8.90 (m, 1H), 8.10 – 7.98 (m, 2H), 7.77 (dd, J = 8.9, 4.7 Hz, 1H), 7.67 (dd, J = 9.1, 2.7 Hz, 1H), 7.51 (d, J = 2.6 Hz, 1H), 7.28 (dd, J = 8.4, 2.7 Hz, 1H), 7.12 (dd, J = 10.3, 7.7 Hz, 1H), 4.70 (t, J = 7.8 Hz, 2H), 4.23 – 4.14 (m, 2H), 3.26 (t, J = 7.9 Hz, 2H), 1.41 (t, J = 6.9 Hz, 3H).	DMSO	>98	W
856				2 HCl	1H NMR (300 MHz, DMSO) δ 9.54 (d, J = 1.7 Hz, 1H), 9.19 (d, J = 8.1 Hz, 1H), 8.98 (d, J = 4.3 Hz, 1H), 8.15 – 8.02 (m, 2H), 7.90 – 7.72 (m, 2H), 7.60 (d, J = 2.6 Hz, 1H), 7.53 – 7.41 (m, 1H), 7.40 – 7.05 (m, 5H), 5.34 (s, 2H), 4.59 (t, J = 7.8 Hz, 2H), 3.22 (t, J = 7.5 Hz, 2H).	DMSO	>98	W
857				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.56 (s, 1H), 9.49 (d, *J* = 1.8 Hz, 1H), 9.11 (d, *J* = 8.0 Hz, 1H), 8.95 (dd, *J* = 5.4, 1.3 Hz, 1H), 8.26 (dd, *J* = 24.6, 3.5 Hz, 2H), 8.12 – 7.95 (m, 3H), 7.71 (dt, *J* = 9.1, 4.5 Hz, 2H), 7.56 (dd, *J* = 19.7, 9.1 Hz, 1H), 4.75 (s, 2H), 2.72 (d, *J* = 5.0 Hz, 3H).	DMSO	>98	Method W
858					^{1}H NMR (400 MHz, DMSO) δ 9.77 (br s, *J* = 81.7 Hz, 1H), 9.50 (d, *J* = 1.5 Hz, 1H), 8.71 – 8.57 (m, 2H), 8.22 – 8.07 (m, 1H), 7.97 (t, *J* = 5.1 Hz, 1H), 7.87 (d, *J* = 9.1 Hz, 1H), 7.81 – 7.39 (m, 4H), 5.01 (s, 2H), 3.07 (s, 3H), 2.90 (s, 3H).	DMSO	>98	Method W

447

859				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.62 (s, 1H), 9.50 (d, *J* = 1.7 Hz, 1H), 9.01 (d, *J* = 8.1 Hz, 1H), 8.90 (dd, *J* = 5.3, 1.5 Hz, 1H), 8.32 (d, *J* = 2.3 Hz, 1H), 8.20 – 8.09 (m, 1H), 7.95 (dd, *J* = 8.5, 4.7 Hz, 2H), 7.83 – 7.74 (m, 1H), 7.67 (dd, *J* = 9.1, 2.6 Hz, 1H), 7.55 (dd, *J* = 19.7, 9.1 Hz, 1H), 5.15 (s, 2H), 4.29 – 3.00 (m, 8H).	DMSO	>98	Method W
860				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.39 (s, 1H), 9.51 (d, *J* = 1.6 Hz, 1H), 8.81 (dd, *J* = 19.3, 6.0 Hz, 2H), 8.29 (s, 1H), 8.16 (dd, *J* = 10.6, 7.5 Hz, 1H), 7.94 (d, *J* = 9.0 Hz, 1H), 7.77 (s, 2H), 7.69 – 7.51 (m, 2H), 4.67 (s, 2H), 3.99 (s, 2H), 3.81 (br s, 4H), 3.70 (br s, 4H).	DMSO	>98	Method W
861				3 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.82 (s, 1H), 9.50 (d, *J* = 1.3 Hz, 1H), 9.02 (d, *J* = 8.0 Hz, 1H), 8.90 (d, *J* = 4.4 Hz, 1H), 8.46 (s, 1H), 8.21 – 8.10 (m, 1H), 8.03 – 7.90 (m, 2H), 7.84 (d, *J* = 8.7 Hz, 1H), 7.68 (dd, *J* = 9.1, 2.3 Hz, 1H), 7.55 (dd, *J* = 19.6, 9.3 Hz, 1H), 4.67 (s, 2H), 3.23 – 3.05 (m, 6H), 2.10 – 1.78 (m, 4H).	DMSO	>98	Method W
862				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.77 (s, 1H), 9.49 (d, *J* = 1.6 Hz, 1H), 9.12 (d, *J* = 8.1 Hz, 1H), 8.99 – 8.91 (m, 1H), 8.23 (d, *J* = 2.1 Hz, 1H), 8.12 – 7.99 (m, 3H), 7.78 – 7.71 (m, 1H), 7.66-7.54 (m, 2H), 4.02 (d, *J* = 6.5 Hz, 2H), 2.24 – 2.00 (m, 1H), 1.07 (d, *J* = 6.7 Hz, 6H).	DMSO	>98	Method W

448

863				2 HCl	^{1}H NMR (400 MHz, $CDCl_3$) δ10.71 (s, 1H), 9.80 (s, 1H), 9.40 (d, *J* = 8.2 Hz, 1H), 8.95 (d, *J* = 5.2 Hz, 1H), 8.54 (d, *J* = 2.4 Hz, 1H), 8.24 (d, *J* = 9.2 Hz, 1H), 8.08 (dd, *J* = 8.0, 5.6 Hz, 1H), 7.86 – 7.76 (m, 1H), 7.69 (d, *J* = 8.7 Hz, 1H), 7.56 (d, *J* = 8.8, 2.2 Hz, 1H), 7.31 (s, 1H), 5.08 (s, 2H), 3.69 (t, *J* = 6.8 Hz, 2H), 3.55 (t, *J* = 6.9 Hz, 2H), 2.13 – 2.01 (m, 2H), 1.98 – 1.85 (m, 2H).	DMSO	>98	Method W
864				2 HCl	1H NMR (400 MHz, DMSO) δ 10.62 (s, 1H), 9.50 (d, *J* = 1.9 Hz, 1H), 9.12 (d, *J* = 8.2 Hz, 1H), 8.96 (dd, *J* = 5.5, 1.4 Hz, 1H), 8.27 (d, *J* = 2.6 Hz, 1H), 8.20 (d, *J* = 8.0 Hz, 1H), 8.15 – 7.97 (m, 3H), 7.75 (ddd, *J* = 11.9, 7.4, 3.3 Hz, 2H), 7.56 (dt, *J* = 10.6, 9.1 Hz, 1H), 4.74 (s, 2H), 4.07 – 3.93 (m, 1H), 1.13 (d, *J* = 6.6 Hz, 6H)..	DMSO	>98	Method W
865				3 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.83 (s, 1H), 9.51 (d, *J* = 1.8 Hz, 1H), 9.15 (d, *J* = 8.2 Hz, 1H), 8.97 (dd, *J* = 5.4, 1.3 Hz, 1H), 8.82 – 8.74 (m, 1H), 8.55 (d, *J* = 2.6 Hz, 1H), 8.28 – 8.19 (m, 1H), 8.16 – 8.01 (m, 3H), 7.94 (d, *J* = 7.9 Hz, 1H), 7.85 – 7.75 (m, 2H), 7.70 (dd, *J* = 7.0, 5.8 Hz, 1H), 7.61 – 7.49 (m, 1H), 5.63 (s, 2H).	DMSO	>98	Method W
866				4 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.62 (s, 1H), 9.50 (d, *J* = 1.8 Hz, 1H), 9.11 (d, *J* = 8.1 Hz, 1H), 8.95 (d, *J* = 5.4 Hz, 1H), 8.76 (d, *J* = 5.0 Hz, 1H), 8.42 (s, 1H), 8.18 (t, *J* = 7.8 Hz, 1H), 8.08 – 7.96 (m, 4H), 7.89 (d, *J* = 7.8 Hz, 1H), 7.80 (dd, *J* = 9.1, 2.6 Hz, 1H), 7.64 (t, *J* = 8.2 Hz, 2H), 7.24 (d, *J* = 8.3 Hz, 1H), 5.57 (s, 2H).	DMSO	>98	Method W

449

867				HCl	1H NMR (300 MHz, DMSO) d 9.58 (s, 1H), 9.05 (d, J = 8.2 Hz, 1H), 8.98 (d, J = 8.1 Hz, 1H), 8.88 (d, J = 5.1 Hz, 1H), 8.47 (s, 1H), 8.05 - 7.85 (m, 4H), 7.71 (m, 1H), 7.61 (d, J = 8.1 Hz, 2H), 7.24 (dd, J = 7.6 Hz, 1H).	DMSO	94	Method X (K2CO3, DMF-THF (1 :1), rt)
868				2 HCl	1H NMR (300 MHz, DMSO) δ 13.07 (s, 1H), 9.59 (d, J = 1.4 Hz, 1H), 9.13 (d, J = 8.1 Hz, 1H), 8.97 (d, J = 7.8 Hz, 1H), 8.92 (d, J = 4.1 Hz, 1H), 8.49 (s, 1H), 8.08 - 7.92 (m, 4H), 7.80 - 7.64 (m, 3H), 7.26 (td, J = 7.8, 1.1 Hz, 1H), 7.14 (d, J = 1.5 Hz, 1H), 7.09 (dd, J = 7.9, 1.6 Hz, 1H), 6.95 (d, J = 7.9 Hz, 1H), 6.03 (s, 2H), 5.19 (s, 2H).	DMSO	99	Method W
869				3HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.67 (s, 1H), 9.40 (d, *J* = 7.6 Hz, 1H), 9.01 (d, *J* = 8.4 Hz, 2H), 8.93 (d, *J* = 8.4 Hz, 1H), 8.31 (d, *J* = 7.6 Hz, 1H), 8.22 (t, *J* = 7.2 Hz, 1H), 8.01 (d, *J* = 9.2 Hz, 1H), 7.97 – 7.92 (m, 2H), 7.79 – 7.71 (m, 3H), 7.33 (t, *J* = 8.0 Hz, 1H), 5.54 (s, 2H).	DMSO	98	Method X
870				2HCl	^{1}H-NMR (400 MHz, CD3OD): δ 9.62 (d, *J* = 6.9 Hz, 1H), 9.40 (d, *J* = 8.2 Hz, 1H), 8.99 (d, *J* = 5.3 Hz, 1H), 8.82 (t, *J* = 8.2 Hz, 1H), 8.22 (dd, *J* = 8.1, 5.7 Hz, 1H), 8.02 – 7.88 (m, 2H), 7.76 – 7.60 (m, 3H), 7.31 (t, *J* = 7.6 Hz, 1H), 4.81 (q, *J* = 8.1 Hz, 2H).	MeOD	95	Method W
871				4HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 12.96 (s, 1H), 9.59 (s, 1H), 9.24 (d, *J* = 8.1 Hz, 1H), 9.00 (s, 1H), 8.80 (d, *J* = 5.7 Hz, 2H), 8.50 (s, 1H), 8.22 (t, *J* = 7.2 Hz, 1H), 8.09 (d, *J* = 9.2 Hz, 2H), 7.99 – 7.79 (m, 5H), 7.74 – 7.54 (m, 6H), 7.30 (t, *J* = 7.5 Hz, 1H), 5.55 (s, 2H).	DMSO-d_6	95	Method X

450

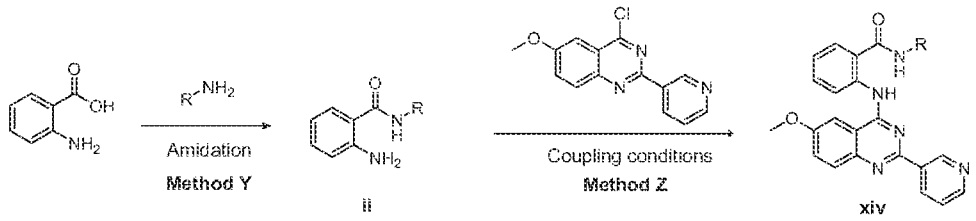
872				2HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 12.82 (s, 1H), 9.58 (s, 1H), 9.13 (d, *J* = 6.9 Hz, 1H), 8.93 (s, 1H), 8.82 (d, *J* = 8.0 Hz, 1H), 8.43 (s, 1H), 8.04 – 7.88 (m, 4H), 7.74 – 7.69 (m, 3H), 7.28 (t, *J* = 7.6 Hz, 1H), 7.01 – 6.91 (m, 2H), 6.87 – 6.85 (m, 2H), 4.74 – 4.70 (m, 1H), 4.55 – 4,.53 (m, 1H), 4.50 – 4.47 (m, 1H), 4.29 – 4.24 (m, 1H).	DMSO	95	Method X
873				3HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 13.07 (s, 1H), 9.61 (s, 1H), 9.05 – 9.00 (m, 2H), 8.88 (d, *J* = 4 Hz, 1H), 8.51 (s, 1H), 8.25 (s, 1H), 8.11 – 8.08 (m, 2H), 7.99 – 7.97 (m, 3H), 7.91 – 7.88 (m, 2H), 7.76 – 7.72 (m, 2H), 7.47 (dd, *J* = 2.0, 8.8 Hz, 1H), 7.27 (t, *J* = 8.8 Hz, 1H), 5.61 (s, 2H).	DMSO	95	Method X
874				2HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 12.89 (s, 1H), 10.72 (s, 1H), 9.83 (s, 1H), 9.38 (d, *J* = 8.2 Hz, 1H), 9.22 (d, *J* = 5.6 Hz, 1H), 9.03 (d, *J* = 8.3 Hz, 1H), 8.51 (s, 1H), 8.37 – 8.27 (m, 1H), 8.02 – 7.86 (m, 3H), 7.71 (t, *J* = 7.6 Hz, 1H), 7.55 (d, *J* = 9.0 Hz, 1H), 7.51 (s, 1H), 7.25 (t, *J* = 7.5 Hz, 1H), 4.71 (d, *J* = 7.3 Hz, 2H), 1.56 (s, 1H), 0.81 – 0.64 (m, 4H).	DMSO	95	Method X
875				3HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 12.88 (s, 1H), 9.57 (s, 1H), 9.24 (d, *J* = 8.1 Hz, 1H), 9.01 (d, *J* = 5.3 Hz, 1H), 8.73 (d, *J* = 8.2 Hz, 1H), 8.49 (s, 1H), 8.37 (t, *J* = 7.8 Hz, 1H), 8.10 (dd, *J* = 11.3, 7.0 Hz, 2H), 7.97 (d, *J* = 7.8 Hz, 2H), 7.86 (s, 2H), 7.80 (d, *J* = 7.1 Hz, 2H), 7.71 (t, *J* = 7.8 Hz, 1H), 7.30 (t, *J* = 7.5 Hz, 1H), 5.65 (s, 2H), 2.78 (s, 3H).	DMSO	95	Method X
876				CF3COOH	^{1}H-NMR (400 MHz, DMSO-d_6): δ 12.93 (s, 1H), 10.74 (s, 1H), 9.75 (s, 1H), 9.40 (s, 1H), 9.05 (d, J = 8.0 Hz, 2H), 8.99 (d, J = 6.0 Hz, 1H), 7.99 (s, 1H), 7.98 – 7.96 (m, 1H), 7.89 – 7.86 (m, 2H), 7.72 – 7.51 (m, 2H), 7.24 (t, J = 6.0 Hz, 1H), 5.84 (s, 2H), 3.60 – 3.56 (m, 2H), 3.43 – 3.39 (m, 2H), 2.06 – 2.01 (m, 2H), 1.99 – 1.84 (m, 2H).	DMSO	95	Method W

451

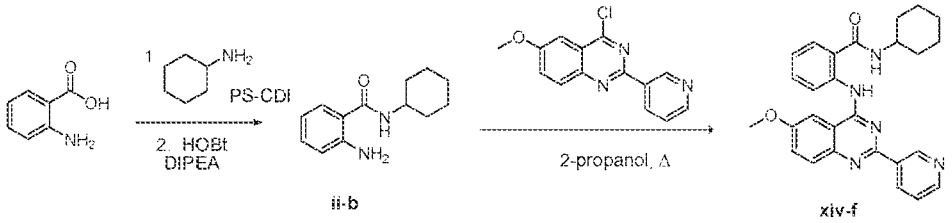
1757					^{1}H NMR (400 MHz, DMSO) δ 9.32 – 9.27 (m, 1H), 8.66 (dd, *J* = 4.8, 1.7 Hz, 1H), 8.64 – 8.60 (m, 1H), 8.50 – 8.43 (m, 1H), 8.10 – 8.03 (m, 1H), 7.93 – 7.80 (m, 4H), 7.68 – 7.60 (m, 2H), 7.59 – 7.49 (m, 2H), 7.39 (ddd, *J* = 7.5, 4.8, 1.1 Hz, 1H), 5.43 (s, 2H).	DMSO	>98	Method W using K_2CO_3 instead of Cs_2CO_3

452

Scheme 27: General route for the synthesis of compounds with general formula xiv



Scheme 28: Representative synthesis of compounds of formula xiv (see Scheme 27)

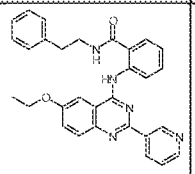
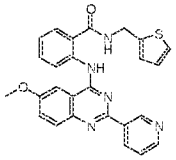
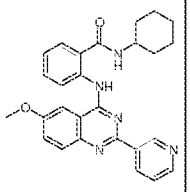
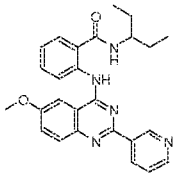
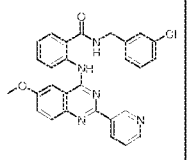
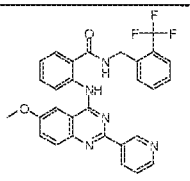
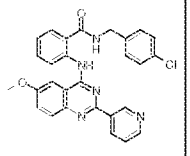
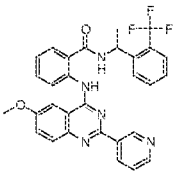
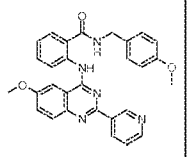
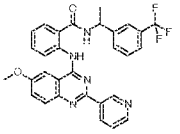
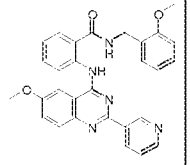
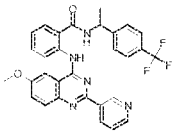
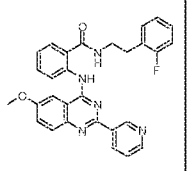
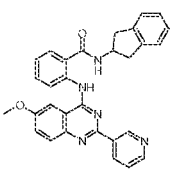


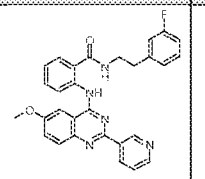
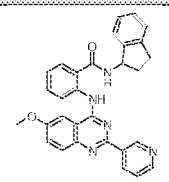
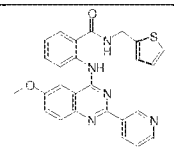
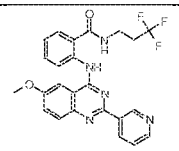
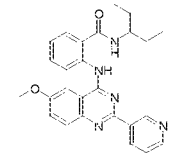
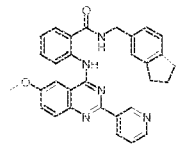
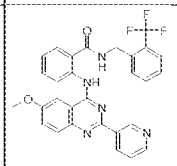
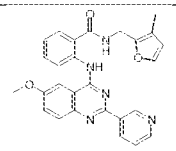
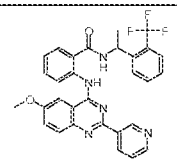
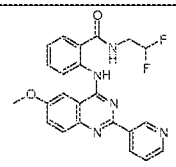
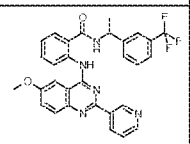
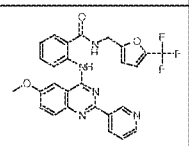
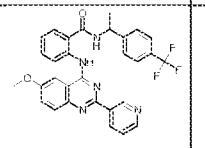
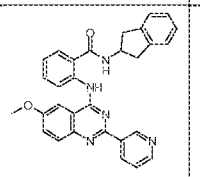
Method Y: 2-Amino-N-cyclohexyl-benzamide (ii-b) To a dry reaction vial was added cyclohexylamine (40 uμmol, 1.0 eq) and PS-carbodiimide resin (72 μmol, 1.8 eq). The solution of 2-amino-benzoic acid (44 μmol, 1.1 eq), diisopropyl ethyl amine (10 μLl) and HOBt (44 μmol, 1.1 eq) in THF (500 μL) was added to the above vial. The reaction mixture was heated at 40^{0}C for 6 h on a shaker. The resin was removed by filtration and washed with 10% MeOH/CH_2Cl_2. The solvent was removed *in vacuo* and the residue was applied to solid phase extraction cartridge (basic silica, 200 mg) and eluted with 50% EtOAc/CH_2Cl_2. After removal of the solvents, the crude 2-amino-N-cyclohexyl-benzamide was obtained and used for the following reaction.

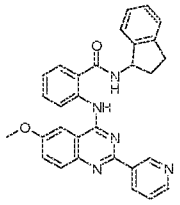
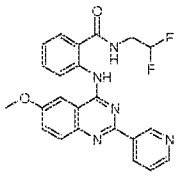
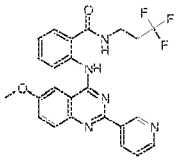
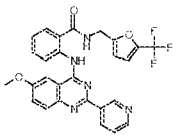
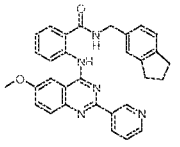
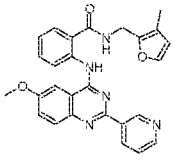
Method Z: N-Cyclohexyl-2-(6-methoxy-2-pyridin-3-yl-quinazolin-4-ylamino)-benzamide (xiv-f) To the crude amide was added the solution of 4-chloro-6-methoxy-2-pyridin-3-yl-quinazoline (20 μmol) in 2-propanol (200 μL). The mixture was refluxed for 8 h. After evaporation, the residue was dissolved in 5%TFA/MeOH-DMF(1:1) and purified by **PREP-HPLC Condition D**. The target fraction was lyophilized to afford the titled compound whose structure was finally confirmed by LCMS using LCMS **Method E.**

The compounds in the following table were prepared in a manner analogous to that described in **Scheme 27**, replacing cyclohexylamine with the appropriate amine.

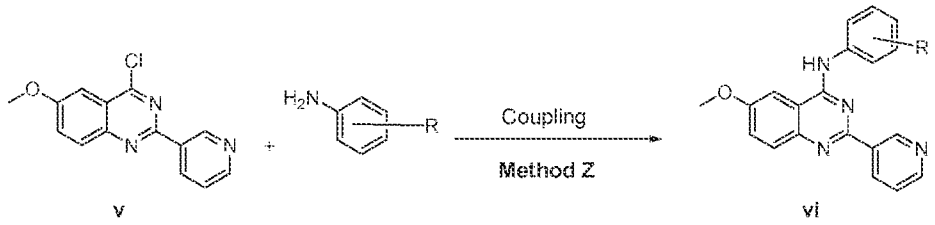
Table 7:

Number	Product	Exact Mass	LCMS (M+1)	Method of Coupling	Number	Product	Exact Mass	LCMS (M+1)	Method of Coupling
877		489	490	Methods Y, Z	884		467	468	Methods Y, Z
878		453	454	Methods Y, Z	885		441	442	Methods Y, Z
879		495	496	Methods Y, Z	886		529	530	Methods Y, Z
880		495	496	Methods Y, Z	887		543	544	Methods Y, Z
881		491	492	Methods Y, Z	888		543	544	Methods Y, Z
882		491	492	Methods Y, Z	889		543	544	Methods Y, Z
883		493	494	Methods Y, Z	890		487	488	Methods Y, Z

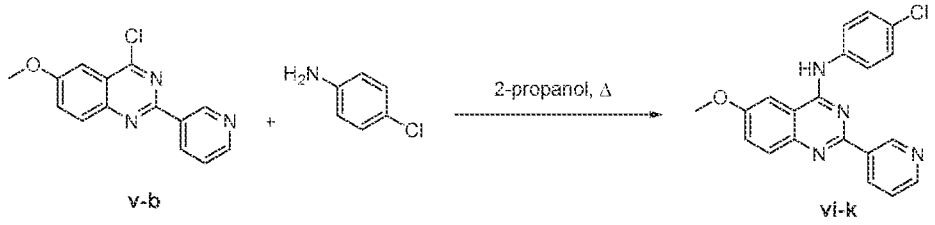
Number	Product	Exact Mass	LCMS (M+1)	Method of Coupling	Number	Product	Exact Mass	LCMS (M+1)	Method of Coupling
891		493	494	Methods Y, Z	**898**		487	488	Methods Y, Z
892		467	468	Methods Y, Z	**899**		467	468	Methods Y, Z
893		441	442	Methods Y, Z	**900**		501	502	Methods Y, Z
894		529	530	Methods Y, Z	**901**		465	466	Methods Y, Z
895		543	544	Methods Y, Z	**902**		435	436	Methods Y, Z
896		543	544	Methods Y, Z	**903**		519	520	Methods Y, Z
897		543	544	Methods Y, Z	**904**		487	488	Methods Y, Z

Number	Product	Exact Mass	LCMS (M+1)	Method of Coupling	Number	Product	Exact Mass	LCMS (M+1)	Method of Coupling
905		487	488	Methods Y, Z	**909**		435	436	Methods Y, Z
906		467	468	Methods Y, Z	**910**		519	520	Methods Y, Z
907		501	502	Methods Y, Z					
908		465	466	Methods Y, Z					

Scheme 29: General route for the synthesis of compounds with general formula vi



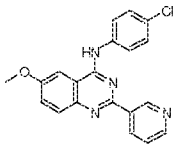
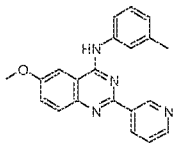
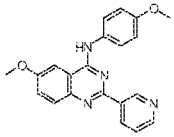
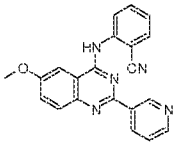
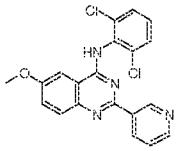
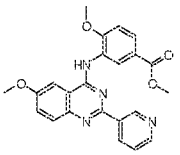
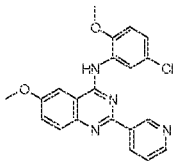
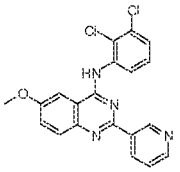
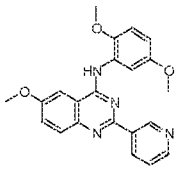
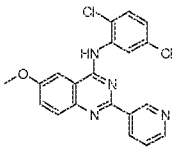
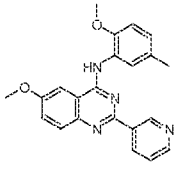
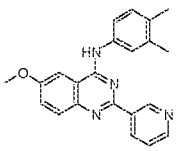
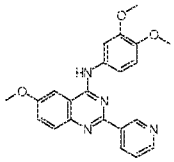
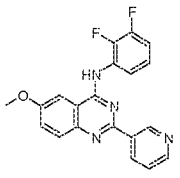
Scheme 30: Representative synthesis of compounds of formula vi-b (see Scheme 29)

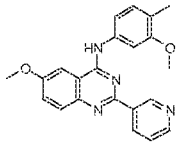
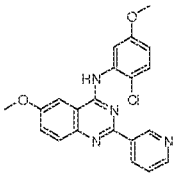
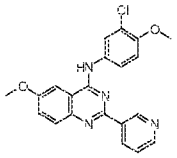
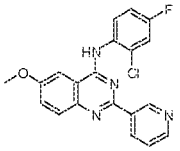
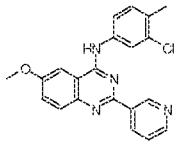
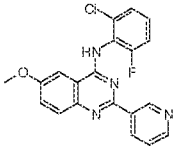
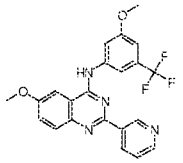
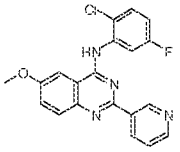
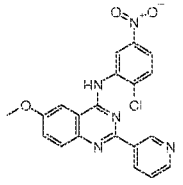
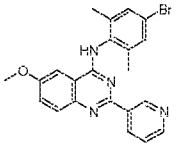
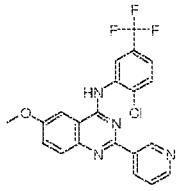
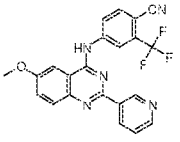
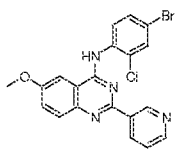
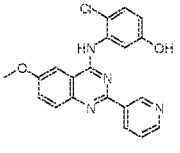


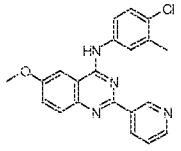
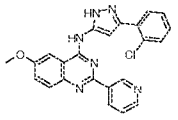
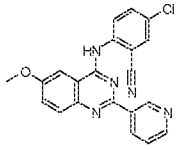
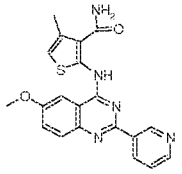
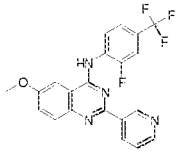
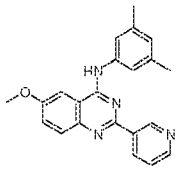
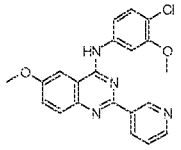
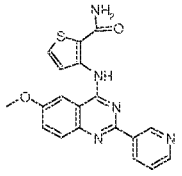
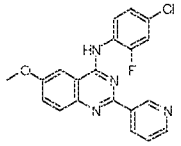
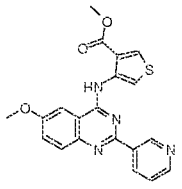
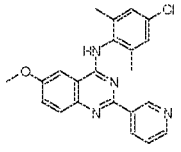
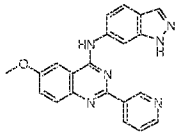
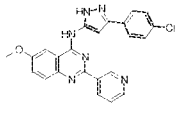
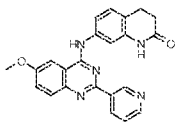
Method Z: Synthesis of N-(4-chlorophenyl)-6-methoxy-2-(pyridin-3-yl)quinazolin-4-amine (vi-k) To 4-chloroaniline (24 μmol) was added the solution of 4-chloro-6-methoxy-2-pyridin-3-yl-quinazoline (20 μmol) in 2-propanol (200 μL). The mixture was refluxed for 8 h. After evaporation, the residue was dissolved in 5%TFA/MeOH-DMF(1:1) and purified by **PREP-HPLC Condition D.** The target fraction was lyophilized to afford the titled compound as the TFA salt whose structure was finally confirmed by LCMS using LCMS **Method E.**

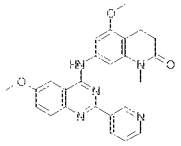
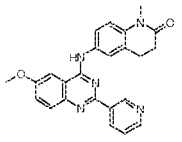
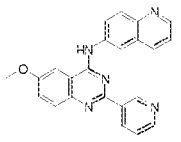
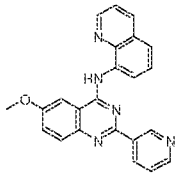
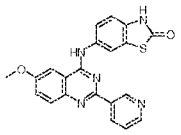
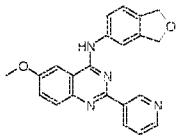
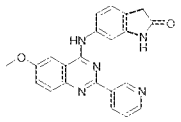
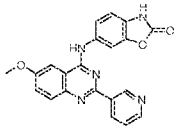
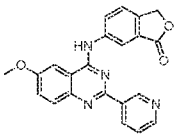
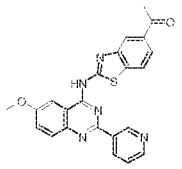
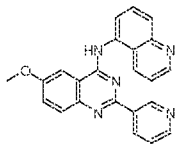
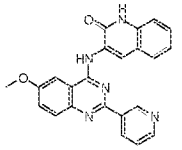
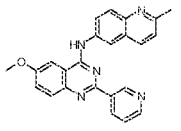
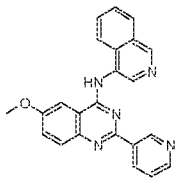
The compounds in the following table were prepared in a manner analogous to that described in **Scheme 29**, replacing 4-chloroaniline with the appropriate aniline.

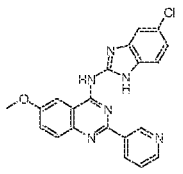
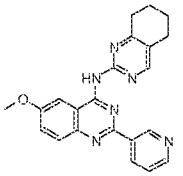
Table 8:

Number	Product	Exact Mass	LCMS (M+1)	Method of Coupling	Number	Product	Exact Mass	LCMS (M+1)	Method of Coupling
911		362	363	Method Z	918		342	343	Method Z
912		358	359	Method Z	919		353	354	Method Z
913		396	397	Method Z	920		416	417	Method Z
914		392	393	Method Z	921		396	397	Method Z
915		388	389	Method Z	922		396	397	Method Z
916		372	373	Method Z	923		356	357	Method Z
917		388	389	Method Z	924		364	365	Method Z

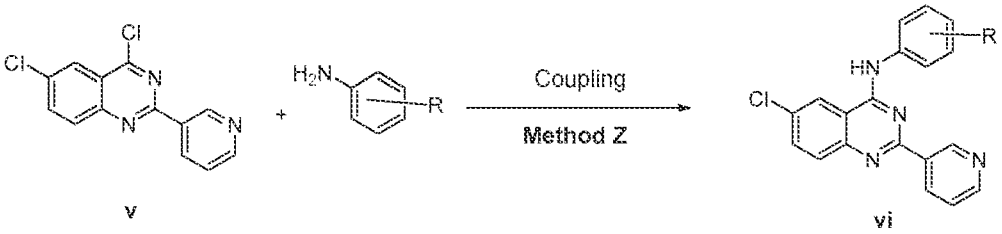
925		372	373	Method Z	932		392	393	Method Z
926		392	393	Method Z	933		380	381	Method Z
927		376	377	Method Z	934		380	381	Method Z
928		426	427	Method Z	935		380	381	Method Z
929		407	408	Method Z	936		434	435	Method Z
930		430	431	Method Z	937		421	422	Method Z
931		440	441	Method Z	938		378	379	Method Z

939		376	377	Method Z	**946**		428	429	Method Z
940		387	388	Method Z	**947**		391	392	Method Z
941		414	415	Method Z	**948**		356	357	Method Z
942		392	393	Method Z	**949**		377	378	Method Z
943		380	381	Method Z	**950**		392	393	Method Z
944		390	391	Method Z	**951**		368	369	Method Z
945		428	429	Method Z	**952**		397	398	Method Z

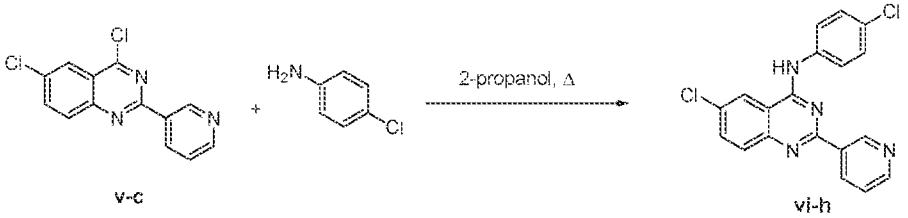
953		441	442	Method Z	**960**		411	412	Method Z
954		379	380	Method Z	**961**		379	380	Method Z
955		401	402	Method Z	**962**		370	371	Method Z
956		383	384	Method Z	**963**		385	386	Method Z
957		382	383	Method Z	**964**		427	428	Method Z
958		379	380	Method Z	**965**		395	396	Method Z
959		393	394	Method Z	**966**		379	380	Method Z

967		402	403	Method Z	968		384	385	Method Z

Scheme 31: General route for the synthesis of compounds with general formula vi



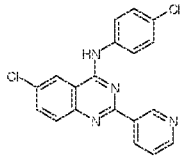
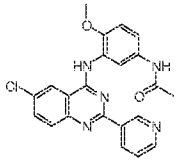
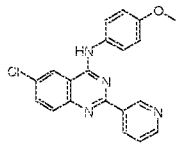
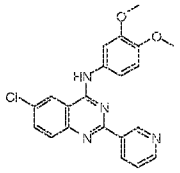
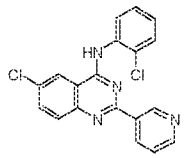
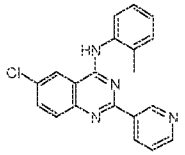
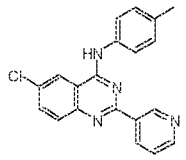
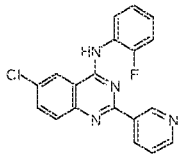
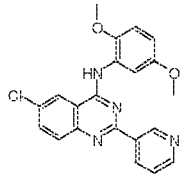
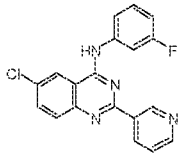
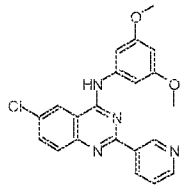
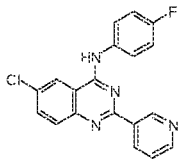
Scheme 32: Representative synthesis of compounds of formula vi (see Scheme 31)

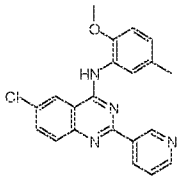
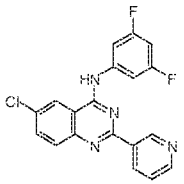
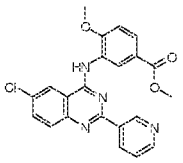
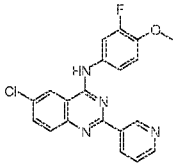
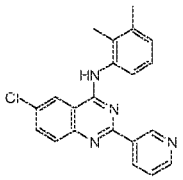
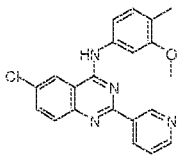
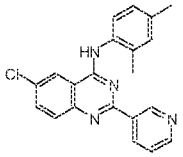
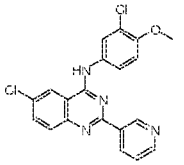
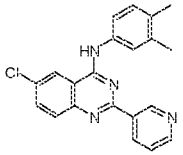
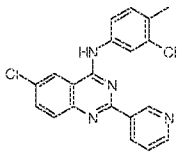
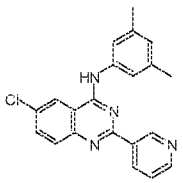
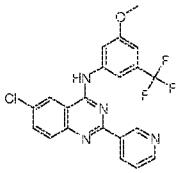
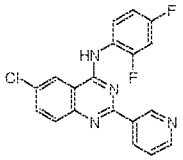
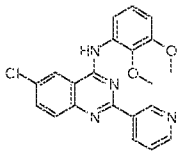


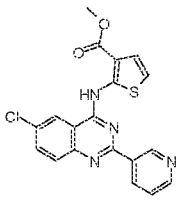
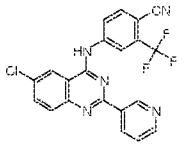
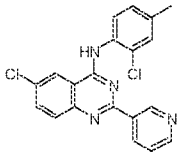
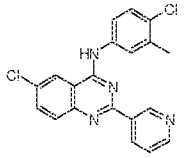
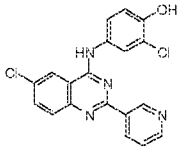
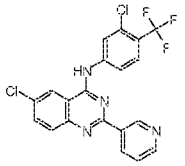
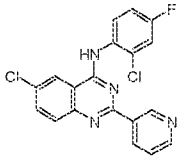
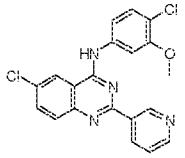
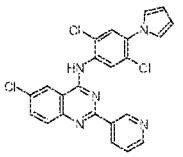
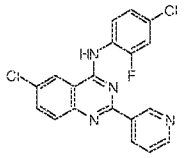
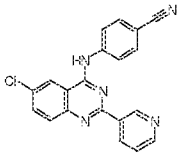
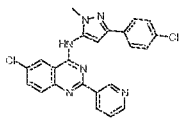
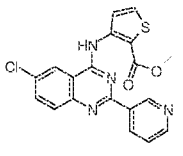
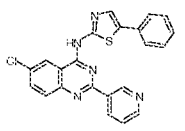
Method Z: Synthesis of 6-chloro-N-(4-chlorophenyl)-2-(pyridin-3-yl)quinazolin-4-amine (vi-c): To 4-chloroaniline (24 μmol) was added the solution of 4,6-dichloro-2-(pyridin-3-yl)quinazoline (20 μmol) in 2-propanol (200 μL). The mixture was refluxed for 8 h. After evaporation, the residue was dissolved in 5%TFA/MeOH-DMF(1:1) and purified by **PREP-HPLC Condition D**. The target fraction was lyophilized to afford the titled compound as the TFA salt whose structure was finally confirmed by LCMS using LCMS **Method E**.

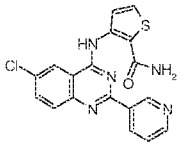
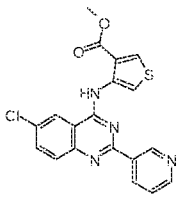
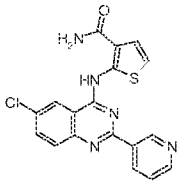
The compounds in the following table were prepared in a manner analogous to that described in **Scheme 31**, replacing 4-chloroaniline with the appropriate aniline.

Table 9:

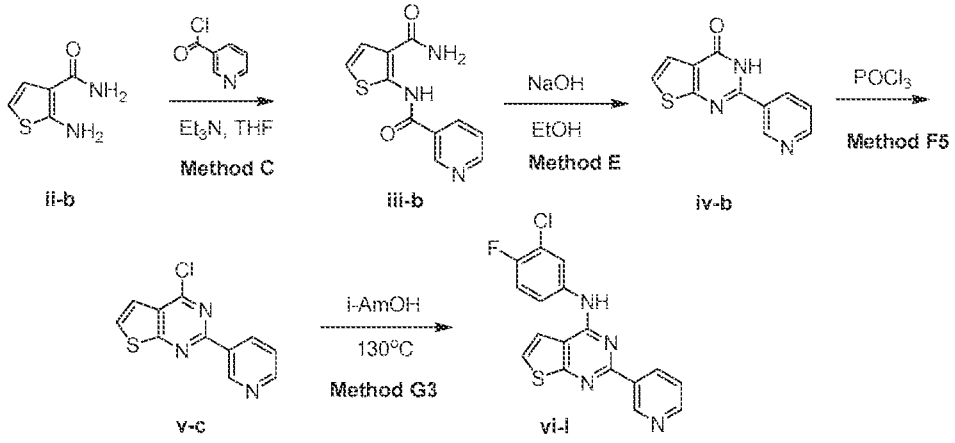
Number	Product	Exact Mass	LCMS (M+1)	Method of Coupling	Number	Product	Exact Mass	LCMS (M+1)	Method of Coupling
969		366	367	Method Z	**975**		419	420	Method Z
970		362	363	Method Z	**976**		392	393	Method Z
971		366	367	Method Z	**977**		346	347	Method Z
972		346	347	Method Z	**978**		350	351	Method Z
973		392	393	Method Z	**979**		350	351	Method Z
974		392	393	Method Z	**980**		350	351	Method Z

981		376	377	Method Z	988		368	369	Method Z
982		420	421	Method Z	989		380	381	Method Z
983		360	361	Method Z	990		376	377	Method Z
984		360	361	Method Z	991		396	397	Method Z
985		360	361	Method Z	992		380	381	Method Z
986		360	361	Method Z	993		430	431	Method Z
987		368	369	Method Z	994		392	393	Method Z

995		396	397	Method Z	**1002**		425	426	Method Z
996		380	381	Method Z	**1003**		380	381	Method Z
997		382	383	Method Z	**1004**		434	435	Method Z
998		384	385	Method Z	**1005**		396	397	Method Z
999		465	466	Method Z	**1006**		384	385	Method Z
1000		357	358	Method Z	**1007**		446	447	Method Z
1001		396	397	Method Z	**1008**		415	416	Method Z

1009		381	382	Method Z	1011		396	397	Method Z
1010		381	382	Method Z					

Scheme 33: Representative synthesis of thiophene analogs of formula vi (see Scheme 4)



N-(3-Carbamoylthiophen-2-yl)nicotinamide (iii-b) To a solution of 2-aminothiophene-3-carboxamide (800 mg, 5.63 mmol, 1.0 eq.) in THF (15 mL) and Et_3N (626 mg, 6.19 mmol, 1.1 eq.) was added nicotinoyl chloride (795 mg, 5.63 mmol, 1.0 eq.) in anhydrous THF (15 mL) dropwise. The resulted mixture was stirred at room temperature overnight. After the reaction was completed, the volatiles were evaporated. The residue was washed with CH_2Cl_2 (20 mL). The resulting solid was collected and dried *in vacuo* to give 1.50 g of N-(3-carbamoylthiophen-2-

yl)nicotinamide as a brown solid (quantitative yield). LCMS m/z = 248.1(M+1) (Method B) (retention time = 1.34 min).

2-(Pyridin-3-yl) thieno [2, 3-d] pyrimidin-4(3H)-one (iv-b) A mixture of N-(3-carbamoylthiophen-2-yl)nicotinamide (1.50 g salt, 6.07 mmol, 1.0 eq.) in EtOH (300 mL) was added NaOH (1.50 g, 37.5 mmol, 6.18 eq.). The resulting mixture was stirred at 80°C for 7 days. After the reaction was completed, the volatiles were removed *in vacuo*. Water (20 mL) was added to the residue and the pH was adjusted to around 2 by adding dilute HCl (2N in water). The solution was concentrated *in vacuo* to give 11.0 g of the HCl salt as a beige solid. LCMS m/z = 230.0 (M+1) (Method B) (retention time = 1.21 min). The crude product containing salts were used for the next step without further purification.

4-Chloro-2-(pyridin-3-yl) thieno [2, 3-d] pyrimidine (v-c) The suspension of 2-(pyridin-3-yl)thieno[2,3-d]pyrimidin-4(3H)-one (6.0 g, containing salts) in $POCl_3$ (30 mL) was stirred at 120°C for 10 h. After the reaction was completed, the mixture was added to ice-water slowly. The pH was adjusted to ~7 by slowly adding $NH_3.H_2O$ at 0°C, then a precipitate formed. The solid was collected and 540 mg of 4-chloro-2-(pyridin-3-yl) thieno [2, 3-d] pyrimidine was obtained as a brown solid. LCMS m/z = 247.9, 250.0(M+1) (Method B) (retention time = 1.85 min).

N-(3-Chloro-4-fluorophenyl)-2-(pyridin-3-yl)thieno[2,3-d]pyrimidin-4-amine (vi-l) A mixture of 4-chloro-2-(pyridin-3-yl)thieno[2,3-d]pyrimidine (80 mg, 0.32 mmol, 1.0 eq.) and 3-chloro-4-fluorobenzenamine (93 mg, 0.64 mmol, 2.0 eq.) in *i*-AmOH (8 mL) was stirred at 130 °C overnight. A yellow precipitate formed and was collected and washed with MeOH (10 mL). The solid was suspended in H_2O (10 mL) and NH_3-H_2O (1 mL) was added. After filtration and drying *in vacuo*, 23.0 mg of the product was obtained as a yellow solid (20.0%). LCMS m/z = 357.0, 359.0 (M+1) (Method B) (retention time = 1.96 min). ^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.99 (s, 1H), 9.48 (d, *J* = 1.6 Hz, 1H), 8.70 – 8.67 (m, 1H), 8.63 (d, *J* = 8.0 Hz, 1H), 8.27 (dd, *J* = 6.8, 2.6 Hz, 1H), 7.76 – 7.93 (m, 3H), 7.54 – 7.57 (m, 2H).

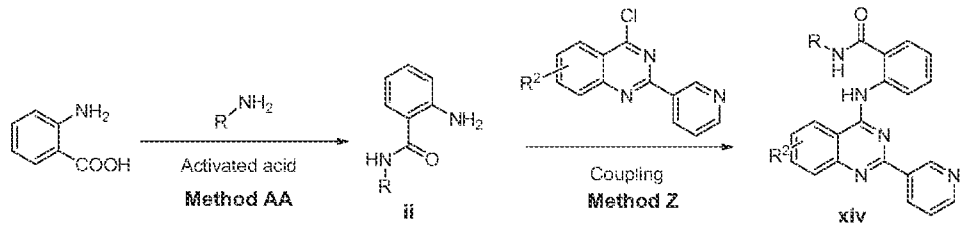
The compounds in the following table were prepared in a manner analogous to that described in **Scheme 33**, replacing 4-fluoro-3-chloroaniline with the appropriate aniline.

Table 10:

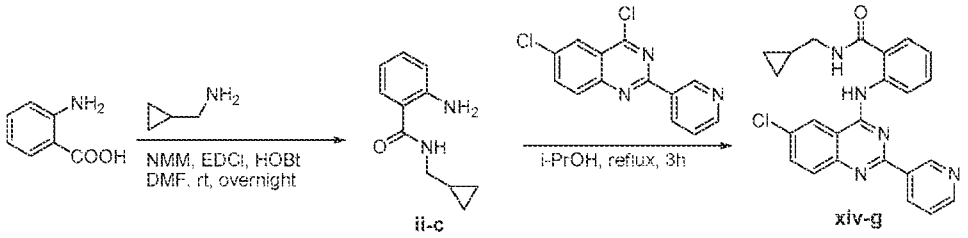
Number	PRODUCT	Salt type	Molecular Mass	^{1}H-NMR	^{1}H-NMR Solvent	LCMS	LCMS Protocol	Purity percent	Method for Coupling
1012			347.39	1H-NMR (400 MHz, DMSO-d6): δ 12.69 (s, 1H), 9.55 (d, J = 1.3 Hz, 1H), 9.00 (d, J = 8.0 Hz, 1H), 8.44 (s, 1H), 8.60 – 8.78 (m, 2H), 7.82 – 8.00 (m, 3H), 7.42 – 7.79 (m, 3H), 7.20 (t, J = 7.2 Hz, 1H).	DMSO	348.1 (M+1)	Method B (NH4HCO3)	95	Method C, G3
1013			370.38	1H-NMR (400 MHz, DMSO-d6): δ 9.96 (s, 1H), 9.51 (d, J = 1.2 Hz, 1H), 8.60 – 8.77 (m, 2H), 7.98 – 7.94 (m, 2H), 7.71 – 7.86 (m, 2H), 7.56 – 7.50 (m, 1H), 7.30 (t, J = 74.0 Hz, 1H), 6.96 (dd, J = 8.8, 2.0 Hz, 1H).	DMSO	371.0 (M+1)	Method B (NH4HCO3)	95	Method C, G3
1014			388.37	1H-NMR (400 MHz, DMSO-d6): δ 10.04 (s, 1H), 9.50 (d, J = 1.6 Hz, 1H), 8.58 – 8.75 (m, 2H), 8.18 (s, 1H), 7.77 – 8.00 (m, 3H), 7.50 – 7.65 (m, 2H), 7.08 – 7.18 (m, 1H)	DMSO	389.0 (M+1)	Method B (NH4HCO3)	95	Method C, G3
1015			356.8	1H-NMR (400 MHz, DMSO-d6): δ 9.99 (s, 1H), 9.48 (d, J = 1.6 Hz, 1H), 8.70 – 8.67 (m, 1H), 8.63 (d, J = 8.0 Hz, 1H), 8.27 (dd, J = 6.8, 2.6 Hz, 1H), 7.76 – 7.93 (m, 3H), 7.54 – 7.57 (m, 2H).	DMSO	357.0, 359.0 (M+1)	Method B (NH4HCO3)	95	Method C, G3

470

Scheme 34: General route for the synthesis of compounds with general formula xiv



Scheme 35: Representative synthesis of compounds of formula xiv-g (see Scheme 34)



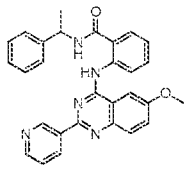
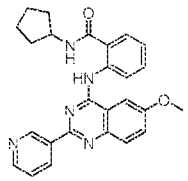
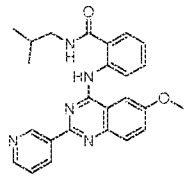
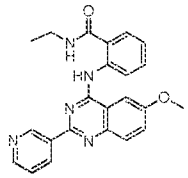
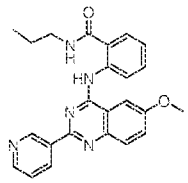
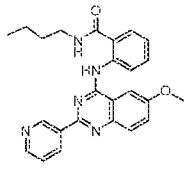
Method AA: 2-Amino-*N*-(cyclopropylmethyl)benzamide (ii-c) A 100 mL round bottom flask was charged with anthranilic acid (500 mg, 3.65 mmol), added DMF (15 mL) under nitrogen atmosphere and stirring. Then, added N-methylmorpholine (1 mL, 9.12 mmol), aminomethylcyclopropane (311 mg, 4.38 mmol), N-ethyl-N'-dimethylaminopropylcarbodiimide (EDCI) (840 mg, 4.38 mmol) and HOBt (670 mg, 4.38 mmol). The reaction mixture was stirred at room temperature overnight. The reaction mixture was quenched with water and extracted with diethyl ether (50 mL x 2). The organic extracts were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated to afford amorphous colorless 2-amino-*N*-(cyclopropylmethyl)benzamide (500 mg, 72% yield), which was checked by NMR and used for next step without further purification. ^{1}H-NMR (Bruker 300 MHz, DMSO-d6) δ 0.20-1.01 (m, 4H), 1.01-1.04 (m, 1H), 3.06-3.11 (m, 2H), 6.37-8.21 (m, 7H).

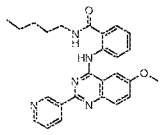
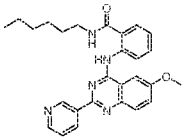
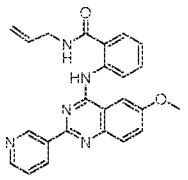
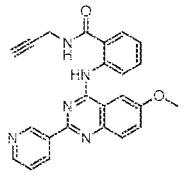
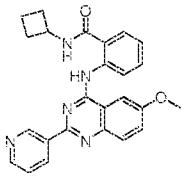
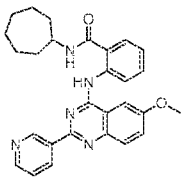
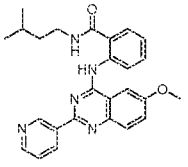
Method Z: 2-(6-chloro-2-(pyridin-3-yl)quinazolin-4-ylamino)-*N*-(cyclopropylmethyl) benzamide (xiv-g): A 100 mL round bottom flask was charged

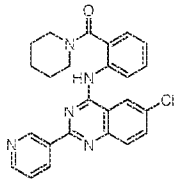
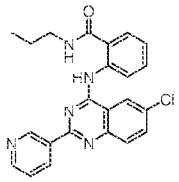
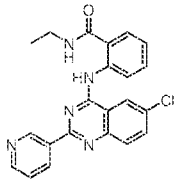
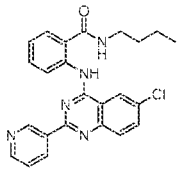
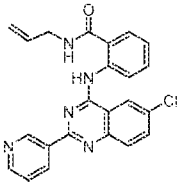
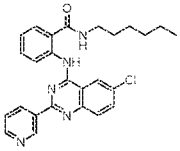
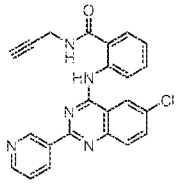
with 4,6-dichloro-2-(pyridin-3-yl)quinazoline **(synthesized as described in Scheme 1 and 4, substituting 5-chloro-2-nitrobenzoic acid for 2-nitro-5-propoxy-benzoic acid)** (150 mg, 0.54 mmol) and 2-amino-*N*-(cyclopropylmethyl)benzamide) (310 mg, 1.63 mmol) and anhydrous *i*-PrOH (20 mL) was added and refluxed for 3h. The reaction mixture was cooled to room temperature and Et_3N (3eq) was added. The solvent was removed *in vacuo*. To the crude product was added a water-methanol mixture (5:1, 50 mL), and then sonicated for 5 min. The solidified compound was collected by filtration, and the solid was recrystallized from hot methanol and washed with water. The product was dried at 50 °C to give 2-(6-chloro-2-(pyridin-3-yl)quinazolin-4-ylamino)-*N*-(cyclopropylmethyl)benzamide as a colorless cotton (220 mg, 94%). The structure was confirmed by NMR and elemental analysis. ^{1}H NMR (Bruker 300 MHz, DMSO-d_6) ppm 0.20-0.98 (m, 5H), 3.07-3.21 (m, 2H), 7.24-8.26 (m, 7H), 8.68-9.55 (m, 5H), 12.22 (s, 1H). CHN Calcd. C: 67.05; H: 4.69; N: 16.29 Found C: 67.15; H: 4.89; N: 16.25

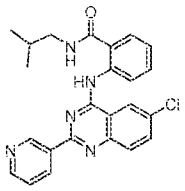
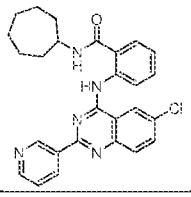
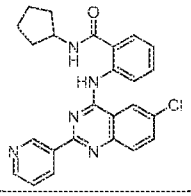
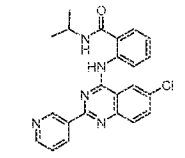
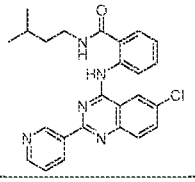
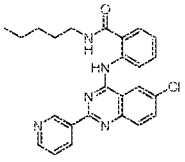
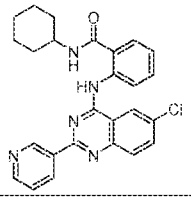
The compounds in the following table were prepared in a manner analogous to that described in **Scheme 34**, replacing aminomethylcyclopropane with the appropriate amine.

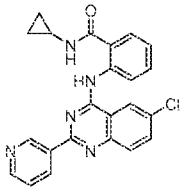
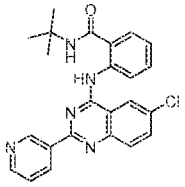
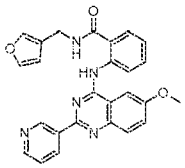
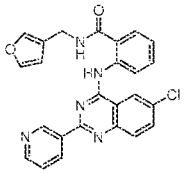
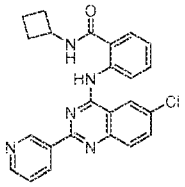
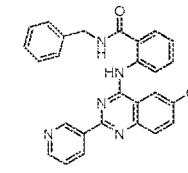
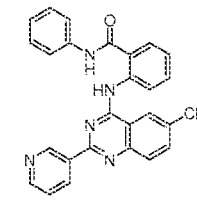
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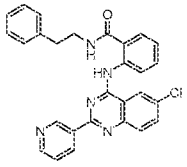
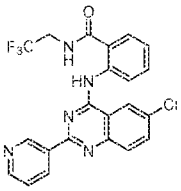
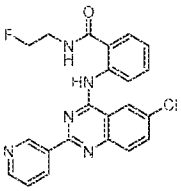
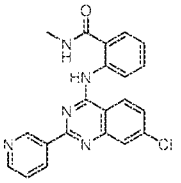
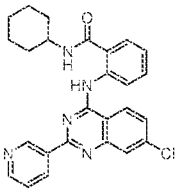
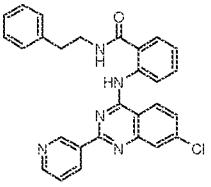
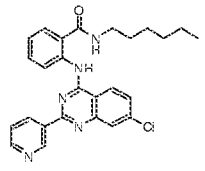
Number	Product	^{1}H NMR	^{1}H NMR Solvent	Purity percent	Method of Coupling
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1017		^{1}H NMR (DMSO-d_6) ppm 1.49-1.62 (m, 8H), 3.99 (s, 3H), 4.24-4.26 (m, 1H), 7.24-7.71 (m, 7H), 8.65-9.55 (m, 5H), 12.19 (s, 1H).	DMSO	>98	Method Z
1018		^{1}H NMR (DMSO-d_6) ppm 0.88-1.99 (m, 7H), 3.14-3.16 (m, 2H), 3.02 (s, 3H), 7.57-7.91 (m, 7H), 8.68-9.55 (m, 5H), 12.19 (s, 1H).	DMSO	>98	Method Z
1019		^{1}H NMR (DMSO-d_6) ppm 1.07-1.12 (m, 3H), 3.44-3.52 (m, 2H), 4.01 (s, 3H), 7.24-786 (m, 8H), 8.68-9.55 (m, 5H), 12.19 (s, 1H).	DMSO	>98	Method Z
1020		1H NMR (DMSO-d_6) ppm 0.87-0.92 (m, 3H), 1.53-1.62 (m, 2H,), 3.30-3.32 (m, 2H), 3.98 (s, 3H), 7.21-7 89 (m, 7H), 8.67-9 55 (m, 5H), 12.38 (s, 1H).	DMSO	>98	Method Z
1021		1H NMR (DMSO-d_6) ppm 0.83-1.51 (m, 7H), 3.30-3.32 (m, 2H), 3.99 (s, 3H), 7.24-7.90 (m, 7H), 8.67-9.55 (m, 5H), 12.38 (s, 1H).	DMSO	>98	Method Z

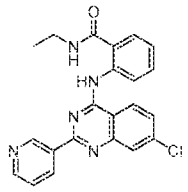
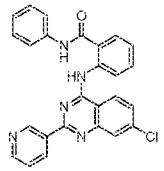
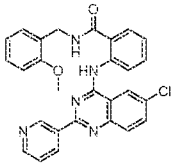
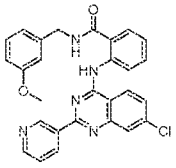
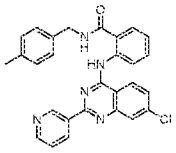
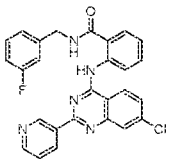
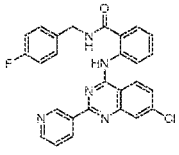
1022		1H NMR (DMSO-d_6) ppm 0.79-1.52 (m, 9H), 3.25-3.30 (m, 2H), 3.98 (s, 3H), 7.21-7.88 (m, 7H), 8.68-9.55 (m, 5H), 12.30 (s, 1H).	DMSO	>98	Method Z
1023		1H NMR (DMSO-d_6) ppm 0.80-1.49 (m, 11H), 3.26-3.30 (m, 2H), 3.99 (s, 3H), 7.24-7.90 (m, 7H), 8.67-9.56 (m, 5H), 12.30 (s, 1H).	DMSO	>98	Method Z
1024		1H NMR (DMSO-d_6) ppm 3.99-4.10 (m, 5H), 5.07-5.33 (m, 2H), 5.89-5.91(m, 1H), 7.24-7.90 (m, 7H), 8.68-9.55 (m, 5H), 12.30 (s, 1H).	DMSO	>98	Method Z
1025		1H NMR (DMSO-d_6) ppm 3.13 (s, 1H), 3.99-4.12 (m, 5H), 7.21-7.89 (m, 7H), 8.67-9.54 (m, 5H), 12.30 (s, 1H).	DMSO	>98	Method Z
1026		1H NMR (DMSO-d_6) ppm 1.68-2.22 (m, 6H), 3.99 (s, 3H), 4.24-4.26 (m, 1H), 7.22-7.92 (m, 7H), 8.66-9.55 (m, 5H), 12.30 (s, 1H).	DMSO	>98	Method Z
1027		1H NMR (DMSO-d_6) ppm 1.41-1.86 (m, 12H), 3.90 (br s, 4H), 7.23-7.89 (m, 7H), 8.63-9.55 (m, 5H), 12.30 (s, 1H).	DMSO	>98	Method Z
1028		1H NMR (DMSO-d_6) ppm 0.85-1.60 (m, 9H), 3.27-3.33 (m, 2H), 3.99 (s, 3H), 7.21-7.91 (m, 7H), 8.68-9.55 (m, 5H), 12.19 (s, 1H).	DMSO	>98	Method Z

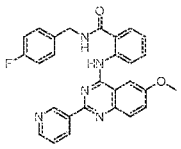
1029		1H NMR (DMSO-d_6) ppm 1.03-1.34 (m, 6H), 3.17-3.31 (m, 4H), 7.40-7.88 (m, 7H), 8.55-10.03 (m, 5H), 12.32 (s, 1H).	DMSO	>98	Method Z
1030		1H NMR (DMSO-d_6) ppm 0.83-1.52 (m, 5H), 3.20-3.29 (m, 2H), 7.27-8.21 (m, 7H), 8.67-9.53 (m, 5H), 12.33 (s, 1H).	DMSO	>98	Method Z
1031		1H NMR (DMSO-d_6) ppm 1.02-1.07 (m, 3H), 3.24-3.32 (m, 2H), 7.27-8.22 (m, 7H), 8.67-9.53 (m, 5H), 12.34 (s, 1H).	DMSO	>98	Method Z
1032		1H NMR (DMSO-d_6) ppm 0.75-1.37 (m, 7H), 3.18-3.20 (m, 2H), 7.21-8.19 (m, 7H), 8.64-9.48 (m, 5H), 12.15 (s, 1H).	DMSO	>98	Method Z
1033		1H NMR (DMSO-d_6) ppm 3.90-3.92 (m, 2H), 5.02-5.17 (m, 2H), 5.81-5.86 (m, 1H), 7.27-8.23 (m, 7H), 8.68-9.55 (m, 5H), 12.25 (s, 1H).	DMSO	>98	Method Z
1034		1H NMR (DMSO-d_6) ppm 0.78-1.42 (m, 11H), 3.20-3.29 (m, 2H), 7.25-7.91 (m, 7H), 8.23-9.53 (m, 5H), 12.17 (s, 1H).	DMSO	>98	Method Z
1035		^{1}H NMR (DMSO-d_6) ppm 3.06 (s, 1H), 4.05-4.08 (m, 2H), 7.28-8.22 (m, 7H), 8.65-9.51 (m, 5H), 12.12 (s, 1H).	DMSO	>98	Method Z

1036		1H NMR (DMSO-d_6) ppm 0.88-1.92 (m, 7H), 3.05-3.16 (m, 2H), 7.23-7.94 (m, 7H), 8.22-9.54 (m, 5H), 12.21 (s, 1H).	DMSO	>98	Method Z
1037		1H NMR (DMSO-d_6) ppm 1.37-1.79 (m, 12H), 3.90-3.96 (m, 1H), 7.25-8.24 (m, 7H), 8.55-9.52 (m, 5H), 12.07 (s, 1H).	DMSO	>98	Method Z
1038		1H NMR (DMSO-d_6) ppm 1.49-1.85 (m, 8H), 4.24-4.26 (m, 1H), 7.23-7.69 (m, 6H), 7.85-9.53 (m, 6H), 12.06 (s, 1H).	DMSO	>98	Method Z
1039		1H NMR (DMSO-d_6) ppm 1.12-1.14 (m, 6H), 4.11-4.18 (m, 1H), 7.23-7.94 (m, 8H), 8.33-9.53 (m, 4H), 12.30 (s, 1H).	DMSO	>98	Method Z
1040		1H NMR (DMSO-d_6) ppm 0.84-1.16 (m, 9H), 3.28-3.34 (m, 2H), 7.23-7.91 (m, 6H), 8.25-9.53 (m, 6H), 12.16 (s, 1H).	DMSO	>98	Method Z
1041		1H NMR (DMSO-d_6) ppm 0.79-1.52 (m, 9H), 3.25-3.32 (m, 2H), 7.24-7.91 (m, 6H), 8.23-9.53 (m, 6H), 12.18 (s, 1H).	DMSO	>98	Method Z
1042		1H NMR (DMSO-d_6) ppm 1.04-1.81 (m, 10H), 3.77-3.82 (m, 1H), 7.21-8.05 (m, 8H), 8.65-9.52 (m, 4H), 11.96 (s, 1H).	DMSO	>98	Method Z

1043		1H NMR (DMSO-d_6) ppm 0.47-0.67 (m, 4H), 2.85-2.88 (m, 1H), 7.26-8.26 (m, 7H), 8.66-9.52 (m, 5H), 12.26 (s, 1H).	DMSO	>98	Method Z
1044		1H NMR (DMSO-d_6) ppm 1.14 (s, 9H), 7.30-7.93 (m, 7H), 8.21-9.50 (m, 5H), 12.22 (s, 1H).	DMSO	>98	Method Z
1045		1H NMR (DMSO-d_6) ppm 3.98 (s, 3H), 4.36 (s, 2H), 6.47 (s, 1H), 7.21-7.91 (m, 9H), 8.68-9.56 (m, 5H), 12.22 (s, 1H).	DMSO	>98	Method Z
1046		1H NMR (DMSO-d_6) ppm 4.30 (s, 2H), 6.42 (s, 1H), 7.28-8.24 (m, 9H), 8.70-9.53 (m, 5H), 12.22 (s, 1H).	DMSO	>98	Method Z
1047		1H NMR (DMSO-d_6) ppm 1.69-2.55 (m, 6H), 4.41-4.44 (m, 1H), 7.23-8.24 (m, 7H), 8.65-9.54 (m, 5H), 12.06 (s, 1H).	DMSO	>98	Method Z
1048		1H NMR (DMSO-d_6) ppm 4.55 (s, 2H), 7.17-8.21 (m, 12H), 8.65-9.54 (m, 5H), 12.06 (s, 1H).	DMSO	>98	Method Z
1049		1H NMR (DMSO-d_6) ppm 7.02-8.67 (m, 15H), 9.47 (s, 1H), 10.04 (s, 1H), 12.06 (s, 1H).	DMSO	>98	Method Z

1050		1H NMR (DMSO-d_6) ppm 2.75-2.80 (m, 2H), 3.48-3.54 (m, 2H), 7.08-8.20 (m, 12H), 8.69-9.56 (m, 5H), 12.16 (s, 1H).	DMSO	>98	Method Z
1051		1H NMR (DMSO-d_6) ppm 4.01-4.10 (m, 2H), 7.28-8.27 (m, 7H), 8.59-9.51 (m, 5H), 11.45 (s, 1H).	DMSO	>98	Method Z
1052		1H NMR (DMSO-d_6) ppm 4.38-4.57 (m, 4H), 7.27-8.24 (m, 7H), 8.69-9.56 (m, 5H), 12.10 (s, 1H).	DMSO	>98	Method Z
1053		1H NMR (DMSO-d_6) ppm 2.85-2.92 (br s, 3H), 7.20-8.22 (m, 7H), 8.67-9.56 (m, 5H), 12.61 (s, 1H).	DMSO	>98	Method Z
1054		1H NMR (DMSO-d_6) ppm 1.04-1.81 (m, 10H), 3.77-3.82 (m, 1H), 7.24-8.05 (m, 8H), 8.65-9.52 (m, 4H), 12.27 (s, 1H).	DMSO	>98	Method Z
1055		1H NMR (DMSO-d_6) ppm 2.49-2.51 (m, 2H), 3.57-3.59 (m, 2H), 7.21-8.16 (m, 12H), 8.69-9.56 (m, 5H), 12.16 (s, 1H).	DMSO	>98	Method Z
1056		1H NMR (DMSO-d_6) ppm 0.79-1.44 (m, 11H), 3.26-3.30 (m, 2H), 7.24-7.92 (m, 7H), 8.67-9.52 (m, 5H), 12.45 (s, 1H).	DMSO	>98	Method Z

1057		1H NMR (DMSO-d_6) ppm 1.04-1.16 (m, 3H), 3.33-3.38 (m, 2H), 7.20-8.22 (m, 7H), 8.60-9.53 (m, 5H), 12.34 (s, 1H).	DMSO	>98	Method Z
1058		1H NMR (DMSO-d_6) ppm 7.09-8.68 (m, 15H), 9.51 (s, 1H), 10.34 (s, 1H), 12.06 (s, 1H).	DMSO	>98	Method Z
1059		1H NMR (DMSO-d_6) ppm 3.78 (s, 3H), 4.43 (s, 2H), 6.77-8.23 (m, 11H), 8.68-9.54 (m, 5H), 12.06 (s, 1H).	DMSO	>98	Method Z
1060		1H NMR (DMSO-d_6) ppm 3.69 (s, 3H), 4.48 (s, 2H), 6.89-8.15 (m, 11H), 8.68-9.54 (m, 5H), 12.44 (s, 1H).	DMSO	>98	Method Z
1061		1H NMR (DMSO-d_6) ppm 2.24 (s, 3H), 4.46 (s, 2H), 7.03-8.13 (m, 11H), 8.67-9.54 (m, 5H), 12.21 (s, 1H).	DMSO	>98	Method Z
1062		1H NMR (DMSO-d_6) ppm 4.51 (s, 2H), 7.11-8.14 (m, 11H), 8.67-9.54 (m, 5H), 12.34 (s, 1H).	DMSO	>98	Method Z
1063		1H NMR (DMSO-d_6) ppm 4.47 (s, 2H), 7.05-8.14 (m, 11H), 8.67-9.54 (m, 5H), 12.37 (s, 1H).	DMSO	>98	Method Z

1064		1H NMR (DMSO-d_6) ppm 3.95 (s, 3H), 4.47 (s, 2H), 7.05-8.14 (m, 11H), 8.67-9.54 (m, 5H), 12.32 (s, 1H).	DMSO	>98	Method Z

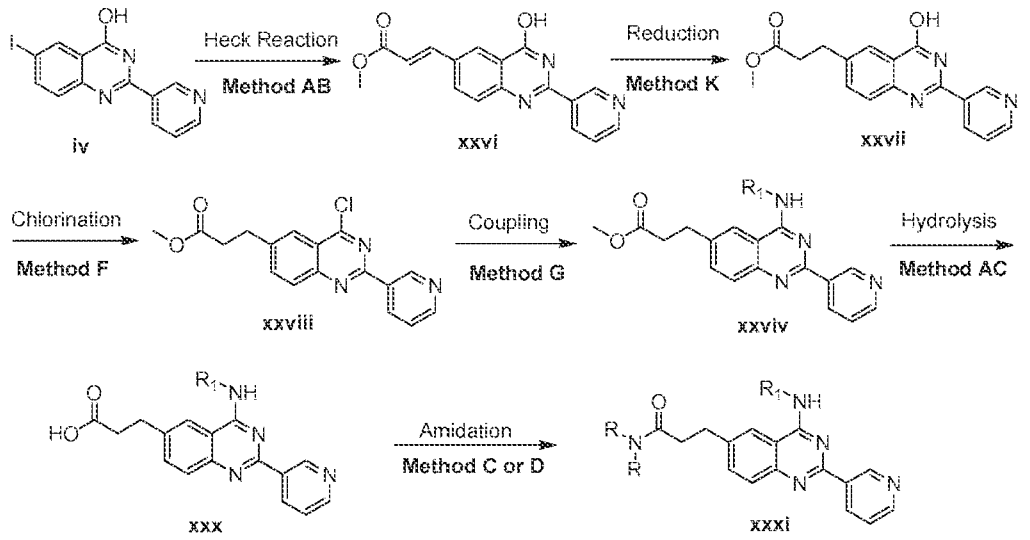
Number	Starting Material R^1	Starting Material R^2	Product	Salt Type	^{1}H NMR	H NMR Solvent	Purity percent	Method of Coupling
1065					^{1}H NMR (DMSO-d_6) ppm 4.52 (d, 2H, J = 5.8 Hz), 7.21-7.30 (m, 5H), 7.50 (t, J = 7.9 Hz, 1H), 7.68 (t, J = 7.8 Hz, 1H), 7.89-7.92 (m, 3H), 8.21 (d, J = 1.8 Hz, 1H), 8.65-8.70 (m, 3H), 8.99 (s, 1H), 9.52 (s, 1H), 11.88 (s, 1H)	DMSO	>98	Method Y, Z
1066					^{1}H NMR (DMSO-d_6) ppm 4.49 (d, 2H, J = 5.6 Hz), 7.24-7.35 (m, 5H), 7.50 (t, J = 7.2 Hz, 1H), 7.70 (t, J = 7.8 Hz, 1H), 7.91-7.95 (m, 3H), 8.22 (d, J = 1.5 Hz, 1H), 8.67-8.73 (m, 3H), 9.19 (s, 1H), 9.53 (s, 1H), 11.96 (s, 1H)	DMSO	>98	Method Y, Z
1067					^{1}H NMR (DMSO-d_6) ppm 4.58 (d, 2H, J = 5.7 Hz), 7.16-7.36 (m, 5H), 7.50 (t, J = 7.5 Hz, 1H), 7.69 (t, J = 7.5 Hz, 1H), 7.88-7.96 (m, 3H), 8.22 (d, J = 1.5 Hz, 1H), 8.65-8.69 (m, 3H), 8.98 (s, 1H), 9.52 (s, 1H), 11.87 (s, 1H)	DMSO	>98	Method Y, Z
1068					^{1}H NMR (DMSO-d_6) ppm 4.47 (d, 2H, J = 5.6 Hz), 7.30 (br s, 5H), 7.54 (t, J = 7.7 Hz, 1H), 7.70 (t, J = 7.8 Hz, 1H), 7.88-7.96 (m, 3H), 8.15 (d, J = 1.5 Hz, 1H), 8.68-8.81 (m, 3H), 8.98 (s, 1H), 9.52 (s, 1H), 12.29 (s, 1H)	DMSO	>98	Method Y, Z

481

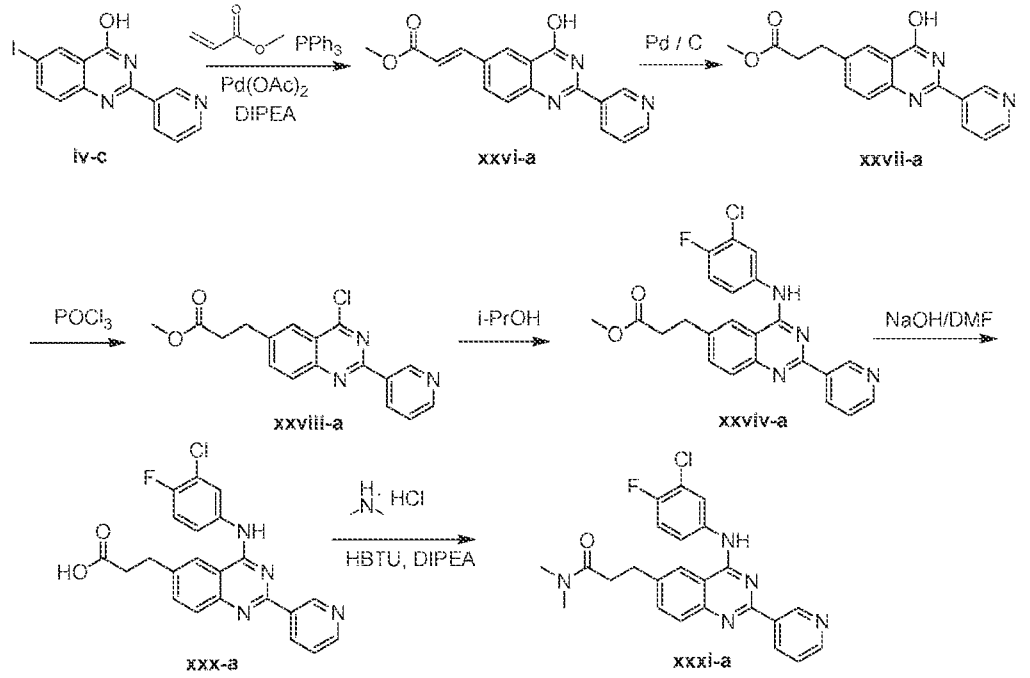
1069					^{1}H NMR (DMSO-d_6) ppm 4.57 (d, 2H, J = 5.6 Hz), 7.23-7.29 (m, 5H), 7.39 (t, J = 7.9 Hz, 1H), 7.71 (t, J = 7.9 Hz, 1H), 7.94-7.99 (m, 3H), 8.15 (d, J = 1.4 Hz, 1H), 8.68-8.84 (m, 3H), 9.24 (s, 1H), 9.55 (s, 1H), 12.23 (s, 1H)	DMSO	>98	Method Y, Z
1070					^{1}H NMR (DMSO-d_6) ppm 4.50 (d, 2H, J = 5.5 Hz), 7.25-7.53 (m, 5H), 7.69 (t, J = 7.1 Hz, 1H), 7.73 (t, J = 7.0 Hz, 1H), 7.94-8.15 (m, 3H), 8.18 (d, J = 1.4 Hz, 1H), 8.68-8.82 (m, 3H), 9.24 (s, 1H), 9.54 (s, 1H), 12.21 (s, 1H)	DMSO	>98	Method Y, Z
1071					^{1}H NMR (DMSO-d_6) ppm 3.90 (s, 3H), 4.56 (d, 2H, J = 5.6 Hz), 7.22-7.44 (m, 7H), 7.44 (t, J = 7.9 Hz, 1H), 7.74 (t, J = 7.9 Hz, 1H), 7.94-7.99 (m, 2H), 8.68-8.81 (m, 3H), 9.24 (s, 1H), 9.55 (s, 1H), 12.19 (s, 1H)	DMSO	>98	Method Y, Z
1072				HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 12.17 (s, 1H), 9.52 (s, 1H), 9.08 (s, 1H), 8.95 (d, J = 7.6 Hz, 1H), 8.85 (s, 1H), 8.66 (d, J = 7.8 Hz, 1H), 7.91 (t, J = 9.4 Hz, 2H), 7.84 (s, 1H), 7.75 – 7.67 (m, 1H), 7.65 (s, 1H), 7.59 (d, J = 8.1 Hz, 1H), 7.30 (t, J = 7.3 Hz, 1H), 4.47 (d, J = 47.3 Hz, 2H), 4.26 (d, J = 6.8 Hz, 2H), 3.58 – 3.50 (m, 2H), 1.47 (t, J = 6.7 Hz, 3H).	DMSO	95	Method Y, Z

482

Scheme 36: General route for the synthesis of compounds with general formula xxxi



Scheme 37: Representative synthesis of compounds of formula xxxi-a: (see Scheme 36)



Method AB: Methyl 3-(4-hydroxy-2-(pyridin-3-yl)quinazolin-6-yl)acrylate (xxvi-a) To a solution of 6-iodo-2-(pyridin-3-yl) quinazolin-4-ol **(synthesized as described**

in Scheme 1 and 4, substituting 5-iodo-2-nitrobenzoic acid for 2-nitro-5-propoxy-benzoic acid) (3.00 g, 8.6 mmol, 1.0 eq.), $Pd(OAc)_2$ (48 mg, 0.21 mmol, 0.025 eq.) and PPh_3 (113 mg, 0.43 mmol, 0.05 eq.) in DMF (8 mL) was added methyl acrylate (3.22 g, 25.8 mmol, 3.0 eq.) and DIPEA (1.22 g, 9.46 mmol, 1.1 eq.) under Ar atmosphere. The mixture was stirred at 110 °C overnight. After cooling, the mixture was filtered and the solid was washed with ethyl acetate three times to afford 1.30 g of **xxxvi-a** as green solid (yield 49%). LCMS m/z = 308.0 (M +1) (Method B) (retention time = 1.41 min).

Methyl 3-(4-hydroxy-2-(pyridin-3-yl) quinazolin-6-yl)propanoate (xxvii-a) Methyl 3-(4-hydroxy-2-(pyridin-3-yl) quinazolin-6-yl) propanoate was prepared in a manner analogous to that described for 2-amino-5-methoxybenzoic acid in **Method K**, replacing 5-methoxy-2-nitrobenzoic acid with methyl 3-(4-hydroxy-2-(pyridin-3-yl)quinazolin-6-yl)acrylate to afford 1.40 g of **xxvii-a** in quantitative yield as a yellow solid. LCMS m/z = 310.0 (M +1) (Method B) (retention time = 1.42 min).

3-(4-Chloro-2-pyridin-3-yl-quinazolin-6-yl)-propionic acid methyl ester (xxviii-a) 3-(4-Chloro-2-pyridin-3-yl-quinazolin-6-yl)-propionic acid methyl ester (**prepared in a manner analogous to that described for 4-chloro-6-propoxy-2-pyridin-3-yl-quinazoline using Method F, replacing 6-propoxy-2-pyridin-3-yl-1H-quinazolin-4-one with methyl 3-(4-hydroxy-2-(pyridin-3-yl)quinazolin-6-yl)propanoate**) was obtained in quantitative yield to give 1.50 g of **xxvii-a** as a red solid. LCMS m/z = 328.1, 330.0 (M +1) (Method B) (retention time = 1.86 min).

3-[4-(3-Chloro-4-fluoro-phenylamino)-2-pyridin-3-yl-quinazolin-6-yl]-propionic acid methyl ester (xxviv-a) 3-[4-(3-Chloro-4-fluoro-phenylamino)-2-pyridin-3-yl-quinazolin-6-yl]-propionic acid methyl ester (**prepared in a manner analogous to that described for 2-(6-propoxy-2-pyridin-3-yl-quinazolin-4-ylamino)-benzamide in Method G1, replacing 4,7-dichloro-2-(4-chlorophenyl)quinazoline and 2-aminobenzamide with 3-(4-chloro-2-pyridin-3-yl-quinazolin-6-yl)-propionic acid methyl ester and 3-chloro-4-fluoro-phenylamine**) was obtained in a 43% yield to

give 1.04 g of **xxviv-a** as a yellow solid. LCMS m/z = 437.1, 439.1 (M +1) (Method B) (retention time = 1.62 min).

Method AC: 3-(4-(3-Chloro-4-fluorophenylamino)-2-(pyridin-3-yl) quinazolin-6-yl)propanoic acid (xxx-a) To a solution of 3-[4-(3-chloro-4-fluoro-phenylamino)-2-pyridin-3-yl-quinazolin-6-yl]-propionic acid methyl ester (1.04 g, 2.39 mmol, 1.0 eq.) in DMF (20 mL) was added a solution of NaOH (0.57 g, 14.3 mmol, 6.0 eq.) in H_2O (8 mL). The mixture was stirred at room temperature for 2 h. 50 mL of water was added to the mixture. After filtration, the resulting filter cake was washed with water and dried *in vacuo* to give 933 mg of **xxx-a** as a yellow solid (yield 93%). LCMS m/z = 423.1, 425.1 (M +1) (Method A) (retention time = 1.51 min).

3-(4-(3-Chloro-4-fluorophenylamino)-2-(pyridin-3-yl)quinazolin-6-yl)-N,N-dimethyl propanamide (xxxi-a) 3-(4-(3-Chloro-4-fluorophenylamino)-2-(pyridin-3-yl)quinazolin-6-yl)-N,N-dimethyl propanamide **(prepared in a manner analogous to that described for 2-benzamido-5-methoxy-3-methylbenzamide in Method D, replacing nicotinic acid and 2-amino-5-methoxy-3-methylbenzamide with 3-(4-(3-chloro-4-fluorophenylamino)-2-(pyridin-3-yl)quinazolin-6-yl)propanoic acid and dimethylamine hydrochloride)** was obtained in 90% yield to give 891 mg of **xxxi-a** as a yellow solid. LCMS m/z = 450.0, 452.0 (M +1) (Method B) (retention time = 1.834min). ^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.95 (s, 1H), 9.51 (d, *J* = 1.6 Hz, 1H), 8.69 – 8.63 (m, 2H), 8.38 (s, 1H), 8.28 (dd, *J* = 6.8, 2.4 Hz, 1H), 7.94 – 7.90 (m, 1H), 7.81 (s, 2H), 7.55 – 7.51 (m, 2H), 3.04 (t, *J* = 7.6 Hz, 2H), 2.99 (s, 3H), 2.85 (s, 3H), 2.77 (t, *J* = 8.0 Hz, 2H).

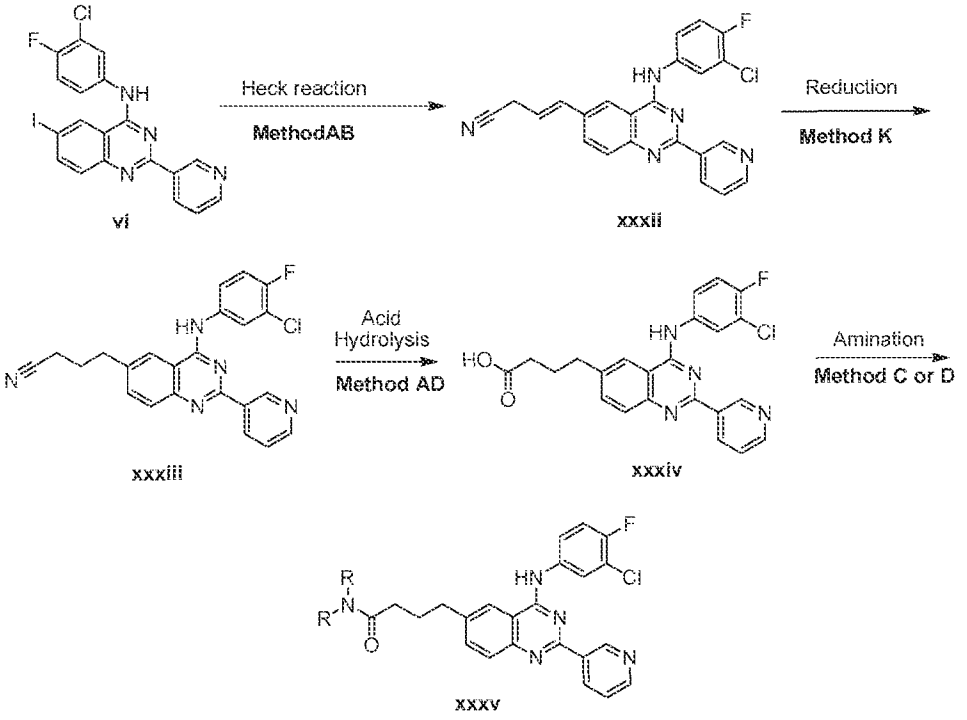
The compounds in the following table were prepared in a manner analogous to that described in **Scheme 36**, replacing dimethylamine with the appropriate amine and 4-fluoro, 3-chloro aniline with the appropriate aniline.

Table 12:

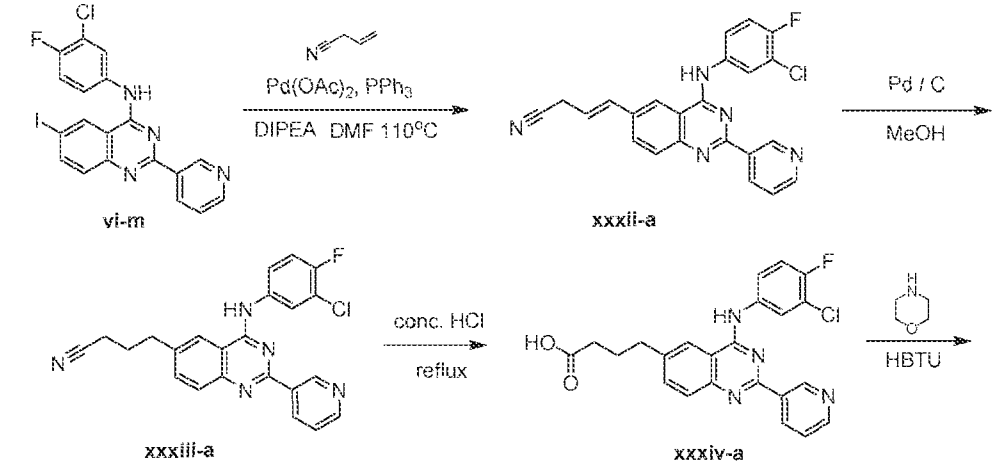
Number	PRODUCT	Salt type	Molecular Mass	^{1}H-NMR	^{1}H-NMR Solvent	LCMS	LCMS Protocol	Purity percent	Method for Coupling
1073			421.85	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.01 (s, 1H), 9.52 (s, 1H), 8.65 – 8.69 (m, 2H), 8.39 (s, 1H), 8.28 (d, *J* = 5.2 Hz, 1H), 7.92 – 7.93 (m, 1H), 7.82 (q, *J* = 8.0 Hz, 2H), 7.52 – 7.57 (m, 2H), 7.35 (s, 1H), 6.84 (s, 1H), 3.05 (t, *J* = 7.2 Hz, 2H), 2.51 – 2.54 (m, 2H).	DMSO	422.1 (M+1)	Method B (NH4HCO3)	95	Method C
1074			435.43	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.01 (s, 1H), 9.55 (d, *J* = 2.4 Hz, 1H), 8.68 – 8.70 (m, 2H), 8.47 (s, 1H), 7.97 – 7.99 (m, 1H), 7.79 – 7.86 (m, 3H), 7.50 – 7.55 (m, 2H), 7.36 (s, 1H), 7.30 (t, *J* = 73.6 Hz, 1H), 6.99 (dd, *J* = 8.4, 2.4Hz, 1H), 6.82 (s, 1H), 3.05 (t, *J* = 8.0 Hz, 2H), 2.52 (t, *J* = 8.4 Hz, 2H).	DMSO	436.2 (M+1)	Method B (NH4HCO3)	95	Method C
1075			435.88	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.00 (s, 1H), 9.52 (s, 1H), 8.65 – 8.69 (m, 2H), 8.39 (s, 1H), 8.27 – 8.29 (m, 1H), 7.79 (dd, *J* = 9.2, 2.4 Hz, 1H), 7.76 – 7.85 (m, 3H), 7.52 – 7.57 (m, 2H), 3.05 (t, *J* = 7.6 Hz, 2H), 2.57 (d, *J* = 4.4 Hz, 3H), 2.52 – 2.54 (m, 2H).	DMSO	436.1 (M+1)	Method B (NH4HCO3)	95	Method D
1076			449.91	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.95 (s, 1H), 9.51 (d, *J* = 1.6 Hz, 1H), 8.63 – 8.69 (m, 2H), 8.38 (s, 1H), 8.28 (dd, *J* = 6.8, 2.4 Hz, 1H), 7.90 – 7.94 (m, 1H), 7.81 (s, 2H), 7.51 – 7.55 (m, 2H), 3.04 (t, *J* = 7.6 Hz, 2H), 2.99 (s, 3H), 2.85 (s, 3H), 2.77 (t, *J* = 8.0 Hz, 2H).	DMSO	450.0 (M+1)	Method B (NH4HCO3)	95	Method D
1077			540.01	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.01 (s, 1H), 9.52 (d, *J* = 1.6 Hz, 1H), 8.61 – 8.74 (m, 2H), 8.41 (s, 1H), 8.28 (dd, *J* = 6.8, 2.6 Hz, 1H), 7.80 – 7.99 (m, 3H), 7.46 – 7.63 (m, 2H), 3.89 (s, 4H), 3.20 (s, 2H), 3.08 (t, *J* = 7.4 Hz, 4H), 2.90 (t, *J* = 7.6 Hz, 2H).	DMSO	540.2, 542.2 (M+1)	Method B (NH4HCO3)	95	Method D

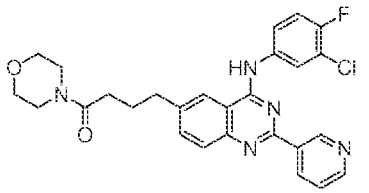
486

Scheme 38: General route for the synthesis of compounds with general formula xxxv:



Scheme 39: Representative synthesis of compounds of formula xxxv-a: (see Scheme 38)





xxxv-a (Compound 1078)

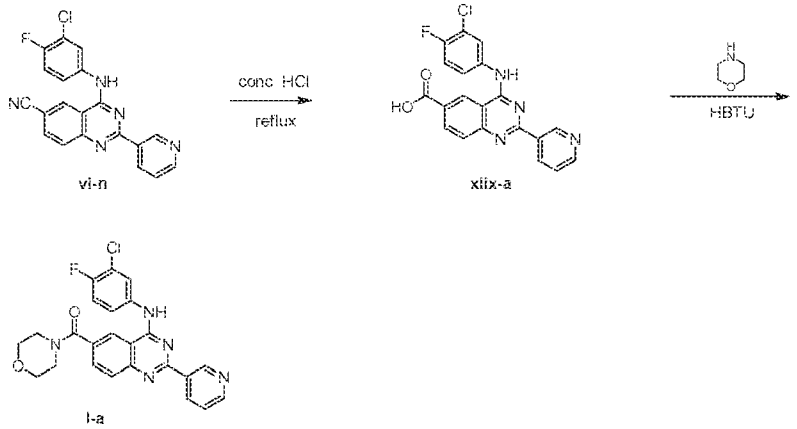
(*E*)-4-[4-(3-Chloro-4-fluoro-phenylamino)-2-pyridin-3-yl-quinazolin-6-yl]-but-3-enenitrile (xxxii-a) (*E*)-4-[4-(3-Chloro-4-fluoro-phenylamino)-2-pyridin-3-yl-quinazolin-6-yl]-but-3-enenitrile **(prepared in a manner analogous to that described for (E)-methyl 3-(4-hydroxy-2-(pyridin-3-yl)quinazolin-6-yl)acrylate using Method AB, replacing 6-iodo-2-(pyridin-3-yl)quinazolin-4-ol and methyl acrylate with N-(3-chloro-4-fluorophenyl)-6-iodo-2-(pyridin-3-yl)quinazolin-4-amine and but-3-enenitrile)** was obtained in a 48% yield to give 400 mg of **xxxii-a** as grey solid. LCMS m/z = 416.0 (M +1) (Method B) (retention time = 1.99 min).

4-[4-(3-Chloro-4-fluoro-phenylamino)-2-pyridin-3-yl-quinazolin-6-yl]-butyronitrile (xxxiii-a) 4-[4-(3-Chloro-4-fluoro-phenylamino)-2-pyridin-3-yl-quinazolin-6-yl]-butyronitrile **(prepared in a manner analogous to that described for 2-amino-5-methoxybenzoic acid in Method K, replacing 5-methoxy-2-nitrobenzoic acid with (E)-4-(4-(3-chloro-4-fluorophenylamino)-2-(pyridin-3-yl)quinazolin-6-yl)but-3-enenitrile)** was obtained in a 95% yield to give 190 mg of **xxxiii-a** as a brown solid. LCMS m/z = 418.1(M +1) (Method B) (retention time = 1.95 min).

Method AD: 4-(4-(3-chloro-4-fluorophenylamino)-2-(pyridin-3-yl)quinazolin-6-yl)butanoic acid (xxxiv-a) 4-[4-(3-Chloro-4-fluoro-phenylamino)-2-pyridin-3-yl-quinazolin-6-yl]-butyronitrile (190 mg, 046 mmol, 1.0 eq.) was treated with concentrated HCl (8 mL). The mixture was stirred at 100 °C for 2 days. The volatiles were removed *in vacuo*, and the residue was washed with water to afford 70 mg of **xxxiv-a** in a 35% yield as a yellow solid. LCMS m/z = 437.1, 439.1 (M +1) (Method B) (retention time = 1.46 min).

4-(4-(3-Chloro-4-fluorophenylamino)-2-(pyridin-3-yl) quinazolin-6-yl)-1-morpholino butan-1-one (xxxv-a) 4-(4-(3-chloro-4-fluorophenylamino)-2-(pyridin-3-yl) quinazolin-6-yl)-1-morpholinobutan-1-one was prepared in a manner analogous to that described for 2-benzamido-5-methoxy-3-methylbenzamide in **Method D**, replacing nicotinic acid and 2-amino-5-methoxy-3-methylbenzamide with 4-(4-(3-chloro-4-fluorophenylamino)-2-(pyridin-3-yl)quinazolin-6-yl) butanoic acid and morpholine to give 32 mg of **xxxv-a** in a 40% yield as a beige solid. LCMS m/z = 506.2, 508.1 (M +1) (Method B) (retention time = 1.85 min). ^{1}H NMR (400 MHz, DMSO-d_6) : δ 10.04 (s, 1H), 9.52 (d, *J* = 1.6 Hz, 1H), 8.69 – 8.65 (m, 2H), 8.39 – 8.38 (m, 1H), 8.27 (dd, J = 6.8, 2.8 Hz, 1H), 7.94 – 7.90 (m, 1H), 7.86 – 7.84 (m, 1H), 7.80 – 7.77 (m, 1H), 7.57 – 7.52 (m, 2H), 3.56 – 3.53 (m, 4H), 3.46 – 3.41 (m, 4H), 2.85 (t, *J* = 8.0 Hz, 2H), 2.40 (t, *J* = 7.6 Hz, 2H), 1.97 (t, *J* = 7.6 Hz, 2H).

Scheme 40: Representative synthesis of compounds of formula I-a



The compounds in the following table were prepared in a manner analogous to that described in **Scheme 38** in the synthesis of 4-(4-(3-Chloro-4-fluorophenyl amino)-2-(pyridin-3-yl) quinazolin-6-yl)-1-morpholino butan-1-one, replacing (*E*)-4-[4-(3-Chloro-4-fluoro-phenylamino)-2-pyridin-3-yl-quinazolin-6-yl]-but-3-enenitrile with 4-(3-chloro-4-fluorophenylamino)-2-(pyridin-3-yl)quinazoline-6-carbonitrile.

Table 13:

Number	PRODUCT	Salt type	Molecular Mass	^{1}H-NMR	^{1}H-NMR Solvent	LCMS	LCMS Protocol	Purity percent	Method for Coupling
1078			411.46	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.64 (d, *J* = 1.6 Hz, 1H), 8.78 (td, *J* = 7.9, 1.8 Hz, 1H), 8.71 (dd, *J* = 4.7, 1.6 Hz, 1H), 7.94 (d, *J* = 9.2 Hz, 1H), 7.59 (brs, 1H), 7.58 (dd, *J* = 7.6, 4.8 Hz, 1H), 7.52 (dd, *J* = 9.2, 2.8 Hz, 1H), 7.16 (t, *J* = 7.6 Hz, 1H), 7.08 (d, *J* = 6.4 Hz, 1H), 6.84 (dd, *J* = 8.0, 1.1 Hz, 1H), 6.69 (s, 1H), 4.36 (t, *J* = 6.5 Hz, 2H), 4.09 (t, *J* = 6.4 Hz, 2H), 3.46 (s, 3H), 2.30 (s, 3H).	DMSO	412.2 (M+1)	Method B (NH4HCO3)	95	Method C, G
1079			506.96	^{1}H NMR (400 MHz, DMSO-d_6): δ 10.42 (s, 1H), 9.54 (d, *J* = 1.6 Hz, 1H), 9.08 (d, *J* = 1.2 Hz, 1H), 8.73 – 8.65 (m, 3H), 8.28 (dd, *J* = 6.8, 2.4 Hz, 1H), 7.97 – 7.93 (m, 2H), 7.60 – 7.53 (m, 2H), 3.60 – 3.58 (m, 4H), 3.51 – 3.46 (m, 2H), 2.55 – 2.53 (m, 2H), 2.41 – 2.48 (m, 4H).	DMSO	508.1 (M+1) 254.1 254.9 (M/2+1)	Method B (NH4HCO3)	95	Method C, G, C
1080			461.92	^{1}H NMR (400 MHz, DMSO-d_6): δ 10.21 (s, 1H), 9.54 (d, *J* = 1.6 Hz, 1H), 8.72 – 8.67 (m, 2H), 8.64 (d, *J* = 1.2 Hz, 1H), 8.28 (dd, *J* = 7.0, 2.6 Hz, 1H), 7.95 – 7.86 (m, 3H), 7.60 – 7.53 (m, 2H), 3.68 (d, *J* = 2.4 Hz, 2H), 3.37 – 3.34 (m, 2H), 1.65 – 1.51 (m, 6H).	DMSO	462.0 464.0 (M+1) 232.3 (M/2+1)	Method A (TFA)	95	Method C, G, C
1081			479.96	^{1}H NMR (400 MHz, DMSO-d_6): δ 10.20 (s, 1H), 9.53 (d, *J* = 1.6 Hz, 1H), 8.72 – 8.67 (m, 2H), 8.64 (d, *J* = 1.2 Hz, 1H), 8.28 (dd, *J* = 6.8, 2.8 Hz, 1H), 7.97 – 7.90 (m, 3H), 7.60 – 7.54 (m, 2H), 3.97 – 3.94 (m, 2H), 3.66 – 3.60 (m, 2H), 2.77 – 2.67 (m, 4H).	DMSO	480.0 482.0 (M+1) 240.6 (M/2+1)	Method A (TFA)	95	Method C, G, C

1082			421.85	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.20 (s, 1H), 9.55 (d, *J* = 1.6 Hz, 1H), 8.79 – 8.64 (m, 3H), 8.29 (dd, *J* = 6.8, 2.6 Hz, 1H), 8.01 – 7.87 (m, 3H), 7.53 – 7.60 (m, 2H), 3.15 – 3.05 (m, 3H), 3.02 (s, 3H).	DMSO	422.1, 424.1 (M+1)	Method B (NH_4HCO_3)	95	Method C, G, D
1083			463.89	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.22 (s, 1H), 9.55 (d, *J* = 1.4 Hz, 1H), 8.77 – 8.65 (m, 3H), 8.02 – 7.87 (m, 3H), 7.60 – 7.54 (m, 2H), 3.56 – 3.39 (m, 2H), 3.82 – 3.55 (m, 6H).	DMSO	464.1, 466.1 (M+1)	Method B (NH_4HCO_3)	95	Method C, G, D
1084			407.83	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.41 (s, 1H), 9.54 (d, *J* = 1.5 Hz, 1H), 9.08 (d, *J* = 1.3 Hz, 1H), 8.76 – 8.63 (m, 3H), 8.32 – 8.20 (m, 2H), 7.96 – 7.93 (m, 2H), 7.63 – 7.50 (m, 2H), 2.88 (d, *J* = 4.5 Hz, 3H).	DMSO	408.0, 410.0 (M+1)	Method B (NH_4HCO_3)	95	Method C, G, D
1085			447.89	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.23 (s, 1H), 9.55 (d, *J* = 1.5 Hz, 1H), 8.68 – 8.77 (m, 3H), 8.28 (dd, *J* = 6.9, 2.6 Hz, 1H), 8.02 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.99 – 7.90 (m, 2H), 7.53 – 7.58 (m, 2H), 3.57 (t, *J* = 6.8 Hz, 2H), 3.51 (t, *J* = 6.4 Hz, 2H), 1.85 – 1.95 (m, 4H).	DMSO	448.1, 420.1 (M+1)	Method B (NH_4HCO_3)	95	Method C, G, D
1086			476.93	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.22 (s, 1H), 9.54 (d, *J* = 1.5 Hz, 1H), 8.75 – 8.63 (m, 3H), 8.29 (dd, J = 6.8, 2.6 Hz, 1H), 8.01 – 7.84 (m, 3H), 7.60 – 7.53 (m, 2H), 3.72 (d, *J* = 2.2 Hz, 2H), 3.51 – 3.39 (m, 2H), 2.48 – 2.40 (m, 2H), 2.33 (d, *J* = 1.3 Hz, 2H), 2.24 (s, 3H).	DMSO	477.1, 479.1 (M+1) 239.1, 239.9 (M/2+1)	Method B (NH_4HCO_3)	95	Method C, G, D

491

1087			511.96	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.19 (s, 1H), 9.53 (d, J = 1.6 Hz, 1H), 8.59 – 8.82 (m, 3H), 8.26 (dd, J = 6.8, 2.6 Hz, 1H), 7.81 – 8.14 (m, 3H), 7.57 (m, 2H), 3.83 – 4.10 (m, 4H), 3.33 – 3.35 (m, 4H).	DMSO	512.1, 514.1 (M+1)	Method B (NH4HCO3)	95	Method C, G, D
1088			481.91	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.47 (s, 1H), 9.54 (d, J = 1.6 Hz, 1H), 9.23 (d, J = 1.2 Hz, 1H), 8.72 – 8.74 (m, 3H), 8.22 – 8.42 (m, 2H), 7.85 – 8.12 (m, 2H), 7.55 – 7.59 (m, 2H), 4.61 (t, J = 5.4 Hz, 1H), 3.47 (t, J = 5.2 Hz, 2H), 3.37 (s, 6H).	DMSO	482.1, 484.2 (M+1)	Method B (NH4HCO3)	95	Method C, G, D
1089			421.85	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.23 (s, 1H), 9.59 (d, J = 1.2 Hz, 1H), 8.72 – 8.77 (m, 2H), 8.68 (d, J = 8.4 Hz, 1H), 8.34 (dd, J = 7.2, 2.0 Hz, 1H), 7.96 – 8.00 (m, 1H), 7.92 (m, 1H), 7.72 – 7.74 (m, 1H), 7.58 – 7.65 (m, 2H), 3.13 (s, 3H), 3.03 (s, 3H).	DMSO	422.0 (M+1)	Method A (TFA)	95	Method C, G, D
1090			394.79	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.25 (s, 1H), 9.54 (s, 1H), 8.68 – 8.70 (m, 2H), 8.60 (d, J = 8.4 Hz, 1H), 8.37 (s, 1H), 8.32 (dd, J = 7.2, 2.8 Hz, 1H), 8.11 (d, J = 7.2 Hz, 1H), 7.93 –7.97 (m, 1H), 7.51 – 7.58 (m, 2H).	DMSO	395.0 (M+1)	Method A (TFA)	95	Method C, G, D
1091			476.93	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.19 (s, 1H), 9.53 (s, 1H), 8.62 – 8.72 (m, 3H), 8.29 (dd, J = 6.8, 2.4 Hz, 1H), 7.91 – 7.94 (m, 1H), 7.83 (s, 1H), 7.66 (d, J = 8.8 Hz, 1H), 7.53 – 7.59 (m, 2H), 3.69 – 3.71 (s, 2H), 3.36 – 3.38 (s, 2H), 2.42 – 2.44 (s, 2H), 2.30 – 2.32 (s, 2H), 2.23 (s, 3H).	DMSO	477.2 (M+1) 239.1 (1/2M+1)	Method B (NH4HCO3)	95	Method C, G, D

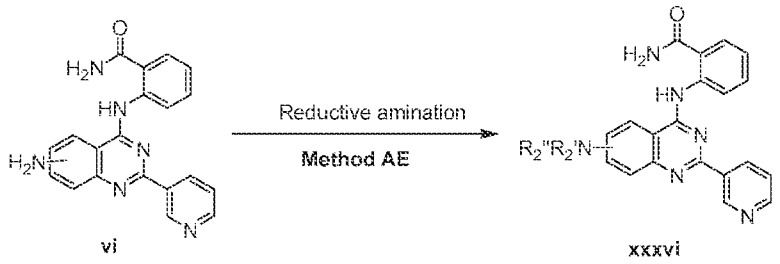
492

1092			463.89	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.18 (s, 1H), 9.52 (s, 1H), 8.62 – 8.71 (m, 3H), 8.28 (d, *J* = 4.8 Hz, 1H), 7.87 – 7.96 (m, 2H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.52 – 7.58 (m, 2H), 3.61 – 3.71 (m, 6H), 3.40 (m, 2H).	DMSO	464.1 (M+1)	Method B (NH4HCO3)	95	Method G, D
1093			393.8	^{1}H-NMR (400 MHz, DMSO-d_6) : δ 10.20 (s, 1H), 9.54 (d, *J* = 1.6 Hz, 1H), 8.62 – 8.72 (m, 3H), 8.42 (d, *J* = 1.2 Hz, 1H), 8.37 (s, 1H), 8.30 (dd, *J* = 7.2, 2.8 Hz, 1H), 8.08 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.91 – 7.95 (m, 1H), 7.71 (s, 1H), 7.53 – 7.60 (m, 2H).	DMSO	394.1 (M+1)	Method B (NH4HCO3)	95	Method G, D
1094			407.83	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.19 (s, 1H), 9.53 (s, 1H), 8.84 (d, *J* = 4.0 Hz, 1H), 8.60 – 8.72 (m, 3H), 8.35 (s, 1H), 8.29 (dd, *J* = 6.8, 2.8 Hz, 1H), 8.05 (d, *J* = 8.4 Hz, 1H), 7.90 – 7.93 (m, 1H), 7.52 – 7.59 (m, 2H), 2.87 (d, *J* = 4.8 Hz, 3H).	DMSO	408.1 (M+1)	Method B (NH4HCO3)	95	Method G, D
1095		HCl	506.96	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.20 (s, 1H), 9.53 (d, *J* = 1.6 Hz, 1H), 8.85 (t, *J* = 5.6 Hz, 1H), 8.61 – 8.72 (m, 3H), 8.36 (d, *J* = 1.2 Hz, 1H), 7.98 (dd, *J* = 6.4, 2.4 Hz, 1H), 8.03 (dd, *J* = 8.8, 1.6 Hz, 1H), 7.91 – 7.95 (m, 1H), 7.52 – 7.59 (m, 2H), 3.60 (t, *J* = 4.4 Hz, 4H), 3.46 – 3.48 (q, *J* = 6.4 Hz, 2H), 2.51– 2.54 (m, 2H), 2.42 – 2.48 (m, 4H).	DMSO	507.1 (M+1) 254.1 (M/2+1)	Method B (NH4HCO3)	95	Method G, C
1096			511.96	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.22 (s, 1H), 9.56 (d, *J* = 1.8 Hz, 1H), 8.61 – 8.79 (m, 3H), 8.31 (dd, *J* = 6.8, 2.6 Hz, 1H), 7.88 – 8.11 (m, 2H), 7.78 (dd, *J* = 8.4, 1.4 Hz, 1H), 7.51 – 7.66 (m, 2H), 4.12 (brs, 2H), 3.76 (brs, 2H), 3.30 – 3.33 (m, 4H).	DMSO	512.1, 514.1 (M+1)	Method B (NH4HCO3)	95	Method G, D

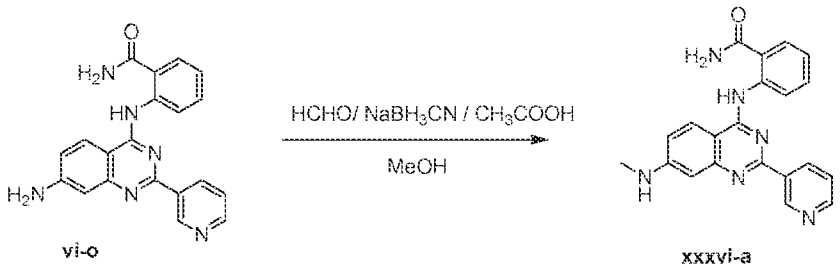
1097			474	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.64 (brs, 1H), 9.53 (s, 1H), 9.44 (t, *J* = 6.4 Hz, 1H), 9.35 (s, 1H), 8.90 (d, *J* = 8.0 Hz, 1H), 8.85 (d, *J* = 4.8 Hz, 1H), 8.35 (dd, *J* = 8.4, 1.2 Hz, 1H), 8.27 (dd, *J* = 6.8, 2.4 Hz, 1H), 8.00 -- 7.97 (m, 2H), 7.82 (dt, *J* = 13.2, 5.2 Hz, 1H), 7.55 (t, *J* = 8.8 Hz, 1H), 4.22 – 4.18 (m, 2H).	DMSO	475.7, 476.6 (M+1)	Method B (NH4HCO3)	95	Method C, G, D

494

Scheme 41: General route for the synthesis of compounds with general formula xxxvi



Scheme 42: Representative synthesis of compounds of formula xxxvi-a: (see Scheme 41)



Method AE: 2-(7-(Methylamino)-2-(pyridin-3-yl)quinazolin-4-ylamino)benzamide (xxxvi-a): A mixture of 2-(7-amino-2-(pyridin-3-yl)quinazolin-4-ylamino)benzamide (160 mg, 0.449 mmol, 1.0 eq.) and HCHO (40%, 37 mg, 0.494 mmol, 1.1 eq.), acetic acid (2 drops) were stirred at room temperature for 0.5 h. $NaBH_3CN$ (34 mg, 0.449 mmol, 1.0 eq.) was added and the mixture was stirred at room temperature overnight. After filtration, the filtrate was concentrated to give the crude product, which was purified by reverse phase chromatography (MeOH / H_2O = 3:7) to afford 28 mg of **xxxvi-a** as a white solid (17%). LCMS m/z = 371.1(M +1), 372.1 (M +2) (Method B) (retention time = 1.60 min). ^{1}H-NMR (400 MHz, DMSO-d_6): δ 12.71 (s, 1H), 9.58 (d, *J* = 1.6 Hz, 1H), 9.14 – 9.12 (m, 1H), 8.74 – 8.69 (m, 2H), 8.45 (s, 1H), 7.93 – 7.91 (m, 1H), 7.85 (d, *J* = 9.2 Hz, 2H), 7.67 – 7.71 (m, 1H), 7.59 – 7.55 (m, 1H), 7.12 – 7.16 (m, 1H), 7.06 – 7.03 (m, 1H), 6.82 – 6.81 (m, 1H), 6.70 (d, *J* = 2.4 Hz, 1H), 2.84 (d, *J* = 4.8 Hz, 3H).

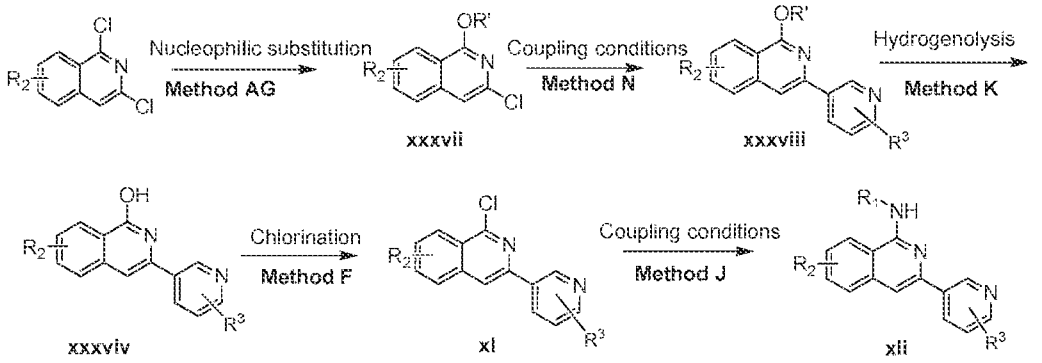
The compounds in the following table were prepared in a manner analogous to that described in **Scheme 41**, replacing formaldehyde with the appropriate aldehyde and 2-aminobenzamide with the appropriate aniline.

Table 14:

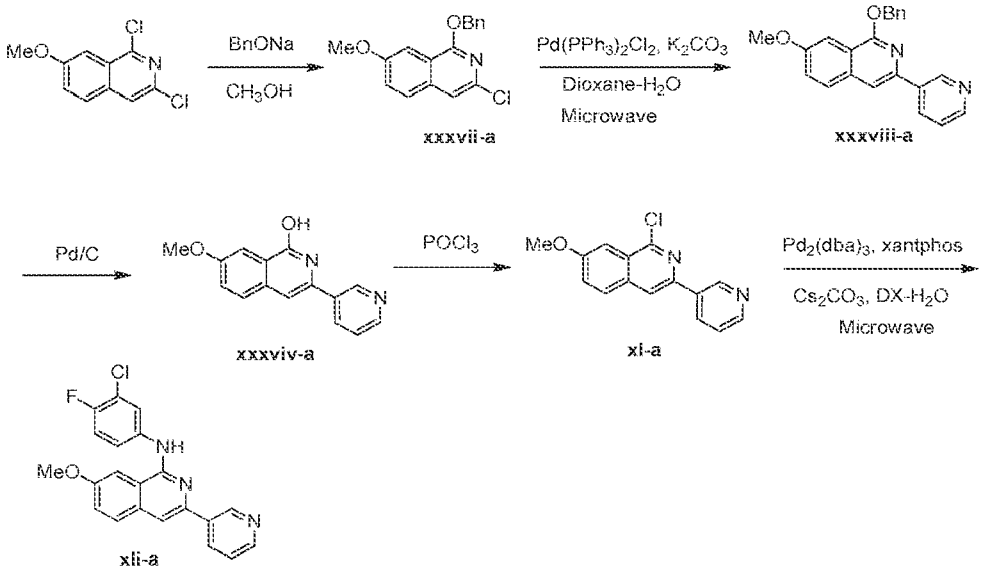
Number	PRODUCT	Salt type	Molecular Mass	^{1}H-NMR	^{1}H-NMR Solvent	LCMS	LCMS Protocol	Purity percent	Method for Coupling
1098			370.41	^{1}H-NMR (400 MHz, DMSO-d_6): δ 12.87 (s, 1H), 9.57 (d, *J* = 1.2 Hz, 1H), 9.25 (d, *J* = 8.8 Hz, 1H), 8.65 – 8.71 (m, 2H), 8.47 (s, 1H), 7.95 – 7.99 (m, 2H), 7.69 – 7.74 (m, 2H), 7.56 (dd, *J* = 7.7, 5.0 Hz, 1H), 7.33 (dd, *J* = 9.1, 1.9 Hz, 1H), 7.16 (t, J = 7.2 Hz, 1H), 6.90 (d, *J* = 1.2 Hz, 1H), 6.62 (d, *J* = 4.8 Hz, 1H), 2.88 (d, *J* = 4.8 Hz, 3H).	DMSO	371.1 (M+1)	Method B (NH_4HCO_3)	95	Method AE
1099			370.41	^{1}H-NMR (400 MHz, DMSO-d_6): δ 12.71 (s, 1H), 9.58 (d, *J* = 1.4 Hz, 1H), 9.13 (d, *J* = 7.7 Hz, 1H), 8.80 – 8.64 (m, 2H), 8.45 (s, 1H), 7.92 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.85 (d, *J* = 9.2 Hz, 2H), 7.76 – 7.62 (m, 1H), 7.57 (dd, *J* = 7.9, 4.8 Hz, 1H), 7.15 (dd, *J* = 11.2, 4.0 Hz, 1H), 7.04 (dd, *J* = 9.0, 2.3 Hz, 1H), 6.81 (q, *J* = 4.8 Hz, 1H), 6.70 (d, *J* = 2.2 Hz, 1H), 2.85 (d, *J* = 4.9 Hz, 3H).	DMSO	371.1 (M+1)	Method B (NH_4HCO_3)	95	Method AE

497

Scheme 43: General route for the synthesis of compounds with general formula xxxxi :



Scheme 44: Representative synthesis of compounds of formula xli-a: (see Scheme 43)



Method AG: 1-(Benzyloxy)-3-chloro-7-methoxyisoquinoline (xxxvii-a) 1,3-dichloro-7-methoxyisoquinoline (2.00 g, 8.8 mmol, 1.0 eq.) was dissolved in 30 mL anhydrous toluene and sodium benzyloxide (2.30 g, 17.6 mmol, 2.0 eq.) was added. The mixture was heated to 80°C for 18h. TLC indicated the reaction was complete.

The mixture was concentrated to give the crude product, which was purified by chromatography on silica gel (eluted with petroleum ether) to give 2.20 g of **xxxvii-a** as a white solid (84.6%). LCMS m/z = 300.1, 302.0 (M+1) (Method B) (retention time = 2.23 min).

1-(Benzyloxy)-7-methoxy-3-(pyridin-3-yl)isoquinoline (xxxviii-a) 1-(Benzyloxy)-7-methoxy-3-(pyridin-3-yl)isoquinoline was prepared using **Method N2.** 1-(Benzyloxy)-3-chloro-7-methoxyisoquinoline (93 mg, 0.5 mmol, 1.0 eq.), potassium carbonate (357mg, 2.5 mmol, 5.0 eq.), and $Pd(PPh_3)_2Cl_2$ (18 mg, 0.026 mmol, 0.05 eq.) was dissolved in the mixed solvent of 1,4-dioxane (3 mL) and water (1 mL). The resulting mixture was stirred at 120°C for 30 min under the microwave condition. The solid was filtrated off and the filtrate was concentrated. The residue was partitioned between ethyl acetate and water. The combined organic layers were washed with brine, dried over anhydrous sodium sulfate. After filtration and evaporation, the residue was purified by silica gel chromatography (petroleum ether/ethyl acetate = 1:10) to afford 100 mg of **xxxviii-a** as a yellow solid (84.7%).

7-Methoxy-3-(pyridin-3-yl)isoquinolin-1-ol (xxxviv-a): 7-Methoxy-3-(pyridin-3-yl)isoquinolin-1-ol **(prepared in a manner analogous to that described for 2-amino-5-methoxybenzoic acid in Method K, replacing 5-methoxy-2-nitrobenzoic acid with1-(benzyloxy)-7-methoxy-3-(pyridin-3-yl) isoquinoline)** was obtained in a 63.6 % yield to give 280 mg of **xxxviv-a** as a yellow solid. This was carried on without further purification.

1-Chloro-7-methoxy-3-(pyridin-3-yl)isoquinoline (xl-a) 1-Chloro-7-methoxy-3-(pyridin-3-yl)isoquinoline **(prepared in a manner analogous to that described for 4-chloro-6-propoxy-2-pyridin-3-yl-quinazoline in Method F1, replacing 6-propoxy-2-pyridin-3-yl-1H-quinazolin-4-one with 3-(pyridin-3-yl)isoquinolin-1-ol)** was obtained in a 73.0% yield to give 60 mg of **xl-a** as a brown solid. MS m / z = 241.1 (M+1) (Method A) (retention time = 1.34 min).

N-(3-Chloro-4-fluorophenyl)-7-methoxy-3-(pyridin-3-yl)isoquinolin-1-amine (xli-a) N-(N-(3-chloro-4-fluorophenyl)-7-methoxy-3-(pyridin-3-yl)isoquinolin-1-amine was prepared using **Method J**. A mixture of 1-chloro-7-methoxy-3-(pyridin-3-yl)isoquinoline (40 mg, 0.17 mmol, 1.0 eq.), 3-chloro-4-fluoro aniline (30 mg, 0.21 mmol, 1.2 eq.), $Pd_2(dba)_3$ (10 mg, 0.011 mmol, 0.06 eq.), Xantphos (15 mg, 0.026 mmol, 0.15 eq.), cesium carbonate (167 mg, 0.52 mmol, 3.0 eq.) was suspended in the mixed solvent of 1,4-dioxane (4 mL) and water (1 mL). The resulting mixture was stirred at 120°C for 30 min under the microwave conditions. After cooling, the resulting mixture was partitioned between water and ethyl acetate. The combined organic layers were washed with water and brine,, dried over anhydrous sodium sulfate. After filtration and evaporation, the residue was purified by prep-HPLC to afford 3 mg of **xli-a** as a yellow solid (yield 5.2%). LCMS m/z = 380.1 (M +1) (Method B). ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.35 (s, 1H), 9.30 (d, *J* = 2.0 Hz, 1H), 8.57 (dd, *J* = 4.7, 1.5 Hz, 1H), 8.41 (td, *J* = 8.0, 1.8 Hz, 1H), 8.30 (dd, *J* = 6.9, 2.6 Hz, 1H), 7.94 – 7.87 (m, 4H), 7.43 – 7.49 (m, 3H), 3.99 (s, 3H).

The compounds in the following table were prepared in a manner analogous to that described in **Scheme 43**, replacing with the appropriate isoquinoline and aniline.

Table 15:

Number	PRODUCT	Salt type	Molecular Mass	^{1}H-NMR	^{1}H-NMR Solvent	LCMS	LCMS Protocol	Purity percent	Method for Coupling
1100			379.81	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.35 (s, 1H), 9.30 (d, *J* = 2.0 Hz, 1H), 8.57 (dd, *J* = 4.7, 1.5 Hz, 1H), 8.41 (td, *J* = 8.0, 1.8 Hz, 1H), 8.30 (dd, *J* = 6.9, 2.6 Hz, 1H), 7.94 – 7.87 (m, 4H), 7.43 – 7.49 (m, 3H), 3.99 (s, 3H).	DMSO	380.1, 382.0 (M+1)	Method B (NH4HCO3)	95	Method J
1101			411.38	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.46 (s, 1H), 9.31 (d, *J* = 1.75 Hz, 1H), 8.57 (dd, *J* = 4.6, 1.3 Hz, 1H), 8.45-8.41 (m, 1H), 8.19 (s, 1H), 7.99 – 7.94 (m, 2H), 7.91 – 7.86 (m, 2H), 7.54 – 7.44 (m, 3H), 7.01 (d, *J* = 8.1 Hz, 1H), 4.00 (s, 3H).	DMSO	412.1 (M+1)	Method B (NH4HCO3)	95	Method J
1102			388.39	^{1}H-NMR (400 MHz, DMSO-d_6): δ 11.35 (s, 1H), 9.34 (d, *J* = 1.9 Hz, 1H), 8.80 (d, *J* = 8.4 Hz, 1H), 8.59 (dd, *J* = 4.7, 1.46 Hz, 1H), 8.49 – 8.45 (m, 1H), 8.26 (s, 1H), 8.13 (s, 1H), 8.02 (s, 1H), 7.97 – 7.92 (m, 1H), 7.61 (td, *J* = 14.9, 7.5 Hz, 1H), 7.56 – 7.46 (m, 3H), 6.95 (dd, *J* = 10.3, 8.3 Hz, 1H), 3.98 (s, 3H).	DMSO	389.1 (M+1)	Method B (NH4HCO3)	95	Method J
1103			370.4	^{1}H-NMR (400 MHz, CDCl3): δ 11.89 (s, 1H), 9.39 (s, 1H), 9.29 (s, 1H), 8.63 – 8.59 (m, 1H), 8.42 – 8.37 (m, 1H), 7.75 (d, *J* = 8.8 Hz, 1H), 7.60 – 7.62 (m, 4H), 7.44 – 7.33 (m, 3H), 7.05 – 7.00 (m, 1H), 4.06 (s, 3H).	CDCl3	371.1 (M+1)	Method B (NH4HCO3)	95	Method J

501

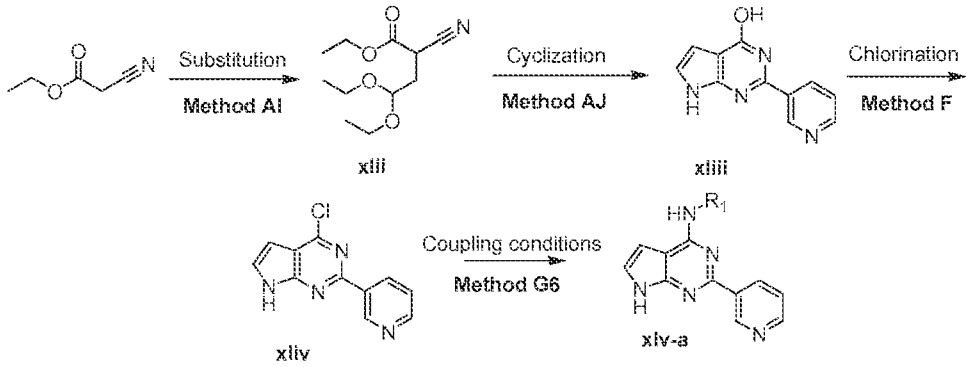
1104			407.37	^{1}H-NMR (400 MHz, CDCl3): δ 9.28 (s, 1H), 8.60 (d, *J* = 4.6 Hz, 1H), 8.34 (d, *J* = 7.8 Hz, 1H), 7.85 (s, 1H), 7.79 (d, *J* = 8.9 Hz, 1H), 7.63 (s, 1H), 7.43 – 7.35 (m, 2H), 7.22 (d, *J* = 8.6 Hz, 1H), 7.17 (s, 1H), 7.09 – 7.03 (m, 2H), 4.00 (s, 3H).	CDCl3	408.1 (M+1)	Method B (NH_4HCO_3)	95	Method J
1105			454.4	^{1}H-NMR (400 MHz, DMSO-d_6): δ 13.00 (s, 1H), 9.43 (d, *J* = 1.2 Hz, 1H), 9.35 (s, 1H), 8.63 (d, *J* = 3.7 Hz, 1H), 8.53 (s, 1H), 8.48 – 8.44 (m, 1H), 8.03 – 8.09 (m, 3H), 7.97 (d, *J* = 8.9 Hz, 1H), 7.65 (d, *J* = 1.8 Hz, 1H), 7.56 – 7.50 (m, 2H), 7.05 (dd, *J* = 8.6, 1.93 Hz, 1H), 4.01 (s, 3H).	DMSO	455.1 (M+1)	Method B (NH_4HCO_3)	95	Method J
1106			455.91	1H-NMR (400 MHz, DMSO-d_6): δ 9.65 (s, 1H), 9.37 (d, *J* = 1.7 Hz, 1H), 8.83 (s, 1H), 8.63 (dd, *J* = 4.7, 1.3 Hz, 1H), 8.54 – 8.43 (m, 1H), 8.35 (dd, *J* = 6.9, 2.6 Hz, 1H), 8.15 (dd, *J* = 8.5, 1.4 Hz, 1H), 8.03 (t, *J* = 4.3 Hz, 2H), 7.91 – 7.95 (m, 1H), 7.46 – 7.55 (m, 5H), 7.11 – 7.01 (m, 1H), 3.91 (s, 3H).	DMSO	456.1, 458.1 (M+1)	Method B (NH_4HCO_3)	95	Method J

502

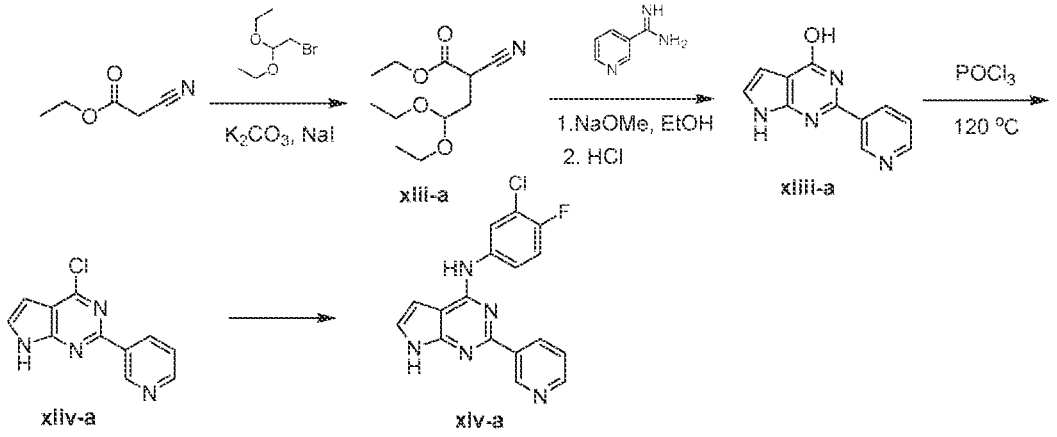
1107				^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.63 (s, 1H), 9.36 (d, J = 1.9 Hz, 1H), 9.19 (d, J = 1.9 Hz, 1H), 8.91 (s, 1H), 8.67 (dd, J = 4.8, 1.5 Hz, 1H), 8.62 (dd, J = 4.7, 1.5 Hz, 1H), 8.53 – 8.44 (m, 1H), 8.35 – 8.32 (m, 2H), 8.19 (dd, J = 8.5, 1.5 Hz, 1H), 8.13 – 8.01 (m, 2H), 7.92 (ddd, J = 9.1, 4.3, 2.7 Hz, 1H), 7.61 (dd, J = 7.9, 4.8 Hz, 1H), 7.55 (dd, J = 8.0, 4.8 Hz, 1H), 7.50 (t, J = 9.1 Hz, 1H).	DMSO	426.7 428.7 (M+H)	Method B (NH4HCO3)	95	Method J

503

Scheme 45: General route for the synthesis of compounds with general formula xxxv-a :



Scheme 46: Representative synthesis of compounds of formula xxxv-a: (see Scheme 45)



Method AI: Ethyl 2-cyano-4,4-diethoxybutanoate (xlii-a) 2-Bromo-1,1-diethoxyethane (4 g, 20 mmol, 1.0 eq.) was added to a mixture of ethyl 2-cyanoacetate (11.4 g, 101 mmol, 5.0 eq.), K_2CO_3 (2.8 g, 20 mmol, 1.0 eq.) and NaI (200 mg, 1.3 mmol, 0.06 eq.), as described in **J. Chem. Soc., 1960, 131-138**. The reaction mixture was refluxed for 4 h at 145 °C. After cooling, the reaction mixture was purified by chromatography on silica gel (eluted with petroleum ether/ethyl acetate (80:1→40: 1→10:1) to give 3.57 g of **xlii-a** as a colorless oil (78%). ^{1}H NMR

(400 MHz, $CDCl_3$): δ 4.70 (t, *J* = 5.6 Hz, 1H), 4.26 (q, *J* = 7.2 Hz, 2H), 3.78 – 3.64 (m, 3H), 3.62 – 3.45 (m, 2H), 2.35 – 2.14 (m, 2H), 1.34 (q, *J* = 7.2 Hz, 3H), 1.25 – 1.16 (m, 6H).

Method AJ: 2-(Pyridin-3-yl)-7H-pyrrolo[2,3-d]pyrimidin-4-ol (xliii) To a solution of nicotinimidamide (5.03 g, 41.6 mmol, 1.2 eq.) in EtOH (100 mL), was added NaOMe (4.8 g, 88.8 mmol, 2.5 eq.). The mixture was stirred at room temperature for 4 h. The reaction mixture was added to ethyl 2-cyano-4,4-diethoxybutanoate (8.00 g, 34.9 mmol, 1 eq.). This mixture was stirred at 105 °C overnight. After cooling, the reaction mixture was acidified with conc. HCl and stirred at room temperature for 2 h. A precipitate formed and was collected and washed with H_2O (20 mL X 2). After lyophilization, 3.10 g of product was obtained as a gray yellow solid (yield 41.8 %). LCMS m/z = 213.1 (M +1) (Method B) (retention time = 1.07 min). ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.26 (s, 1H), 12.04 (s, 1H), 9.23 (d, *J* = 1.6 Hz, 1H), 8.70 (dd, *J* = 4.8, 1.2 Hz, 1H), 8.43 – 8.40 (m, 1H), 7.55 (dd, *J* = 8.0, 4.8 Hz, 1H), 7.12 (d, *J* = 1.6 Hz, 1H), 6.51 (d, *J* = 2.8 Hz, 1H).

4-Chloro-2-(pyridin-3-yl)-7H-pyrrolo[2,3-d]pyrimidine (xlv-a) 4-Chloro-2-(pyridin-3-yl)-7H-pyrrolo[2,3-d]pyrimidine **(prepared in a manner analogous to that described for 4-chloro-6-propoxy-2-pyridin-3-yl-quinazoline in Method F1, replacing 6-propoxy-2-pyridin-3-yl-1H-quinazolin-4-one with 2-(pyridin-3-yl)-7H-pyrrolo[2,3-d] pyrimidin-4-ol)** to give 450 mg of **xliv-a** in a 69.0 % yield as a brown solid. LCMS m/z = 231.0, 233.0 (M +1) (Method B) (retention time = 1.60 min).

N-(3-chloro-4-fluorophenyl)-2-(pyridin-3-yl)-7H-pyrrolo[2,3-d]pyrimidin-4-amine (xlv-a) N-(3-chloro-4-fluorophenyl)-2-(pyridin-3-yl)-7H-pyrrolo[2,3-d]pyrimidin-4-amine **(prepared in a manner analogous to that described for N-(3-chloro-4-fluorophenyl)-6-(3-(dimethylamino)propyl)-2-(pyridin-3-yl)quinazolin-4-amine using Method G6, replacing 3-(4-(3-chloro-4-fluorophenylamino)-2-(pyridin-3-yl)quinazolin-6-yl)propyl methanesulfonate with 4-chloro-2-(pyridin-**

3-yl)-7H-pyrrolo[2,3-d]pyrimidine) to give a 11.3 % yield, 10 mg of **xlv-a** as brown solid. LCMS m/z = 340.1, 342.0 (M +1) (Method B) (retention time = 1.814 min). ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.48 (d, *J* = 1.6 Hz, 1H), 8.62 (dd, *J* = 4.8, 1.6 Hz, 1H), 8.60 – 8.56 (m, 1H), 8.27 (dd, *J* = 6.4, 2.4 Hz, 1H), 8.06 (ddd, *J* = 8.8, 4.0, 2.8 Hz, 1H), 7.71 (d, *J* = 3.6 Hz, 1H), 7.66 (t, *J* = 9.2 Hz, 1H), 7.50 (dd, *J* = 8.0, 4.8 Hz, 1H), 7.41 (br s, 2H), 6.85 (d, *J* = 3.6 Hz, 1H).

The compounds in the following table were prepared in a manner analogous to that described in **Scheme 45**, replacing with the appropriate aniline.

Table 16:

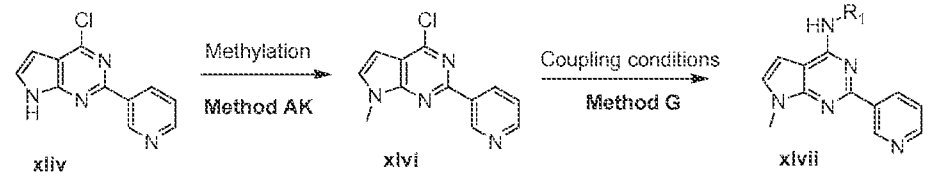
Number	PRODUCT	Salt type	Molecular Mass	^{1}H-NMR	^{1}H-NMR Solvent	LCMS	LCMS Protocol	Purity percent	Method for Coupling
1108			330.34	^{1}H-NMR (400 MHz, DMSO-d_6): δ 12.29 (s, 1H), 12.09 (s, 1H), 9.54 (d, *J* = 1.2 Hz, 1H), 9.11 (d, *J* = 8.4 Hz, 1H), 8.65 – 8.68 (m, 1H), 8.35 (s, 1H), 7.89 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.79 (s, 1H), 7.67 (td, *J* = 8.8, 1.2 Hz, 1H), 7.55 (dd, *J* = 7.2, 4.8 Hz, 1H), 7.43 – 7.41 (m, 1H), 7.10 (td, *J* = 8.0, 1.2 Hz, 1H), 6.49 (d, *J* = 3.6 Hz, 1H).	DMSO	331.1 (M +1)	Method B (NH4HCO3)	95	Method AJ, F, G6
1109			371.32	^{1}H-NMR (400 MHz, DMSO-d_6): δ 12.02 (d, *J* = 1.3 Hz, 1H), 9.75 (s, 1H), 9.50 (d, *J* = 1.5 Hz, 1H), 8.68 – 8.53 (m, 2H), 8.29 (s, 1H), 7.94 – 7.75 (m, 1H), 7.61 – 7.44 (m, 2H), 7.41 – 7.29 (m, 1H), 7.04 (s, 1H), 6.88 (dd, *J* = 3.4, 1.9 Hz, 1H).	DMSO	372.0 (M+1)	Method A (TFA)	95	Method AJ, F, G6
1110			366.32	1H-NMR (400 MHz, DMSO-d6):δ 11.98 (s, 1H), 9.69 (s, 1H), 9.48 (d, J = 1.8 Hz, 1H), 8.64- 8.59 (m, 2H), 8.19 (d, J = 2.0 Hz, 1H), 7.63 (dd, J = 8.8, 2.0 Hz, 1H), 7.54 (dd, J = 7.9, 4.8 Hz, 1H), 7.45 (d, J = 8.8 Hz, 1H), 7.34 (d, J = 3.0 Hz, 1H), 6.	DMSO	368.1 (M+1)	Method A (TFA)	95	Method AJ, F, G6

507

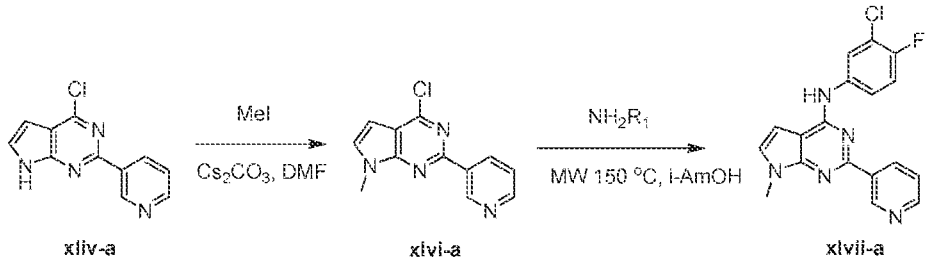
1111			339.75	^{1}H-NMR (400 MHz, DMSO-d_6): δ 11.51 (s, 1H), 8.78 (d, *J* = 8.0 Hz, 2H), 8.17 (d, *J* = 9.2 Hz, 1H), 7.80 (dd, *J* = 9.2, 2.8 Hz, 1H), 7.70 – 7.64 (m, 1H), 7.46 (d, *J* = 2.8 Hz, 1H), 7.41 (d, *J* = 8.0 Hz, 1H), 7.20 (d, *J* = 4.0 Hz, 2H), 7.16 – 7.08 (m, 1H).	DMSO	340.1, 342.0 (M+1)	Method B (NH4HCO3)	95	Method AJ, F, G6

508

Scheme 47: General route for the synthesis of compounds with general formula xxxxvii :



Scheme 48: Representative synthesis of compounds of formula xxxxvii-a: (see Scheme 47)



Method AK: 4-Chloro-7-methyl-2-(pyridin-3-yl)-7H-pyrrolo[2,3-d]pyrimidine (xliv-a) To a solution of 4-chloro-2-(pyridin-3-yl)-7H-pyrrolo[2,3-d]pyrimidine (80 mg, 0.34 mmol, 1.0 eq.) in dry DMF (20 mL) was added Cs_2CO_3 (221 mg, 0.68 mmol, 2.0 eq.) and iodomethane (54.3 mg, 0.38 mmol, 1.1 eq.) at 0 °C. The reaction mixture was warmed to room temperature and stirred for 2.5 h. The reaction mixture was poured into ice water and extracted with EtOAc (20 mL x 3). The combined organic layers were dried over anhydrous Na_2SO_4. After filtration and concentration, the residue was purified by chromatography on silica gel (petroleum ether/ethyl acetate 8:1) to give 65 mg of **xlvi-a** as brown solid (56.7%).

N-(3-chloro-4-fluorophenyl)-7-methyl-2-(pyridin-3-yl)-7H-pyrrolo[2,3-d]pyrimidin-4-amine (xlvii-a) N-(3-chloro-4-fluorophenyl)-7-methyl-2-(pyridin-3-yl)-7H-pyrrolo[2,3-d]pyrimidin-4-amine **(prepared in a manner analogous to that described for N-(3-chloro-4-fluorophenyl)-6-(3-(dimethylamino)propyl)-2-(pyridin-3-yl)quinazolin-4-amine using Method G6, replacing 3-(4-(3-chloro-4-fluorophenylamino)-2-(pyridin-3-yl)quinazolin-6-yl)propyl methanesulfonate**

with 4-chloro-7-methyl-2-(pyridin-3-yl)-7H-pyrrolo[2,3-d]pyrimidine) to give a 70.0 % yield, 30 mg of **xlvii-a** as a brown solid. LCMS m/z = 354.1, 356.1 (M +1) (Method B) (retention time = 1.94 min). ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.97 (s, 1H), 9.53 (s, 1H), 9.15 (d, *J* = 8.0 Hz, 1H), 8.91 (d, *J* = 5.2 Hz, 1H), 8.25 (dd, *J* = 6.8, 2.4 Hz, 1H), 8.04 (dd, *J* = 7.6, 5.6 Hz, 1H), 7.94 – 7.90 (m, 1H), 7.48 – 7.43 (m, 2H), 6.95 (d, *J* = 3.2 Hz, 1H), 3.88 (s, 3H).

The compounds in the following table were prepared in a manner analogous to that described in **Scheme 46**, replacing with the appropriate aniline.

Table 17:

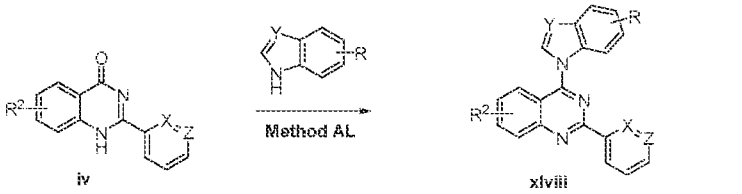
Number	PRODUCT	Salt type	Molecular Mass	^{1}H-NMR	^{1}H-NMR Solvent	LCMS	LCMS Protocol	Purity percent	Method for Coupling
1112		HCl	353.78	^{1}H NMR (400 MHz, DMSO-d_6): δ 9.97 (s, 1H), 9.53 (s, 1H), 9.15 (d, J = 8.0 Hz, 1H), 8.91 (d, J = 5.2 Hz, 1H), 8.25 (dd, J = 6.8, 2.4 Hz, 1H), 8.04 (dd, J = 7.6, 5.6 Hz, 1H), 7.94 – 7.90 (m, 1H), 7.48 – 7.43 (m, 2H), 6.95 (d, J = 3.2 Hz, 1H), 3.88 (s, 3H).	DMSO	354.1, 356.1 (M +1)	Method B (NH4HCO3)	95	Method AK, G6
1113			385.34	^{1}H NMR (400 MHz, DMSO-d_6): δ 9.81 (s, 1H), 9.56 (d, J = 1.6 Hz, 1H), 8.69 – 8.64 (m, 2H), 8.29 (s, 1H), 7.87 (d, J = 8.8 Hz, 1H), 7.55 – 7.51 (m, 2H), 7.41 (d, J = 3.6 Hz, 1H), 7.04 (d, J = 8.0 Hz, 1H), 6.90 (d, J = 3.6 Hz, 1H), 3.87 (s, 3H).	DMSO	386.1 (M +1)	Method B (NH4HCO3)	95	Method AK, G6

511

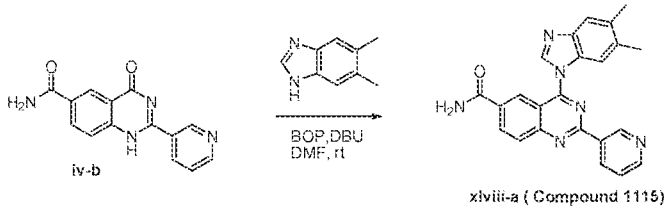
1114				1H-NMR (400 MHz, DMSO-d6):δ 12.32 (s, 1H), 9.61 (s, 1H), 9.11 (d, J = 7.6 Hz, 1H), 9.11 (d, J = 7.6 Hz, 1H), 8.74 (dt, J = 8.0, 1.9 Hz, 1H), 8.67 (d, J = 3.6 Hz, 1H), 8.38 (s, 1H), 8.38 (s, 1H), 7.90 (dd, J = 7.9, 1.4 Hz, 1H), 7.82 (s, 1H), 7.68 (dd	DMSO	344.9 (M +1)	Method B (NH4HCO3)	95	Method AK, G6

512

Scheme 49: General route for the synthesis of compounds with general formula xlviii

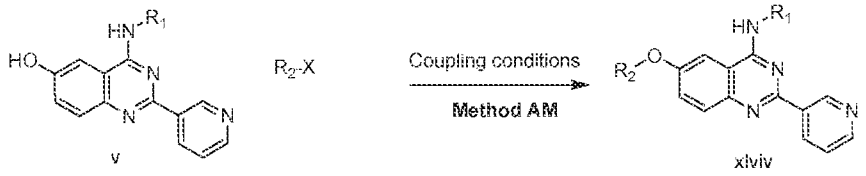


Scheme 50: Representative synthesis of compounds of formula xlviii-a (See Scheme 49)

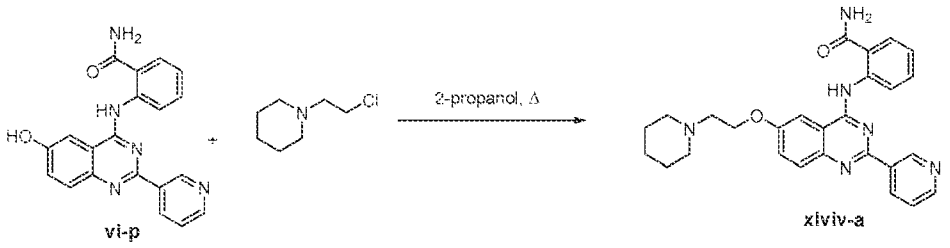


Method AL: 4-(5,6-dimethyl-1H-benzo[d]imidazol-1-yl)-2-(pyridin-3-yl)quinazoline-6-carboxamide (xlviii-a) To a suspension of 4-oxo-2-(pyridin-3-yl)-1,4-dihydroquinazoline-6-carboxamide **(prepared as described in scheme 4)** (100 mg, 0.376 mmol, 1.0 eq.) in dry DMF (20 mL) was added benzotriazole-1-yl-oxy-tris-(dimethylamino)-phosphonium hexafluorophosphate (216 mg, 0.488 mmol, 1.3 eq.) and diaza(1,3)bicyclo[5.4.0]undecene (114.5 mg, 0.752 mmol, 2.0 eq.) following a procedure outlined in ***J. Org. Chem.*, 2007, *72*, 10194–10210**. To the clear solution was then added 5,6-dimethyl-1H-benzo[d]imidazole (165.2 mg, 1.13 mmol, 3.0 eq.) and the mixture was stirred overnight at room temperature. The resultant precipitate was then collected by filtration and washed with dichloromethane, water, and ether. The product was dried *in vacuo* to give 26.3 mg of the desired product (**xlviii-a**) as an off-white solid (6.7 %). LCMS m/z = 395.1 (M +1) (Method C) (retention time = 1.68 min). ^{1}H NMR (300 MHz, DMSO) δ 9.69 (s, 1H), 8.90 (s, 1H), 8.82 (d, J = 15.2 Hz, 2H), 8.66 (s, 1H), 8.54 (d, J = 8.6 Hz, 1H), 8.42 (s, 1H), 8.30 (d, J = 8.5 Hz, 1H), 7.79 (s, 1H), 7.68 (s, 3H), 2.39 (s, 3H), 2.36 (s, 3H).

Scheme 51: General route for the synthesis of compounds with general formula xlviv



Scheme 52: Representative synthesis of compounds of formula xlviv (see Scheme 51)

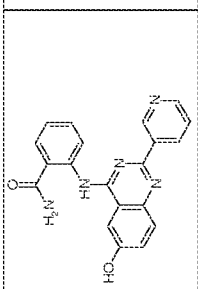
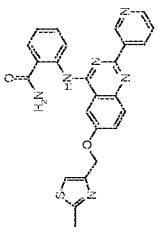
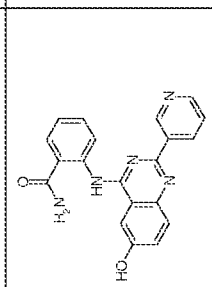
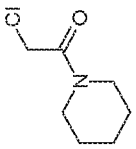
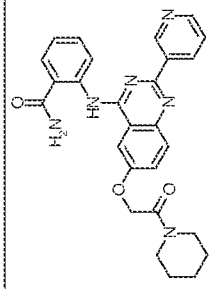
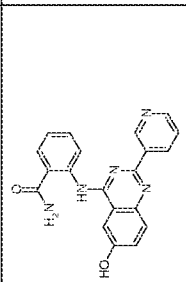
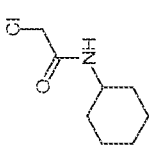
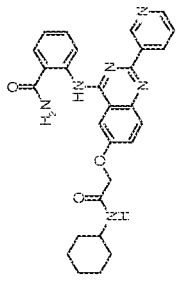
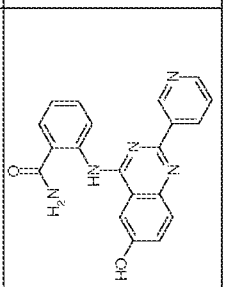
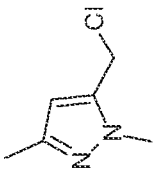
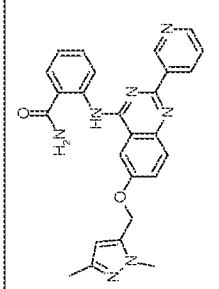


Method AM: Synthesis of 2-(6-(2-(piperidin-1-yl)ethoxy)-2-(pyridin-3-yl)quinazolin-4-ylamino)benzamide (xlviv-a) To 1-(2-chloroethyl)piperidine (45 µmol) was added the solution of 2-(6-hydroxy-2-(pyridin-3-yl)quinazolin-4-ylamino)benzamide (30 µmol) in NMP (200 µL). PS-BEMP (90 µmol) was added to the vials by resin dispenser. After the reaction mixture was heated at 90^0C for 12 h, the residue was diluted with methanol and purified by mass triggered **PREP-HPLC Condition D.** The target fraction was lyophilized to afford the titled compound whose structure was finally confirmed by LCMS using LCMS **Method E.**

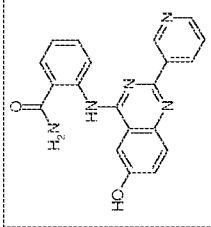
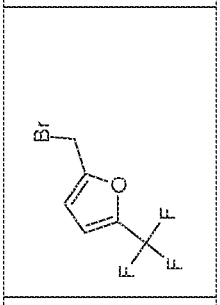
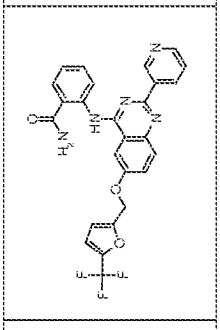
The compounds in the following table were prepared in a manner analogous to that described in **Scheme 51**, replacing 1-(2-chloroethyl)piperidine with the appropriate alkyl halide.

Table 18:

Number	Starting Material 1	Starting Material 2	Product	Salt Type	Exact Mass	Mass Found (M+1)	Purity (%)
1116					468	469	98
1117					454	455	98
1118					456	457	98

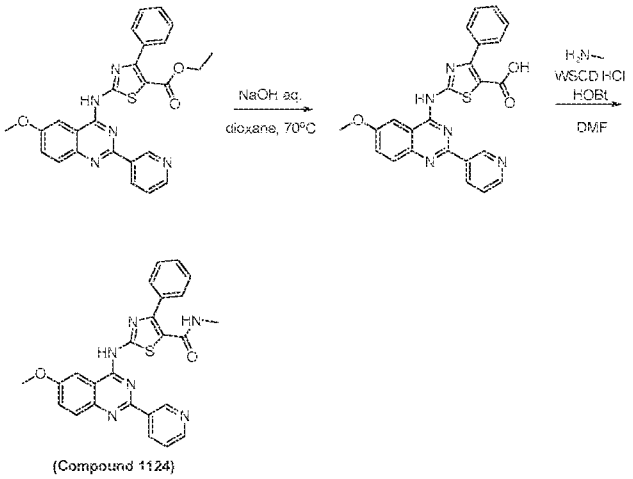
1119					466	469	98
1120					482	483	98
1121				TFA	496	497	98
1122					465	466	98

516

1123					505
					506
					98

517

Scheme 53: Synthesis of 2-(6-methoxy-2-(pyridin-3-yl)quinazolin-4-ylamino)-N-methyl-4-phenylthiazole-5-carboxamide dihydrochloride (Compound 1124)



To a suspension of ethyl 2-(6-methoxy-2-(pyridin-3-yl)quinazolin-4-ylamino)-4-phenylthiazole-5-carboxylate (1.3956 g, 2.89 mmol) in dioxane (40 mL) was added 1N NaOH (20 ml, 20.00 mmol) at room temperature to give a clear solution. The reaction mixture was stirred at room temperature for 1 h and then warmed to 50°C overnight, however starting material remained. An additional 20 mL of 1N NaOH was added and heating was continued at 50°C for 1 h and at 70 °C for 5 h 30 min. The reaction mixture was cooled to room temperature and diluted with water and ethyl acetate. The water phase was removed and adjusted to an acidic pH with 1N HCl (40 mL). A precipitate formed and was collected and washed with water. The product was dried *in vacuo* to give 1.20 g of a brown solid in a 91%yield. ^{1}H NMR (DMSO-d_6) ppm 12.88 (br, 2H), 9.77 (dd, J = 2.12, 0.6 Hz, 1H), 8.92-8.89 (m, 1H), 8.78 (dd, J = 4.8, 1.68 Hz, 1H), 8.32 (br, 1H), 7.96 (d, J = 9.12 Hz, 1H), 7.82-7.80 (m, 2H), 7.70-7.67 (m, 1H), 7.63 (dd, J = 9.12, 2.68 Hz, 1H),7.50-7.44 (m, 3H), 3.98 (s, 3H).

Method AN: 2-(6-methoxy-2-(pyridin-3-yl)quinazolin-4-ylamino)-N-methyl-4-phenylthiazole-5-carboxamide To a suspension of 2-(6-methoxy-2-(pyridin-3-yl)quinazolin-4-ylamino)-4-phenylthiazole-5-carboxylic acid (291.8 mg, 0.641 mmol) in DMF(20 mL) under nitrogen atmosphere was added N-(3-dimethylaminopropyl)-

N'-ethylcarbodiimide hydrochloride (189 mg, 0.986 mmol) and 1-hydroxybenzotriazole hydrate (147 mg, 0.961 mmol) at room temperature. The reaction mixture was stirred at room temperature for 10 min to give a clear solution and methylamine in a methanol solution (4 mL) was added at room temperature. The reaction mixture was stirred at room temperature for 2 h 15 min. Additional methyl amine in a methanol solution (4 mL) was added at room temperature and then heated to 50°C for 1h followed by room temperature for 2 days. The reaction mixture was partitioned between water and ethyl acetate. The water phase was collected and a solid precipitated from the water phase. The solid was filtered and dried in an oven at 60°C to give 107.9 mg (0.23 mmol) as the parent compound. The parent compound was suspended in methanol and 4N HCl in ethyl acetate (ca. 2mL) was added to give a clear solution which precipitated over time. The solid was collected by filtration and dried in oven at 60°C for 2 days to give 82.4 mg of the HCl salt as a yellow solid in 24% yield. ^{1}H NMR (DMSO-d_6) δ 12.77 (brs, 1H), 9.76 (d, J = 1.72 Hz, 1H), 9.18 (d, J = 7.88 Hz, 1H), 8.92 (d J = 5.04 Hz, 1H), 8.35 (brs, 1H), 8.27 (brd, J = 4.56 Hz, 1H), 7.99-7.965 (m, 2H), 7.79 (brd, J = 7.16 Hz, 2H), 7.65 (dd, J = 9.12, 2.56 Hz, 1H), 7.50-7.41 (m, 3H), 4.00 (s, 3H), 2.76 (d, J =4.56 Hz, 3H) . The 1H of 2HCl was not observed.

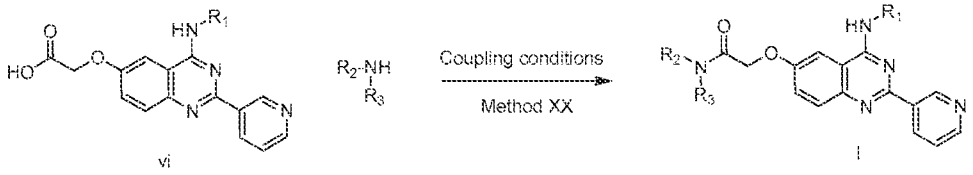
The compounds in the following table were prepared in a manner analogous to that described in **Scheme 53,** replacing N-methyl amine with the appropriate alkyl amine.

Table 19:

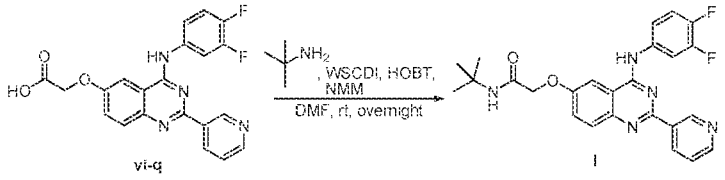
Number	Starting Material 1	Starting Material 2	Product	Salt Type	^{1}H NMR	^{1}H NMR Solvent	Purity percent	Method of Coupling
1124				2 HCl	1H NMR (DMSO-d6) ppm 12.77 (brs, 1H), 9.76 (d, J = 1.72 Hz, 1H), 9.18 (d, J = 7.88 Hz, 1H), 8.92 (d J = 5.04 Hz, 1H), 8.35 (brs, 1H), 8.27 (brd, J = 4.56 Hz, 1H), 7.99-7.965 (m, 2H), 7.79 (brd, J = 7.16 Hz, 2H), 7.65 (dd, J = 9.12, 2.56 Hz, 1H), 7.50-7.41 (m, 3H), 4.00 (s, 3H), 2.76 (d, J =4.56 Hz, 3H) . The 1H of 2HCl was not observed.	DMSO	>98	Method AN
1125				2 HCl	1H NMR (DMSO-d6) ppm 12.75 (brs, 1H), 9.77 (d, J = 1.52 Hz, 1H), 9.13 (brs, 1H), 8.88 (brd, J = 5.08 Hz, 1H), 8.34 (d, J =2.04 Hz, 1H), 7.98 (d, J = 9.12 HZ, 1H), 7.90 (brm, 1H), 7.83-7.80 (m, 2H), 7.66-7.53 (brm, 3H), 7.51-7.42 (m, 3H), 4.00 (s, 3H). The 1H of 2HCl was not observed.	DMSO	>98	Method AN
1126					1H NMR (DMSO-d6) ppm 12.66 (s, 1H), 9.76 (s, 1H), 8.88 (d, J = 7.76 HZ, 1H), 8.75 (d, J = 3.68 Hz, 1H), 8.40-8.20 (br, 2H), 7.94 (br, 1H), 7.80 (d, J =7.16 Hz, 2H), 7.63 (m, 2H), 7.49-7.41 (m, 3H), 3.99 (s, 3H), 3.24 (q, J = 7.24 Hz, 2H), 1.07 (t, J = 7.24 Hz, 3H)	DMSO	>98	Method AN

520

Scheme 54: General route for the synthesis of compounds with general formula I



Scheme 55: Representative synthesis of compounds of formula I-a: (see Scheme 54)



Method AO: *N*-tert-butyl-2-(4-(3,4-difluorophenyl-amino)-2-(pyridin-3-yl)quinazolin-6-yloxy)acetamide To a solution of carboxylic acid derivative (500 mg, 1.2 mmol) in DMF was added 2-aminoisobutane (134 mg, 1.8 mmol), NMM (0.4 mL, 3.6 mmol), WSCDI (282 mg, 1.4 mmol) and HOBT (225 mg, 1.4 mmol). The reaction mixture was stirred at room temperature overnight. The resulting solution was poured into ice-water and the precipitate formed and was filtered off. The solid was washed with water and dried to give 350 mg (62% yield) of desired product. ^{1}H NMR (400 MHz, DMSO) δ 9.86 (s, 1H), 9.49 (d, J = 1.5 Hz, 1H), 8.71 – 8.57 (m, 2H), 8.11 (ddd, J = 13.3, 7.5, 2.5 Hz, 1H), 8.00 – 7.93 (m, 1H), 7.87 (d, J = 9.1 Hz, 1H), 7.67 (ddd, J = 11.7, 7.1, 2.1 Hz, 2H), 7.59 – 7.47 (m, 3H), 4.61 (s, 2H), 1.35 (s, 9H).

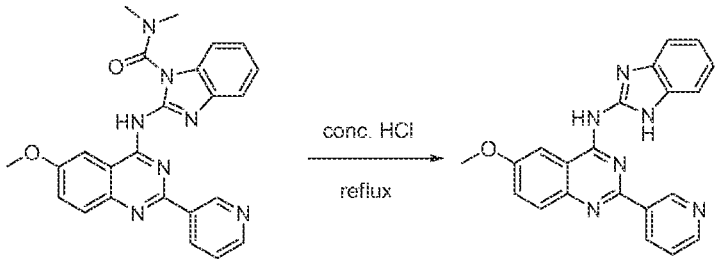
The compounds in the following table were prepared in a manner analogous to that described in **Scheme 54,** replacing 2-aminoisobutane with the appropriate alkyl amine.

Table 20:

Number	Starting Material R^1	Starting Material R^3	Product	Salt Type	^1H NMR	^1H NMR Solvent	Purity percent	Method of Coupling
1127				3 HCl	^1H NMR (400 MHz, DMSO) δ 10.60 (s, 1H), 9.48 (d, J = 1.9 Hz, 1H), 9.14 (dt, J = 8.2, 1.6 Hz, 1H), 8.96 (dd, J = 5.5, 1.3 Hz, 1H), 8.37 (t, J = 6.0 Hz, 1H), 8.24 (d, J = 2.6 Hz, 1H), 8.11 – 7.97 (m, 3H), 7.74 (ddd, J = 11.8, 7.4, 3.3 Hz, 2H), 7.55 (dt, J = 10.5, 9.1 Hz, 1H), 4.79 (s, 2H), 3.01 (t, J = 6.5 Hz, 2H), 1.86 – 1.59 (m, 1H), 0.85 (d, J = 6.7 Hz, 6H).	DMSO	>98	Method AO
1128				3 HCl	^1H NMR (400 MHz, DMSO) δ 10.81 (s, 1H), 9.50 (d, J = 1.9 Hz, 1H), 9.16 (d, J = 8.2 Hz, 1H), 8.98 (dd, J = 5.5, 1.3 Hz, 1H), 8.40 (d, J = 2.5 Hz, 1H), 8.29 (t, J = 6.4 Hz, 1H), 8.18 – 7.95 (m, 3H), 7.83 – 7.67 (m, 2H), 7.55 (dt, J = 10.5, 9.1 Hz, 1H), 4.88 (s, 2H), 2.98 (d, J = 6.4 Hz, 1H), 0.84 (s, 9H).	DMSO	>98	Method AO
1129				2 HCl	^1H NMR (400 MHz, DMSO) δ 10.87 (s, 1H), 9.50 (d, J = 1.9 Hz, 1H), 9.16 (d, J = 8.2 Hz, 1H), 8.98 (dd, J = 5.5, 1.3 Hz, 1H), 8.41 (d, J = 2.5 Hz, 1H), 8.23 – 7.96 (m, 4H), 7.85 – 7.66 (m, 2H), 7.55 (dt, J = 10.5, 9.1 Hz, 1H), 4.85 (s, 2H), 3.80 – 3.43 (m, 1H), 1.65 – 1.21 (m, 4H), 0.81 (t, J = 7.4 Hz, 6H).	DMSO	>98	Method AO

522

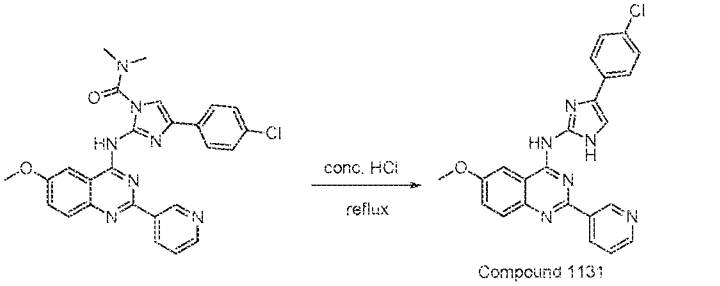
Scheme 56: Synthesis of N-(1H-benzo[d]imidazol-2-yl)-6-methoxy-2-(pyridin-3-yl)quinazolin-4-amine dihydrochloride (Compound 1130)



Compound 1130

2-(6-methoxy-2-(pyridin-3-yl)quinazolin-4-ylamino)-N,N-dimethyl-1H-benzo[d]imidazole-1-carboxamide (334.1 mg, 0.760 mmol) was dissolved in concentrated HCl (0.063 ml, 0.760 mmol). The solution was stirred at room tempertaure overnight and then at 50°C for 3h 30 min followed by 100°C for 3 h. The solid was collected and dried *in vacuo* to give 116.2 mg of a yellow solid in a yield 35%. ^{1}H NMR (DMSO-d_6) δ 13.22 (br, 1H), 9.55 (s, 1H), 8.92 (dd, J = 4.96, 1.36 Hz, 1H), 8.88 (br, 1H), 8.01 (d, J = 9.12 Hz, 1H), 7.92 (br, 1H), 7.83 (br,1H), 7.67 (dd, J = 9.12, 2.80 Hz, 1H), 7.61 (m, 2H), 7.38 (m, 2H), 3.97 (s, 3H) . The 1H of 2HCl and NH - were not observed.

Scheme 57: Synthesis of N-(4-(4-chlorophenyl)-1H-imidazol-2-yl)-6-methoxy-2-(pyridin-3-yl)quinazolin-4-amine dihydrochloride (Compound 1131)

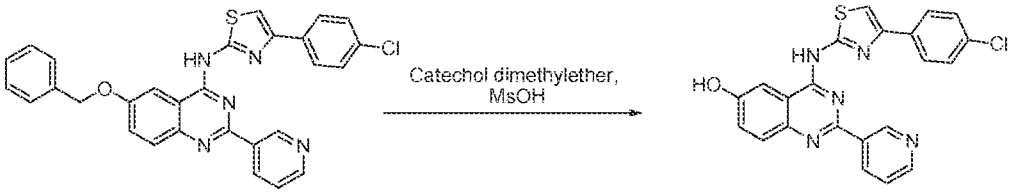


Compound 1131

4-(4-chlorophenyl)-2-(6-methoxy-2-(pyridin-3-yl)quinazolin-4-ylamino)-N,N-dimethyl-1H-imidazole-1-carboxamide and concentrated $HCl_{(aq)}$ (10 mL) were added to a round bottom flask, a precipitate appeared upon refluxing the mixture for 3 h. The

solid was collected (373.4 mg) and trituated with CH_2Cl_2 / methanol overnight. The product was filtered and dried to give 261.7 mg of a solid. A suspension of the product in methanol was added to a 1N solution of NaOH $_{(aq.)}$ (5 mL) followed by CH_2Cl_2 and H_2O. The solid was collected and washed with methanol to give 255.7 mg (0.596 mmol) of the parent product. The free parent was suspended in CH_2Cl_2 /methanol and converted to the HCl salt by addition of a 0.3 ml solution of 4N HCl in ethyl acetate. The HCl salt was collected and dried *in vacuo* to give 248.4 mg as brown solid in a 26% yield. ^{1}H NMR (DMSO-d_6) δ 13.61 (br, 1H), 12.81 (br, 1H), 9.46 (s, 1H), 8.87 (d, J = 5.24 Hz, 1H), 8.70 (br, 1H), 7.91-7.87 (m, 5H), 7.75 (m, 1H), 7.62-7.56 (m, 3H), 3.95 (s, 3H). The 1H of 2HCl was not observed.

Scheme 58: Synthesis of 4-(4-(4-chlorophenyl)thiazol-2-ylamino)-2-(pyridin-3-yl)quinazolin-6-ol (Compound 1132)

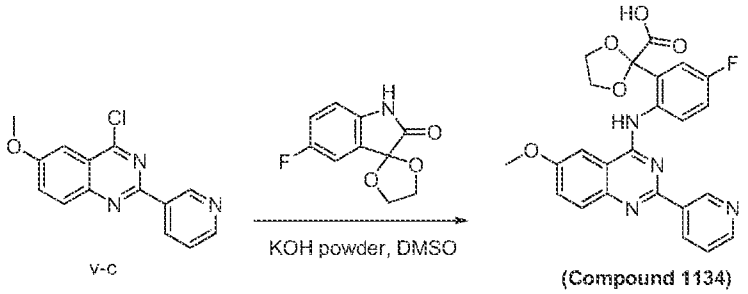


To a mixture of N-(6-(benzyloxy)-2-(pyridin-3-yl)quinazolin-4-yl)-4-(4-chlorophenyl)thiazol-2-amine and catechol, dimethyl ether (0.16 g, 1.15 mmol) was added methanesulfonic acid (4.0 mL). The mixture was stirred for 1 hr and was then poured into water. The slurry was added to a stirring sat. $NaHCO_{3(aq)}$. solution slowly and allowed to stir for 30min. The precipitate was filtered to give a brown solid which was washed with methanol to give 4-(4-(4-chlorophenyl)thiazol-2-ylamino)-2-(pyridin-3-yl)quinazolin-6-ol (0.23g, 91.0 %).

Scheme 59: Synthesis of 4-(4-phenylthiazol-2-ylamino)-2-(pyridin-3-yl)quinazolin-6-ol (Compound 1133) Synthesis of 4-(4-phenylthiazol-2-ylamino)-2-(pyridin-3-yl)quinazolin-6-ol was performed in a similar manner to that described

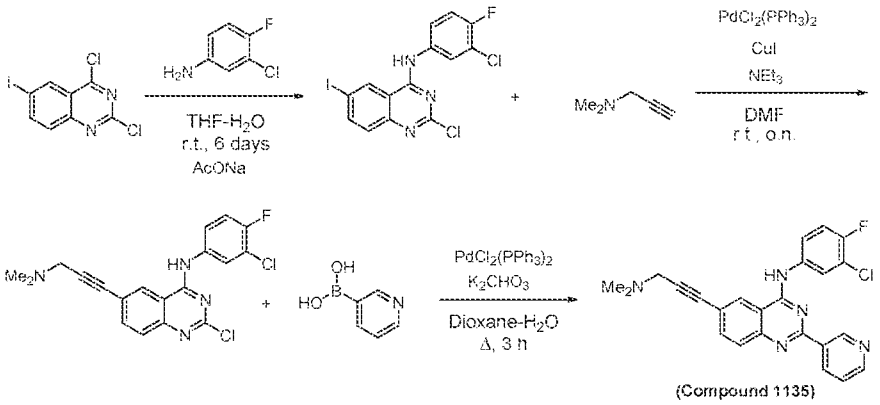
for 4-(4-(4-chlorophenyl)thiazol-2-ylamino)-2-(pyridin-3-yl)quinazolin-6-ol substituting for 4-(4-phenylthiazol-2-ylamino)-2-(pyridin-3-yl)quinazolin-6-ol for the N-(6-(benzyloxy)-2-(pyridin-3-yl)quinazolin-4-yl)-4-(4-chlorophenyl)thiazol-2-amine giving 4-(4-phenylthiazol-2-ylamino)-2-(pyridin-3-yl)quinazolin-6-ol. ^{1}H NMR (300 MHz, DMSO) δ 10.06 – 9.22 (m, 2H), 8.95 (dt, J = 7.9, 1.6 Hz, 1H), 8.62 (dd, J = 4.7, 1.4 Hz, 1H), 7.99 (d, J = 7.5 Hz, 2H), 7.87 (d, J = 2.8 Hz, 1H), 7.59 – 7.47 (m, 2H), 7.45 – 7.32 (m, 3H), 7.30 – 7.09 (m, 2H).

Scheme 60: Synthesis of 2-(5-fluoro-2-(6-methoxy-2-(pyridin-3-yl)quinazolin-4-ylamino)phenyl)-1,3-dioxolane-2-carboxylic acid (Compound 1134)



To a mixture of 4-chloro-6-methoxy-2-(pyridin-3-yl)quinazoline (0.50 g, 1.84 mmol) and 5'-fluorospiro[[1,3]dioxolane-2,3'-indolin]-2'-one (0.42 g, 2.02 mmol) in dry DMSO (4 mL) was added KOH powder (0.11g, 2.02 mmol). The reaction mixture was stirred for 15 h at room temperature and then the reaction mixture was poured into water. The aqueous layer was washed with ethyl acetate (2x 20mL) and the resulting aqueous layer was acidified with 5N HCl to give a precipitate. The solid was filtered to give 2-(5-fluoro-2-(6-methoxy-2-(pyridin-3-yl)quinazolin-4-ylamino)phenyl)-1,3-dioxolane-2-carboxylic acid as a light yellow powder (0.27g, 0.58 mmol, 32 %). LCMS m/z = 432 (M +1) (Method C) ^{1}H NMR (300 MHz, DMSO) δ 9.50 – 9.38 (m, 2H), 8.69 – 8.59 (m, 2H), 8.42 (dd, J = 9.7, 5.3 Hz, 1H), 7.86 (d, J = 9.1 Hz, 1H), 7.64 (d, J = 2.6 Hz, 1H), 7.61 – 7.41 (m, 4H), 4.25 – 4.11 (m, 4H), 3.98 (s, 3H).

Scheme 61: N-(3-chloro-4-fluorophenyl)-6-(3-(dimethylamino)prop-1-ynyl)-2-(pyridin-3-yl)quinazolin-4-amine (compound 1135)



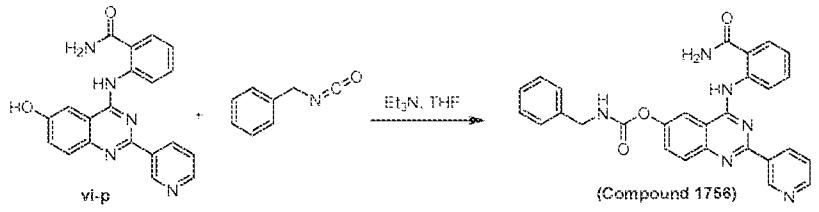
In a 50 mL round-bottomed flask was added 2,4-dichloro-6-iodoquinazoline (0.52 g, 1.6 mmol), 3-chloro-4-fluoroaniline (0.30 g, 2.1 mmol), and sodium acetate (0.20 g, 2.4 mmol) in THF (6 mL) and water (2 mL) to give a brown suspension. After being stirred at room temperature for 6 days, the reaction mixture was diluted with water (15 mL) and extracted with ethyl acetate (2 x 10 mL). The organic layers were combined and washed with brine (1 x 20 mL), dried over Na_2SO_4, filtered and concentrated. The resulting product was washed with CH_2Cl_2 and dried to give 0.51 g of 2-chloro-N-(3-chloro-4-fluorophenyl)-6-iodoquinazolin-4-amine as a light brown solid in a 73 % yield. ^{1}H NMR (300 MHz, DMSO) δ 10.29 (s, 1H), 8.95 (s, 1H), 8.14 (dd, J = 1.5, 9.0 Hz, 1H), 8.06 (dd, J = 2.7, 6.6 Hz, 1H), 7.81 – 7.76 (m, 1H), 7.52 – 7.46 (m, 2H).

In a 50 mL round-bottomed flask was added 2-chloro-N-(3-chloro-4-fluorophenyl)-6-iodoquinazolin-4-amine (200 mg, 0.46 mmol), N,N-dimethylpropargylamine (99 mL, 0.92 mmol), NEt_3 (0.26 mL, 1.84 mmol), CuI (0.88 mg, 4.6 mmol) and $PdCl_2(PPh_3)_2$ (6.5 mg, 9.2 mmol) in DMF (3 mL) to give a light yellow suspension. The mixture was stirred at room temperature overnight under an argon atmosphere. The reaction mixture was diluted with water (10 mL) and ethyl acetate (10 mL) and then a precipitate formed. The resulting precipitate was removed by filtration through Celite. The filtrate was extracted with ethyl acetate (2 x 10 mL). The combined organic layer was washed with water (1 x 15 mL) and brine (1 x 15 mL) and was dried over Na_2SO_4, filtered and concentrated. The residue was purified

by column chromatography on silica gel (eluted with CH_2Cl_2/MeOH 1:0 to 9:1). The desired product was washed with CH_2Cl_2 to give 61 mg of 2-chloro-N-(3-chloro-4-fluorophenyl)-6-(3-(dimethylamino)prop-1-ynyl)quinazolin-4-amine as pale yellow solid in a 34 % yield. LCMS m/z = 389 (M +1) (Method C) (retention time = 2.24 min). ^{1}H NMR (300 MHz, DMSO) δ 10.30 (s, 1H), 8.68 (s, 1H), 8.07 (dd, J = 2.7, 6.9 Hz, 1H), 7.86 (dd, J = 1.8, 8.7 Hz, 1H), 7.81 – 7.70 (m, 1H), 7.68 (d, J = 8.4 Hz, 1 H), 7.49 (t, J = 9.2 Hz, 1 H), 3.52 (s, 2H), 2.28 (s, 6H).

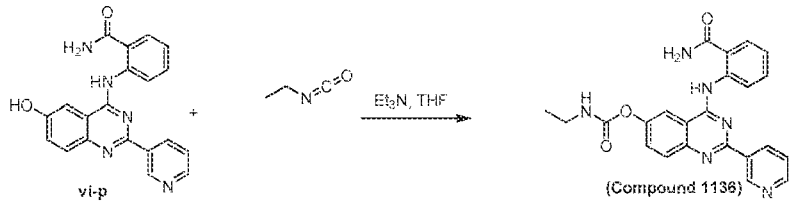
In a 50 mL round-bottomed flask was added 2-chloro-N-(3-chloro-4-fluorophenyl)-6-(3-(dimethylamino)prop-1-ynyl)quinazolin-4-amine (61 mg, 0.16 mmol), 3-pyridineboronic acid (25 mg, 0.20 mmol), K_2CO_3 (0.11 mg, 0.78 mmol) and $PdCl_2(PPh_3)_2$ (5.5 mg, 7.8 mM) in dioxane (2 mL) to give a yellow suspension. The mixture was heated at reflux for 3 h under argon. After cooling to room temperature, water (10 mL) and ethyl acetate (10 mL) were added to the mixture to form a precipitate. The resulting precipitate was filtered through Celite. The filtrate was extracted with ethyl acetate (2 x 10 mL) and the combined organic layers were washed with water (1 x 15 mL) and brine (1 x 15 mL) and then dried over Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography on silica gel (eluted with AcOEt/MeOH 1:0 to 9:1). The desired product was washed with CH_2Cl_2 to give 25 mg of N-(3-chloro-4-fluorophenyl)-6-(3-(dimethylamino)prop-1-ynyl)-2-(pyridin-3-yl)quinazolin-4-amine as a light brown solid in 37 % yield. LCMS m/z = 432 (M +1) (Method C) (retention time = 1.86 min). ^{1}H NMR (300 MHz, DMSO) δ 10.13 (s, 1H), 9.51 (s, 1H), 8.77 – 8.56 (m, 3H), 8.26 (dd, J = 6.9, 2.5 Hz, 1H), 8.02 – 7.78 (m, 3H), 7.64 – 7.47 (m, 2H), 3.54 (s, 2H), 2.30 (s, 6H).

Scheme 62: Synthesis of 4-(2-carbamoylphenylamino)-2-(pyridin-3-yl)quinazolin-6-yl benzylcarbamate (compound 1756)



A mixture of 2-(6-hydroxy-2-(pyridin-3-yl)quinazolin-4-ylamino)benzamide (200 mg, 0.283 mmol), (isocyanatomethyl)benzene (5 mL) and Et_3N (57 mg, 0.283 mmol) in tetrahydrofuran (THF) (10 mL) was stirred at room temperature overnight. Water (10 mL) was added to the above mixture and the mixture was concentrated *in vacuo*. The precipitate was collected by filtration and washed with water (6 mL x 2) to afford 72 mg of the desired product as a white solid in a yield 26.0%. LCMS: rt = 1.829 min, $[MH]^+$ = 491.1 ^{1}H-NMR (400 MHz, DMSO-d_6): δ 13.05 (s, 1H), 9.63 (s, 1H), 9.07 (d, *J* = 8.5 Hz, 1H), 8.87 (d, *J* = 8.0 Hz, 1H), 8.79 (d, *J* = 3.7 Hz, 1H), 8.59 (t, *J* = 6.1 Hz, 1H), 8.49 (s, 1H), 8.02 – 7.89 (m, 4H), 7.82 – 7.68 (m, 3H), 7.46 – 7.22 (m, 6H), 4.35 (d, *J* = 6.1 Hz, 2H).

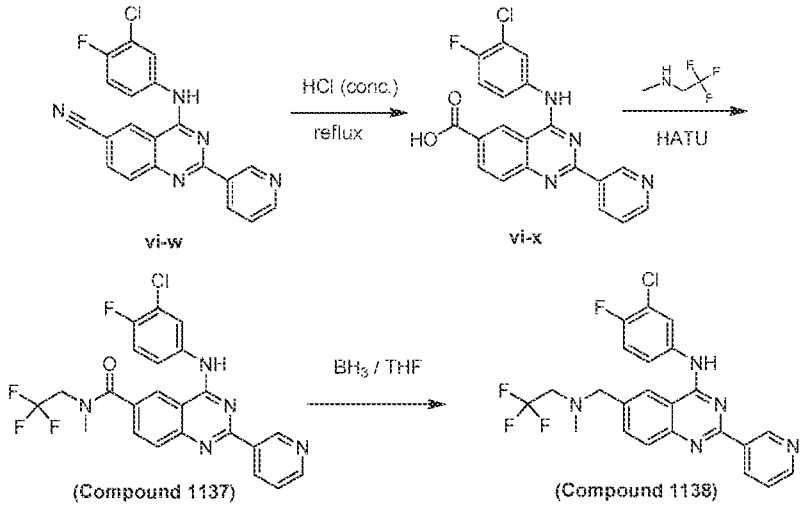
Scheme 63: Synthesis of 4-(2-carbamoylphenylamino)-2-(pyridin-3-yl)quinazolin-6-yl ethylcarbamate (compound 1136)



4-(2-carbamoylphenylamino)-2-(pyridin-3-yl)quinazolin-6-yl ethylcarbamate was synthesized in a similar manner to that described for 4-(2-carbamoylphenylamino)-2-(pyridin-3-yl)quinazolin-6-yl benzylcarbamate substituting isocyanatoethane for (isocyanatomethyl)benzene. The resulting product was analyzed by LCMS: rt = 1.11 min, $[M+1]^+$ = 429.0. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 13.06 (s, 1H), 9.66 (s, 1H), 9.10 (d, *J* = 8.3 Hz, 1H), 8.87 – 8.80 (m, 2H), 8.51 (s, 1H), 8.06 – 7.94 (m, 4H), 7.88

(s, 1H), 7.79 – 7.63 (m, 3H), 7.24 (t, *J* = 7.6 Hz, 1H), 3.22 – 3.11 (m, 2H), 1.14 (t, *J* = 7.2 Hz, 3H).

Scheme 64: 4-(3-chloro-4-fluorophenylamino)-N-methyl-2-(pyridin-3-yl)-N-(2,2,2-trifluoroethyl)quinazoline-6-carboxamide (compound 1137) and N-(3-chloro-4-fluorophenyl)-6-((methyl(2,2,2-trifluoroethyl)amino)methyl)-2-(pyridin-3-yl)quinazolin-4-amine (compound 1138)



A mixture of 4-(3-chloro-4-fluorophenylamino)-2-(pyridin-3-yl)quinazoline-6-carbonitrile (1.5 g, 4.0 mmol) in HCl (conc, 25 mL) was heated to 100 °C and stirred overnight. After cooling and filtration, the solid was washed with water (10 mL) twice to give 1.4 g of the desired product 4-(3-chloro-4-fluorophenylamino)-2-(pyridin-3-yl)quinazoline-6-carboxylic acid as a yellow solid in a 89.0% yield. LCMS: r.t = 1.271 min, $[MH]^+$ = 394.9

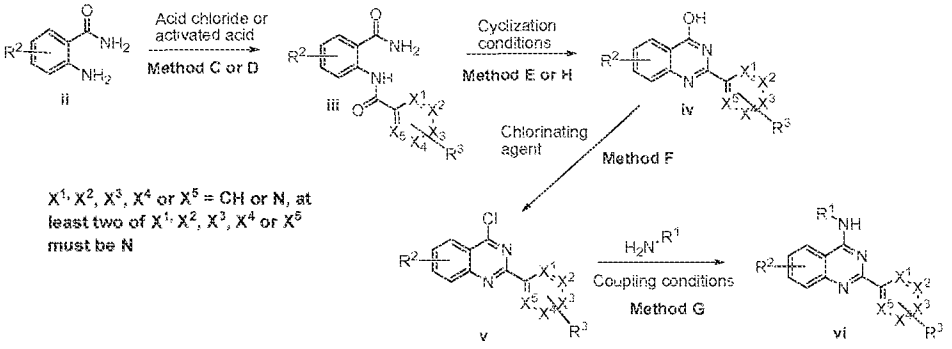
A mixture of 4-(3-chloro-4-fluorophenylamino)-2-(pyridin-3-yl)quinazoline-6-carboxylic acid (900 mg, 2.4 mmol), DIPEA (620 mg, 4.8 mmol) and HATU (1.4 g, 3.6mmol) in DMF (10 mL) was pre-stirred for 20 min, and 2,2,2-trifluoro-N-methylethanamine (360 mg, 2.4 mmol) was added in one portion. The resulting mixture was stirred at room temperature overnight. Water (80 mL) was added and a precipitate formed which was collected and purified by prep-HPLC to afford 490 mg of the desired product 4-(3-chloro-4-fluorophenylamino)-N-methyl-2-(pyridin-3-yl)-

N-(2,2,2-trifluoroethyl)quinazoline-6-carboxamide as a white solid in 42.0% yield. LCMS: r.t = 1.970 min, $[MH]^+$ = 490.0 ^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.79 (brs, 1H), 9.59 (s, 1H), 9.19 (d, J = 7.6 Hz, 1H), 9.04 (d, J = 4.8 Hz, 1H), 8.90 (s, 1H), 8.22 – 8.00 (m, 5H), 7.62 (t, J = 9.2 Hz, 1H), 4.55 – 4.52 (m, 2H), 3.22 (s, 3H).

To a mixture of 4-(3-chloro-4-fluorophenylamino)-N-methyl-2-(pyridin-3-yl)-N-(2,2,2-trifluoroethyl)quinazoline-6-carboxamide (60 mg, 0.12 mmol) in THF (1 mL) was added BH_3-THF (2 mol/L, 1mL). The mixture was stirred at room temperature overnight. Methanol (0.2 mL) was added to quench the reaction mixture. The mixture was purified by prep-HPLC to give the desired product N-(3-chloro-4-fluorophenyl)-6-((methyl(2,2,2-trifluoroethyl)amino)methyl)-2-(pyridin-3-yl)quinazolin-4-amine (GL001H-3309) as a white solid 15 mg in a yield of 26.0%. LCMS: r.t = 2.154 min, $[MH]^+$ = 476.1. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.09 (s, 1H), 9.53 (s, 1H), 8.70 – 8.66 (m, 2H), 8.44 (s, 1H), 8.27 – 8.25 (m, 1H), 7.93 – 7.91 (m, 3H), 7.57 – 7.55 (m, 2H), 3.93 (s, 2H), 3.39 – 3.32 (m, 2H), 2.40 (s, 3H).

Synthesis of 4-(3-chloro-4-fluorophenylamino)-2-(pyridin-3-yl)-N-(2,2,2-trifluoroethyl)quinazoline-6-carboxamide (compound 1139) 4-(3-chloro-4-fluorophenylamino)-2-(pyridin-3-yl)-N-(2,2,2-trifluoroethyl)quinazoline-6-carboxamide was synthesized in a similar manner to that described for 4-(3-chloro-4-fluorophenylamino)-N-methyl-2-(pyridin-3-yl)-N-(2,2,2-trifluoroethyl)quinazoline-6-carboxamide substituting 2,2,2-trifluoroethylamine for 2,2,2-trifluoro-N-methylethylamine. The resulting product was analyzed. LCMS: r.t = 1.934 min, $[M+1]^+$ = 476.0. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.43 (s, 1H), 9.54 (s, 1H), 9.32 (t, J = 6.1 Hz, 1H), 9.14 (s, 1H), 8.72 (d, J = 4.6 Hz, 1H), 8.68 (d, J = 8.0 Hz, 1H), 8.32 (d, J = 8.7 Hz, 1H), 8.27 (dd, J = 6.7, 2.2 Hz, 1H), 7.98 (d, J = 8.7 Hz, 1H), 7.96 – 7.90 (m, 1H), 7.62 – 7.51 (m, 2H), 4.27 – 4.14 (m, 2H).

Scheme 65: General route for the synthesis of compounds with general formula vi



Method E for cyclization

E1: Sodium methoxide/Toluene
E2: NaOH/EtOH

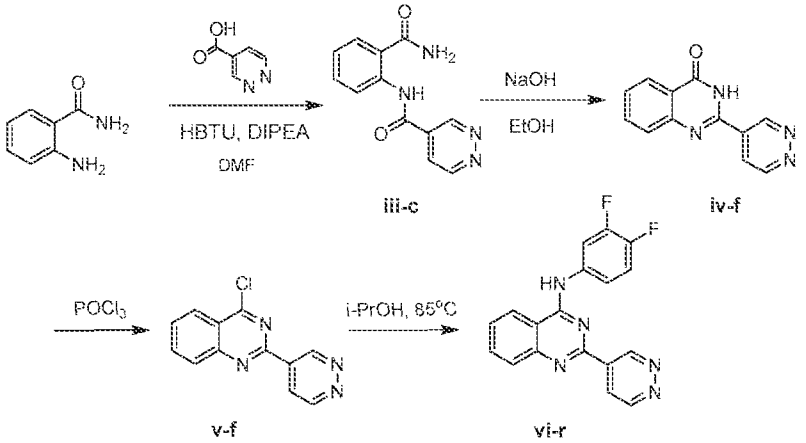
Method G for Coupling Conditions

G1: *i*-PrOH/85-100 °C
G2: THF/reflux
G3: *i*-AmOH/100-130 °C

G4: MeOH/microwave/150 °C
G5: *i*-AmOH/microwave/150 °C

G6: THF/Et_3N/reflux

Scheme 66: Representative synthesis of compounds of formula vi-a with a pyridazine (see Scheme 65)



Method D: N-(2-carbamoylphenyl) pyridazine-4-carboxamide (iii-c) A mixture of pyridazine-4-carboxylic acid (500 mg, 4.0 mmol, 1.0 eq.), 2-aminobenzamide (603 mg, 4.4 mmol, 1.1 eq.) and HBTU (3.0 g, 8.0 mmol, 2.0 eq.) was suspended in 15 mL of DMF. DIPEA (2.0 mL, 1.56 g, 12.0 mmol, 3.0 eq.) was added dropwise at room temperature and was stirred over night. After quenching with water, the resulting precipitate was collected and washed with a small amount of DCM. A white solid (388 mg) was obtained, LCMS m/z = 243.1 (M+1) (Method B) (retention time = 0.99 min), was used in the next step without further purification.

Method E1: 2-(pyridazin-4-yl) quinazolin-4(*3H*)-one (iv-f) A 100 mL round-bottom flask equipped with a Dean-Stark trap was charged with a mixture of N-(2-carbamoylphenyl) pyridazine-4-carboxamide (300 mg, 1.0 eq.), sodium methoxide (401 mg, 7.4 mmol, 6.0 eq.) and 10 mL of anhydrous toluene. The reaction mixture was heated to 110 °C and refluxed overnight. After cooling, the volatiles were removed *in vacuo* and the residue was quenched with a saturated aqueous solution of NH_4Cl (10 mL). The pH of the mixture was adjusted to 3 with 10 % HCl in water. The solution was extracted with DCM (50 ml × 3). The combined organic layers were washed with brine, dried over Na_2SO_4. After filtration and evaporation, 88 mg of a yellow solid was obtained, LCMS m/z = 225.1 (M+1) (Method A) (retention time = 1.10 min) which was used in the next step without further purification.

Method F5: 4-chloro-2-(pyridazin-4-yl)quinazoline (v-f) A 100-mL round-bottom flask was charged with 2-(pyridazin-4-yl) quinazolin-4(*3H*)-one (30 mg) which was suspended in 3 mL of $POCl_3$. The reaction mixture was heated to reflux for 1 h. The reaction mixture turned to a clear brown solution. After cooling, 50 mL of ice/water was carefully added. An aqueous ammonia solution (25% by weight in water) was added dropwise to the mixture with stirring until the pH of the mixture was adjusted to 7~8. An internal temperature of 0 °C was maintained by the addition of ice. The mixture was warmed to room temperature and extracted with DCM (50 ml × 3). The combined organic layers were washed with brine, dried over Na_2SO_4. After filtration and evaporation, 32 mg was obtained as a light brown solid. LCMS m/z = 242.9

(M+1) (Method B) (retention time = 1.65 min). The solid was used directly in the next step without further purification.

Method G1: N-(3,4-difluorophenyl)-2-(pyridazin-4-yl)quinazolin-4-amine (vi-r) (This method is representative of method G1, G2, and G3. These three methods can be implemented in a similar way except for substitution of the appropriate solvent and temperature) The mixture of 4-chloro-2-(pyridazin-4-yl)quinazoline (10 mg, 0.041 mmol, 1 eq.) and 3,4-difluorobenzenamine (11 mg, 0.082 mmol, 2eq.) was suspended in *i*-PrOH. The mixture was heated at 85°C overnight. After cooling, the resulting precipitate was filtered and purified on HPLC (Condition **C**). 7.3 mg of N-(3,4-difluorophenyl)-2-(pyridazin-4-yl)quinazolin-4-amine was obtained (yield 53%). LCMS m/z = 336.0 (M+1) (Method B) (retention time = 1.731 min).^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.23 (s, 1H), 10.00 (dd, *J* = 2.2, 1.3 Hz, 1H), 9.44 (dd, *J* = 5.4, 1.2 Hz, 1H), 8.59 (d, *J* = 8.1 Hz, 1H), 8.39 (dd, *J* = 5.4, 2.4 Hz, 1H), 8.05 – 8.13 (m, 1H), 7.99 (s, 1H), 7.97 (d, *J* = 3.6 Hz, 1H), 7.72 – 7.79 (m, 2H), 7.51 – 7.61 (m, 1H).

The compounds in the following table were prepared in a manner analogous to that described in **Scheme 1 and 64** (prepared according to method **procedure A - G** as designated).

Table 21:

Number	Product	Salt type	Molecular Mass	^{1}H-NMR	^{1}H-NMR Solvent	LCMS	LCMS Protocol	Purity percent	Method for Coupling
1140			402.66	1H-NMR (400 MHz, CD3OD): δ 9.40 (s, 1H), 9.84 – 9.86 (m, 2H), 8.52 (d, J = 8.4 Hz, 1H), 8.15 (s, 1H), 8.02 (s, 1H), 7.84 (dd, J =9.2, 2.4 Hz , 1H), 7.66 – 7.67 (m, 2H).	CD3OD	402.0, 404.0, 405.9 (M+1)	Method B (NH4HCO3)	95	Method C, G1
1141			386.21	1H-NMR (400 MHz, DMSO-d6): δ 10.78 (s, 1H), 9.49 (s, 1H), 8.89 (d, J = 10.8 Hz, 2H), 8.75 (d, J = 8.8 Hz, 1H), 8.44 (dd, J = 6.8, 2.4 Hz, 1H), 8.12 (d, J = 2.0 Hz, 1H), 7.94 – 7.99 (m, 1H), 7.87 (dd, J = 8.8, 2.0 Hz, 1H), 7.56 (t, J = 9.2 Hz, 1H).	DMSO	386.0, 388.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1
1142			369.76	1H-NMR (400 MHz, CD3OD): δ 9.40 (s, 1H), 8.76 (d, J = 10.8 Hz, 2H), 8.40 (d, J = 8.8 Hz, 1H), 8.02 (d, J = 2.0 Hz, 1H), 7.80 – 7.86 (m, 1H), 7.68 (dd, J = 8.8, 1.6 Hz, 1H), 7.52 (d, J = 9.2 Hz, 1H), 7.33 (q, J = 9.2 Hz, 1H).	CD3OD	370.0, 372.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1

534

1143			376.8	1H-NMR (400 MHz, CD3OD): δ 9.55 (s, 1H), 8.80 (d, J = 7.2 Hz, 3H), 8.26 (d, J = 8.8 Hz, 1H), 8.04 (s, 1H), 7.85 (d, J = 6.8 Hz, 1H), 7.72 (d, J = 8.4 Hz, 1H), 7.66 (t, J = 7.2 Hz, 1H), 7.28 (t, J = 7.6 Hz, 1H).	CD3OD	377.1, 379.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1
1144			358.78	1H-NMR (400 MHz, CD3OD): δ 9.39 (d, J = 1.6 Hz, 1H), 8.79 (d, J = 6.8 Hz, 2H), 8.47 (d, J = 9.2 Hz, 1H), 8.20 (s, 1H), 8.05 – 8.10 (m, 2H), 7.77 (dd, J = 8.8, 2.0 Hz, 1H), 7.63 – 7.65 (m, 2H).	CD3OD	359.0, 361.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1
1145			399.78	1H-NMR (400 MHz, DMSO-d6): δ 10.63 (s, 1H), 9.52 (d, J = 1.2 Hz, 1H), 8.86 (t, J = 6.0 Hz, 2H), 8.77 (d, J = 8.4 Hz, 1H), 8.12 (d, J = 15.6 Hz, 2H), 7.85 (d, J = 8.8 Hz, 2H), 7.53 (t, J = 8.0 Hz, 1H), 7.32 (t, J = 74.0 Hz, 1H), 7.04 (dd, J = 8.0, 1.6 Hz, 1H).	DMSO	400.0, 402.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1

535

1146			402.66	1H-NMR (400 MHz, CD3OD): δ 9.40 (s, 1H), 8.85 – 8.88 (m, 2H), 8.53 (d, J = 9.2 Hz, 1H), 8.17 (d, J = 2.0 Hz, 1H), 7.80 – 7.88 (m, 3H), 7.46 (s, 1H).	CD3OD	401.9, 403.9, 405.9 (M+1)	Method B (NH4HCO3)	95	Method C, G1
1147			377.78	1H-NMR (400 MHz, DMSO-d6): δ 12.28 (s, 1H), 9.58 (s, 1H), 9.14 (d, J = 8.4 Hz, 1H), 8.87 (s, 1H), 8.80 (d, J = 2.0 Hz, 1H), 8.28 (d, J = 9.2 Hz, 1H), 8.07 – 8.12 (m, 2H), 7.86 (dd, J = 8.8, 2.0 Hz, 1H), 7.77 (t, J = 8.8 Hz, 1H), 7.26 (t, J = 7.6 Hz, 1H).	DMSO	378.1, 380.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1
1148			381.79	1H-NMR (400 MHz, DMSO-d6): δ 11.69 – 11.49 (m, 1H), 9.40 (d, J = 1.2 Hz, 1H), 9.00 – 8.86 (m, 3H), 8.24 (dd, J = 6.6, 2.1 Hz, 1H), 7.91 (ddd, J = 8.9, 4.2, 2.6 Hz, 1H), 7.71 (d, J = 1.4 Hz, 1H), 7.61 (t, J = 9.0 Hz, 1H), 7.49 (dd, J = 9.2, 2.3 Hz, 1H), 4.00 (s, 3H).	DMSO	382.1, 384.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1

536

1149			395.36	1H-NMR (400 MHz, DMSO-d6): δ 9.96 (s, 1H), 9.57 (d, J = 1.4 Hz, 1H), 8.83 – 8.74 (m, 2H), 8.57 (d, J = 9.1 Hz, 1H), 8.28 (t, J = 2.0 Hz, 1H), 7.86 (dd, J = 8.2, 1.2 Hz, 1H), 7.50 – 7.32 (m, 3H), 7.31 (t, J = 74.0 Hz, 1H), 6.94 (dd, J = 8.0, 2.2 Hz, 1H), 3.98 (s, 3H).	DMSO	396.1, (M+1), 397.2 (M+2)	Method B (NH4HCO3)	95	Method C, G1
1150			383.33	1H-NMR (400 MHz, DMSO-d6): δ 10.27 (s, 1H), 9.57 (s, 1H), 8.80 (dd, J = 19.8, 1.7 Hz, 2H), 8.72 – 8.66 (m, 1H), 8.50 (s, 1H), 8.07 – 7.94 (m, 3H), 7.75 (t, J = 7.2 Hz, 1H), 7.57 (t, J = 8.2 Hz, 1H), 7.14 (d, J = 8.8 Hz, 1H).	DMSO	384.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1
1151			385.42	1H-NMR (400 MHz, DMSO-d6): δ 13.01 (s, 1H), 10.04 (s, 1H), 9.40 (d, J = 5.4 Hz, 1H), 9.20 (d, J = 8.4 Hz, 1H), 8.48 (s, 1H), 8.42 (dd, J = 5.3, 1.9 Hz, 1H), 8.04 – 7.94 (m, 2H), 7.84 (d, J = 9.2 Hz, 1H), 7.75 (t, J = 7.9 Hz, 1H), 7.58 (d, J = 9.2 Hz, 1H), 7.20 (t, J = 7.5 Hz, 1H), 7.13 (s, 1H), 3.15 (s, 6H).	DMSO	386.0 (M+1)	Method A (TFA)	95	Method D, G1
1152		HCl	394.83	1H-NMR (400 MHz, DMSO-d6): δ 10.96 (s, 1H), 9.97 (d, J = 1.1 Hz, 1H), 9.55 (d, J = 5.5 Hz, 1H), 8.61 (dd, J = 5.5, 2.2 Hz, 1H), 8.15 (dd, J = 6.8, 2.6 Hz, 1H), 8.08 (d, J = 9.3 Hz, 1H), 7.94 (ddd, J = 8.9, 4.3, 2.6 Hz, 1H), 7.74 (s, 1H), 7.62 (dd, J = 9.4, 2.5 Hz, 1H), 7.56 (t, J = 9.1 Hz, 1H), 3.16 (s, 6H).	DMSO	395.1, 397.1 (M+1)	Method A (TFA)	95	Method D, G1

537

1153		HCl	408.4	1H-NMR (400 MHz, DMSO-d6): δ 10.71 (brs, 1H), 10.01 – 9.99 (m, 1H), 9.52 (dd, J = 5.5, 1.0 Hz, 1H), 8.60 (dd, J = 5.5, 2.3 Hz, 1H), 8.07 ((d, J = 9.2 Hz 1H), 7.85 – 7.76 (m, 2H), 7.71 (s, 1H), 7.65 (dd, J = 9.3, 2.5 Hz, 1H), 7.56 (t, J = 8.2 Hz, 1H), 7.33 (t, J = 74.0 Hz, 1H), 7.09 (dd, J = 8.1, 2.1 Hz, 1H), 3.17 (s, 6H).	DMSO	409.1 (M+1)	Method A (TFA)	95	Method D, G1
1154			372.38	1H-NMR (400 MHz, DMSO-d6): δ 13.13 (s, 1H), 9.63 (d, J = 1.2 Hz, 1H), 9.34 (d, J = 7.6 Hz, 1H), 8.91 – 8.84 (m, 1H), 8.79 (d, J = 2.4 Hz, 1H), 8.49 (s, 1H), 8.12 (d, J = 9.6 Hz, 1H), 8.03 – 7.85 (m, 2H), 7.75 – 7.61 (m, 1H), 7.48 – 7.30 (m, 2H), 7.28 – 7.06 (m, 1H), 3.99 (s, 3H).	DMSO	373.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1
1155			381.79	1H-NMR (400 MHz, DMSO-d6): δ 10.16 (s, 1H), 9.99 – 9.95 (m, 1H), 9.42 (dd, J = 5.2, 1.2 Hz, 1H), 8.58 – 8.51 (m, 1H), 8.35 (dd, J = 5.2, 2.4 Hz, 1H), 8.21 (dd, J = 6.8, 2.4 Hz, 1H), 7.93 (ddd, J = 8.8, 4.2, 2.7 Hz, 1H), 7.53 (dd, J = 11.7, 6.4 Hz, 1H), 7.32 (dd, J = 6.6, 2.6 Hz, 2H), 3.97 (s, 3H).	DMSO	362.0, 364.0 (M+1)	Method B (NH4HCO3)	95	Method D, G1
1156			395.36	1H-NMR (400 MHz, DMSO-d6) δ 10.07 (s, 1H), 10.01 (d, J = 1.3 Hz, 1H), 9.43 (dd, J = 5.2, 1.2 Hz, 1H), 8.55 (d, J = 10.0 Hz, 1H), 8.40 (dd, J = 5.2, 2.0 Hz, 1H), 7.91 (d, J = 2.0 Hz, 1H), 7.66 – 7.77 (m, 1H), 7.55 – 7.35 (m, 3H), 7.32 (t, J = 74.0 Hz, 1H), 7.01 (dd, J = 8.0, 2.0 Hz, 1H), 3.99 (s, 3H).	DMSO	396.1 (M+1)	Method B (NH4HCO3)	95	Method D, G1

538

1157			376.80	1H-NMR (400 MHz, DMSO-d6): δ 13.34 (s, 1H), 9.61 (s, 1H), 9.28 (d, J = 8.4 Hz, 1H), 8.87 (s, 1H), 8.80 (s, 1H), 8.53 (s, 1H), 8.25 (s, 1H), 7.94 – 8.06 (m, 4H), 7.70 (t, J = 8.0 Hz, 1H), 7.23 (t, J = 7.6 Hz, 1H).	DMSO	377.0, 379.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1
1158			358.78	1H-NMR (400 MHz, DMSO-d6): δ 10.35 (s, 1H), 9.54 (s, 1H), 8.77 – 8.84 (m, 4H), 8.32(d, J = 8.0 Hz, 1H), 8.00 – 8.03 (m, 2H), 7.62 – 7.70 (m, 2H).	DMSO	359.0, 361.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1
1159			386.21	1H-NMR (400 MHz, DMSO-d6): δ 10.55 (s, 1H), 9.50 (s, 1H), 8.83 8.87 (m, 3H), 8.47 – 8.49 (m, 1H), 7.96 – 8.06 (m, 3H), 7.54 (t, J = 9.2 Hz, 1H).	DMSO	386.0, 388.0, 390.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1
1160			402.66	1H-NMR (400 MHz, DMSO-d6): δ 10.54 (s, 1H), 9.53 (s, 1H), 8.84 – 8.86 (m, 3H), 8.62 (d, J = 2.0 Hz, 1H), 8.01 – 8.07 (m, 3H), 7.73 (d, J = 8.8 Hz, 1H).	DMSO	401.9, 403.9, 406.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1

539

1161			402.66	1H-NMR (400 MHz, DMSO-d6): δ 10.42 (s, 1H), 9.55 (d, J = 1.6Hz, 1H), 8.87 – 8.88 (m, 1H), 8.82 (d, J = 2.4 Hz, 1H), 8.36 (d, J = 2.0 Hz, 2H), 8.00 – 8.07 (m, 2H), 7.40 (t, J = 1.6 Hz, 1H).	DMSO	401.9, 403.8, 405.8 (M+1)	Method B (NH4HCO3)	95	Method C, G1
1162			468.25	1H-NMR (400 MHz, DMSO-d6): δ 13.36 (s, 1H), 9.59 (d, J =1.2 Hz, 1H), 9.15 – 9.12 (m, 1H), 8.90 – 8.85 (m, 2H), 8.68 (d, J = 1.2 Hz, 1H), 8.52 (s, 1H), 8.28 – 8.25 (m, 1H), 8.07 (s, 1H), 7.99 – 7.96 (m, 1H), 7.83 (d, J = 8.8Hz, 1H), 7.74 – 7.70 (m, 1H), 7.28 (t, J =7.6 Hz, 1H).	DMSO	469.0 (M+1)	Method B (NH4HCO3)	90	Method C, G1
1163			491.23	1H-NMR (400 MHz, DMSO-d6): δ 10 83 (s, 1H), 9.32 (s, 1H), 9.07 (s, 1H), 8.74 (s, 2H), 8 16 (dd, J = 8.0, 1.6 Hz, 1H), 7.87 (s, 1H), 7.74 – 7.64 (m, 2H), 7.39 (t, J = 8.0 Hz, 1H), 7.16 (t, J = 74.0 Hz, 1H), 6.95 – 6.92 (m, 1H).	DMSO	492.0 (M+1)	Method B (NH4HCO3)	90	Method C, G1
1164			477.66	1H-NMR (400 MHz, DMSO-d6): δ 11.48 (s, 1H), 9.42 (s, 1H), 9.34 (s, 1H), 8.95 – 8.93 (m, 2H), 8.35 – 8.30 (m, 2H), 7.97 – 7.90 (m, 2H), 7.60 (t, J = 9.0 Hz, 1H).	DMSO	478.0, 480.0 (M+1)	Method B (NH4HCO3)	90	Method C, G1

540

1165			413.81	1H-NMR (400 MHz, DMSO-d6): δ 10.07 (s, 1H), 9.99 (s, 1H), 9.40 (d, J = 5.6 Hz, 1H), 8.56 (d, J = 1.6 Hz, 1H), 8.36 (dd, J = 5.2, 2.0 Hz, 1H), 7.87 (m, 1H), 7.81 (m, 1H), 7.53 (t, J = 7.8 Hz, 1H), 7.30 (t, J = 74.0 Hz, 1H), 8.36 (dd, J = 8.4, 2.0 Hz, 1H), 2.70 (s, 3H).	DMSO	414.1, 416.0 (M+1)	Method B (NH4HCO3)	95	Method D, G1
1166			400.24	1H-NMR (400 MHz, DMSO-d6): δ 10.16 (s, 1H), 10.01 (s, 1H), 9.46 (d, J = 5.2 Hz, 1H), 8.56 (d, J = 1.6 Hz, 1H), 8.39 (dd, J = 5.4, 2.2 Hz, 1H), 8.20 (dd, J = 7.2, 2.6 Hz, 1H), 7.95 – 7.91 (m, 1H), 7.89 (s, 1H), 7.57 (t, J = 9.0 Hz, 1H), 2.75 (s, 3H).	DMSO	400.0, 402.0 (M+1)	Method B (NH4HCO3)	95	Method D, G1
1167			409.39	1H-NMR (400 MHz, DMSO-d6): δ 10.05 – 10.3 (m, 2H), 9.45 (dd, J = 5.2, 1.2 Hz, 1H), 8.42 (dd, J = 5.2, 1.2 Hz, 1H), 8.06 (d, J = 2.8 Hz, 1H), 7.97 – 7.94 (m, 2H), 7.86 (dd, J = 8.0, 1.2 Hz, 1H), 7.66 – 7.60 (m, 2H), 7.38 (t, J = 74.0 Hz, 1H), 7.10 – 7.08 (m, 1H), 4.32 (q, J = 6.8 Hz, 2H), 1.51 (t, J =7.0 Hz, 3H).	DMSO	410.1 (M+1)	Method B (NH4HCO3)	95	Method D, G1
1168			379.36	1H-NMR (400 MHz, DMSO-d6): δ 10.13 (s, 1H), 10.07 (d, J = 2.0 Hz, 1H), 9.44 (dd, J = 5.2, 2.4 Hz, 1H), 8.48 – 8.44 (m, 2H), 7.93 (t, J = 2.0 Hz, 1H), 7.86 – 7.84 (m, 2H), 7.66 – 7.62 (m, 1H), 7.54 (t, J = 8.4 Hz, 1H), 7.32 (t, J = 74.0 Hz, 1H), 7.02 (dd, J = 8.0, 2.4 Hz, 1H), 2.77 (s, 3H).	DMSO	380.1 (M+1)	Method B (NH4HCO3)	95	Method D, G1

541

1169			444.23	1H-NMR (400 MHz, DMSO-d6): δ 10.17 (s, 1H), 9.55 (s, 1H), 8.98 (s, 1H), 8.79 (d, J = 12.8 Hz, 2H), 8.26 (s, 1H), 8.08 (d, J = 9.2 Hz, 1H), 7.92 – 7.88 (m, 2H), 7.52 – 7.50 (m, 1H), 7.32 (t, J = 71.6 Hz, 1H), 6.99 (d, J = 7.6 Hz, 1H).	DMSO	444.0, 446.0 (M+1)	Method B (NH4HCO3)	95	Method C,G1
1170			430.66	1H-NMR (400 MHz, DMSO-d6): δ 10.11 (s, 1H), 9.52 (s, 1H), 8.89 (d, J = 1.2 Hz, 1H), 8.83 (s, 1H), 8.77 (d, J = 2.4 Hz, 1H), 8.56 (dd, J = 6.8 , 2.4 Hz, 1H), 8.05 (dd, J = 9.2, 2.0 Hz, 1H), 8.02 – 7.96 (m, 1H), 7.88 (d, J = 8.8 Hz, 1H), 7.49 (t, J = 9.2 Hz, 1H).	DMSO	430.0, 432.0, 434.0 (M+1)	Method B (NH4HCO3)	95	Method C,G1
1171			386.41	1H-NMR (400 MHz, DMSO-d6): δ 13.07 (s, 1H), 9.63 (s, 2H), 9.33 (s, 1H), 8.95 (d, J = 8.0 Hz, 1H), 8.50 (s, 1H), 7.99 – 7.94 (m, 3H), 7.76 – 7.71 (m, 1H), 7.62 – 7.59 (m, 2H), 7.24 (t, J = 7.4 Hz, 1H), 4.23 (q, J = 7.0 Hz, 2H), 1.46 (t, J = 7.0 Hz, 3H).	DMSO	387.1 (M+1)	Method B (NH4HCO3)	95	Method C,G1
1172			372.38	1H-NMR (400 MHz, DMSO-d6): δ 13.11 (s, 1H), 9.61 (s, 2H), 9.34 (s, 1H), 8.91 (d, J = 8.0 Hz, 1H), 8.49 (s, 1H), 7.98 – 7.95 (m, 3H), 7.72 (t, J = 8.0 Hz, 1H), 7.62 –7.60 (m, 2H), 7.24 (t, J = 7.6 Hz, 1H), 3.97 (s, 3H).	DMSO	373.1 (M+1)	Method B (NH4HCO3)	95	Method C,G1

542

1173		HCl	379.32	1H-NMR (400 MHz, DMSO-d6): δ 10.55 (brs, 1H), 9.59 (s, 2H), 9.35 (s, 1H), 8.68 (d, J = 8.4 Hz, 1H), 8.09 – 8.07 (m, 1H), 8.00 – 7.96 (m, 2H), 7.76 – 7.72 (m, 1H), 7.67 (dd, J = 8.8, 2.0 Hz, 1H), 7.53 (d, J = 8.8 Hz, 1H).	DMSO	380.0 (M+1)	Method B (NH4HCO3)	95	Method C,G1
1174		HCl	464.47	1H-NMR (400 MHz, DMSO-d6): δ 10.14 (s, 1H), 9.59 (s, 1H), 8.80 (m, 2H), 8.62 (d, J = 7.6 Hz,1H), 8.30 (s, 1H), 7.90 (s, 2H), 7.70 (d, J = 7.6 Hz, 1H), 7.53 – 7.45 (m, 1H), 7.39 – 6.66 (m, 1H), 7.30 (t, J = 74.1 Hz, 1H),3.73 (s, 2H), 3.63 – 3.58 (m, 4H), 2.48 – 2.43 (m, 4H).	DMSO	465.1 (M+1)	Method B (NH4HCO3)	95	Method C,G1
1175			357.37	1H-NMR (400 MHz, DMSO-d6): δ 9.70 (s, 1H), 9.43 (d, J = 8.4 Hz, 1H), 8.90 (s, 1H), 8.78 (d, J = 2.0 Hz, 1H), 8.22 (d, J = 8.0 Hz, 1H), 8.11 (d, J = 8.0 Hz, 1H), 7.80 (d, J = 2.8 Hz, 1H), 7.60 – 7.65 (m, 2H), 7.09 – 7.13 (m, 3H), 2.76 (s, 3H).	DMSO	358.0 (M+1)	Method B (NH4HCO3)	95	Method C,G1

543

1176			365.79	1H-NMR (400 MHz, DMSO-d6): δ 10.02 (s, 1H), 9.62 (s, 1H), 8.85 (s, 1H), 8.76 (d, J = 2.4 Hz, 1H), 8.45 (d, J = 8.0 Hz, 1H), 8.03 – 8.07 (m, 1H), 7.81 (d, J = 6.8 Hz, 1H), 7.61 (t, J = 7.6 Hz, 1H), 7.49 (t, J = 9.2 Hz, 1H), 2.75 (s, 3H).	DMSO	366.0, 368.0 (M+1)	Method B (NH4HCO3)	95	Method C,G1
1177			379.36	1H-NMR (400 MHz, DMSO-d6): δ 10.02 (s, 1H), 9.64 (s, 1H), 8.83 (s, 1H), 8.76 (d, J = 2.0 Hz, 1H), 8.50 (d, J = 8.0 Hz, 1H), 8.38 (s, 1H), 7.92 (d, J = 8.4 Hz, 1H), 7.81 (d, J = 6.8 Hz, 1H), 7.61 (t, J = 7.8 Hz, 1H), 7.49 (t, J = 8.4 Hz, 1H), 7.32 (t, J = 74.0 Hz, 1H), 6.95 (d, J = 7.2 Hz, 1H), 2.75 (s, 3H).	DMSO	380.0 (M+1)	Method B (NH4HCO3)	95	Method C,G1
1178			382.25	1H-NMR (400 MHz, DMSO-d6): δ 10.21 (s, 1H), 9.62 (s, 1H), 8.86 (t, J = 2.4 Hz, 1H), 8.78 (t, J = 3.2 Hz, 2H), 8.52 (d, J = 8.4 Hz, 1H), 8.10 – 8.13 (m, 1H), 7.83 (d, J = 7.2 Hz, 1H), 7.68 (d, J = 9.2 Hz, 1H), 7.63 (t, J = 7.6 Hz, 1H), 2.75 (s, 3H).	DMSO	381.9, 383.9 (M+1)	Method B (NH4HCO3)	95	Method C,G1

544

1179			349.34	1H-NMR (400 MHz, DMSO-d6): δ 10.21 (s, 1H), 9.60 (s, 1H), 8.87 (s, 1H), 8.78 (d, J = 2.4 Hz, 1H), 8.50 – 8.60 (m, 2H), 7.80 – 7.85 (m, 2H), 7.61 (t, J = 7.8 Hz, 1H), 7.46 – 7.54(m, 1H), 2.74 (s, 3H).	DMSO	350.0 (M+1)	Method B (NH4HCO3)	95	Method C,G1
1180			382.25	1H-NMR (400 MHz, DMSO-d6): δ 10.20 (s, 1H), 9.62 (s, 1H), 8.85 (s, 1H), 8.77 (d, J = 2.8 Hz, 1H), 8.47 – 8.52 (m, 3H), 7.81 (d, J = 3.2 Hz, 1H), 7.60 (t, J = 7.8 Hz, 1H), 7.31 (t, J = 1.6 Hz, 1H) , 2.51 (s, 3H).	DMSO	381.9, 383.9 (M+1)	Method B (NH4HCO3)	95	Method C,G1
1181			338.37	1H-NMR (400 MHz, DMSO-d6): δ 10.21 (s, 1H), 9.64 (s, 1H), 8.86 (d, J = 9.2 Hz, 2H), 8.76 (d, J = 8.0 Hz, 1H), 8.51 (d, J = 8.0 Hz, 1H), 8.38 (d, J = 8.4 Hz, 1H), 7.84 (d, J = 7.2 Hz, 1H), 7.61 – 7.65 (m, 3H), 2.76 (s, 3H).	DMSO	339.0 (M+1)	Method B (NH4HCO3)	95	Method C,G1
1182			383.33	1H-NMR (400 MHz, DMSO-d6): δ 10.24 (s, 1H), 9.99 (s, 1H), 9.41 (d, J = 5.2 Hz, 1H), 8.62 (d, J = 8.4 Hz, 1H), 8.36 – 8.38 (m, 1H), 8.10 (s, 1H), 7.95 – 7.98 (m, 3H), 7.73 – 7.74 (m, 1H), 7.62 (t, J = 8.0 Hz, 1H), 7.20 (d, J = 8.0 Hz, 1H).	DMSO	384.2 (M+1)	Method B (NH4HCO3)	95	Method D, G1

545

1183			365.34	1H-NMR (400 MHz, DMSO-d6): δ 10.19(s, 1H), 10.01(s, 1H), 9.41 – 9.43 (m, 1H), 8.63(d, J = 8.0 Hz, 1H), 8.39 – 8.41 (m, 1H), 7.93 – 7.97 (m, 3H), 7.84(d, J = 8.4 Hz, 1H), 7.74 (m, 1H), 7.54 – 7.56 (m, 1H), 7.32 (t, J = 74.0 Hz, 1H), 7.02 – 7.04 (m, 1H).	DMSO	366.2 (M+1)	Method B (NH4HCO3)	95	Method D, G1
1184			398.25	1H-NMR (400 MHz, DMSO-d6): δ 10.27 (s, 1H). 9.96 (s, 1H), 9.44 (d, J = 4.8 Hz, 1H), 8.40 – 8.41 (m, 1H), 8.29 (d, J = 2.0 Hz, 1H), 8.06 (d, J = 2.4 Hz, 1H), 7.99 – 8.02 (m, 1H), 7.89 (d, J = 8.8 Hz, 1H), 7.71 (d, J = 8.8 Hz, 1H), 7.56 – 7.58 (m, 1H), 3.99 (s, 3H).	DMSO	398.0, 400.0, 402.0 (M+1)	Method B (NH4HCO3)	95	Method D, G1
1185			381.79	1H-NMR (400 MHz, DMSO-d6): δ 9.92 (s, 1H), 9.36 – 9.38 (m, 1H), 8.27 – 8.29 (m, 1H), 8.14 – 8.16 (m, 1H), 7.51 (s, 1H), 7.83 – 7.91 (m, 3H), 7.51 – 7.56 (m, 2H), 3.97 (s, 3H).	DMSO	382.1, 384.1 (M+1)	Method B (NH4HCO3)	95	Method D, G1
1186			365.34	1H-NMR (400 MHz, DMSO-d6): δ 9.95 – 10.00 (m, 2H), 9.40(d, J = 5.6 Hz, 1H), 8.32 – 8.33 (m, 1H), 8.06 (m, 1H), 7.96 (s, 1H), 7.89 (d, J = 9.2 Hz, 1H), 7.69 (m, 1H), 7.54 – 7.59 (m, 2H), 3.98 (s, 3H).	DMSO	366.1 (M+1)	Method B (NH4HCO3)	95	Method D, G1

546

1187			354.36	1H-NMR (400 MHz, DMSO-d6): δ 10.00(s, 1H), 9.90 (m, 1H), 9.35 – 9.36 (m, 1H), 8.23 – 8.30 (m, 3H), 7.84 – 7.90 (m, 2H), 7.62 – 7.71 (m, 2H), 7.54 – 7.57 (m, 1H), 3.96 (s, 3H).	DMSO	355.1 (M+1)	Method B (NH4HCO3)	95	Method D, G1
1188			413.35	1H-NMR (400 MHz, DMSO-d6): δ 9.96 – 10.0 (m, 2H), 8.39 – 8.40 (m, 1H), 8.31 – 8.33 (m, 1H), 8.07 (s, 1H), 7.86 – 7.96 (m, 3H), 7.57 – 7.67 (m, 2H), 7.22 (d, J = 8.0 Hz, 1H), 4.01 (s, 3H).	DMSO	414.1 (M+1)	Method B (NH4HCO3)	95	Method D, G1
1189			373.36	1H-NMR (400 MHz, DMSO-d6): δ 12.15 (s, 1H), 10.02 (s, 1H), 9.41 (d, J = 5.2 Hz, 1H), 8.94 (d, J = 7.6 Hz, 1H), 8.41 (m, 1H), 8.09 (d, J = 7.6 Hz, 1H), 7.93 (d, J = 8.8 Hz, 1H), 7.80 (t, J = 8.4 Hz, 1H), 7.60 – 7.62 (m, 2H), 7.25 (t, J = 7.6 Hz, 1H), 4.01 (s, 3H).	DMSO	374.1, 376.1 (M+1)	Method B (NH4HCO3)	95	Method D, G1

547

1190			398.25	1H-NMR (400 MHz, DMSO-d6): δ 9.95 (s,1H), 9.54 (s,1H), 8.81 – 8.82 (m, 1H), 8.74 (d, J = 2.0 Hz, 1H), 8.66 (d, J = 2.4 Hz, 1H), 8.06 (dd, J = 8.8, 2.4 Hz, 1H), 8.00 (d, J = 2.4 Hz, 1H), 7.92 (d, J = 8.8 Hz, 1H), 7.70 (d, J = 8.8 Hz, 1H), 7.60 (dd, J = 8.8, 2.4 Hz, 1H), 3.40 (s, 3H).	DMSO	397.9, 400.0, 401.9 (M+1)	Method B (NH4HCO3)	95	Method D, G6
1191			381.79	1H-NMR (400 MHz, DMSO-d6): δ 9.90 (s,1H), 9.52 (s,1H), 8.81 (m, 1H), 8.73 (d, J = 2.4 Hz, 1H), 8.53 (dd, J = 6.8, 2.4 Hz, 1H), 7.96 – 8.03 (m, 2H), 7.91 (d, J = 9.2 Hz, 1H), 7.59 (dd, J = 5.2, 2.4 Hz, 1H), 7.51 (t, J = 8.8 Hz, 1H), 3.40 (s, 3H).	DMSO	382.0, 384.0 (M+1)	Method B (NH4HCO3)	95	Method D, G6
1192			365.34	1H-NMR (400 MHz, DMSO-d6): δ 9.89 (s, 1H), 9.52 – 9.53 (m, 1H), 8.81 – 8.82 (m, 1H), 8.73 (d, J = 2.4 Hz, 1H), 8.45 – 8.51 (m, 1H), 7.98 (m, 1H), 7.90 (d, J = 9.2 Hz, 1H), 7.75 – 7.78 (m, 1H), 7.47 – 7.59 (m, 2H), 3.40 (s, 3H).	DMSO	366.0 (M+1)	Method B (NH4HCO3)	95	Method D, G6

548

1193			354.36	1H-NMR (400 MHz, DMSO-d6): δ 10.06 (s, 1H), 9.54 (s, 1H), 8.74 – 8.81 (m, 3H), 8.35 (d, J = 8.4 Hz, 1H), 8.04 (m, 1H), 7.92 – 7.95 (m, 1H), 7.59 – 7.69 (m, 3H), 3.40 (s, 3H).	DMSO	355.0 (M+1)	Method B (NH4HCO3)	95	Method D, G6
1194			398.25	1H-NMR (400 MHz, DMSO-d6): δ 9.91 (s, 1H), 9.55 (d, J = 1.2 Hz, 1H), 8.81 (t, J = 2.0 Hz, 1H), 8.74 (d, J = 2.4 Hz, 1H), 8.39 (d, J = 1.6 Hz, 1H), 7.97 (d, J = 2.8 Hz, 1H), 7.92 (d, J = 8.8 Hz, 1H), 7.59 (dd, J = 8.8, 2.4 Hz, 1H), 7.32 (t, J = 1.6 Hz, 1H), 3.40 (s, 3H).	DMSO	396.0, 399.9, 402.0 (M+1)	Method B (NH4HCO3)	95	Method D, G6
1195			395.36	1H-NMR (400 MHz, DMSO-d6): δ 9.91 (s, 1H), 9.55 (m, 1H), 8.74 – 8.79 (m, 2H), 8.25 (s, 1H), 8.03 (d, J = 2.4 Hz, 1H), 7.92 (d, J = 9.2 Hz, 1H), 7.86 (d, J = 8.4 Hz, 1H), 7.60 (dd, J = 9.2, 2.4 Hz, 1H), 7.48 – 7.52 (m, 1H), 7.34 (t, J = 74.0 Hz, 1H), 6.96 – 6.98 (m, 1H), 3.40 (s, 3H).	DMSO	396.1 (M+1)	Method B (NH4HCO3)	95	Method D, G6

549

1196			377.78	1H-NMR (400 MHz, DMSO-d6): δ 12.26 (s, 1H), 9.94 (s, 1H), 9.41 – 9.42 (m, 1H), 8.75 (d, J = 8.0 Hz, 1H,), 8.33 – 8.34 (m, 1H), 8.19 (d, J = 8.4 Hz, 1H), 8.05 (d, J = 7.6 Hz, 1H), 7.93 (m, 1H), 7.75 – 7.77 (m, 2H), 7.05 – 7.30 (m, 2H)	DMSO	378.0, 380.0 (M+1)	Method B (NH4HCO3)	95	Method D, G6
1197			343.34	1H-NMR (400 MHz, DMSO-d6): δ 13.86 (s, 1H), 12.39 (s, 1H), 9.62 (d, J = 0.8 Hz, 1H), 9.29 (d, J = 8.0 Hz, 1H), 8.87 (s, 1H), 8.80 (d, J = 2.4 Hz, 1H), 8.27 (d, J = 8.0 Hz, 1H), 8.12 (dd, J = 8.0, 1.6 Hz, 1H), 7.97 – 8.05 (m, 3H), 7.75 – 7.79 (m, 2H), 7.24 (t, J = 7.6 Hz, 1H).	DMSO	344.0 (M+1)	Method B (NH4HCO3)	95	Method D, G6
1198			372.38	1H-NMR (400 MHz, DMSO-d6): δ 13.05 (s, 1H), 9.99 (s, 1H), 9.39 (d, J = 5.2 Hz, 1H), 9.05 (d, J = 8.4 Hz, 1H), 8.47 (s, 1H), 8.36 – 8.38 (m, 1H), 7.85 – 7.96 (m, 3H), 7.71 (t, J = 7.6 Hz, 1H), 7.46 – 7.60 (m, 2H), 7.20 (t, J = 7.6 Hz, 1H), 3.95 (s, 3H).	DMSO	373.0 (M+1)	Method B (NH4HCO3)	95	Method D, G1

550

1199			376.8	1H-NMR (400 MHz, DMSO-d6): δ 13.15 (s, 1H), 10.00 (s, 1H), 9.44 (d, J = 4.2 Hz, 1H), 8.95 (d, J = 8.4 Hz, 1H), 8.49 (s, 1H), 8.40 – 8.42 (m, 1H), 8.15 (d, J = 9.2 Hz, 1H), 7.91 – 7.97 (m, 3H), 7.80 (t, J = 7.6 Hz, 1H), 7.73 (t, J = 7.6 Hz, 1H), 7.25 (t, J = 7.2 Hz, 1H).	DMSO	377.0, 379.0 (M+1)	Method B (NH4HCO3)	95	Method D, G1
1200			399.78	1H-NMR (400 MHz, DMSO-d6): δ 12.29 (s, 1H), 9.98 (s, 1H), 9.42 (d, J = 5.2 Hz, 1H), 8.66 (d, J = 9.2 Hz, 1H), 8.36 – 8.38 (m, 1H), 8.00 (d, J = 1.5 Hz, 1H), 7.89 (s, 1H), 7.79 – 7.81 (m, 2H), 7.49 – 7.57 (m, 1H), 7.31 (t, J = 74.0 Hz, 1H), 7.04 (dd, J = 8.0, 1.2 Hz, 1H).	DMSO	400.0, 401.9 (M+1)	Method A (TFA)	95	Method D, G1
1201			386.21	1H-NMR (400 MHz, DMSO-d6): δ 9.94 (s, 1H), 9.43 (d, J = 5.2 Hz, 1H), 8.72 (d, J = 8.8 Hz, 1H), 8.33 (dd, J = 5.6, 2.4 Hz, 1H), 8.21 (dd, J = 6.4, 1.6 Hz, 1H), 7.93 – 7.96 (m, 2H), 7.78 (dd, J = 8.6, 2.0 Hz, 1H), 7.54 (t, J = 9.2 Hz, 2H).	DMSO	386.0 387.8 (M+1)	Method A (TFA)	95	Method D, G1

551

1202			369.76	1H-NMR (400 MHz, DMSO-d6): δ 10.28 (s, 1H), 9.95 (m, 1H), 9.44 – 9.45 (m, 1H), 8.60 (d, J = 8.8 Hz, 1H), 8.32 – 8.34 (m, 1H), 8.02 – 8.08 (m, 1H), 7.98 (d, J = 6.4 Hz, 1H), 7.79 (dd, J = 9.2, 2.4 Hz, 1H), 7.70 – 7.72 (m, 1H), 7.56 (q, J = 9.2 Hz, 1H).	DMSO	369.9, 371.0 (M+1)	Method A (TFA)	95	Method D, G1
1203			358.78	1H-NMR (400 MHz, DMSO-d6): δ 10.36 (s, 1H), 9.92 (s, 1H), 9.42 (d, J = 4.8 Hz, 1H), 8.59 (d, J = 8.4 Hz, 1H), 8.23 – 8.33 (m, 3H), 7.96 (d, J = 1.6 Hz, 1H), 7.65 – 7.79 (m, 3H).	DMSO	359.0, 361.0 (M+1)	Method B (NH4HCO3)	95	Method D, G1
1204			402.66	1H-NMR (400 MHz, DMSO-d6): δ 10.32 (s, 1H), 9.96 (s, 1H), 9.44 (d, J = 5.2 Hz, 1H), 8.60 (d, J = 8.4 Hz, 1H), 8.28 – 8.35 (m, 2H), 7.94 – 7.99 (m, 2H), 7.79 (d, J = 8.8 Hz, 1H), 7.73 (d, J = 8.8 Hz, 1H).	DMSO	401.9, 403.9, 405.9 (M+1)	Method B (NH4HCO3)	95	Method D, G1
1205			402.66	1H-NMR (400 MHz, DMSO-d6): δ 9.90 (s, 1H), 9.42 (d, J = 4.8 Hz, 1H), 8.58 (d, J = 8.8 Hz, 1H), 8.27 (s, 1H), 8.07 (s, 2H), 7.92 (s, 1H), 7.73 (d, J = 8.0 Hz, 1H), 7.36 (s, 1H).	DMSO	401.9, 403.9, 405.9 (M+1)	Method B (NH4HCO3)	95	Method D, G1

552

1206			351.76	1H-NMR (400 MHz, DMSO-d6): δ 10.59 (s, 1H), 9.43 (m, 1H), 9.07 (d, J = 5.2 Hz, 1H), 8.71 (d, J = 8.4 Hz, 1H), 8.50 (dd, J = 6.4, 2.0 Hz, 1H), 8.31 (dd, J = 5.2, 0.8 Hz, 1H), 8.00 – 8.09 (m, 3H), 7.80 (t, J = 7.2 Hz, 1H), 7.53 (t, J = 9.2 Hz, 1H).	DMSO	352.0, 354.0 (M+1)	Method B (NH4HCO3)	95	Method D, G1
1207			342.35	1H-NMR (400 MHz, DMSO-d6): δ 13.31 (s, 1H), 9.38 – 9.43 (m, 2H), 9.05 (d, J = 5.2 Hz, 1H), 8.52 (s, 1H), 8.47 (d, J = 5.2 Hz, 1H), 8.25 (d, J = 8.0 Hz, 1H), 7.95 – 8.04 (m, 4H), 7.82 (t, J = 7.2 Hz, 1H), 7.70 (t, J = 7.6 Hz, 1H), 7.22 (t, J = 7.6 Hz, 1H).	DMSO	343.1 (M+1)	Method B (NH4HCO3)	95	Method D, G1
1208			365.34	1H-NMR (400 MHz, DMSO-d6): δ 10.13 (s, 1H), 9.37 (d, J = 1.2 Hz, 1H), 9.01 (d, J = 5.2 Hz, 1H), 8.68 (d, J = 8.4 Hz, 1H), 8.40 (dd, J = 5.2, 1.2 Hz, 1H), 8.28 (t, J = 1.2 Hz, 1H), 7.92 – 8.00 (m, 3H), 7.77 – 7.79 (m, 1H), 7.47 – 7.52 (m, 1H), 7.34 (t, J = 74.0 Hz, 1H), 6.97 (dd, J = 8.4, 2.4 Hz, 1H).	DMSO	366.1 (M+1)	Method B (NH4HCO3)	95	Method D, G1

553

1209		HCl (batch 02)	351.76	1H-NMR (400 MHz, DMSO-d6): δ 10.82 (s, 1H), 9.59 (s, 2H), 9.36 (s, 1H), 8.74 (d, J = 8.4 Hz, 1H), 8.22 (dd, J = 6.8, 2.4 Hz, 1H), 8.07 (d, J = 8.4 Hz, 1H), 8.00 (t, J = 7.6 Hz, 1H), 7.90 – 7.94 (m, 1H), 7.75 (t, J = 7.2 Hz, 1H), 7.56 (t, J = 9.2 Hz, 1H).	DMSO	352.0, 354.1 (M+1)	Method B (NH4HCO3)	95	Method D, G1
1210			342.35	1H-NMR (400 MHz, DMSO-d6): δ 13.17 (s, 1H), 9.65 (s, 2H), 9.36 (s, 1H), 8.93 (d, J = 8.0 Hz, 1H), 8.51 (s, 1H), 8.23 (d, J = 8.4 Hz, 1H), 7.92 – 8.02 (m, 4H), 7.72 – 7.79 (m, 2H), 7.26 (t, J = 7.6 Hz, 1H).	DMSO	343.1 (M+1)	Method B (NH4HCO3)	95	Method D, G4
1211			365.34	1H-NMR (400 MHz, DMSO-d6): δ 10.15 (s, 1H), 9.62 (s, 2H), 9.32 (s, 1H), 8.63 (d, J = 8.0 Hz, 1H), 7.94 – 7.97 (m, 3H), 7.81 (dd, J = 8.4, 1.2 Hz, 1H), 7.69 – 7.74 (m, 1H), 7.50 – 7.55 (m, 1H), 7.31 (t, J = 74.0 Hz, 1H), 7.01 (dd, J = 8.4, 2.4 Hz, 1H).	DMSO	366.1 (M+1)	Method B (NH4HCO3)	95	Method D, G6

554

1212			399.78	1H-NMR (400 MHz, DMSO-d6): δ 10.27 (s, 1H), 10.01 – 10.02 (m, 1H), 9.44 – 9.46 (m, 1H), 8.62 (d, J = 8.4 Hz, 1H), 8.40 (dd, J = 5.2, 2.0Hz, 1H), 8.04 (t, J = 1.6 Hz, 1H), 8.00 (d, J = 3.2 Hz, 2H), 7.94 (m, 1H), 7.76 – 7.80 (m, 1H), 7.38 (t, J = 73.6 Hz, 1H), 7.16 (t, J = 2.0 Hz, 1H),.	DMSO	400.0, 402.0 (M+1)	Method B (NH4HCO3)	95	Method D, G6
1213			398.79	1H-NMR (400 MHz, DMSO-d6): δ 10.16 (s, 1H), 9.56(m, 1H), 8.69 – 8.72 (m, 2H), 8.59 (d, J = 8.0 Hz, 1H), 8.08 (d, J = 1.6 Hz, 1H), 7.94 – 7.97 (m, 2H), 7.69–7.73 (m, 1H), 7.55 – 7.58 (m, 1H), 7.36 (t, J = 73.6 Hz, 1H), 7.13 (t, J = 2.0 Hz, 1H).	DMSO	399.0, 401.1 (M+1)	Method B (NH4HCO3)	95	Method D, G6
1214			365.34	1H-NMR (400 MHz, DMSO-d6): δ 11.17 (s, 1H), 9.49 (s, 1H), 8.88 – 8.92 (m, 3H), 8.16 (d, J = 8.0 Hz, 1H), 8.07 (t, J = 7.6 Hz, 2H), 7.84 (t, J = 8.0 Hz, 2H), 7.57 (t, J = 8.0 Hz, 1H), 7.36 (t, J = 74.0 Hz, 1H), 7.10 – 7.12 (m,1H).	DMSO	366.1 (M+1)	Method B (NH4HCO3)	95	Method D, G6
1215			368.22	1H-NMR (400 MHz, DMSO-d6): δ 10.23 (s, 1H), 10.00 (s, 1H), 9.44 (d, J = 5.2 Hz, 1H), 8.58 (d, J = 8.0 Hz, 1H), 8.38 (dd, J = 2.4, 5.2 Hz, 1H), 8.32 (d, J = 2.0 Hz, 1H), 7.96 – 8.00 (m, 3H), 7.73 – 7.77 (m, 2H).	DMSO	367.8, 369.8, 371.8 (M+1)	Method B (NH4HCO3)	95	Method D, G1

555

1216			351.76	1H-NMR (400 MHz, DMSO-d6): δ 10.21 (s, 1H), 9.99 (s, 1H), 9.43 (d, J = 5.2 Hz, 1H), 8.58 (d, J = 8.4 Hz, 1H), 8.38 (dd, J = 5.2, 2.0 Hz, 1H), 8.22 (dd, J = 7.0, 2.6 Hz, 1H), 7.89 – 7.93 (m, 3H), 7.68 – 7.72 (m, 1H), 7.55 (t, J = 8.6 Hz, 1H).	DMSO	351.9, 353.8 (M+1)	Method B (NH4HCO3)	95	Method D, G1
1217			324.34	1H-NMR (400 MHz, DMSO-d6): δ 10.32 (s, 1H), 9.99 (dd, J = 2.0, 1.2 Hz, 1H), 9.44 (dd, J = 5.2, 0.8 Hz, 1H), 8.61 (d, J = 8.4 Hz, 1H), 8.38 – 8.40 (m, 2H), 8.28 – 8.31 (m, 1H), 7.99 (s, 1H), 7.97 (d, J = 3.6 Hz, 1H), 7.66 – 7.80 (m, 3H).	DMSO	325.0 (M+1)	Method B (NH4HCO3)	95	Method D, G1
1218			368.22	1H-NMR (400 MHz, DMSO-d6): δ 11.94 (s, 1H), 9.44 (d, J = 0.8 Hz, 1H), 9.06 (d, J = 8.0 Hz, 1H), 9.00 (d, J = 2.4 Hz, 1H), 8.97 (t, J = 1.8 Hz, 1H), 8.38 (d, J = 2.4 Hz, 1H), 8.38 (d, J = 2.4 Hz, 1H), 8.12 (t, J = 7.4 Hz, 1H), 8.00 (dd, J = 8.6, 2.2 Hz, 1H), 7.86 (t, J = 7.6 Hz, 1H), 7.82 (d, J = 8.8 Hz, 1H).	DMSO	367.9, 369.9, 371.8 (M+1)	Method B (NH4HCO3)	95	Method D, G6

556

1219			351.76	1H-NMR (400 MHz, DMSO-d6): δ 11.62 (s, 1H), 9.40 (d, J = 0.8 Hz, 1H), 8.60 – 8.83 (m, 3H), 8.32 (dd, J = 6.6, 2.2 Hz, 1H), 8.20 (d, J = 8.6 Hz, 1H), 8.09 (t, J = 7.4 Hz, 1H), 7.95 – 8.00 (m, 1H), 7.65 (t, J = 7.8 Hz, 1H), 7.61 (t, J = 9.2 Hz, 1H).	DMSO	352.0, 354.0 (M+1)	Method B (NH4HCO3)	95	Method D, G6
1220			335.31	1H-NMR (400 MHz, DMSO-d6): δ 11.05 (s, 1H), 9.48 (d, J = 0.8 Hz, 1H), 8.91 – 8.93 (m, 2H), 8.81 (d, J = 8.4 Hz, 1H), 8.28 – 8.33 (m, 1H), 8.14 (d, J = 8.4 Hz, 1H), 8.06 (t, J = 7.6 Hz, 1H), 7.77 – 7.85 (m, 2H), 7.56 – 7.63 (m, 1H)	DMSO	336.1 (M+1)	Method B (NH4HCO3)	95	Method D, G6
1221			324.34	1H-NMR (400 MHz, DMSO-d6): δ 12.09 (s, 1H), 9.40 (d, J = 1.6 Hz, 1H), 9.10 (d, J = 8.4 Hz, 1H), 9.00 (d, J = 2.0 Hz, 1H), 8.97 (t, J = 2.0 Hz, 1H), 8.49 (s, 1H), 8.26 – 8.30 (m, 2H), 8.12 – 8.06 (m, 1H), 7.87 – 7.91 (m, 1H), 7.76 – 7.84 (m, 2H)	DMSO	324.9 (M+1)	Method B (NH4HCO3)	95	Method D, G6
1222			368.22	1H-NMR (400 MHz, DMSO-d6): δ 10.21 (s, 1H), 9.59 (d, J = 1.2 Hz, 1H), 8.85 (t, J = 1.8 Hz, 1H), 8.78 (d, J = 2.0 Hz, 1H), 8.64 (d, J = 8.4 Hz, 1H), 8.42 (d, J = 1.6 Hz, 2H), 7.96 – 8.02 (m, 2H), 7.74 – 7.78 (m, 1H), 7.35 (d, J = 1.6 Hz, 1H).	DMSO	368.0, 370.0, 372.0 (M+1)	Method B (NH4HCO3)	95	Method D, G6

557

1223			368.22	1H-NMR (400 MHz, DMSO-d6): δ 10.26 (s, 1H), 10.00 (s, 1H), 9.45 (d, J = 5.2 Hz, 1H), 8.56 (d, J = 8.4 Hz, 1H), 8.38 (dd, J = 5.0, 1.8 Hz, 1H), 8.09 (s, 2H), 7.94 (s, 1H), 7.92 (d, J = 9.2 Hz, 1H), 7.70 – 7.74 (m, 1H), 7.35 (s, 1H).	DMSO	368.1, 370.1 (M+1)	Method B (NH4HCO3)	95	Method D, G1
1224			413.81	1H-NMR (400 MHz, DMSO-d6): δ 10.05 (s, 1H), 9.63 (s, 1H), 8.82 (s, 1H), 8.78 (s, 1H), 8.66 (s, 1H), 8.31 (s, 1H), 7.89 – 7.91 (m, 2H), 7.49 (d, J = 8.0 Hz, 1H), 7.31 (t, J = 73.6 Hz, 1H), 6.96 (d, J = 7.6 Hz, 1H), 2.74 (s, 3H).	DMSO	414.0 416.0 (M+1)	Method B (NH4HCO3)	95	Method C, G3
1225			400.24	1H-NMR (400 MHz, DMSO-d6): δ 9.90 (s, 1H), 9.54 (s, 1H), 8.77 – 8.80 (m, 2H), 8.60 (s, 1H), 8.50 (s, 1H), 7.99 (s, 1H), 7.76 (s, 1H), 7.44 (s, 1H), 2.67 (s, 3H).	DMSO	400.0 401.9 (M+1)	Method B (NH4HCO3)	95	Method C, G3

558

1226			390.83	1H-NMR (400 MHz, DMSO-d6): δ 13.33 (s, 1H), 9.67 (s, 1H), 9.36 (d, J = 8.0Hz, 1H), 8.88 (s, 1H), 8.79 (s, 1H), 8.52 (s, 1H), 8.08 (s, 1H), 8.04 (s, 1H), 7.97 (d, J = 7.2 Hz, 1H), 7.88 (s, 1H), 7.69 (d, J = 7.2 Hz,1H), 7.21 (t, J = 7.6 Hz, 1H), 2.75 (s, 3H).	DMSO	391.0 392.0 (M+1)	Method A (TFA)	95	Method C, G3
1227			391.81	1H-NMR (400 MHz, DMSO-d6): δ 16.00 (s, 1H), 9.69 (s, 1H), 9.39 (d, J = 8.4 Hz, 1H), 8.90 (s, 1H), 8.79 (s, 1H), 8.29 (s, 1H), 8.13 (d, J = 7.6 Hz, 1H), 7.82 (s, 1H), 7.50 (t, J = 7.6 Hz, 1H), 7.06 (t, J = 7.2 Hz, 1H), 2.73 (s, 3H).	DMSO	392.0 393.1 (M+1)	Method A (TFA)	95	Method C, G3
1228			372.81	1H-NMR (400 MHz, DMSO-d6): δ 10.07 (s, 1H), 9.57 (s, 1H), 8.82 (s, 2H), 8.76 (s, 1H), 8.57 (s, 1H), 8.32 (d, J = 7.6 Hz, 1H), 7.81 (s, 1H), 7.57 – 7.63 (m, 2H), 2.70 (s, 3H)	DMSO	373.0 374.0 (M+1)	Method B (NH4HCO3)	95	Method C, G3
1229			416.69	1H-NMR (400 MHz, DMSO-d6): δ 10.09 (s, 1H), 9.63 (d, J = 1.2 Hz, 1H), 8.85 (dd, J = 2.4, 1.6 Hz, 1H), 8.78 (d, J = 2.4 Hz, 2H), 8.63 (d, J = 1.6 Hz, 1H), 8.45 (s, 2H), 7.34 (t, J = 2.0 Hz, 1H), 2.74 (s, 3H).	DMSO	416.9 417.9 (M+1)	Method B (NH4HCO3)	95	Method C, G3

559

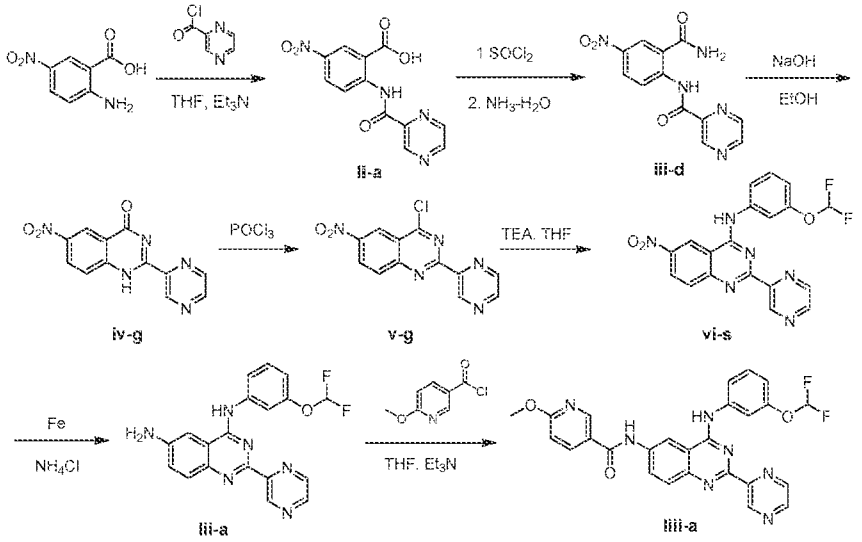
1230		HCl	351.76	1H-NMR (400 MHz, DMSO-d6): δ 10.42 (s, 1H), 9.60 (s, 2H), 9.34 (s, 1H), 8.64 (d, J = 8.4 Hz, 1H), 8.24 (dd, J = 8.4, 2.4 Hz, 1H), 7.98 – 7.92 (m, 3H), 7.76 – 7.71 (m, 1H), 7.56 (t, J = 8.8 Hz, 1H).	DMSO	352.0, 354.0 (M+1)	Method B (NH4HCO3)	95	Method C, G1
1231		HCl	383.33	1H-NMR (400 MHz, DMSO-d6): δ 10.58 (s, 1H), 9.61 (s, 2H), 9.34 (s, 1H), 8.71 (d, J = 8.4 Hz, 1H), 8.13 (s, 1H), 8.04 – 7.93 (m, 3H), 7.78 – 7.73 (m, 1H), 7.62 (t, J = 8.4 Hz, 1H), 7.21 (d, J = 8.0 Hz,1H).	DMSO	384.1 (M+1)	Method B (NH4HCO3)	95	Method C, G1
1232			421.25	1H-NMR (400 MHz, DMSO-d6): 10.34 (s, 1H), 9.58 (s, 1H), 9.27 – 9.25 (m, 1H), 8.84 – 8.77 (m, 2H), 9.52 (s, 1H), 8.35 (s, 1H), 8.07 – 7.67 (m, 5H), 7.20 (t, J = 7.5 Hz, 1H).	DMSO	421.0, 423.0 (M+1)	Method B (NH4HCO3)	95	Method C, G6
1233				1H-NMR (400 MHz, DMSO-d6): δ 13.15 (s, 1H), 10.00 (s, 1H), 9.44 (d, J = 5.2 Hz, 1H), 8.95 (d, J = 8.4 Hz, 1H), 8.48 (s, 1H), 8.42 – 8.40 (m, 1H), 8.16 (d, J = 9.2 Hz, 1H), 7.97 – 7.91 (m, 3H), 7.81 – 7.73 (m, 2H), 7.25 (t, J = 2.4 Hz, 1H).	DMSO	377.0 (M+1)	Method B (NH4HCO3)	95	Method G

560

1234				1H-NMR (400 MHz, DMSO-d6): δ 9.95 (s, 1H), 9.54 (s, 1H), 8.82 (s, 1H), 8.74 (d, J = 2.0 Hz, 1H), 8.66 (d, J = 2.4 Hz, 1H), 8.07 (dd, J = 8.8, 2.4 Hz, 1H), 8.00 (d, J = 2.4 Hz, 1H), 7.92 (d, J = 8.8 Hz, 1H), 7.70 (d, J = 8.8 Hz, 1H), 7.60 (dd, J = 8.8, 2.4 Hz, 1H), 4.00 (s, 3H).	DMSO	397.9, 400.0 (M+1)	Method B (NH4HCO3)	95	Method G

561

Scheme 67: Representative synthesis of compounds of formula with a pyrazine liii-a (see Scheme 65)



Method C: 5-Nitro-2-(pyrazine-2-carboxamido)benzoic acid (li-a) To a solution of pyrazine-2-carboxylic acid (1.36 g, 10.9 mmol, 1eq.) in $SOCl_2$ (20 mL) was added DMF (2 drops). The mixture was stirred at 60 °C for 20 min. The volatiles were removed *in vacuo* to give crude pyrazine-2-carbonyl chloride, which was used in the next step directly. To a suspension of 2-amino-5-nitrobenzoic acid (2.00 g, 10.9 mmol, 1.0 eq.) in THF (50 mL) was added Et_3N (1.09 g) and pyrazine-2-carbonyl chloride in anhydrous THF (50 mL) dropwise. The resulting mixture was stirred at room temperature for 18 h. After the reaction was completed, the volatiles were removed. The residue was suspended in H_2O (10 mL) and the pH was adjusted to 5 by slow addition of 2N HCl in water. The resulting solid was collected and dried *in vacuo* to give 3.12 g of 5-nitro-2-(pyrazine-2-carboxamido)benzoic acid as a brown solid (99%). LCMS m/z = 289.0 (M+1) (Method B) (retention time = 1.24 min).

Method A: N-(2-carbamoyl-4-nitrophenyl)pyrazine-2-carboxamide (iii-d) A mixture of 5-nitro-2-(pyrazine-2-carboxamido)benzoic acid (3.12 g, 10.8 mmol) in $SOCl_2$ (20 mL) was stirred at 80 °C for 2 h. After cooling, the volatiles were removed and the residue was suspended in DCM (150 mL), and a solution of $NH_3.H_2O$ (25%

by weight in water, 40 mL) was added and stirred for 4 h. The resulting precipitate was collected and dried *in vacuo* to give 2.42 g of N-(2-carbamoyl-4-nitrophenyl)pyrazine-2-carboxamide as a dark red solid (74.6%). LCMS m/z = 288.0 (M+1) (Method B) (retention time = 1.11 min).

Method E2: 6-nitro-2-(pyrazin-2-yl)quinazolin-4(1H)-one (iv-g) To a mixture of N-(2-carbamoyl-4-nitrophenyl)pyrazine-2-carboxamide (2.42 g, 8.43 mmol, 1.0 eq.) in EtOH (60 mL) was added NaOH (1.98 g, 49.5 mmol, 5.0 eq.). The resulting mixture was stirred at room temperature for 18 h. After the reaction was completed, the volatiles were removed *in vacuo*. The residue was partitioned between H_2O (50 mL) and ethyl acetate (50 mL). The aqueous layer was neutralized to pH 5 by slow addition of aqueous citric acid. The resulting precipitate was collected and dried to give 2.00 g of 6-nitro-2-(pyrazin-2-yl)quinazolin-4(3H)-one as a yellow solid (88%). LCMS m/z = 270.1 (M+1) (Method A) (retention time = 1.36 min).

Method F2: 4-Chloro-6-nitro-2-(pyrazin-2-yl)quinazoline (v-g) To a mixture of 6-nitro-2-(pyrazin-2-yl)quinazolin-4(3H)-one (1.00 g, 3.7 mmol) in $POCl_3$ (10 mL) was added *N,N*-dimethylbenzenamine (0.1 mL). The resulting mixture was stirred at 120°C for 2 h. After the reaction was completed, $POCl_3$ was removed *in vacuo*, and the residue was co-evaporated with toluene twice to give a dark crude product, which was used for the next step without further purification.

Method G6: N-(3-(difluoromethoxy)phenyl)-6-nitro-2-(pyrazin-2-yl)quinazolin-4-amine (vi-s) A mixture of 4-chloro-6-nitro-2-(pyrazin-2-yl)quinazoline (1.00 g, crude, 3.7 mmol, 1.0 eq.), 3-(difluoromethoxy)benzenamine (600 mg, 3.7 mmol, 1.0 eq.) and Et_3N (1.00 g, 10 mmol, 3.0 eq) in THF (80 mL) was stirred at 75 °C for 18 h. After cooling, the volatiles were removed *in vacuo* and the residue was washed with H_2O (100 mL x 2). The solid was dried *in vacuo* to afford 1.40 g of N-(3-(difluoromethoxy)phenyl)-6-nitro-2-(pyrazin-2-yl)quinazolin-4-amine as a black solid (90.2% of two steps). LCMS m/z = 411.0 (M+1) (Method A) (retention time = 1.61 min).

Method B: N^4-(3-(difluoromethoxy)phenyl)-2-(pyrazin-2-yl)quinazoline-4,6-diamine (lii-a) To a mixture of N-(3-(difluoromethoxy)phenyl)-6-nitro-2-(pyrazin-2-yl) quinazolin -4-amine (1.40 g, 3.4 mmol, 1.0 eq.) in MeOH-H_2O (v/v, 3:1, 110 mL) was added NH_4Cl (1.80 g, 34 mmol, 10.0 eq.) and Fe (1.91 g, 34 mmol, 10.0 eq.). The resulting mixture was stirred at 60 °C for 3 h. After the reaction was completed, the mixture was cooled to room temperature, and the iron was filtered off. The filtrate was concentrated to 15 mL and a precipitate formed and was collected and dried *in vacuo* to give 1.13 g of N^4-(3-(difluoromethoxy)phenyl)-2-(pyrazin-2-yl)quinazoline-4,6-diamine as a pale yellow solid (87.5%). LCMS m/z = 381.1 (M+1) (Method B) (retention time = 1.60 min). ^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.69 (s, 1H), 9.52 (d, *J* = 1.2 Hz, 1H), 8.75 (d, *J* = 2.4 Hz, 1H), 8.69 (d, *J* = 2.4 Hz, 1H), 8.30 (s, 1H), 7.87 (dd, *J* = 8.4, 0.8 Hz, 1H), 7.72 (d, *J* = 8.8 Hz, 1H), 7.49 – 7.42 (m, 2H), 7.33 – 7.32 (m, 1H), 7.31 (t, *J* = 74.Hz, 1H), 5.85 (s, 2H).

Method C: N-(4-(3-(difluoromethoxy)phenylamino)-2-(pyrazin-2-yl)quinazolin-6-yl)-6-methoxynicotinamide (liii-a) To a solution of 6-methoxynicotinic acid (100 mg, 0.65 mmol) in $SOCl_2$ (2 mL) was added DMF (1 drop). The mixture was stirred at 60 °C for 20 min. The volatiles were removed *in vacuo* to give 6-methoxynicotinoyl chloride, which was used for the next step directly. To a suspension of N^4-(3-(difluoromethoxy)phenyl)-2-(pyrazin-2-yl)quinazoline-4,6-diamine (130 mg, 0.34 mmol, 0.5 eq.) in THF (5 mL) and Et_3N (101 mg, 1 mmol , 3.0 eq) was added 6-methoxynicotinoyl chloride in anhydrous THF (5 mL) dropwise. The resulting mixture was stirred at room temperature for 18 h. The volatiles were removed *in vacuo*. The residue was washed with MeOH and re-crystallized from THF/MeOH twice, and purified by reverse phase chromatography PREP-HPLC (A = NH_4HCO_3-H_2O, 10 mmol/L, B = MeOH) to afford 33 mg of N-(4-(3-(difluoromethoxy)phenylamino)-2-(pyrazin-2-yl)quinazolin-6-yl)-6-methoxynicotinamide as a pale yellow solid (18.8%). LCMS m/z = 516.1 (M+1), 258.6 (M/2+1) (Method A) (retention time = 1.57 min). ^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.71 (s, 1H), 10.18 (s, 1H), 9.57 (d, *J* = 1.6 Hz, 1H), 9.01 (d, *J* = 1.6 Hz, 1H),

8.91 (d, J = 2.4 Hz, 1H), 8.81 (t, J = 2.0 Hz, 1H), 8.76 (d, J = 2.4 Hz, 1H), 8.34 (dd, J = 8.8, 2.8 Hz, 1H), 8.23 (s, 1H), 8.08 (dd, J = 8.8, 2.0 Hz, 1H), 8.00 (d, J = 9.2 Hz, 1H), 7.90 (d, J = 9.2 Hz, 1H), 7.46 – 7.50 (m, 1H), 7.32 (t, J = 74.4 Hz, 1H), 7.02 (d, J = 8.8 Hz, 1H), 6.95 (dd, J = 8.0, 2.0 Hz, 1H), 3.97 (s, 3H).

The compounds in the following table were prepared in a manner analogous to that described in **Scheme 67** (prepared according to method **procedure A - G** as designated).

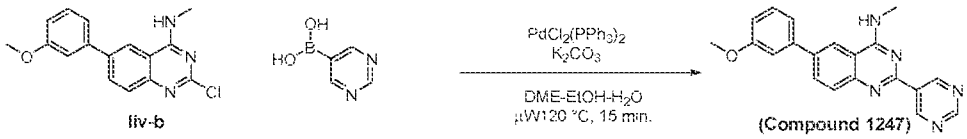
Table 22:

Number	PRODUCT	Salt type	Molecular Mass	^{1}H-NMR	^{1}H-NMR Solvent	LCMS	LCMS Protocol	Purity percent	Method for Coupling
1242			422.39	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.10 – 10.45 (m, 2H), 9.68 (s, 1H), 8.45 – 9.10 (m, 2H), 7.68 – 8.37 (m, 4H), 7.36 – 7.52 (m, 2H), 7.02 – 7.08 (m, 1H), 2.21 (s, 3H).	DMSO	423.0 (M+1)	Method A (TFA)	95	Method C, G4, C
1243			515.47	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.71 (s, 1H), 10.18 (s, 1H), 9.57 (d, *J* = 1.6 Hz, 1H), 9.01 (d, *J* = 1.6 Hz, 1H), 8.91 (d, *J* = 2.4 Hz, 1H), 8.81 (t, *J* = 2.0 Hz, 1H), 8.76 (d, *J* = 2.4 Hz, 1H), 8.34 (dd, *J* = 8.8, 2.8 Hz, 1H), 8.23 (s, 1H), 8.08 (dd, *J* = 8.8, 2.0 Hz, 1H), 8.00 (d, *J* = 9.2 Hz, 1H), 7.90 (d, *J* = 9.2 Hz, 1H), 7.46 – 7.50 (m, 1H), 7.32 (t, *J* = 74.4 Hz, 1H), 7.02 (d, *J* = 8.8 Hz, 1H), 6.95 (dd, *J* = 8.0, 2.0 Hz, 1H), 3.97 (s, 3H).	DMSO	516.2 (M+1)	Method B (NH4HCO3)	95	Method C, G4, C
1244			514.48	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.56 (s, 1H), 10.16 (s, 1H), 9.57 (s, 1H), 9.00 (d, *J* = 1.6 Hz, 1H), 8.81 (d, *J* = 2.4 Hz, 1H), 8.76 (d, *J* = 2.8 Hz, 1H), 8.23 (s, 1H), 8.07 – 8.12 (m, 3H), 7.99 (d, *J* = 9.2 Hz, 1H), 7.89 (d, *J* = 9.2 Hz, 1H), 7.46 – 7.50 (m, 1H), 7.32 (t, *J* = 72.8 Hz, 1H), 7.11 – 7.13 (m, 2H), 6.95 (dd, *J* = 8.4, 2.4 Hz, 1H), 3.87 (s, 3H).	DMSO	515.2 (M+1)	Method B (NH4HCO3)	95	Method C, G4, C
1245			520.53	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.30 (s, 1H), 10.16 (s, 1H), 9.54 (s, 1H), 8.89 (s, 1H), 8.79 (t, *J* = 2.4 Hz, 1H), 8.74 (d, *J* = 2.8 Hz, 1H), 8.20 (s, 1H), 7.93 (s, 2H), 7.87 (d, *J* = 8.4 Hz, 1H), 7.48 (dd, *J* = 10.0, 2.0 Hz, 1H), 7.31 (t, *J* = 74.0 Hz, 1H), 6.94 (dd, *J* = 8.4, 2.0 Hz, 1H), 3.26 (s, 3H), 3.18 – 3.22 (m, 1H), 1.91 – 1.96 (m, 2H), 1.66 – 1.78 (m, 2H), 1.53 – 1.63 (m, 2H), 1.38 – 1.49 (m, 2H).	DMSO	521.2 (M+1)	Method B (NH4HCO3)	95	Method C, G4, C

1246			492.48	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.35 (s, 1H), 10.15 (s, 1H), 9.54 (s, 1H), 8.90 (d, *J* = 2.0 Hz, 1H), 8.80 (dd, *J* = 2.4, 1.2 Hz, 1H), 8.75 (d, *J* = 2.4 Hz, 1H), 8.19 (s, 1H), 7.95 (d, *J* = 8.8 Hz, 1H), 7.86 – 7.91 (m, 2H), 7.48 (dd, *J* = 10.8, 2.8 Hz, 1H), 7.31 (t, *J* = 74.4 Hz, 1H), 6.94 (dd, *J* = 7.6, 2.0 Hz, 1H), 3.94 – 3.97 (m, 2H), 3.40 – 3.43 (m, 2H), 2.70 – 2.73 (m, 1H), 1.65 – 1.78 (m, 4H).	DMSO	493.2 (M+1)	Method B (NH4HCO3)	95	Method C, G4, C

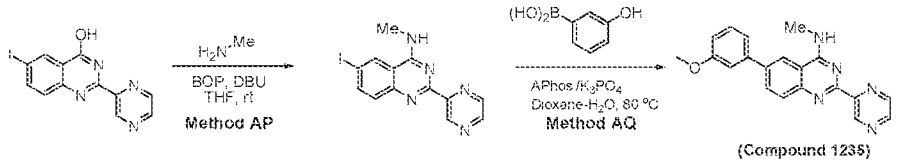
567

Scheme 68: Synthesis of 6-(3-methoxyphenyl)-N-methyl-2-(pyrimidin-5-yl)quinazolin-4-amine (Compound 1247)



Method BF : 6-(3-methoxyphenyl)-N-methyl-2-(pyrimidin-5-yl)quinazolin-4-amine (compound 1247) In a 10 mL microwave vial was added 2-chloro-6-(3-methoxyphenyl)-N-methylquinazolin-4-amine (0.080 g, 0.267 mmol), pyrimidine-5-boronic acid (0.099 g, 0.801 mmol), dichlorobis(triphenylphosphine)palladium (II) ($Pd(PPh_3)_2Cl_2$) (9.37 mg, 0.013 mmol), and potassium carbonate (0.111 g, 0.801 mmol) in DME (3 mL), EtOH (1.286 mL), and water (0.857 mL) to give a yellow suspension. The vial was irradiated at 120 °C for 15 min under argon. Water (10 mL) was added to the mixture and extracted with ethyl acetate (2 x 10 mL). The organic layers were combined and washed with brine (1 x 20 mL) and then dried over $MgSO_4$, filtered and concentrated. The residue was washed with MeOH-CH_2Cl_2 and dried to give 35 mg of 6-(3-methoxyphenyl)-N-methyl-2-(pyrimidin-5-yl)quinazolin-4-amine as a white solid (38 %). LCMS m/z = 344 (M +1) (Method D) (retention time = 1.78 min). ^{1}H NMR (300 MHz, DMSO) δ 9.79 - 9.59 (m, 2H), 9.30 (s, 1H), 8.72 (d, J = 4.6 Hz, 1H), 8.59 (s, 1H), 8.16 (d, J = 8.6 Hz, 1H), 7.85 (d, J = 8.7 Hz, 1H), 7.53 - 7.28 (m, 3H), 7.00 (d, J = 6.8 Hz, 1H), 3.86 (s, 3H), 3.18 (d, J = 3.9 Hz, 3H).

Scheme 69: Synthesis of 6-(3-methoxyphenyl)-N-methyl-2-(pyridin-3-yl)quinazolin-4-amine (Compound 1235)



In a 100 mL round-bottomed flask was added 6-iodo-2-(pyrazin-2-yl)quinazolin-4(3H)-one (0.500 g, 1.428 mmol), BOP (0.821 g, 1.857 mmol), and 1,8-diazabicyclo[5.4.0]undec-7-ene (0.426 ml, 2.86 mmol) in DMF (10 mL) to give a colorless solution. Methylamine, 2M in THF (2.142 ml, 4.28 mmol) was added and stirred at room temperature overnight. The reaction mixture was diluted with water (50 mL) and then a precipitate formed. The resulting solid was collected by filtration and dried to give 0.515 g of 6-iodo-N-methyl-2-(pyrazin-2-yl)quinazolin-4-amine as a pale brown solid in a 99 % yield. LCMS m/z = 364 (M +1) (Method D) (retention time = 1.25 min). ^{1}H NMR (300 MHz, DMSO) δ 9.60 (s, 1H), 8.89 - 8.65 (m, 3H), 8.65 - 8.48 (m, 1H), 8.06 (d, *J* = 8.7 Hz, 1H), 7.59 (d, *J* = 8.7 Hz, 1H), 3.11 (d, *J* = 4.2 Hz, 3H).

In a 50 mL round-bottomed flask was added 6-iodo-N-methyl-2-(pyrazin-2-yl)quinazolin-4-amine (0.100 g, 0.275 mmol), 3-methoxyphenylboronic acid (0.063 g, 0.413 mmol), bis(di-tert-butyl(4-dimethylaminophenyl)phosphine) dichloropalladium(II) (0.016 g, 0.022 mmol), and potassium phosphate tribasic monohydrate (0.190 g, 0.826 mmol) in dioxane (5 mL) and water (0.5 mL) to give a brown suspension. The reaction mixture was heated at 80 °C overnight under argon. After cooling to room temperature, the reaction mixture was diluted with water (10 mL) and then a precipitate formed. The resulting solid was collected by filtration and washed with ethyl acetate and dried to give 25 mg of 6-(3-methoxyphenyl)-N-methyl-2-(pyrazin-2-yl)quinazolin-4-amine as a pale yellow solid in a 26 % yield. LCMS m/z = 344 (M +1) (Method D) (retention time = 1.43 min). ^{1}H NMR (300 MHz, DMSO) δ 9.64 (s, 1H), 8.85 - 8.78 (m, 1H), 8.77 - 8.71 (m, 1H), 8.70 - 8.63 (m, 1H), 8.63 - 8.55 (m, 1H), 8.18 (d, *J* = 8.8 Hz, 1H), 7.89 (d, *J* = 8.9 Hz, 1H), 7.53 - 7.31 (m, 3H), 7.09 - 6.92 (m, 1H), 3.86 (s, 3H), 3.17 (d, *J* = 3.6 Hz, 3H).

The compounds in the following table were prepared in a manner analogous to that described in **Scheme 69** (prepared according to method **described for 6-(3-methoxyphenyl)-N-methyl-2-(pyridin-3-yl)quinazolin-4-amine**).

Table 23:

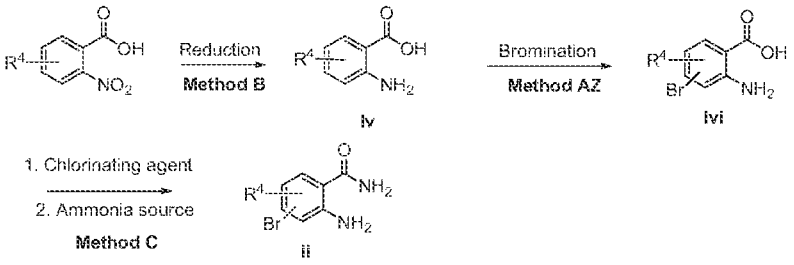
Number	PRODUCT	Salt type	Molecular Mass	^{1}H-NMR	^{1}H-NMR Solvent	LCMS	LCMS Protocol	Purity percent	Method for Coupling
1235			343.38	1H NMR (300 MHz, DMSO) δ 9.64 (s, 1H), 8.85 – 8.78 (m, 1H), 8.77 – 8.71 (m, 1H), 8.70 – 8.63 (m, 1H), 8.63 – 8.55 (m, 1H), 8.18 (d, J = 8.8 Hz, 1H), 7.89 (d, J = 8.9 Hz, 1H), 7.53 – 7.31 (m, 3H), 7.09 – 6.92 (m, 1H), 3.86 (s, 3H), 3.17 (d, J = 3.6 Hz, 3H).	DMSO	344 (M+1)	Method D	100	Method AP/AQ
1236			338.37	1H NMR (300 MHz, DMSO) δ 9.64 (s, 1H), 8.87 – 8.61 (m, 4H), 8.24 (d, J = 8.8 Hz, 1H), 8.15 – 7.98 (m, 4H), 7.92 (d, J = 8.7 Hz, 1H), 3.17 (d, J = 4.0 Hz, 3H).	DMSO	339 (M+1)	Method D	100	Method C,G1
1237		2HCl		^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.17 (s, 1H), 9.54 (d, *J* = 5.2 Hz, 1H), 9.36 (s, 1H), 8.63 (s, 2H), 8.13 – 8.06 (m, 2H), 7.58 – 7.51 (m, 2H), 7.43 – 7.38 (m, 1H), 3.23 (d, *J* = 4.0 Hz, 3H).	DMSO	350.1, 351.1, (M+1)	Method B (NH_4HCO_3)	95	Method C, G1
1238		2HCl		^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.14 (s, 1H), 9.50 (d, *J* = 5.2 Hz, 1H), 9.24 (s, 1H), 8.60 (dd, *J* = 5.4, 1.8 Hz, 1H), 8.55 (s, 1H), 8.04 (q, *J* = 8.8 Hz, 2H), 7.76 (dd, *J* = 15.4, 9.0 Hz, 1H), 7.51 – 7.45 (m, 1H), 7.32 (dt, *J* = 8.4, 2.0 Hz, 1H), 3.23 (d, *J* = 4.4 Hz, 3H).	DMSO	350.0, 351.0, (M+1)	Method B (NH_4HCO_3)	95	Method C, G1

570

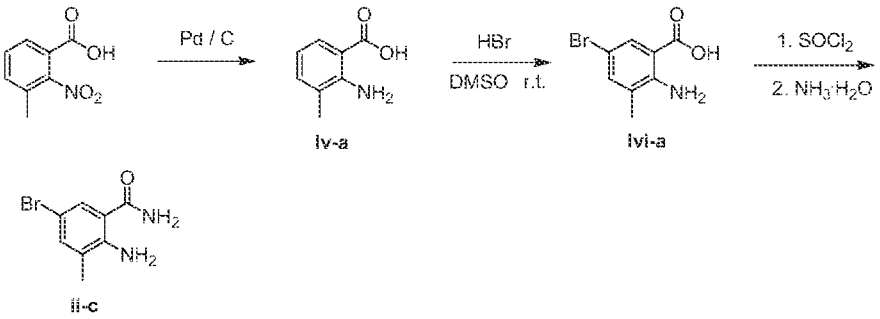
1239				^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.73 (s, 1H), 9.32 (s, 1H), 8.74 (d, *J* = 4.4 Hz, 1H), 8.51 (s, 1H), 8.03 (d, *J* = 8.7 Hz, 1H), 7.92 (d, *J* = 8.6 Hz, 1H), 7.54 – 7.49 (m, 2H), 7.42 – 7.37 (m, 1H), 4.12 (q, *J* = 5.2 Hz, 1H), 3.17 (t, *J* = 4.5 Hz, 3H).	DMSO	350.1 (M+1)	Method B (NH_4HCO_3)	95	Method C, G1
1240		2HCl		^{1}H-NMR (400 MHz, CD3OD): δ 9.77 (s, 1H), 8.85 (d, *J* = 11.4 Hz, 2H), 8.42 (s, 1H), 8.19 – 8.03 (m, 2H), 7.60 (dd, *J* = 15.6, 7.8 Hz, 1H), 7.10 (t, *J* = 8.4 Hz, 2H), 3.38 (s, 3H).	CD3OD	350.1 (M+1)	Method B (NH_4HCO_3)	95	Method C, G1
1241		2HCl		^{1}H-NMR (400 MHz, DMSO): δ 10.84 (d, *J* = 1.8 Hz, 1H), 9.87 (s, 1H), 9.06 (d, *J* = 13.6 Hz, 2H), 8.90 (s, 1H), 8.32 (t, *J* = 9.8 Hz, 2H), 7.67 – 7.35 (m, 3H), 3.39 (s, 3H).	DMSO	349.9 (M+1)	Method B (NH_4HCO_3)	95	Method C, G1

571

Scheme 70: General route for the synthesis of compounds with general formula ii



Scheme 71: Representative synthesis of compounds of formula ii (see Scheme 70)



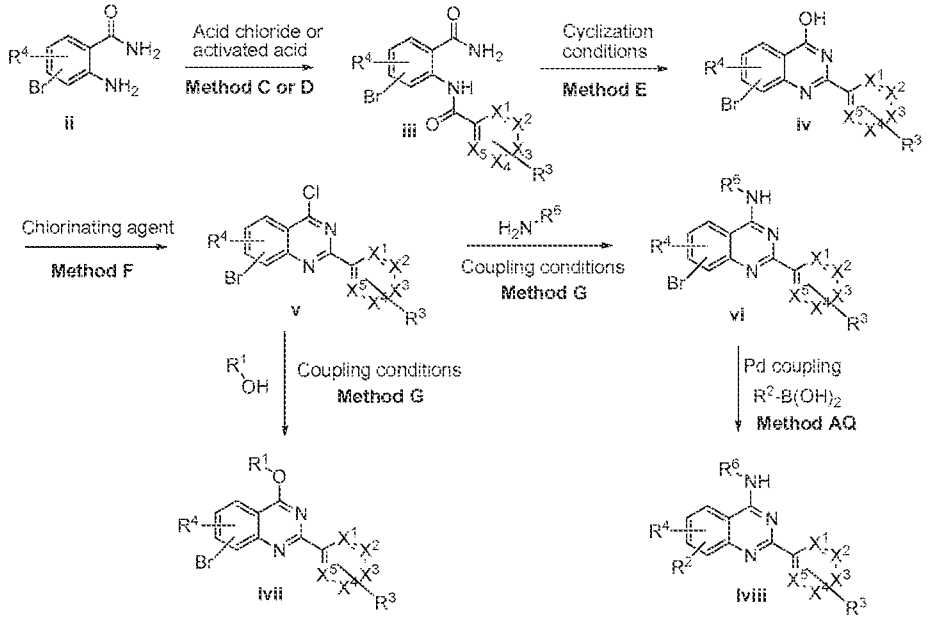
Method B2: 2-Amino-3-methylbenzoic acid (Iv-a) Pd/C catalyst (150 mg) was suspended in a solution of 3-methyl-2-nitrobenzoic acid (1.50 g, 8.28 mmol. 1.0 eq) in THF (60 mL), the mixture was stirred under H_2 atmosphere at room temperature overnight. The Pd/C was removed by filtration over Celite and the THF was removed *in vacuo* to give 1.23 g of **Iv-a** as a white solid (yield 98 %). LCMS m/z = 152.1 (M+1) (Method B) (retention time = 0.73 min). The product was used further without purification.

Method AZ: 2-Amino-5-bromo-3-methylbenzoic acid (Ivi-a) To a solution of 2-amino-3-methylbenzoic acid (1.23 g, 8.14 mmol, 1.0 eq) in 15 mL of DMSO was added 40% HBr (6.00 mL, 44.7 mmol, 5 eq). The resulting mixture was stirred at room temperature overnight. A white precipitate formed during the course of the reaction. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ resulting in a white solid that was filtered and dried *in vacuo* to yield 950 mg in 51%

yield of **lvi-a** as white solid. LCMS m/z = 229.9 (M+1) (Method B) (retention time = 1.20 min).

Method C: 2-Amino-5-bromo-3-methylbenzamide (ii-c) A mixture of 2-amino-5-bromo-3-methylbenzoic acid (950 mg, 4.15 mmol) and $SOCl_2$ (20 mL) was stirred at 80°C for 2 h. After the reaction was completed, the mixture was cooled to room temperature. The $SOCl_2$ was removed *in vacuo* and the residue was dissolved in anhydrous THF (10 mL). The THF solution was then added dropwise to a 28% by weight solution of NH_3-H_2O (10 mL). After 1 h, the resulting precipitate was collected and dried *in vacuo* to give 820 mg of **ii-c** as a yellow solid (87%). LCMS m/z = 288.9, 230.9 (M+1) (Method B) (retention time = 1.49 min).

Scheme 72: General route for the synthesis of compounds with general formula lvii and lviii



X^1, X^2, X^3, X^4 or X^5 = CH or N, at least one X^1, X^2, X^3, X^4 or X^5 must be N

Method G for Coupling Conditions

G1: *i*-PrOH/85-100 °C

G2: THF/heat
G3: *i*-AmOH/100-130 °C

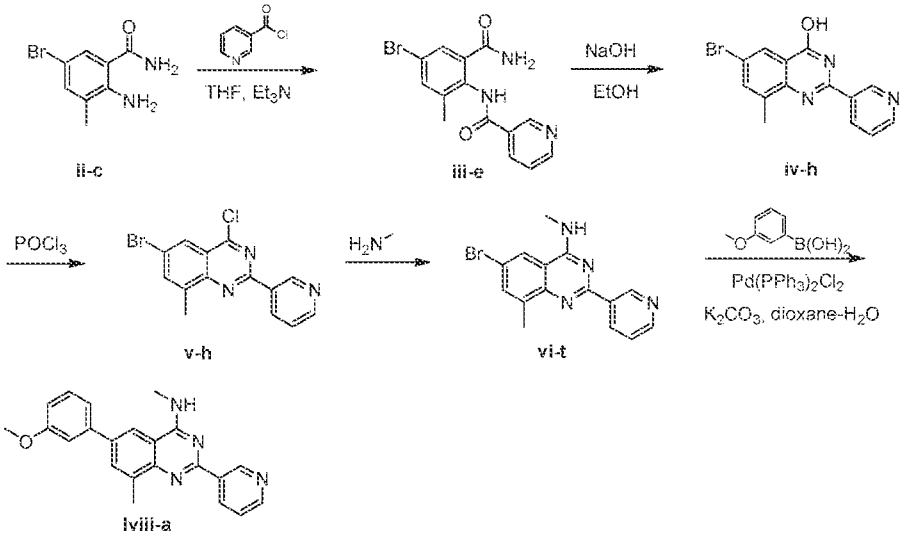
G4: MeOH/microwave/150 °C
G5: *i*-AmOH/ microwave/150 °C

G6: THF/Et_3N/reflux
G7: THF-H_2O/NaOAc/rt-60 °C
G8: NaH/THF
G9: *n*-BuLi/THF
G10: LHMDS/THF
G11: LDA/THF
G12: K_2CO_3/DMF/60 °C
G13: Cs_2CO_3/DMA/80 °C
G14: NaOtBu/DMF/Microwave/100 °C

Method AQ for Coupling Conditions

AQ1: $Pd(PPh_3)_2Cl_2$/ K_2CO_3/ Dioxane-H_2O
AQ2: $Pd_2(APhos)_2Cl_2$/K_3PO_4/Dioxane-H_2O
AQ3: $Pd(PPh_3)_4$/ K_3PO_4/Dioxane-H_2O
AQ4: $Pd(dppf)Cl_2$-CH_2Cl_2/ K_3PO_4/ Dioxane-H_2O
AQ5: $Pd(OAc)_2Cl_2$/ S-Phos/K_3PO_4/Dioxane-H_2O
AQ6: $Pd(dppf)Cl_2$-CH_2Cl_2/ Na_2CO_3/ Dioxane-H_2O

Scheme 73: Representative synthesis of compounds of formula lvii and lviii (see Scheme 72)



Method C: N-(4-bromo-2-carbamoyl-6-methylphenyl)nicotinamide (iii-e) To a solution of 2-amino-5-bromo-3-methylbenzamide (820 mg, 3.55 mmol, 1.0 eq.) in THF (15 mL) and Et_3N (0.7 mL) was added nicotinoyl chloride (551 mg, 3.91 mmol, 1.1 eq.) in anhydrous THF (15 mL) dropwise. The resulting mixture was stirred at room temperature overnight. After the reaction was completed, the resultant precipitate was filtered and dried *in vacuo* to give 1.74 g of crude **iii-e** as a yellow solid. LCMS m/z = 333.8, 335.8 (M+1) (Method B) (retention time = 1.42 min).

Method E: 6-Bromo-8-methyl-2-(pyridin-3-yl)quinazolin-4-ol (iv-h) A mixture of N-(4-bromo-2-carbamoyl-6-methylphenyl)nicotinamide (1.74 g salt, 5.22 mmol, 1.0 eq) in EtOH (50 mL) was treated with NaOH (1.04 g, 26.1 mmol, 5.0 eq). The resulting mixture was stirred at room temperature overnight. After the reaction was completed, the volatiles were removed *in vacuo*. Water (30 mL) was added to the residue and the mixture was adjusted to pH ~ 1 or 2 by slow addition of aqueous HCl. The resultant precipitate was collected and dried to give 870 mg of **iv-h** as a yellow solid (77% yield after two steps). LCMS m/z = 315.7, 317.7 (M+1) (Method B) (retention time = 1.74 min).

Method F5: 6-Bromo-4-chloro-8-methyl-2-(pyridin-3-yl)quinazoline (v-h) 6-Bromo-8-methyl-2-(pyridin-3-yl)quinazolin-4-ol (870 mg, 2.76 mmol) was added to $POCl_3$ (10 mL). The resulting mixture was stirred at 120°C overnight. After the reaction was completed, the mixture was carefully poured into ice-water. The pH was adjusted to 7 by slow addition of NH_4OH at 0°C. The resultant solid was collected to give 1.00 g of **v-h** as a beige solid (quantitative yield). LCMS m/z = 333.9, 335.9 (M+1) (Method B) (retention time = 2.23 min).

Method G6: 6-Bromo-N, 8-dimethyl-2-(pyridin-3-yl)quinazolin-4-amine (vi-t) A mixture of 6-bromo-4-chloro-8-methyl-2-(pyridin-3-yl)quinazoline (200 mg, 0.60 mmol, 1.0 eq.), methylamine (81 mg, 1.20 mmol, 2.0 eq.) and Et_3N (0.2 mL) in *i*-PrOH (10 mL) was stirred at 85 °C overnight. The resultant yellow precipitate was

collected to afford 125 mg of **vi-t** as a beige solid (63.4%). LCMS m/z = 328.8, 330.8 (M+1) (Method B) (retention time = 1.95 min).

Method G2: 7-bromo-N-methyl-2-(pyridin-3-yl)quinazolin-4-amine (vi-u) To a suspension of 7-bromo-4-chloro-2-(pyridin-3-yl)quinazoline (5.0 g, 0.0156 mol) in THF (100 mL) was added dropwise a methylamine solution (40 wt. % in H_2O) (24 ml, 0.272 mmol) with cooling. The suspension was stirred at 60 °C for 3h, cooled, filtered, and dried to give the title compound. (3.62 g, 73.5 %)

Method AQ1: 6-(3-Methoxyphenyl)-N, 8-dimethyl-2-(pyridin-3-yl) quinazolin-4-amine (lviii-a) (This method is representative of method AQ2 and can be implemented in a similar way except for substitution of the appropriate catalyst and base) To a mixture of 6-bromo-N,8-dimethyl-2-(pyridin-3-yl)quinazolin-4-amine (130 mg, 0.396 mmol, 1.0 eq), 3-methoxyphenylboronic acid (60 mg, 0.396 mmol, 1.0 eq), K_2CO_3 (295 mg, 2.14 mmol, 5.4 eq.) in dioxane (8 mL) and H_2O (4 mL) was added $Pd(PPh_3)_2Cl_2$ (15 mg, 0.021 mmol, 0.054 eq) under N_2 atmosphere. The resulting mixture was stirred at 120℃ under N_2 atmosphere overnight. After the reaction was completed, the mixture was filtered, and the filtrate was concentrated *in vacuo*. The residue was purified by reverse phase HPLC column to afford 11 mg of **lviii-a** as a white solid (yield 7.8%). LCMS m/z = 357.2, (M+1) (Method B (retention time = 2.11 min). 1H NMR (400 MHz, DMSO-d_6): δ 9.68 (d, *J* = 1.2 Hz, 1H), 8.75 (d, *J* = 8.0 Hz, 1H), 8.62 (d, *J* = 4.6 Hz, 1H), 8.49 (d, *J* = 4.4 Hz, 1H), 8.35 (s, 1H), 7.97 (s, 1H), 7.49 (dd, *J* = 7.8, 4.8 Hz, 1H), 7.44 – 7.29 (m, 3H), 6.93 (dd, *J* = 6.8, 2.4 Hz, 1H), 3.81 (s, 3H), 3.12 (d, *J* = 4.4 Hz, 3H), 2.68 (s, 3H).

Method AQ3: 6-(4-Fluorophenyl)-N,8-dimethyl-2-(pyridin-3-yl)quinazolin-4-amine dihydrochloride (lviii-b) 6-Bromo-N,8-dimethyl-2-(pyridin-3-yl)quinazolin-4-amine (340mg, 1.03 mmol), 3-fluorobenzeneboronic acid (217 mg, 1.55 mmol), K_3PO_4 (658 mg, 3.10 mmol) and $Pd(PPh_3)_4$ (59.7 mg, 0.052 mmol) were dissolved in the mixed solvent of 1,4-dioxane (10 mL) and water (1 mL). The resulting mixture

was stirred at 90°C for 6 hours under a nitrogen atmosphere. After the reaction was completed, water was added to the mixture and stirred for 30 minutes. The resulting precipitate was collected by filtration and purified by column chromatography on NH-silica gel (eluted with THF) to give a yellow powder. The solid was suspended in ethanol and 5N HCl (1 mL) was added to the mixture. The mixture was sonicated for 10 min and the resulting precipitate was collected by filtration and dried to give 304 mg of 6-(3-fluorophenyl)-N,8-dimethyl-2-(pyridin-3-yl)quinazolin-4-amine dihydrochloride as a yellow powder in 71% yield.

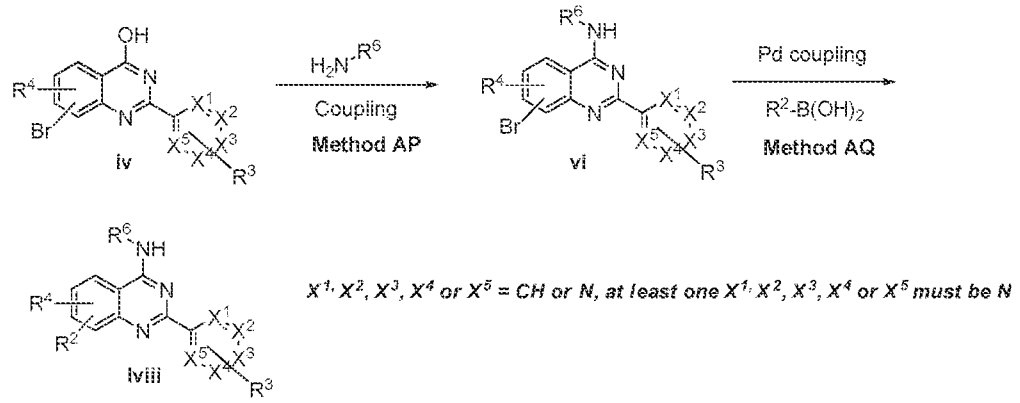
Method AQ4: 6-(2,4-Difluorophenyl)-N,5-dimethyl-2-(pyridin-3-yl)quinazolin-4-amine(lviii-c) 6-Bromo-N,5-dimethyl-2-(pyridin-3-yl)quinazolin-4-amine (350mg, 1.06 mmo l), 2,4-difluorophenylboronic acid (252 mg, 1.595 mmol), K_3PO_4 (677 mg, 3.19 mmol) and $Pd(dppf)Cl_2$-CH_2Cl_2 (87 mg, 0.106 mmol) were dissolved in the mixed solvent of 1,4-dioxane (10 mL) and water (1 mL). The resulting mixture was stirred at 90°C for 2.5 hours under N_2. After the reaction was completed, water was added to the mixture and extracted with ethyl acetate. The combined organic layers were washed with water and brine, dried over Na_2SO_4. After filtration and evaporation, the crude product was purified by column chromatography on NH-silica gel (eluted with isocratic 33%ethyl acetate/67%hexane) to give a white powder. The solid was suspended in ethanol and 5N HCl (1.0 mL) was added to the mixture. The mixture was sonicated for 10 min and the resultant precipitate was collected by filtration and dried to give 139 mg of 6-(2,4-difluorophenyl)-N,5-dimethyl-2-(pyridin-3-yl)quinazolin-4-amine dihydrochloride as a pale yellow powder in a 30% yield.

Method AQ5: 7-(3-fluorophenyl)-N,6-dimethyl-2-(pyridin-3-yl)quinazolin-4-amine dihydrochloride (lviii-d) A mixture of 7-chloro-N,6-dimethyl-2-(pyridin-3-yl)quinazolin-4-amine (400 mg, 1.40 mmol), 3-fluorophenylboronic acid (294 g, 2.10 mmol), $Pd(OAc)_2$ (15.8 mg, 0.070 mmol), 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl (86.7 mg, 0.211 mmol), K_3PO_4 (900 mg, 4.23 mmol) in dioxane (10 mL) and water (2 mL) was stirred under reflux for 2.5 h. Ethyl acetate (20 mL) was added to the cooled mixture and a precipiate formed and was filtered. The solid

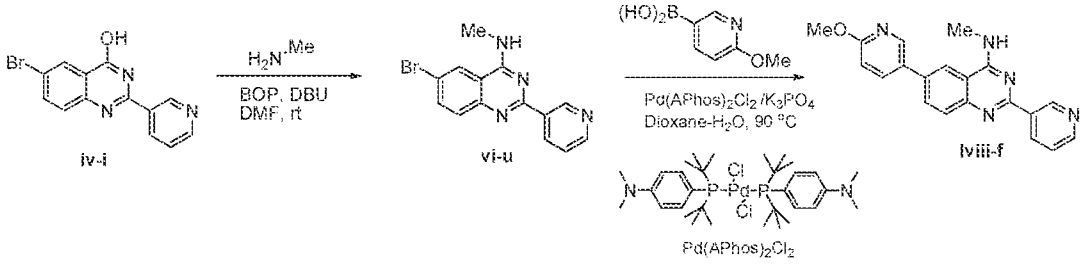
was recrystallized from DMF and water to give the title compound as free form. The solid was suspended in ethyl acetate (10 mL) and 4N HCl in ethyl acetate (1.0 mL) was added. The resulting solid was subjected to sonication for 20 min, filtered and dried to give the title compound as the bis-HCl salt (0.10 g, 18.7 %).

Method AQ6:7-(3,4-difluorophenyl)-N,8-dimethyl-2-(pyridin-3-yl)quinazolin-4-amine dihydrochloride (lviii-e) To a suspension of 3,4-difluorophenylboronic acid (389 mg, 2.46 mmol) and 7-bromo-N,8-dimethyl-2-(pyridin-3-yl)quinazolin-4-amine (395.4 mg, 1.201 mmol) in dioxane/H_2O (2/1) (30 mL) under a nitrogen atmosphere was added Na_2CO_3 (633.2mg, 5.97 mmol) and (1,1'-bis(diphenylphosphino)ferrocene)-dichloropalladium(II) (98 mg, 0.120 mmol) at room temperature. The mixture was stirred at 100°C for 1.5 h. Water was added to the reaction mixture and then a precipitate formed. The solid was filtered and washed with water and dried. The dried solid was then heated in a methanol/dioxane mixture to give a clear solution and filtered through Celite. The filtrate was concentrated to give the crude product. The crude product was sonicated in methanol/CH_2Cl_2 for ca.15 min and filtered to give 305.2 mg of a pale brown solid as the parent compound. To a suspension of parent compound in methanol was added 4N HCl in ethyl acetate (ca. 4 mL) to give a clear solution. The solution was concentrated and recystallized from ethanol to give the HCl salt. The salt was collected and dried in an oven at 60°C to give 231.3 mg in a 44% yield as pale yellow solid. ^{1}H NMR (DMSO-d_6) δ 9.73 (s, 1H), 9.37 (brd, J = 8.08 Hz, 1H), 8.97 (brd, J = 5.24 Hz, 1H), 8.77 (brs, 1H), 8.20 (d, J =8.48 Hz, 1H), 8.10-8.07 (brm, 1H), 7.63-7.55 (brm, 2H), 7.47 (d, J =8.48 Hz, 1H), 7.32 (brm, 1H), 3.20 (d, J = 4.20 Hz, 3H), 2.65 (s, 3H). The 1H of 2HCl was not observed.

Scheme 74: General route for the synthesis of compounds with general formula lviii



Scheme 75: Representative synthesis of compounds of formula lviii (see Scheme 74)



Method AP: 6-bromo-*N*-methyl-2-(pyridine-3-yl)quinazoline-4-amine (vi-u) To a solution of 6-bromo-2-(pyridin-3-yl)quinazolin-4(3H)-one (5.00 g, 16.6 mmol), (benzotriazol-1-yloxy)tris(dimethylamino)phosphonium hexafluorophosphate (BOP) (9.52 g, 21.5 mmol), and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (4.94 ml, 33.1 mmol) in DMF (50 mL) was added methylamine, 2M in THF (16.6 mL, 33.1 mmol). The mixture was stirred overnight at room temperature. Water (100 mL) was added to the mixture and stirred. The resultant precipitate was collected by filtration and dried to give 5.15 g of 6-bromo-N-methyl-2-(pyridin-3-yl)quinazolin-4-amine as pale yellow solid (99 %). LCMS m/z = 315 (M +1) (Method D) (retention time = 1.34 min). ^{1}H NMR (300 MHz, DMSO) δ 9.60 (dd, *J* = 2.1, 0.8 Hz, 1H), 8.79 – 8.70 (m, 1H), 8.67 (dd, *J* = 4.8, 1.7 Hz, 1H), 8.57 (s, 1H), 8.51 (d, *J* = 2.0 Hz, 1H), 7.90 (dd, *J*

= 8.9, 2.1 Hz, 1H), 7.71 (d, *J* = 8.9 Hz, 1H), 7.52 (ddd, *J* = 7.9, 4.8, 0.9 Hz, 1H), 3.13 (d, *J* = 4.5 Hz, 3H).

Method AQ2: 6-(6-methoxypyridin-3-yl)-*N*-methyl-2-(pyridine-3-yl)quinazoline-4-amine (lviii-f) To a 1 dram reaction vial was added 6-bromo-*N*-methyl-2-(pyridine-3-yl)quinazoline-4-amine (35 mg, 0.111 mmol), 6-methoxypyridin-3-ylboronic acid (20.4 mg, 0.133 mmol), $Pd(APhos)_2Cl_2$ (3.2 mg, 0.004mmol) and potassium phosphate monohydrate (77 mg, 0.33 mmol) in a mixture of dioxane-water (9:1, 2 mL). The reaction mixture was heated to 90 °C for 14 h after which it was cooled to room temperature and diluted with water (5 mL). The resultant precipitate was collected by filtration and recrystallized from methanol to give 6-(6-methoxypyridin-3-yl)-*N*-methyl-2-(pyridine-3-yl)quinazoline-4-amine as a pale yellow solid (19.1 mg, 51%). LCMS m/z = 344 (M +1) (Method C) (retention time = 2.01 min). ^{1}H NMR (300 MHz, DMSO) δ 9.64 (d, *J* = 1.3 Hz, 1H), 8.84 – 8.74 (m, 1H), 8.68 (dd, *J* = 6.2, 1.7 Hz, 2H), 8.57 (d, *J* = 1.6 Hz, 2H), 8.16 (ddd, *J* = 14.4, 8.7, 2.2 Hz, 2H), 7.85 (d, *J* = 8.7 Hz, 1H), 7.54 (dd, *J* = 7.9, 4.8 Hz, 1H), 7.00 (d, *J* = 8.7 Hz, 1H), 3.93 (s, 3H), 3.18 (d, *J* = 4.3 Hz, 3H).

The compounds in the following table were prepared in a manner analogous to that described in **Scheme 72 or 74**, replacing methylamine with the appropriate amine and 6-methoxypyridin-3-ylboronic acid with the appropriate boronic acid.

Table 24:

Number	Product	Salt	Molecular Mass	^{1}H-NMR	^{1}H-NMR Solvent	LCMS	Retention Time	LCMS Protocol	Purity percent	Method for Coupling
1248		HCl	342.4	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.66 (s, 1H), 8.50 – 8.89 (m, 3H), 8.16 (d, *J* = 8.2 Hz, 1H), 7.86 (d, *J* = 8.6 Hz, 1H), 7.30 – 7.61 (m, 4H), 7.01 (d, *J* = 6.4 Hz, 1H), 3.88 (s, 3H), 3.32 (brs, 1H), 3.19 (s, 3H).	DMSO	343.1 (M+1)		Method B (NH4HCO3)	95	Method AQ1
1249			372.4	1H-NMR (400 MHz, DMSO-d6): δ 9.63 (s, 1H), 8.77 (d, J = 7.9 Hz, 1H), 8.67 (d, J = 3.7 Hz, 1H), 8.50 (s, 1H), 8.11 (s, 1H), 7.56 -7.53 (m, 2H), 7.48 -7.40 (m, 3H), 7.01 (d, J = 3.9 Hz, 1H), 4.07 (s, 3H), 3.88 (s, 3H), 3.17 (d, J = 4.0 Hz, 3H).	DMSO	372.9 (M+1)		Method B (NH4HCO3)	95	Method AQ1
1250			356.4	1H-NMR (400 MHz, DMSO-d6): δ 9.63 (s, 1H), 8.79 – 8.74 (m, 1H), 8.69 (d, J = 4.0 Hz, 1H), 7.67 (d, J = 8.4 Hz, 1H), 7.60 (d, J = 8.8 Hz, 1H), 7.57 – 7.51 (m, 1H), 7.42 (t, J = 8.0 Hz, 1H), 7.37 – 7.30 (m,1H), 7.02 – 6.92 (m, 3H), 3.82 (s, 3H), 3.16 (d, J = 4.0 Hz, 3H), 2.69 (s, 3H).	DMSO	357.1 (M+1)		Method B (NH4HCO3)	95	Method AQ1
1251			356.4	1H-NMR (400 MHz, DMSO-d6): δ 9.68 (d, J = 1.2 Hz, 1H), 8.75 (d, J = 8.0 Hz, 1H), 8.62 (d, J = 4.6 Hz, 1H), 8.49 (d, J = 4.4 Hz, 1H), 8.35 (s, 1H), 7.97 (s, 1H), 7.49 (dd, J = 7.8, 4.8 Hz, 1H), 7.44 – 7.29 (m, 3H), 6.93 (dd, J = 6.8, 2.4 Hz, 1H), 3.81 (s, 3H), 3.12 (d, J = 4.4 Hz, 3H), 2.68 (s, 3H).	DMSO	357.2 (M+1)		Method B (NH4HCO3)	95	Method AQ1
1252			329.3	1H NMR (300 MHz, DMSO) δ 9.31 (s, 1H), 8.76 (d, J = 4.7 Hz, 1H), 8.51 (d, J = 8.0 Hz, 1H), 8.37 (d, J = 2.0 Hz, 1H), 8.16 (dd, J = 8.5, 2.2 Hz, 1H), 7.84 (d, J = 8.4 Hz, 1H), 7.59 (dd, J = 7.9, 4.8 Hz, 1H), 7.49 – 7.23 (m, 3H), 6.99 (d, J = 6.7 Hz, 1H), 3.85 (s, 3H).	DMSO	330 (M+1)	1.76	Method D	100	

581

1253		HCl	342.4	1H NMR (300 MHz, DMSO) δ 10.11 (s, 1H), 9.63 (s, 1H), 9.07 – 8.86 (m, 2H), 8.58 (s, 1H), 8.16 (s, 2H), 7.92 – 7.77 (m, 1H), 7.54 – 7.36 (m, 2H), 7.20 (d, J = 8.6 Hz, 1H), 7.16 – 7.07 (m, 1H), 3.81 (s, 3H), 3.29 (d, J = 3.9 Hz, 3H).	DMSO	343 (M+1)	1.47	Method D	100	Method AQ2
1254			330.3	1H NMR (300 MHz, DMSO) δ 9.59 (s, 1H), 8.73 (d, J = 8.3 Hz, 1H), 8.65 (d, J = 4.7 Hz, 1H), 8.37 – 8.22 (m, 1H), 8.18 – 8.05 (m, 1H), 7.76 (d, J = 9.0 Hz, 1H), 7.71 (s, 1H), 7.56 – 7.43 (m, 2H), 4.58 (s, 2H), 3.14 (d, J = 4.4 Hz, 3H), 2.69 (d, J = 4.6 Hz, 3H).	DMSO	331 (M+1)	1.52	Method D	100	Method AQ2
1255			312.4	1H NMR (300 MHz, DMSO) δ 9.64 (s, 1H), 8.88 – 8.47 (m, 4H), 8.25 – 8.05 (m, 1H), 7.97 – 7.72 (m, 3H), 7.67 – 7.35 (m, 4H), 3.18 (d, J = 4.4 Hz, 3H).	DMSO	313 (M+1)	1.46	Method D	100	Method AQ2
1256		HCl	337.4	1H NMR (300 MHz, DMSO) δ 9.93 (s, 1H), 9.63 (s, 1H), 9.00 (d, J = 8.3 Hz, 1H), 8.95 – 8.82 (m, 2H), 8.46 – 8.32 (m, 2H), 8.25 (d, J = 7.0 Hz, 1H), 8.13 (d, J = 8.4 Hz, 1H), 7.92 (d, J = 7.2 Hz, 1H), 7.88 – 7.70 (m, 2H), 3.29 (d, J = 4.2 Hz, 3H).	DMSO	338 (M+1)	1.50	Method D	100	Method AQ2
1257			337.4	1H NMR (300 MHz, DMSO) δ 9.64 (s, 1H), 8.77 (d, J = 7.9 Hz, 1H), 8.73 – 8.59 (m, 3H), 8.21 (d, J = 8.8 Hz, 1H), 8.11 – 7.94 (m, 4H), 7.87 (d, J = 8.7 Hz, 1H), 7.54 (dd, J = 7.9, 4.8 Hz, 1H), 3.18 (d, J = 4.0 Hz, 3H).	DMSO	338 (M+1)	1.50	Method D	100	Method AQ2

582

1258			346.8	1H NMR (300 MHz, DMSO) δ 9.64 (s, 1H), 8.77 (d, J = 7.9 Hz, 1H), 8.72 – 8.52 (m, 3H), 8.14 (d, J = 8.7 Hz, 1H), 7.97 – 7.74 (m, 3H), 7.68 – 7.45 (m, 3H), 3.18 (d, J = 4.0 Hz, 3H).	DMSO	347 (M+1)	1.60	Method D	100	Method AQ2
1259			346.8	1H NMR (300 MHz, DMSO) δ 9.64 (s, 1H), 8.78 (d, J = 8.0 Hz, 1H), 8.72 – 8.54 (m, 3H), 8.17 (d, J = 8.7 Hz, 1H), 7.94 (s, 1H), 7.90 – 7.78 (m, 2H), 7.61 – 7.42 (m, 3H), 3.19 (d, J = 4.4 Hz, 3H).	DMSO	347 (M+1)	1.66	Method D	100	Method AQ2
1260			372.4	1H NMR (300 MHz, DMSO) δ 9.63 (s, 1H), 8.77 (dd, J = 7.9, 1.8 Hz, 1H), 8.67 (d, J = 4.7 Hz, 1H), 8.46 (d, J = 4.4 Hz, 1H), 8.26 (s, 1H), 7.95 – 7.84 (m, 1H), 7.75 (d, J = 8.6 Hz, 1H), 7.53 (dd, J = 7.9, 4.8 Hz, 1H), 7.35 (d, J = 8.3 Hz, 1H), 6.77 – 6.60 (m, 2H), 3.80 (ss, 6H), 3.14 (d, J = 4.3 Hz, 3H).	DMSO	373 (M+1)	1.49	Method D	100	Method AQ2
1261			348.3	1H NMR (300 MHz, DMSO) δ 9.63 (s, 1H), 8.77 (dd, J = 8.0, 1.9 Hz, 1H), 8.66 (d, J = 4.6 Hz, 1H), 8.59 (s, 2H), 8.21 – 8.09 (m, 1H), 8.02 – 7.88 (m, 1H), 7.84 (d, J = 8.7 Hz, 1H), 7.71 (s, 1H), 7.67 – 7.58 (m, 1H), 7.53 (dd, J = 7.6, 5.1 Hz, 1H), 3.18 (d, J = 4.4 Hz, 3H).	DMSO	349 (M+1)	1.61	Method D	100	Method AQ2
1262			313.4	1H NMR (300 MHz, DMSO) δ 9.65 (s, 1H), 9.09 (s, 1H), 8.78 (d, J = 8.0 Hz, 1H), 8.73 – 8.55 (m, 4H), 8.30 – 8.14 (m, 2H), 7.89 (d, J = 8.6 Hz, 1H), 7.63 – 7.47 (m, 2H), 3.19 (d, J = 4.3 Hz, 3H).	DMSO	314 (M+1)	1.70	Method C	96	Method AQ2

583

1263			343.4	1H NMR (300 MHz, DMSO) δ 9.64 (d, J = 1.3 Hz, 1H), 8.84 – 8.74 (m, 1H), 8.66 (dd, J = 6.2, 1.7 Hz, 2H), 8.57 (d, J = 1.6 Hz, 2H), 8.16 (ddd, J = 14.4, 8.7, 2.2 Hz, 2H), 7.85 (d, J = 8.7 Hz, 1H), 7.54 (dd, J = 7.9, 4.8 Hz, 1H), 7.00 (d, J = 8.7 Hz, 1H), 3.93 (s, 3H), 3.18 (d, J = 4.3 Hz, 3H).	DMSO	344.1 (M+1)	1.94	Method C	95	Method AQ2
1264			356.4	1H NMR (300 MHz, DMSO) δ 10.76 (s, 1H), 9.75 (d, J = 1.6 Hz, 1H), 9.23 (d, J = 8.2 Hz, 1H), 9.05 - 8.86 (m, 2H), 8.41 - 8.24 (m, 2H), 8.24 - 8.05 (m, 2H), 7.96 (dd, J = 8.1, 5.2 Hz, 1H), 6.56 (d, J = 9.5 Hz, 1H), 4.81 (s, 2H), 3.34 (s, 3H), 3.29 (d, J = 4.3 Hz, 3H).	DMSO	357.1 (M+1)	2.13	Method C	100	Method AQ2
1265			342.4	1H NMR (300 MHz, DMSO) d 9.64 (s, 1H), 8.78 (dd, J = 8.0, 1.9 Hz, 1H), 8.67 (dd, J = 6.3, 4.7 Hz, 2H), 8.58 (s, 1H), 8.17 - 8.06 (m, 1H), 7.86 (d, J = 8.7 Hz, 1H), 7.79 (s, 1H), 7.72 (d, J = 7.6 Hz, 1H), 7.60 - 7.44 (m, 2H), 7.37 (d, J = 7.5 Hz, 1H), 5.31 (t, J = 5.4 Hz, 1H), 4.62 (d, J = 4.9 Hz, 2H), 3.18 (d, J = 4.4 Hz, 3H).	DMSO	343.1 (M+1)	1.76	Method C	99	Method AQ2
1266			344.4	1H NMR (300 MHz, DMSO) δ 9.65 (d, J = 2.1 Hz, 1H), 8.92 – 8.59 (m, 3H), 8.59 – 8.47 (m, 1H), 8.40 – 8.11 (m, 2H), 8.04 (d, J = 8.5 Hz, 1H), 7.56 (dd, J = 7.9, 4.8 Hz, 1H), 6.95 (d, J = 8.6 Hz, 1H), 4.29 (s, 3H), 3.93 (s, 3H).	DMSO	345.1 (M+1)	2.32	Method C	100	Method AQ2
1267			329.4	1H NMR (300 MHz, DMSO) δ 12.77 (s, 1H), 9.33 (d, J = 1.7 Hz, 1H), 8.77 (dd, J = 4.7, 1.5 Hz, 1H), 8.60 - 8.46 (m, 1H), 8.23 (d, J = 8.3 Hz, 1H), 8.04 (d, J = 1.5 Hz, 1H), 7.87 (dd, J = 8.3, 1.8 Hz, 1H), 7.67 - 7.53 (m, 1H), 7.52 - 7.29 (m, 3H), 7.04 (ddd, J = 7.7, 2.4, 1.5 Hz, 1H), 3.57 (s, 3H).	DMSO	330 (M+1)	1.76	Method C	100	Method AQ2

584

1268			342.4	1H NMR (300 MHz, DMSO) δ 9.65 (dd, J = 2.1, 0.8 Hz, 1H), 8.84 – 8.74 (m, 1H), 8.68 (dd, J = 4.7, 1.7 Hz, 1H), 8.52 (d, J = 4.4 Hz, 1H), 8.30 (d, J = 8.6 Hz, 1H), 8.03 (d, J = 1.7 Hz, 1H), 7.85 (dd, J = 8.5, 1.8 Hz, 1H), 7.54 (ddd, J = 8.0, 4.8, 0.8 Hz, 1H), 7.47 – 7.34 (m, 3H), 7.08 – 6.96 (m, 1H), 3.34 (s, 3H), 3.17 (d, J = 4.4 Hz, 3H).	DMSO	343.3 (M+1)	2.09	Method C		Method AQ2
1269			342.4	1H NMR (300 MHz, DMSO) δ 9.53 (d, J = 2.0 Hz, 1H), 8.65 (dd, J = 5.9, 3.5 Hz, 2H), 8.51 (d, J = 4.2 Hz, 1H), 8.23 (d, J = 8.3 Hz, 1H), 7.84 (d, J = 7.3 Hz, 1H), 7.65 - 7.25 (m, 5H), 7.00 (dd, J = 8.1, 2.6 Hz, 1H), 3.33 (s, 3H), 3.17 (d, J = 4.2 Hz, 3H).	DMSO	343.3 (M+1)	2.16	Method C	100	Method AQ2
1270		2HCl	374.5	1H NMR (300 MHz, DMSO) δ 10.67 (s, 1H), 9.69 (s, 1H), 9.12 (d, J = 11.6 Hz, 2H), 8.97 (d, J = 5.0 Hz, 1H), 8.43 (d, J = 7.4 Hz, 1H), 8.31 (d, J = 8.6 Hz, 1H), 8.20 (s, 1H), 8.07 (s, 1H), 7.98 – 7.86 (m, 1H), 7.77 (s, 2H), 3.31 (d, J = 3.9 Hz, 3H), 2.90 (s, 3H).	DMSO	375.1 (M+1)	1.67	Method C	95	Method AQ2
1271			374.5	1H NMR (300 MHz, DMSO) δ 9.70 – 9.57 (m, 1H), 8.84 – 8.72 (m, 1H), 8.73 – 8.62 (m, 3H), 8.19 (dd, J = 8.7, 1.9 Hz, 1H), 8.06 (d, J = 8.4 Hz, 2H), 7.86 (dd, J = 10.6, 8.5 Hz, 3H), 7.60 – 7.49 (m, 1H), 3.19 (d, J = 4.4 Hz, 2H), 2.81 (s, 3H).	DMSO	375.1 (M+1)	1.64	Method C	95	Method AQ2
1272		2HCl	425.5	1H NMR (300 MHz, DMSO) δ 10.54 (s, 1H), 9.70 (d, J = 1.7 Hz, 1H), 9.12 (d, J = 6.1 Hz, 1H), 8.98 (dd, J = 5.5, 4.0 Hz, 2H), 8.37 (dd, J = 26.8, 7.9 Hz, 2H), 8.09 – 7.84 (m, 3H), 7.63 (t, J = 7.7 Hz, 1H), 7.49 (d, J = 7.6 Hz, 1H), 3.67 (bs, 8H), 3.31 (d, J = 4.3 Hz, 3H).	DMSO	426.2 (M+1)	1.72	Method C	95	Method AQ2

585

1273		HCl	342.4	1H NMR (300 MHz, DMSO) δ 9.64 (s, 1H), 8.77 (d, J = 7.9 Hz, 1H), 8.71 – 8.65 (m, 1H), 8.60 (s, 1H), 8.53 (s, 1H), 8.10 (d, J = 8.7 Hz, 1H), 7.87 – 7.77 (m, 3H), 7.59 – 7.49 (m, 1H), 7.10 (d, J = 8.7 Hz, 2H), 3.83 (d, J = 0.9 Hz, 3H), 3.19 (s, 3H).	DMSO	343.1 (M+1)	2.06	Method C	100	Method AQ2
1274			329.4	1H NMR (300 MHz, DMSO) δ 9.34 (d, J = 1.5 Hz, 1H), 8.74 (dd, J = 4.8, 1.6 Hz, 1H), 8.53 (d, J = 8.0 Hz, 1H), 8.32 (d, J = 2.1 Hz, 1H), 8.10 (dd, J = 8.5, 2.3 Hz, 1H), 7.79 (d, J = 8.6 Hz, 1H), 7.76 (s, 1H), 7.73 (s, 1H), 7.58 (dd, J = 8.0, 4.8 Hz, 1H), 7.07 (d, J = 8.8 Hz, 2H), 3.82 (s, 3H).	DMSO	330.0 (M+1)	1.75	Method C	100	Method AQ2
1275			343.4	1H NMR (300 MHz, DMSO) δ 9.65 (d, J = 1.5 Hz, 1H), 8.84 – 8.65 (m, 4H), 8.31 (d, J = 5.4 Hz, 1H), 8.24 (dd, J = 8.7, 1.9 Hz, 1H), 7.87 (d, J = 8.7 Hz, 1H), 7.59 – 7.46 (m, 2H), 7.33 (d, J = 0.9 Hz, 1H), 3.93 (s, 3H), 3.20 (d, J = 4.4 Hz, 3H).	DMSO	344.1 (M+1)	1.95	Method C	95	Method AQ2
1276			331.3	1H NMR (300 MHz, DMSO) δ 9.63 (d, J = 1.4 Hz, 1H), 8.81 - 8.74 (m, 1H), 8.73 (d, J = 2.3 Hz, 1H), 8.68 (dd, J = 4.7, 1.7 Hz, 1H), 8.66 - 8.56 (m, 2H), 8.44 (td, J = 8.2, 2.6 Hz, 1H), 8.18 (dd, J = 8.7, 2.0 Hz, 1H), 7.87 (d, J = 8.7 Hz, 1H), 7.54 (dd, J = 7.9, 4.8 Hz, 1H), 7.38 (dd, J = 8.5, 2.9 Hz, 1H), 3.18 (d, J = 4.4 Hz, 3H).	DMSO	332.1 (M+1)	1.89	Method C	100	Method AQ2
1277			425.5	1H NMR (300 MHz, DMSO) δ 9.63 (d, J = 1.4 Hz, 1H), 8.77 (d, J = 8.0 Hz, 1H), 8.70 - 8.59 (m, 3H), 8.15 (dd, J = 8.7, 1.6 Hz, 1H), 7.92 (d, J = 8.2 Hz, 2H), 7.85 (d, J = 8.7 Hz, 1H), 7.62 - 7.48 (m, 3H), 3.62 (s, J = 54.7 Hz, 8H), 3.17 (d, J = 4.2 Hz, 3H).	DMSO	426.2 (M+1)	1.69	Method C	100	Method AQ2

586

1278			343.4	1H NMR (300 MHz, DMSO) δ 9.67 (d, J = 1.5 Hz, 1H), 8.86 – 8.77 (m, 1H), 8.74 (dd, J = 4.7, 1.6 Hz, 1H), 8.37 – 8.25 (m, 2H), 8.06 (d, J = 8.7 Hz, 1H), 7.60 (dd, J = 7.9, 4.1 Hz, 1H), 7.50 – 7.30 (m, 3H), 7.02 (dd, J = 7.9, 1.4 Hz, 1H), 4.31 (s, 3H), 3.87 (s, 3H).	DMSO	344.2 (M+1)	2.47	Method C	100	Method AQ2

587

Number	Starting Material 1	Starting Material 2	Product	Salt type	^{1}H NMR	^{1}H NMR Solvent	Purity percent	Method of Coupling	LCMS	LCMS Method
1279				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 9.69 (d, *J* = 1.8 Hz, 1H), 9.40 – 9.33 (m, 1H), 9.03 – 8.93 (m, 2H), 8.64 – 8.59 (m, 1H), 8.18 – 8.14 (m, 1H), 8.13 – 8.05 (m, 3H), 8.04 – 7.97 (m, 2H), 3.21 (d, *J* = 4.4 Hz, 3H), 2.77 (s, 3H).	DMSO	>98	AQ3		
1280				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 9.71 – 9.65 (m, 1H), 9.44 – 9.36 (m, 1H), 9.06 – 8.94 (m, 2H), 8.59 – 8.54 (m, 1H), 8.19 – 8.10 (m, 2H), 7.79 – 7.71 (m, 2H), 7.61 – 7.54 (m, 1H), 7.29 – 7.22 (m, 1H), 3.21 (d, *J* = 3.9 Hz, 3H), 2.76 (s, 3H).	DMSO	>98	AQ3		
1281				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 9.72 – 9.65 (m, 1H), 9.43 – 9.36 (m, 1H), 9.04 – 8.91 (m, 2H), 8.63 – 8.55 (m, 1H), 8.36 – 8.31 (m, 1H), 8.26 – 8.20 (m, 1H), 8.20 – 8.11 (m, 2H), 7.91 – 7.85 (m, 1H), 7.78 – 7.70 (m, 1H), 3.22 (d, *J* = 4.2 Hz, 3H), 2.76 (s, 3H).	DMSO	>98	AQ3		

1282				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 9.70 – 9.65 (m, 1H), 9.37 (d, *J* = 8.2 Hz, 1H), 9.03 – 8.90 (m, 2H), 8.49 – 8.42 (m, 1H), 8.12 (dd, *J* = 8.1, 5.6 Hz, 1H), 8.08 – 8.03 (m, 1H), 7.88 – 7.78 (m, 2H), 7.15 – 7.04 (m, 2H), 3.84 (s, 3H), 3.21 (d, *J* = 3.9 Hz, 3H), 2.76 (s, 3H).	DMSO	>98	AQ3		
1283				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 9.73 – 9.67 (m, 1H), 9.36 (d, *J* = 7.4 Hz, 1H), 9.02 – 8.96 (m, 1H), 8.82 (s, 1H), 8.26 – 8.19 (m, 1H), 8.15 – 8.07 (m, 1H), 7.89 – 7.83 (m, 1H), 7.47 – 7.38 (m, 2H), 7.21 – 7.15 (m, 1H), 7.14 – 7.06 (m, 1H), 3.81 (s, 3H), 3.19 (d, J= 4.5 Hz, 3H), 2.77 (s, 3H).	DMSO	>98	AQ3		
1284				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 9.72 (d, *J* = 1.8 Hz, 1H), 9.34 – 9.28 (m, 1H), 8.95 (dd, *J* = 5.4, 1.4 Hz, 1H), 8.88 – 8.78 (m, 1H), 8.38 (d, *J* = 1.5 Hz, 1H), 8.07 – 8.00 (m, 2H), 7.95 – 7.90 (m, 1H), 7.90 – 7.83 (m, 1H), 7.76 (dd, *J* = 7.8, 0.7 Hz, 1H), 7.68 – 7.63 (m, 1H), 3.19 (d, *J* = 4.5 Hz, 3H), 2.77 (s, 3H).	DMSO	>98	AQ3		
1285					^{1}H NMR (400 MHz, DMSO) δ 9.63 (dd, *J* = 2.1, 0.8 Hz, 1H), 8.80 – 8.75 (m, 1H), 8.69 (dd, *J* = 3.7, 1.8 Hz, 1H), 7.72 (d, *J* = 8.5 Hz, 1H), 7.61 (d, *J* = 8.5 Hz, 1H), 7.58 – 7.49 (m, 2H), 7.46 – 7.40 (m, 1H), 7.39 – 7.32 (m, 1H), 7.28 – 7.18 (m, 1H), 3.18 (d, *J* = 4.4 Hz, 3H), 2.64 (s, 3H).	DMSO	>98	AQ4		

589

1286				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 9.67 – 9.60 (m, 1H), 9.06 – 8.88 (m, 3H), 8.12 (d, *J* = 8.8 Hz, 1H), 7.91 – 7.79 (m, 2H), 7.53 – 7.40 (m, 2H), 7.34 – 7.24 (m, 1H), 3.34 (d, *J* = 4.6 Hz, 3H), 2.66 (s, 3H).	DMSO	>98	AQ4		
1287				HCl	^{1}H NMR (400 MHz, DMSO) δ 9.62 – 9.57 (m, 1H), 8.94 – 8.86 (m, 2H), 8.62 (s, 1H), 7.95 (d, *J* = 8.5 Hz, 1H), 7.86 – 7.75 (m, 2H), 7.52 – 7.36 (m, 2H), 7.35 – 7.28 (m, 1H), 3.31 (d, *J* = 4.5 Hz, 3H), 2.67 (s, 3H).	DMSO	>98	AQ4		
1288				HCl	^{1}H NMR (400 MHz, DMSO) δ 9.63 – 9.58 (m, 1H), 8.95 – 8.86 (m, 2H), 8.73 (s, 1H), 8.01 (d, *J* = 8.5 Hz, 1H), 7.87 – 7.75 (m, 2H), 7.61 – 7.50 (m, 1H), 7.45 – 7.33 (m, 3H), 3.32 (d, *J* = 4.5 Hz, 3H), 2.66 (s, 3H).	DMSO	>98	AQ4		
1289				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 9.64 – 9.60 (m, 1H), 9.00 – 8.86 (m, 3H), 8.06 (d, *J* = 8.5 Hz, 1H), 7.91 – 7.79 (m, 2H), 7.65 – 7.55 (m, 1H), 7.37 – 7.29 (m, 1H), 7.29 – 7.22 (m, 2H), 3.35 (d, *J* = 4.6 Hz, 3H), 2.72 (s, 3H).	DMSO	>98	AQ4		
1290				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 9.69 – 9.64 (m, 1H), 9.14 – 8.99 (m, 2H), 8.96 (dd, *J* = 5.0, 1.5 Hz, 1H), 8.15 (d, *J* = 8.6 Hz, 1H), 7.90 – 7.81 (m, 2H), 7.50 – 7.34 (m, 4H), 3.35 (d, *J* = 4.6 Hz, 3H), 2.72 (s, 3H).	DMSO	>98	AQ4		

590

1291				HCl	^{1}H NMR (300 MHz, $CDCl_3$) δ 9.63 (s, 2H), 8.96 (d, *J* = 8.2 Hz, 1H), 8.90 (d, *J* = 5.0 Hz, 1H), 8.50 (s, 1H), 8.16 – 7.99 (m, 2H), 7.82 (dd, *J* = 8.0, 4.9 Hz, 1H), 7.71 – 7.62 (m, 1H), 7.61 – 7.47 (m, 3H), 3.26 (d, *J* = 4.5 Hz, 3H).	DMSO	>98	G2/AQ3		
1292				2 HCl	^{1}H NMR (300 MHz, $CDCl_3$) δ 10.27 (s, 1H), 9.69 (s, 1H), 9.09 (d, *J* = 8.1 Hz, 1H), 8.97 (d, *J* = 5.0 Hz, 1H), 8.56 (s, 1H), 8.32 (d, *J* = 8.6 Hz, 1H), 8.04 (d, *J* = 8.7 Hz, 1H), 7.89 (dd, *J* = 8.0, 5.1 Hz, 1H), 7.45 – 7.26 (m, 4H), 3.29 (d, *J* = 4.2 Hz, 3H), 2.32 (s, 3H).	DMSO	>98	G2/AQ3		
1293				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 10.40 (s, 1H), 9.73 (s, 1H), 9.15 (d, *J* = 7.9 Hz, 1H), 8.98 (d, *J* = 5.1 Hz, 1H), 8.67 (s, 1H), 8.33 (d, *J* = 8.6 Hz, 1H), 8.18 (d, *J* = 8.7 Hz, 1H), 7.91 (dd, *J* = 7.9, 5.2 Hz, 1H), 7.45 (m, 2H), 7.20 (d, *J* = 8.2 Hz, 1H), 7.12 (t, *J* = 7.5 Hz, 1H), 3.82 (s, 3H), 3.29 (d, *J* = 4.1 Hz, 3H).	DMSO	>98	G2/AQ3		
1294					^{1}H NMR (300 MHz, $CDCl_3$) δ 9.66 (s, 1H), 8.80 (d, *J* = 7.9 Hz, 1H), 8.74 – 8.67 (m, 1H), 8.60 (m, 1H), 8.49 (s, 1H), 8.00 (dd, *J* = 18.5, 10.4 Hz, 2H), 7.96 – 7.81 (m, 2H), 7.76 (d, *J* = 7.6 Hz, 1H), 7.65 (t, *J* = 7.6 Hz, 1H), 7.56 (dd, *J* = 7.6, 5.0 Hz, 1H), 3.18 (d, *J* = 4.2 Hz, 3H).	DMSO	>98	G2/AQ3		

591

1295				2 HCl	^{1}H NMR (300 MHz, $CDCl_3$) δ 9.88 (s, 1H), 9.66 (s, 1H), 9.01 (d, *J* = 8.3 Hz, 1H), 8.90 (d, *J* = 4.2 Hz, 1H), 8.70 (s, 1H), 8.27 – 8.08 (m, 2H), 7.81 (dd, *J* = 8.0, 5.1 Hz, 1H), 7.72 (t, *J* = 7.6 Hz, 1H), 7.60 – 7.48 (m, 1H), 7.48 – 7.27 (m, 2H), 3.27 (d, *J* = 4.3 Hz, 3H).	DMSO	>98	G2/AQ3		
1296				2 HCl	^{1}H NMR (300 MHz, $CDCl_3$) δ 9.63 (m, 2H), 8.93 (d, *J* = 7.7 Hz, 1H), 8.88 (d, *J* = 4.1 Hz, 1H), 8.76 (s, 1H), 8.29 (d, *J* = 8.4 Hz, 1H), 8.07 (d, *J* = 8.8 Hz, 1H), 7.94 (dd, *J* = 8.6, 5.5 Hz, 2H), 7.82 – 7.73 (m, 1H), 7.41 (t, *J* = 8.7 Hz, 2H), 3.28 (d, *J* = 4.3 Hz, 3H).	DMSO	>98	G2/AQ3		
1297				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 9.82 (s, 1H), 9.64 (d, *J* = 1.7 Hz, 1H), 9.00 (d, *J* = 8.0 Hz, 1H), 8.95 – 8.86 (m, 2H), 8.69 (t, *J* = 1.9 Hz, 1H), 8.51 – 8.34 (m, 2H), 8.30 (dd, *J* = 7.9, 1.8 Hz, 1H), 8.13 (d, *J* = 8.7 Hz, 1H), 7.93 – 7.76 (m, 2H), 3.30 (d, *J* = 4.5 Hz, 3H).	DMSO	>98	G2/AQ3		
1298				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 10.30 (s, 1H), 9.70 (d, *J* = 2.1 Hz, 1H), 9.11 (d, *J* = 8.2 Hz, 1H), 9.04 – 8.83 (m, 1H), 8.56 (s, 1H), 8.26 (d, *J* = 8.6 Hz, 1H), 8.01 – 7.80 (m, 3H), 7.78 – 7.64 (m, 1H), 7.60 (t, *J* = 7.2 Hz, 1H), 7.54 (d, *J* = 7.2 Hz, 1H), 3.29 (d, *J* = 4.4 Hz, 3H), 2.44 (s, 3H).	DMSO	>98	G2/AQ3		

592

1299					^{1}H NMR (300 MHz, DMSO) δ 10.50 (s, 1H), 9.66 (s, 1H), 9.09 (d, *J* = 8.2 Hz, 1H), 9.01 (s, 1H), 8.94 (d, *J* = 5.0 Hz, 1H), 8.40 (d, *J* = 8.7 Hz, 1H), 8.28 (d, *J* = 8.8 Hz, 1H), 8.13 – 8.00 (m, 4H), 7.88 (dd, *J* = 8.0, 5.2 Hz, 1H), 3.30 (d, *J* = 4.1 Hz, 3H), 2.62 (s, 3H).	DMSO	>98	G2/AQ3		
1300				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 10.49 (s, 1H), 9.66 (s, 1H), 9.09 (d, *J* = 7.9 Hz, 1H), 9.01 (s, 1H), 8.95 (d, *J* = 5.0 Hz, 1H), 8.40 (d, *J* = 8.6 Hz, 1H), 8.29 (d, *J* = 8.7 Hz, 1H), 8.15 – 7.94 (m, 4H), 7.88 (dd, *J* = 7.9, 5.2 Hz, 1H), 3.31 (d, *J* = 4.1 Hz, 3H), 2.63 (s, 3H).	DMSO	>98	G2/AQ3		
1301				3 HCl	^{1}H NMR (300 MHz, DMSO) δ 10.97 (s, 1H), 9.71 (d, *J* = 2.0 Hz, 1H), 9.29 (s, 1H), 9.15 (d, *J* = 8.0 Hz, 1H), 8.98 (dd, *J* = 5.0, 1.3 Hz, 1H), 8.49 – 8.38 (m, 1H), 8.34 (d, *J* = 8.8 Hz, 1H), 8.21 (s, 1H), 7.92 (dd, *J* = 8.1, 5.1 Hz, 1H), 7.84 (s, 1H), 7.69 – 7.52 (m, 2H), 3.31 (d, *J* = 4.3 Hz, 3H), 3.23 (s, 6H).	DMSO	>98	G2/AQ3		
1302				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 10.33 (s, 1H), 9.73 (d, *J* = 1.7 Hz, 1H), 9.20 (d, *J* = 8.0 Hz, 1H), 9.00 (d, *J* = 4.2 Hz, 1H), 8.68 (s, 1H), 8.32 (d, *J* = 8.6 Hz, 1H), 8.16 (d, *J* = 7.9 Hz, 1H), 8.01 – 7.93 (m, 2H), 7.90 (t, *J* = 7.2 Hz, 1H), 7.74 (dd, *J* = 15.4, 7.7 Hz, 2H), 3.24 (t, *J* = 18.2 Hz, 3H).	DMSO	>98	G2/AQ3		

1303				HCl	^{1}H NMR (300 MHz, DMSO) δ 10.46 (s, 1H), 9.76 (d, *J* = 2.1 Hz, 1H), 9.21 (d, *J* = 8.2 Hz, 1H), 9.00 (dd, *J* = 5.1, 1.2 Hz, 1H), 8.58 (d, *J* = 1.3 Hz, 1H), 8.41 (d, *J* = 8.6 Hz, 1H), 8.08 – 7.86 (m, 2H), 7.36 – 7.09 (m, 3H), 3.29 (d, *J* = 4.3 Hz, 3H), 2.33 (s, 3H), 2.17 (s, 3H).	DMSO	>98	G2/AQ3		
1304					^{1}H NMR (300 MHz, DMSO) δ 9.65 (d, *J* = 2.1 Hz, 1H), 8.79 (dt, *J* = 8.0, 1.9 Hz, 1H), 8.69 (dd, *J* = 4.7, 1.6 Hz, 1H), 8.46 (d, *J* = 4.5 Hz, 1H), 8.20 (d, *J* = 1.7 Hz, 1H), 7.83 (d, *J* = 8.5 Hz, 1H), 7.75 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.54 (dd, *J* = 7.9, 4.8 Hz, 1H), 7.28 – 7.02 (m, 3H), 3.33 (s, 6H), 3.15 (d, *J* = 4.4 Hz, 3H), 2.51 (dt, *J* = 3.6, 1.7 Hz, 1H), 2.35 (s, 3H), 2.27 (s, 3H).	DMSO	>98	G2/AQ3		
1305				HCl	^{1}H NMR (300 MHz, DMSO) δ 10.48 (s, 1H), 9.70 (s, 1H), 9.11 (d, *J* = 7.8 Hz, 1H), 8.97 (d, *J* = 4.7 Hz, 1H), 8.90 (s, 1H), 8.36 (d, *J* = 8.6 Hz, 1H), 8.29 (d, *J* = 8.7 Hz, 1H), 7.98 – 7.80 (m, 1H), 7.74 (s, 1H), 7.65 (d, *J* = 7.5 Hz, 1H), 7.30 (d, *J* = 7.8 Hz, 1H), 3.32 (d, *J* = 4.0 Hz, 3H), 2.33 (d, *J* = 10.0 Hz, 3H), 2.29 (s, 3H).	DMSO	>98	G2/AQ3		
1306				HCl	^{1}H NMR (300 MHz, DMSO) δ 10.45 – 10.35 (m, 1H), 9.69 (s, 1H), 9.09 (s, 1H), 8.99 (s, 1H), 8.88 (s, 1H), 8.37 (d, *J* = 8.6 Hz, 1H), 8.28 (d, *J* = 8.7 Hz, 1H), 7.94 (s, 1H), 7.54 (s, 1H), 7.11 (s, 1H), 3.34 (d, *J* = 4.3 Hz, 3H), 2.40 (s, 3H).	DMSO	>98	G2/AQ3		

594

1307				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 10.28 (s, 1H), 9.84 – 9.66 (m, 1H), 9.17 (d, *J* = 8.1 Hz, 1H), 8.99 (d, *J* = 5.0 Hz, 1H), 8.46 (s, 1H), 8.36 (d, *J* = 8.6 Hz, 1H), 7.98 – 7.80 (m, 2H), 7.41 (t, *J* = 8.4 Hz, 1H), 6.83 (d, *J* = 8.4 Hz, 2H), 3.71 (s, 6H), 3.29 (d, *J* = 4.2 Hz, 3H).	DMSO	>98	G2/AQ3		
1308				HCl	^{1}H NMR (300 MHz, DMSO) δ 9.64 (s, 1H), 8.96 – 8.91 (m, 1H), 8.89 – 8.83 (m, 2H), 8.41 (d, *J* = 9.1 Hz, 2H), 8.38 – 8.32 (m, 1H), 8.16 (d, *J* = 9.0 Hz, 2H), 8.02 (d, *J* = 9.1 Hz, 1H), 7.81 – 7.73 (m, 1H), 3.27 (d, *J* = 4.3 Hz, 3H).	DMSO	>98	G2/AQ3		
1309					^{1}H NMR (300 MHz, DMSO) δ 9.64 (d, *J* = 2.0 Hz, 1H), 8.78 (ddd, *J* = 14.6, 8.2, 6.5 Hz, 1H), 8.70 (dd, *J* = 4.7, 1.4 Hz, 1H), 8.56 (d, *J* = 4.3 Hz, 1H), 8.33 (d, *J* = 1.5 Hz, 1H), 8.06 (dd, *J* = 8.6, 1.4 Hz, 1H), 7.81 (d, *J* = 8.6 Hz, 1H), 7.56 (dd, *J* = 7.9, 4.8 Hz, 1H), 7.34 (t, *J* = 7.5 Hz, 2H), 7.20 – 7.00 (m, 2H), 3.16 (d, *J* = 4.4 Hz, 3H).	DMSO	>98	G2/AQ3		
1310				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 10.63 (s, 1H), 9.69 (s, 1H), 9.16 (s, 1H), 9.10 (d, *J* = 7.9 Hz, 1H), 8.97 (d, *J* = 5.0 Hz, 1H), 8.52 (s, 1H), 8.45 (d, *J* = 8.7 Hz, 1H), 8.29 (d, *J* = 8.7 Hz, 2H), 8.07 (d, *J* = 7.8 Hz, 1H), 8.01 – 7.84 (m, 2H), 7.63 (t, *J* = 7.8 Hz, 1H), 7.54 (s, 1H), 3.31 (d, *J* = 4.3 Hz, 3H).	DMSO	>98	G2/AQ3		

595

1311				HCl	^{1}H NMR (300 MHz, DMSO) δ 10.20 (s, 1H), 9.65 (s, 1H), 9.02 (s, 1H), 8.95 (s, 2H), 8.43 (d, *J* = 8.7 Hz, 1H), 8.26 – 8.14 (m, 1H), 8.04 (dd, *J* = 18.8, 8.1 Hz, 4H), 7.88 (s, 1H), 7.47 (s, 1H), 3.32 (s, 3H), 3.17 (d, *J* = 1.8 Hz, 9H).	DMSO	>98	G2/AQ3		
1312				HCl	^{1}H NMR (300 MHz, DMSO) δ 9.79 (s, 1H), 9.66 (d, *J* = 1.7 Hz, 1H), 9.02 (d, *J* = 8.1 Hz, 1H), 8.96 – 8.86 (m, 1H), 8.57 (s, 1H), 8.18 (d, *J* = 8.7 Hz, 1H), 8.05 (dd, *J* = 8.7, 1.4 Hz, 1H), 7.82 (dd, *J* = 8.1, 5.0 Hz, 1H), 7.79 – 7.72 (m, 1H), 7.64 – 7.45 (m, 2H), 3.25 (d, *J* = 4.4 Hz, 3H).	DMSO	>98	G2/AQ3		
1313				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 10.01 (s, 1H), 9.65 (s, 1H), 9.06 (d, *J* = 7.8 Hz, 1H), 8.95 (d, *J* = 4.8 Hz, 1H), 8.59 (s, 1H), 8.21 (d, *J* = 8.6 Hz, 1H), 8.07 (d, *J* = 9.1 Hz, 1H), 7.95 – 7.77 (m, 2H), 7.66 – 7.52 (m, 2H), 3.27 (d, *J* = 4.3 Hz, 3H), 3.17 (d, *J* = 0.7 Hz, 1H).	DMSO	>98	G2/AQ3		
1314				HCl	^{1}H NMR (300 MHz, DMSO) δ 10.10 (s, 1H), 9.69 (s, 1H), 9.13 (d, *J* = 8.0 Hz, 1H), 8.98 (d, *J* = 5.1 Hz, 1H), 8.62 (s, 1H), 8.27 (d, *J* = 8.6 Hz, 1H), 8.13 (d, *J* = 8.3 Hz, 1H), 8.02 – 7.83 (m, 1H), 7.77 – 7.65 (m, 2H), 7.60 (d, *J* = 8.5 Hz, 1H), 3.29 (d, *J* = 3.9 Hz, 3H).	DMSO	>98	G2/AQ3		

596

1315				HCl	^{1}H NMR (300 MHz, DMSO) δ 9.62 (s, 1H), 9.02 – 8.93 (m, 1H), 8.89 (d, *J* = 4.5 Hz, 1H), 8.80 (s, 1H), 8.35 (d, *J* = 8.7 Hz, 1H), 8.18 (s, 1H), 8.04 (d, *J* = 8.7 Hz, 1H), 7.96 – 7.75 (m, 2H), 3.29 (d, *J* = 4.2 Hz, 3H).	DMSO	>98	G2/AQ3		
1316				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 10.36 (s, 1H), 9.67 (s, 1H), 9.13 (d, *J* = 8.2 Hz, 1H), 9.01 – 8.82 (m, 2H), 8.40 (d, *J* = 9.1 Hz, 1H), 8.26 (d, *J* = 8.7 Hz, 1H), 7.97 (s, 2H), 7.90 (dd, *J* = 8.0, 5.2 Hz, 1H), 7.65 (s, 1H), 3.31 (d, *J* = 4.3 Hz, 3H).	DMSO	>98	G2/AQ3		
1317					^{1}H NMR (300 MHz, DMSO) δ 9.65 (d, *J* = 1.9 Hz, 1H), 8.89 – 8.75 (m, 1H), 8.74 – 8.67 (m, 1H), 8.67 – 8.56 (m, 1H), 8.48 (s, 1H), 8.06 – 7.94 (m, 1H), 7.87 (d, *J* = 8.7 Hz, 1H), 7.68 – 7.51 (m, 2H), 7.46 (td, *J* = 9.6, 4.7 Hz, 1H), 7.39 – 7.21 (m, 1H), 3.18 (d, *J* = 4.4 Hz, 3H).	DMSO	>98	G2/AQ3		
1318				HCl	^{1}H NMR (300 MHz, DMSO) δ 10.57 (s, 1H), 9.69 (d, *J* = 2.0 Hz, 1H), 9.15 (d, *J* = 8.0 Hz, 1H), 9.02 (s, 1H), 8.97 (d, *J* = 4.4 Hz, 1H), 8.40 (d, *J* = 8.8 Hz, 1H), 8.29 (d, *J* = 8.7 Hz, 1H), 7.91 (dd, *J* = 8.0, 5.2 Hz, 1H), 7.77 – 7.63 (m, 2H), 7.37 – 7.18 (m, 1H), 3.29 (d, *J* = 4.3 Hz, 3H).	DMSO	>98	G2/AQ3		
1319					^{1}H NMR (300 MHz, $CDCl_3$) δ 9.58 (d, *J* = 2.0 Hz, 1H), 8.78 – 8.60 (m, 2H), 8.35 (d, *J* = 1.7 Hz, 1H), 8.11 – 7.84 (m, 3H), 7.78 (d, *J* = 8.6 Hz, 1H), 7.54 (dd, *J* = 7.9, 4.8 Hz, 1H), 7.48 – 7.34 (m, 2H), 7.17 (d, *J* = 8.1 Hz, 1H), 7.10 (t, *J* = 7.4 Hz, 1H), 3.81 (s, 3H).	DMSO	>98	G2/AQ3		

597

1320					^{1}H NMR (300 MHz, $CDCl_3$) δ 9.62 (d, *J* = 2.1 Hz, 1H), 8.82 – 8.72 (m, 1H), 8.72 – 8.66 (m, 1H), 8.30 (s, 1H), 7.93 (dd, *J* = 8.7, 1.2 Hz, 1H), 7.86 (d, *J* = 8.6 Hz, 1H), 7.54 (dd, *J* = 7.9, 4.8 Hz, 1H), 7.50 – 7.33 (m, 2H), 7.18 (d, *J* = 8.3 Hz, 1H), 7.09 (t, *J* = 7.5 Hz, 1H), 3.82 (s, 3H), 3.46 (s, 6H).	DMSO	>98	G2/AQ3		
1321					^{1}H NMR (300 MHz, $CDCl_3$) δ 9.59 (d, *J* = 2.1 Hz, 1H), 8.76 – 8.66 (m, 2H), 8.50 (s, 2H), 8.06 (brs, 1H), 7.99 (dt, *J* = 8.6, 1.7 Hz, 1H), 7.86 (d, *J* = 8.7 Hz, 1H), 7.75 – 7.63 (m, 1H), 7.54 (dd, *J* = 7.9, 4.8 Hz, 1H), 7.52 – 7.44 (m, 1H), 7.44 – 7.32 (m, 2H).	DMSO	>98	G2/AQ3		
1322					^{1}H NMR (300 MHz, $CDCl_3$) δ 9.59 (d, *J* = 2.1 Hz, 1H), 8.79 – 8.62 (m, 3H), 8.21 (dd, *J* = 8.8, 1.9 Hz, 1H), 8.10 (brs, 2H), 7.86 (d, *J* = 8.7 Hz, 1H), 7.80 – 7.69 (m, 2H), 7.68 – 7.49 (m, 2H), 7.32 – 7.20 (m, 1H).	DMSO	>98	G2/AQ3		
1323					^{1}H NMR (300 MHz, $CDCl_3$) δ 9.58 (d, *J* = 2.0 Hz, 1H), 8.80 – 8.64 (m, 2H), 8.62 (d, *J* = 1.8 Hz, 1H), 8.14 (dd, *J* = 8.7, 1.9 Hz, 1H), 8.07 (brs, 2H), 7.98 – 7.87 (m, 2H), 7.85 (d, *J* = 8.7 Hz, 1H), 7.54 (dd, *J* = 7.9, 4.8 Hz, 1H), 7.38 (t, *J* = 8.8 Hz, 2H).	DMSO	>98	G2/AQ3		

598

1324					^{1}H NMR (300 MHz, $CDCl_3$) δ 9.65 – 9.57 (m, 1H), 8.82 – 8.70 (m, 1H), 8.70 – 8.63 (m, 1H), 8.36 (d, *J* = 1.8 Hz, 1H), 8.11 (dd, *J* = 8.7, 1.7 Hz, 1H), 7.89 (d, *J* = 8.7 Hz, 1H), 7.72 – 7.60 (m, 2H), 7.60 – 7.47 (m, 2H), 7.32 – 7.18 (m, 1H), 3.49 (s, 6H).	DMSO	>98	G2/AQ3		
1325					^{1}H NMR (400 MHz, DMSO) δ 9.64 (d, *J* = 1.4 Hz, 1H), 8.78 (dt, *J* = 8.3, 1.8 Hz, 1H), 8.69 (dd, *J* = 4.7, 1.8 Hz, 1H), 8.61 – 8.46 (m, 2H), 8.40 (d, *J* = 1.6 Hz, 1H), 7.99 (dd, *J* = 9.0, 1.8 Hz, 1H), 7.83 (d, *J* = 9.0 Hz, 1H), 7.54 (dd, *J* = 8.4, 4.5 Hz, 1H), 3.99 (d, *J* = 8.9 Hz, 6H), 3.17 (d, *J* = 4.6 Hz, 3H).	DMSO	>98	G2/AQ3		
1326					^{1}H NMR (300 MHz, DMSO) δ 9.64 – 9.55 (m, 1H), 8.81 – 8.62 (m, 3H), 8.40 (s, 1H), 8.23 (dd, *J* = 8.8, 1.4 Hz, 1H), 8.13 (d, *J* = 7.7 Hz, 1H), 8.00 (d, *J* = 7.7 Hz, 2H), 7.89 (d, *J* = 8.7 Hz, 1H), 7.69 (t, *J* = 7.7 Hz, 1H), 7.54 (dd, *J* = 7.9, 4.8 Hz, 1H), 2.71 (s, 3H).	DMSO	>98	G2/AQ3		
1327					^{1}H NMR (300 MHz, DMSO) δ 9.58 (d, *J* = 2.1 Hz, 1H), 8.76 – 8.65 (m, 3H), 8.24 (dd, *J* = 8.7, 1.8 Hz, 1H), 8.19 – 7.93 (m, 6H), 7.88 (d, *J* = 8.8 Hz, 1H), 7.54 (dd, *J* = 7.9, 4.8 Hz, 1H), 2.65 (s, 3H).	DMSO	>98	G2/AQ3		

599

1328					^{1}H NMR (300 MHz, DMSO) δ 9.60 (d, J = 1.8 Hz, 1H), 8.73 (dt, J = 8.0, 1.8 Hz, 1H), 8.69 (dd, J = 4.8, 1.6 Hz, 1H), 8.37 (s, 1H), 7.99 (brs, 2H), 7.92 – 7.81 (m, 2H), 7.67 – 7.60 (m, 1H), 7.60 – 7.52 (m, 2H), 7.52 – 7.43 (m, 2H).	DMSO	>98	G2/AQ3		
1329					^{1}H NMR (300 MHz, DMSO) δ 9.60 (d, J = 2.0 Hz, 1H), 8.77 – 8.65 (m, 3H), 8.19 (dd, J = 8.7, 1.8 Hz, 1H), 8.09 (brs, 2H), 7.99 – 7.94 (m, 1H), 7.90 – 7.79 (m, 2H), 7.63 – 7.51 (m, 2H), 7.48 (d, J = 8.1 Hz, 1H).	DMSO	>98	G2/AQ3		
1330					^{1}H NMR (300 MHz, DMSO) δ 9.65 (s, 1H), 8.87 – 8.75 (m, 1H), 8.70 (s, 1H), 8.55 (s, 1H), 8.41 (s, 1H), 8.25 (s, 1H), 8.09 – 7.76 (m, 3H), 7.62 – 7.44 (m, 1H), 7.18 (s, 1H), 3.93 (s, 3H), 3.17 (s, 3H).	DMSO	>98	G2/AQ3		
1331					^{1}H NMR (300 MHz, DMSO) δ 9.61 (s, 1H), 8.75 (d, J = 7.6 Hz, 1H), 8.68 (s, 1H), 8.45 (s, 1H), 8.18 (d, J = 9.2 Hz, 1H), 8.07 (d, J = 8.2 Hz, 2H), 8.01 – 7.87 (m, 3H), 7.55 (s, 1H), 3.51 (s, 6H), 2.63 (s, 3H).	DMSO	>98	G2/AQ3		
1332					^{1}H NMR (300 MHz, DMSO) δ 9.63 (s, 1H), 8.83 – 8.72 (m, 1H), 8.70 (d, J = 3.8 Hz, 1H), 8.21 (s, 1H), 7.89 (q, J = 8.6 Hz, 2H), 7.74 – 7.41 (m, 5H), 3.47 (s, 6H).	DMSO	>98	G2/AQ3		

1333					^{1}H NMR (300 MHz, DMSO) δ 9.62 (d, *J* = 2.0 Hz, 1H), 8.76 (dt, *J* = 7.9, 1.8 Hz, 1H), 8.70 (dd, *J* = 4.8, 1.6 Hz, 1H), 8.38 (d, *J* = 1.9 Hz, 1H), 8.13 (dd, *J* = 8.7, 1.9 Hz, 1H), 7.98 – 7.84 (m, 2H), 7.78 (d, *J* = 7.6 Hz, 1H), 7.66 – 7.41 (m, 3H), 3.51 (s, 6H).	DMSO	>98	G2/AQ3		
1334				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 9.81 – 9.63 (m, 1H), 9.18 (d, *J* = 8.4 Hz, 1H), 9.07 – 8.89 (m, 1H), 8.39 (d, *J* = 8.7 Hz, 1H), 8.31 (d, *J* = 1.7 Hz, 1H), 8.22 – 8.07 (m, 1H), 8.02 (dd, *J* = 8.7, 1.7 Hz, 1H), 7.98 – 7.91 (m, 1H), 7.91 – 7.83 (m, 1H), 7.80 – 7.68 (m, 2H), 3.65 (s, 6H).	DMSO	>98	G2/AQ3		
1335					^{1}H NMR (300 MHz, DMSO) δ 9.65 – 9.62 (m, 1H), 8.82 – 8.75 (m, 1H), 8.73 – 8.68 (m, 1H), 8.61 – 8.56 (m, 1H), 8.50 (d, *J* = 2.0 Hz, 1H), 8.34 – 8.20 (m, 3H), 7.97 (d, *J* = 8.7 Hz, 1H), 7.82 (t, *J* = 8.0 Hz, 1H), 7.57 (dd, *J* = 8.3, 5.2 Hz, 1H), 3.54 (s, 6H).	DMSO	>98	G2/AQ3		
1336					^{1}H NMR (300 MHz, DMSO) δ 9.61 (d, *J* = 1.8 Hz, 1H), 8.80 – 8.72 (m, 1H), 8.72 – 8.67 (m, 1H), 8.47 (d, *J* = 1.6 Hz, 1H), 8.39 – 8.29 (m, 2H), 8.19 (dd, *J* = 8.7, 1.8 Hz, 1H), 8.14 – 8.07 (m, 2H), 7.94 (d, *J* = 8.7 Hz, 1H), 7.55 (dd, *J* = 7.9, 4.8 Hz, 1H), 3.52 (s, 6H).	DMSO	>98	G2/AQ3		

1337				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 9.67 – 9.61 (m, 1H), 8.82 – 8.73 (m, 1H), 8.73 – 8.65 (m, 1H), 8.39 (s, 1H), 8.03 – 7.96 (m, 3H), 7.90 – 7.72 (m, 2H), 7.72 – 7.60 (m, 1H), 7.56 (dd, *J* = 7.6, 5.1 Hz, 1H), 3.53 (s, 6H).	DMSO	>98	G2/AQ3		
1338					^{1}H NMR (300 MHz, DMSO) δ 9.65 (d, *J* = 2.1 Hz, 1H), 8.78 (dt, *J* = 8.1, 1.8 Hz, 1H), 8.71 – 8.59 (m, 3H), 8.19 (dd, *J* = 8.6, 1.7 Hz, 1H), 8.07 – 7.95 (m, 2H), 7.93 – 7.81 (m, 2H), 7.54 (dd, *J* = 7.9, 4.7 Hz, 1H), 7.47 – 7.34 (m, 2H), 3.23 – 3.20 (m, 3H).	DMSO	>98	G2/AQ3		
1339					^{1}H NMR (300 MHz, DMSO) δ 9.68 – 9.64 (m, 1H), 8.83 – 8.75 (m, 1H), 8.69 (d, *J* = 4.7 Hz, 1H), 8.56 – 8.45 (m, 2H), 8.17 – 8.05 (m, 1H), 8.05 – 7.87 (m, 4H), 7.58 – 7.40 (m, 3H), 3.18 (d, *J* = 4.1 Hz, 3H).	DMSO	>98	G2/AQ3		
1340					^{1}H NMR (300 MHz, DMSO) δ 9.67 (d, *J* = 1.5 Hz, 1H), 8.80 (dt, *J* = 7.9, 1.9 Hz, 1H), 8.69 (dd, *J* = 4.8, 1.7 Hz, 1H), 8.57 – 8.41 (m, 2H), 8.08 (dd, *J* = 6.1, 2.6 Hz, 1H), 7.99 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.92 (d, *J* = 8.6 Hz, 1H), 7.84 (d, *J* = 5.6 Hz, 1H), 7.62 – 7.44 (m, 4H), 3.17 (d, *J* = 4.5 Hz, 3H).	DMSO	>98	G2/AQ3		

602

1341					^{1}H NMR (300 MHz, DMSO) δ 9.66 (d, *J* = 1.5 Hz, 1H), 8.79 (dt, *J* = 7.9, 1.9 Hz, 1H), 8.68 (dd, *J* = 4.8, 1.7 Hz, 1H), 8.65 (d, *J* = 1.9 Hz, 1H), 8.61 – 8.53 (m, 1H), 8.35 (d, *J* = 1.6 Hz, 1H), 8.21 (dd, *J* = 8.7, 2.0 Hz, 1H), 8.16 (d, *J* = 8.4 Hz, 1H), 7.92 – 7.80 (m, 3H), 7.59 – 7.48 (m, 2H), 3.21 (d, *J* = 4.5 Hz, 3H).	DMSO	>98	G2/AQ3		
1342					^{1}H NMR (300 MHz, DMSO) δ 9.66 (d, *J* = 1.6 Hz, 1H), 8.79 (dt, *J* = 8.0, 1.9 Hz, 1H), 8.73 – 8.61 (m, 3H), 8.50 (s, 1H), 8.24 (dd, *J* = 8.7, 1.9 Hz, 1H), 8.04 (d, *J* = 8.4 Hz, 1H), 7.96 – 7.82 (m, 3H), 7.60 – 7.50 (m, 2H), 3.21 (d, *J* = 4.4 Hz, 3H).	DMSO	>98	G2/AQ3		
1343				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 10.41 (brs, 1H), 9.75 (d, *J* = 1.7 Hz, 1H), 9.24 – 9.19 (m, 1H), 9.01 (dd, *J* = 5.2, 1.5 Hz, 1H), 8.90 (d, *J* = 1.5 Hz, 1H), 8.46 (d, *J* = 8.7 Hz, 1H), 8.39 (dd, *J* = 8.7, 1.7 Hz, 1H), 8.06 – 7.91 (m, 2H), 7.86 (d, *J* = 5.5 Hz, 1H), 7.66 – 7.52 (m, 3H), 3.29 (d, *J* = 4.5 Hz, 3H).	DMSO	>98	G2/AQ3		
1344				HCl	^{1}H NMR (300 MHz, DMSO) δ 10.33 (brs, 1H), 9.78 (d, *J* = 2.0 Hz, 1H), 9.23 (d, *J* = 8.1 Hz, 1H), 9.01 (d, *J* = 5.0 Hz, 1H), 8.73 (s, 1H), 8.48 (d, *J* = 8.6 Hz, 1H), 8.14 (d, *J* = 8.6 Hz, 1H), 8.05 (d, *J* = 8.0 Hz, 2H), 7.95 (dd, *J* = 8.1, 5.2 Hz, 1H), 7.79 (d, *J* = 8.1 Hz, 1H), 7.72 – 7.50 (m, 4H), 3.27 (d, *J* = 4.3 Hz, 3H).	DMSO	>98	G2/AQ3		

1345					^{1}H NMR (300 MHz, DMSO) δ 9.68 (d, *J* = 1.4 Hz, 1H), 8.85 – 8.77 (m, 1H), 8.77 – 8.62 (m, 3H), 8.40 (s, 1H), 8.30 (dd, *J* = 8.7, 1.6 Hz, 1H), 8.14 – 7.95 (m, 4H), 7.91 (d, *J* = 8.7 Hz, 1H), 7.63 – 7.50 (m, 3H), 3.22 (d, *J* = 4.3 Hz, 3H).	DMSO	>98	G2/AQ3		
1346					^{1}H NMR (300 MHz, DMSO) δ 9.67 (d, *J* = 2.0 Hz, 1H), 8.80 (dt, *J* = 8.0, 1.9 Hz, 1H), 8.69 (dd, *J* = 4.7, 1.7 Hz, 1H), 8.67 – 8.55 (m, 2H), 8.25 (dd, *J* = 8.7, 1.8 Hz, 1H), 8.13 – 8.09 (m, 1H), 7.92 – 7.77 (m, 4H), 7.71 (d, *J* = 7.8 Hz, 1H), 7.67 – 7.47 (m, 4H), 7.47 – 7.37 (m, 1H), 3.20 (d, *J* = 4.4 Hz, 3H).	DMSO	>98	G2/AQ3		
1347					^{1}H NMR (300 MHz, DMSO) δ 9.68 – 9.65 (m, 1H), 8.79 (dt, *J* = 8.0, 1.9 Hz, 1H), 8.69 (dd, *J* = 4.8, 1.7 Hz, 1H), 8.68 – 8.60 (m, 2H), 8.20 (dd, *J* = 8.7, 1.9 Hz, 1H), 7.99 – 7.95 (m, 2H), 7.92 – 7.81 (m, 3H), 7.80 – 7.73 (m, 2H), 7.61 – 7.46 (m, 3H), 7.46 – 7.36 (m, 1H), 3.20 (d, *J* = 4.4 Hz, 3H).	DMSO	>98	G2/AQ3		
1348					^{1}H NMR (300 MHz, DMSO) δ 9.66 (d, *J* = 1.5 Hz, 1H), 8.80 (dt, *J* = 7.9, 1.9 Hz, 1H), 8.70 (dd, *J* = 4.7, 1.7 Hz, 1H), 8.55 (d, *J* = 4.6 Hz, 1H), 8.32 (d, *J* = 8.6 Hz, 1H), 8.04 (d, *J* = 1.8 Hz, 1H), 7.92 – 7.84 (m, 3H), 7.60 – 7.50 (m, 3H), 7.50 – 7.42 (m, 1H), 3.18 (d, *J* = 4.5 Hz, 3H).	DMSO	>98	G2/AQ3		

604

1349				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 10.23 (brs, 1H), 9.67 (d, *J* = 2.1 Hz, 1H), 9.04 (d, *J* = 7.7 Hz, 1H), 8.98 – 8.91 (m, 1H), 8.57 (d, *J* = 8.7 Hz, 1H), 8.48 (s, 1H), 8.08 (d, *J* = 8.3 Hz, 1H), 7.91 – 7.76 (m, 3H), 7.22 – 7.10 (m, 2H), 3.85 (s, 3H), 3.31 (d, *J* = 4.4 Hz, 3H).	DMSO	>98	G2/AQ3		
1350				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 10.48 (brs, 1H), 9.74 (d, *J* = 1.9 Hz, 1H), 9.19 (d, *J* = 8.3 Hz, 1H), 9.07 – 8.97 (m, 1H), 8.71 (d, *J* = 8.8 Hz, 1H), 8.64 (s, 1H), 8.36 (s, 1H), 8.19 (d, *J* = 7.6 Hz, 1H), 8.16 – 8.06 (m, 2H), 7.95 (dd, *J* = 8.1, 5.0 Hz, 1H), 7.75 (t, *J* = 7.7 Hz, 1H), 3.31 (d, *J* = 4.4 Hz, 3H), 2.71 (s, 3H).	DMSO	>98	G2/AQ3		
1351				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 10.47 (brs, 1H), 9.73 (d, *J* = 1.3 Hz, 1H), 9.19 (d, *J* = 8.3 Hz, 1H), 9.03 – 8.94 (m, 1H), 8.69 – 8.62 (m, 2H), 8.15 – 8.07 (m, 3H), 8.02 – 7.77 (m, 3H), 3.29 (d, *J* = 4.3 Hz, 3H), 2.65 (s, 3H).	DMSO	>98	G2/AQ3		
1352				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 10.44 (brs, 1H), 9.74 (s, 1H), 9.19 (d, *J* = 7.3 Hz, 1H), 8.99 (d, *J* = 5.2 Hz, 1H), 8.68 (d, *J* = 8.4 Hz, 1H), 8.37 (s, 1H), 8.03 – 7.90 (m, 1H), 7.83 (d, *J* = 8.2 Hz, 1H), 7.72 – 7.62 (m, 1H), 7.53 (d, *J* = 9.6 Hz, 3H), 3.32 (d, *J* = 4.0 Hz, 3H).	DMSO	>98	G2/AQ3		

1353				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 10.48 (brs, 1H), 9.77 (s, 1H), 9.29 – 9.23 (m, 1H), 9.05 – 8.97 (m, 1H), 8.74 – 8.59 (m, 2H), 8.20 – 8.08 (m, 1H), 8.02 – 7.95 (m, 1H), 7.90 (s, 1H), 7.84 – 7.79 (m, 1H), 7.68 – 7.57 (m, 2H), 3.35 – 3.29 (m, 3H).	DMSO	>98	G2/AQ3		
1354				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 10.35 (brs, 1H), 9.72 (d, *J* = 2.0 Hz, 1H), 9.21 – 9.11 (m, 1H), 8.98 (dd, *J* = 5.1, 1.4 Hz, 1H), 8.65 (d, *J* = 8.7 Hz, 1H), 8.59 (s, 1H), 8.09 (dd, *J* = 8.8, 1.7 Hz, 1H), 7.95 – 7.82 (m, 3H), 7.70 – 7.60 (m, 2H), 3.30 (d, *J* = 4.4 Hz, 3H).	DMSO	>98	G2/AQ3		
1355				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 10.51 (brs, 1H), 9.77 (d, *J* = 1.9 Hz, 1H), 9.22 (d, *J* = 8.2 Hz, 1H), 9.01 (dd, *J* = 5.1, 1.4 Hz, 1H), 8.69 (s, 1H), 8.40 (d, *J* = 8.7 Hz, 1H), 8.17 (dd, *J* = 8.7, 1.6 Hz, 1H), 7.96 (dd, *J* = 8.1, 5.2 Hz, 1H), 7.30 – 7.15 (m, 2H), 7.10 (dd, *J* = 7.3, 1.9 Hz, 1H), 3.89 (s, 3H), 3.59 (s, 3H), 3.30 (d, *J* = 4.5 Hz, 3H).	DMSO	>98	G2/AQ3		
1356				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 10.42 (s, 1H), 9.71 (d, *J* = 1.8 Hz, 1H), 9.12 (d, *J* = 8.1 Hz, 1H), 8.97 (dd, *J* = 5.1, 1.5 Hz, 1H), 8.71 (s, 1H), 8.30 (d, *J* = 8.7 Hz, 1H), 8.19 (dd, *J* = 8.7, 1.6 Hz, 1H), 7.90 (dd, *J* = 7.9, 5.1 Hz, 1H), 7.18 – 7.06 (m, 2H), 7.01 (dd, *J* = 8.9, 3.1 Hz, 1H), 3.81 (s, 3H), 3.76 (s, 3H), 3.30 (d, *J* = 4.4 Hz, 3H).	DMSO	>98	G2/AQ3		

1357				HCl	^{1}H NMR (300 MHz, DMSO) δ 10.21 (brs, 1H), 9.63 (s, 1H), 8.99 (d, *J* = 8.0 Hz, 1H), 8.93 (d, *J* = 3.7 Hz, 1H), 8.87 (s, 1H), 8.37 (d, *J* = 8.9 Hz, 1H), 8.15 (d, *J* = 8.2 Hz, 1H), 7.91 – 7.78 (m, 1H), 7.05 (d, *J* = 2.1 Hz, 2H), 6.66 – 6.58 (m, 1H), 3.87 (s, 6H), 3.31 (d, *J* = 4.2 Hz, 3H).	DMSO	>98	G2/AQ3		
1358				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 10.43 (brs, 1H), 9.73 (d, *J* = 1.8 Hz, 1H), 9.17 (d, *J* = 8.2 Hz, 1H), 8.99 (dd, *J* = 5.0, 1.3 Hz, 1H), 8.69 (d, *J* = 8.6 Hz, 1H), 8.49 (s, 1H), 8.05 – 7.88 (m, 2H), 7.71 (t, *J* = 7.9 Hz, 1H), 7.64 – 7.50 (m, 1H), 7.50 – 7.33 (m, 2H), 3.32 (d, *J* = 4.3 Hz, 3H).	DMSO	>98	G2/AQ3		
1359				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 10.29 (s, 1H), 9.70 (d, *J* = 1.7 Hz, 1H), 9.14 (d, *J* = 8.3 Hz, 1H), 8.97 (dd, *J* = 5.1, 1.3 Hz, 1H), 8.63 (d, *J* = 8.7 Hz, 1H), 8.58 (s, 1H), 8.15 – 8.04 (m, 1H), 7.90 (dd, *J* = 8.0, 5.1 Hz, 1H), 7.75 – 7.57 (m, 3H), 7.43 – 7.30 (m, 1H), 3.30 (d, *J* = 4.3 Hz, 3H).	DMSO	>98	G2/AQ3		
1360				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 10.41 (brs, 1H), 9.73 (d, *J* = 1.9 Hz, 1H), 9.16 (d, *J* = 8.3 Hz, 1H), 8.98 (dd, *J* = 5.1, 1.4 Hz, 1H), 8.65 (d, *J* = 8.8 Hz, 1H), 8.60 (s, 1H), 8.12 – 8.02 (m, 1H), 8.00 – 7.84 (m, 3H), 7.49 – 7.33 (m, 2H), 3.30 (d, *J* = 4.4 Hz, 3H).	DMSO	>98	G2/AQ3		

1361				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 10.39 (s, 1H), 9.71 (d, *J* = 1.8 Hz, 1H), 9.17 – 9.08 (m, 1H), 8.97 (dd, *J* = 5.1, 1.5 Hz, 1H), 8.64 (d, *J* = 8.7 Hz, 1H), 8.58 (s, 1H), 8.07 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.88 (dd, *J* = 8.1, 5.2 Hz, 1H), 7.70 – 7.58 (m, 2H), 7.46 (t, *J* = 7.6 Hz, 1H), 7.33 (d, *J* = 7.4 Hz, 1H), 3.30 (d, *J* = 4.4 Hz, 3H), 2.43 (s, 3H).	DMSO	>98	G2/AQ3		
1362				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 10.37 (brs, 1H), 9.70 (d, *J* = 1.7 Hz, 1H), 9.10 (d, *J* = 8.1 Hz, 1H), 8.96 (dd, *J* = 5.0, 1.4 Hz, 1H), 8.62 (d, *J* = 8.7 Hz, 1H), 8.58 (s, 1H), 8.08 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.87 (dd, *J* = 7.9, 5.0 Hz, 1H), 7.74 (d, *J* = 8.2 Hz, 2H), 7.39 (d, *J* = 8.0 Hz, 2H), 3.30 (d, *J* = 4.4 Hz, 3H), 2.40 (s, 3H).	DMSO	>98	G2/AQ3		
1363				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 9.82 (brs, 1H), 9.65 (s, 1H), 9.14 – 9.02 (m, 1H), 9.02 – 8.90 (m, 1H), 8.64 – 8.51 (m, 1H), 8.20 (s, 1H), 8.07 (d, *J* = 7.8 Hz, 1H), 8.00 – 7.85 (m, 3H), 7.85 – 7.66 (m, 2H), 3.30 (s, 3H).	DMSO	>98	G2/AQ3		

1364				HCl	^{1}H NMR (300 MHz, DMSO) δ 9.83 (brs, 1H), 9.68 – 9.63 (m, 1H), 9.12 – 9.02 (m, 1H), 9.01 – 8.91 (m, 1H), 8.56 (d, *J* = 9.2 Hz, 1H), 8.42 (s, 1H), 8.35 (s, 1H), 8.19 (d, *J* = 8.7 Hz, 1H), 8.13 (d, *J* = 9.3 Hz, 1H), 7.97 (d, *J* = 7.8 Hz, 1H), 7.93 – 7.84 (m, 1H), 7.79 (t, *J* = 8.2 Hz, 1H), 3.28 (d, *J* = 4.5 Hz, 3H).	DMSO	>98	G2/AQ3		
1365				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 10.27 (brs, 1H), 9.72 (s, 1H), 9.23 – 9.10 (m, 1H), 8.98 (s, 1H), 8.77 – 8.55 (m, 2H), 8.18 – 7.86 (m, 6H), 3.34 – 3.27 (m, 3H).	DMSO	>98	G2/AQ3		
1366					^{1}H NMR (300 MHz, DMSO) δ 9.66 (d, *J* = 2.0 Hz, 1H), 8.79 (dt, *J* = 7.9, 1.9 Hz, 1H), 8.69 (dd, *J* = 4.7, 1.6 Hz, 1H), 8.65 – 8.53 (m, 2H), 8.22 – 8.12 (m, 3H), 7.92 (dd, *J* = 8.8, 1.5 Hz, 1H), 7.86 (d, *J* = 8.7 Hz, 1H), 7.80 (d, *J* = 8.8 Hz, 1H), 7.54 (dd, *J* = 7.9, 4.8 Hz, 1H), 4.11 (s, 3H), 3.20 (d, *J* = 4.4 Hz, 3H).	DMSO	>98	G2/AQ3		
1367					^{1}H NMR (300 MHz, DMSO) δ 11.10 (s, 1H), 9.63 (d, *J* = 2.0 Hz, 1H), 8.85 (d, *J* = 1.7 Hz, 1H), 8.81 – 8.70 (m, 2H), 8.39 (dd, *J* = 8.9, 1.9 Hz, 1H), 8.15 – 8.02 (m, 5H), 7.60 (dd, *J* = 8.0, 4.8 Hz, 1H), 2.65 (s, 3H), 2.61 (s, 3H).	DMSO	>98	G2/AQ3		

1368				HCl	^{1}H NMR (300 MHz, DMSO) δ 9.72 (d, *J* = 1.8 Hz, 1H), 9.27 – 9.21 (m, 1H), 8.97 (dd, *J* = 5.3, 1.4 Hz, 1H), 8.50 (dd, *J* = 8.8, 2.1 Hz, 1H), 8.34 (d, *J* = 1.9 Hz, 1H), 8.30 (d, *J* = 8.8 Hz, 1H), 8.15 – 8.09 (m, 2H), 8.09 – 7.98 (m, 3H), 3.55 (s, 3H), 2.65 (s, 3H), 2.22 (s, 3H).	DMSO	>98	G2/AQ3		
1369				HCl	^{1}H NMR (300 MHz, DMSO) δ 11.16 (s, 1H), 9.67 (s, 1H), 9.20 (d, *J* = 8.2 Hz, 1H), 8.97 (d, *J* = 4.3 Hz, 1H), 8.75 (s, 1H), 8.23 (d, *J* = 8.7 Hz, 1H), 8.14 (d, *J* = 8.8 Hz, 1H), 8.02 (dd, *J* = 8.0, 5.5 Hz, 1H), 7.66 – 7.47 (m, 2H), 7.47 – 7.34 (m, 1H), 2.56 (s, 3H).	DMSO	>98	G2/AQ3		
1370				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 10.17 (brs, 1H), 9.68 (d, *J* = 2.0 Hz, 1H), 9.06 (d, *J* = 8.0 Hz, 1H), 8.95 (dd, *J* = 5.0, 1.4 Hz, 1H), 8.77 (s, 1H), 8.31 (s, 2H), 8.16 (d, *J* = 2.1 Hz, 1H), 7.87 (dd, *J* = 7.8, 5.2 Hz, 1H), 7.72 (d, *J* = 7.8 Hz, 1H), 7.61 – 7.47 (m, 2H), 7.19 (d, *J* = 1.4 Hz, 1H), 3.31 (d, *J* = 4.4 Hz, 3H).	DMSO	>98	G2/AQ3		
1371				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 10.28 (brs, 1H), 9.71 (s, 1H), 9.16 (d, *J* = 7.9 Hz, 1H), 8.98 (d, *J* = 4.2 Hz, 1H), 8.67 (d, *J* = 8.9 Hz, 1H), 8.45 (s, 1H), 8.01 – 7.83 (m, 2H), 7.68 – 7.50 (m, 2H), 7.50 – 7.35 (m, 1H), 3.31 (d, *J* = 4.1 Hz, 3H).	DMSO	>98	G2/AQ3		

1372				HCl	^{1}H NMR (300 MHz, DMSO) δ 9.72 – 9.45 (m, 2H), 8.95 (d, *J* = 7.6 Hz, 1H), 8.88 (d, *J* = 3.8 Hz, 1H), 8.49 (d, *J* = 8.5 Hz, 1H), 8.13 (s, 1H), 7.91 – 7.75 (m, 3H), 7.53 – 7.43 (m, 1H), 7.36 – 7.25 (m, 1H), 3.27 (d, *J* = 4.3 Hz, 3H).	DMSO	>98	G2/AQ3		
1373				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 10.04 (brs, 1H), 9.70 (s, 1H), 9.22 – 9.07 (m, 1H), 8.93 (s, 1H), 8.62 (d, *J* = 7.6 Hz, 1H), 8.55 (s, 1H), 8.06 (d, *J* = 8.9 Hz, 1H), 7.99 – 7.79 (m, 2H), 7.79 – 7.55 (m, 2H), 3.33 – 3.27 (m, 3H).	DMSO	>98	G2/AQ3		
1374				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 9.64 (s, 1H), 9.34 (brs, 1H), 9.06 – 8.92 (m, 1H), 8.86 (s, 1H), 8.50 – 8.37 (m, 1H), 8.25 (s, 1H), 8.11 – 7.95 (m, 1H), 7.85 – 7.74 (m, 1H), 7.74 – 7.57 (m, 2H), 7.43 – 7.29 (m, 1H), 3.28 – 3.21 (m, 3H).	DMSO	>98	G2/AQ3		
1375				HCl	^{1}H NMR (300 MHz, DMSO) δ 9.63 (d, *J* = 1.6 Hz, 1H), 9.38 (brs, 1H), 9.01 – 8.91 (m, 1H), 8.84 (dd, *J* = 5.0, 1.6 Hz, 1H), 8.60 (s, 1H), 8.08 (s, 2H), 7.76 (dd, *J* = 7.9, 5.1 Hz, 1H), 7.64 – 7.38 (m, 2H), 3.26 (d, *J* = 3.7 Hz, 3H).	DMSO	>98	G2/AQ3		

611

1376				HCl	^{1}H NMR (300 MHz, DMSO) δ 9.88 (brs, 1H), 9.65 (s, 1H), 9.18 – 8.99 (m, 1H), 8.90 (s, 1H), 8.70 (s, 1H), 8.31 – 8.03 (m, 2H), 7.94 – 7.77 (m, 2H), 7.77 – 7.57 (m, 1H), 3.28 (s, 3H).	DMSO	>98	G2/AQ3		
1377				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 10.33 (s, 1H), 9.67 (s, 1H), 9.10 (d, *J* = 7.8 Hz, 1H), 9.02 (s, 1H), 8.92 (d, *J* = 5.0 Hz, 1H), 8.35 (d, *J* = 8.8 Hz, 1H), 8.25 (d, *J* = 8.8 Hz, 1H), 8.03 – 7.76 (m, 3H), 3.31 (s, 3H).	DMSO	>98	G2/AQ3		
1378				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 9.66 (d, *J* = 1.7 Hz, 1H), 9.56 – 9.34 (m, 1H), 9.26 – 9.10 (m, 1H), 9.05 (d, *J* = 4.7 Hz, 1H), 8.44 (s, 1H), 8.19 (dd, *J* = 8.1, 5.7 Hz, 1H), 7.95 (d, *J* = 11.5 Hz, 1H), 7.63 – 7.45 (m, 2H), 7.45 – 7.26 (m, 1H), 3.19 (d, *J* = 4.4 Hz, 3H).	DMSO	>98	G2/AQ3		
1379				HCl	^{1}H NMR (300 MHz, DMSO) δ 9.67 – 9.59 (m, 1H), 9.38 (d, *J* = 8.3 Hz, 1H), 9.22 – 9.10 (m, 1H), 9.03 (d, *J* = 4.9 Hz, 1H), 8.37 (s, 1H), 8.16 (dd, *J* = 8.1, 5.6 Hz, 1H), 7.89 (d, *J* = 11.6 Hz, 1H), 7.78 (td, *J* = 8.9, 6.6 Hz, 1H), 7.54 – 7.36 (m, 1H), 7.30 (td, *J* = 8.3, 2.0 Hz, 1H), 3.18 (d, *J* = 4.4 Hz, 3H).	DMSO	>98	G2/AQ3		

612

1380				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 9.72 (d, *J* = 1.6 Hz, 1H), 9.25 – 9.14 (m, 1H), 8.99 (dd, *J* = 5.2, 1.5 Hz, 1H), 8.51 (s, 1H), 8.44 (d, *J* = 8.7 Hz, 1H), 8.26 – 8.11 (m, 1H), 7.94 (dd, *J* = 8.0, 5.2 Hz, 1H), 7.65 – 7.49 (m, 2H), 7.49 – 7.29 (m, 1H), 3.69 (s, 6H).	DMSO	>98	G2/AQ3		
1381				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 9.71 (s, 1H), 9.18 (d, *J* = 8.0 Hz, 1H), 8.98 (d, *J* = 5.1 Hz, 1H), 8.49 – 8.36 (m, 2H), 8.16 (d, *J* = 8.8 Hz, 1H), 7.99 – 7.86 (m, 1H), 7.86 – 7.72 (m, 1H), 7.46 (t, *J* = 10.2 Hz, 1H), 7.29 (t, *J* = 8.5 Hz, 1H), 3.69 (s, 6H).	DMSO	>98	G2/AQ3		
1382				HCl	^{1}H NMR (300 MHz, DMSO) δ 10.25 (brs, 1H), 9.66 (d, *J* = 1.6 Hz, 1H), 9.04 (d, *J* = 8.2 Hz, 1H), 8.94 (dd, *J* = 5.0, 1.6 Hz, 1H), 8.70 (s, 1H), 8.23 (d, *J* = 8.8 Hz, 1H), 8.16 (dd, *J* = 8.7, 1.5 Hz, 1H), 7.84 (dd, *J* = 8.0, 5.1 Hz, 1H), 7.71 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.65 – 7.55 (m, 2H), 3.90 (s, 3H), 3.29 (d, *J* = 4.5 Hz, 3H), 2.64 (s, 3H).	DMSO	>98	G2/AQ3		
1383				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 10.18 (brs, 1H), 9.68 (d, *J* = 1.8 Hz, 1H), 9.17 (d, *J* = 8.0 Hz, 1H), 8.99 (dd, *J* = 5.2, 1.4 Hz, 1H), 8.86 (s, 1H), 8.31 (d, *J* = 8.7 Hz, 1H), 8.22 (d, *J* = 8.8 Hz, 1H), 7.97 (dd, *J* = 8.0, 5.3 Hz, 1H), 7.64 – 7.49 (m, 2H), 7.49 – 7.34 (m, 1H), 4.06 – 3.92 (m, 2H), 3.73 (t, *J* = 5.5 Hz, 2H), 3.33 (s, 3H).	DMSO	>98	G2/AQ3		

613

1384				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 10.18 (brs, 1H), 9.67 (d, *J* = 1.6 Hz, 1H), 9.14 (d, *J* = 8.1 Hz, 1H), 8.99 (dd, *J* = 5.2, 1.5 Hz, 1H), 8.80 (s, 1H), 8.29 (d, *J* = 8.7 Hz, 1H), 8.18 (d, *J* = 8.7 Hz, 1H), 7.95 (dd, *J* = 8.2, 5.2 Hz, 1H), 7.79 (td, *J* = 8.9, 6.6 Hz, 1H), 7.50 (ddd, *J* = 11.6, 9.3, 2.6 Hz, 1H), 7.33 (td, *J* = 8.3, 2.3 Hz, 1H), 4.08 – 3.94 (m, 3H), 3.73 (t, *J* = 5.5 Hz, 3H), 3.32 (s, 3H).	DMSO	>98	G2/AQ3		
1385				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 10.33 (brs, 1H), 9.70 (d, *J* = 1.7 Hz, 1H), 9.15 (d, *J* = 8.2 Hz, 1H), 8.99 (dd, *J* = 5.2, 1.5 Hz, 1H), 8.81 (s, 1H), 8.33 (d, *J* = 8.7 Hz, 1H), 8.18 (d, *J* = 8.7 Hz, 1H), 7.95 (dd, *J* = 8.1, 5.2 Hz, 1H), 7.81 (td, *J* = 8.9, 6.6 Hz, 1H), 7.49 (ddd, *J* = 11.5, 9.3, 2.5 Hz, 1H), 7.32 (td, *J* = 8.5, 2.2 Hz, 1H), 3.96 – 3.78 (m, 2H), 3.48 (t, *J* = 6.1 Hz, 2H), 3.27 (s, 3H), 2.14 – 1.93 (m, 2H).	DMSO	>98	G2/AQ3		
1386				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 9.73 (s, 1H), 9.17 (d, *J* = 8.4 Hz, 1H), 8.99 (s, 1H), 8.52 (s, 1H), 8.43 (d, *J* = 8.8 Hz, 1H), 8.21 (d, *J* = 9.0 Hz, 1H), 8.02 – 7.90 (m, 1H), 7.87 – 7.78 (m, 1H), 7.57 – 7.38 (m, 1H), 7.38 – 7.24 (m, 1H), 4.31 – 4.18 (m, 4H), 2.08 (s, 4H).	DMSO	>98	G2/AQ3		

614

1387				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 9.68 (d, *J* = 1.7 Hz, 1H), 9.17 (d, *J* = 8.3 Hz, 1H), 8.99 (dd, *J* = 5.2, 1.5 Hz, 1H), 8.34 (d, *J* = 8.6 Hz, 1H), 8.24 – 8.12 (m, 2H), 7.97 (dd, *J* = 8.0, 5.2 Hz, 1H), 7.81 (td, *J* = 8.9, 6.6 Hz, 1H), 7.49 (ddd, *J* = 11.6, 9.3, 2.5 Hz, 1H), 7.30 (td, *J* = 8.4, 2.1 Hz, 1H), 4.16 (brs, 4H), 1.80 (brs, 6H).	DMSO	>98	G2/AQ3		
1388				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 9.70 (d, *J* = 1.7 Hz, 1H), 9.26 (d, *J* = 8.3 Hz, 1H), 9.01 (dd, *J* = 5.3, 1.4 Hz, 1H), 8.37 – 8.19 (m, 2H), 8.15 (d, *J* = 8.7 Hz, 1H), 8.02 (dd, *J* = 8.1, 5.3 Hz, 1H), 7.81 (td, *J* = 8.9, 6.5 Hz, 1H), 7.48 (ddd, *J* = 11.6, 9.3, 2.6 Hz, 1H), 7.30 (td, *J* = 8.4, 2.3 Hz, 1H), 4.23 – 4.12 (m, 4H), 3.90 – 3.80 (m, 4H).	DMSO	>98	G2/AQ3		
1389				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 9.68 (d, *J* = 1.7 Hz, 1H), 9.17 (d, *J* = 8.2 Hz, 1H), 8.99 (dd, *J* = 5.2, 1.5 Hz, 1H), 8.34 (d, *J* = 8.7 Hz, 1H), 8.27 – 8.13 (m, 2H), 7.97 (dd, *J* = 8.1, 5.4 Hz, 1H), 7.67 – 7.48 (m, 2H), 7.41 (ddd, *J* = 14.7, 9.9, 4.9 Hz, 1H), 4.16 (brs, 4H), 1.80 (brs, 6H).	DMSO	>98	G2/AQ3		

615

1390				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 9.70 (d, *J* = 1.8 Hz, 1H), 9.26 (d, *J* = 8.3 Hz, 1H), 9.01 (dd, *J* = 5.3, 1.4 Hz, 1H), 8.36 – 8.23 (m, 2H), 8.18 (d, *J* = 8.7 Hz, 1H), 8.03 (dd, *J* = 8.0, 5.4 Hz, 1H), 7.64 – 7.46 (m, 2H), 7.46 – 7.29 (m, 1H), 4.23 – 4.16 (m, 4H), 3.85 (d, *J* = 4.7 Hz, 4H).	DMSO	>98	G2/AQ3		
1391				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 9.68 (d, *J* = 1.7 Hz, 1H), 9.18 (d, *J* = 8.2 Hz, 1H), 9.00 (dd, *J* = 5.2, 1.2 Hz, 1H), 8.62 (s, 1H), 8.39 (d, *J* = 8.7 Hz, 1H), 8.21 (d, *J* = 8.8 Hz, 1H), 7.98 (dd, *J* = 8.0, 5.2 Hz, 1H), 7.64 – 7.47 (m, 2H), 7.46 – 7.27 (m, 1H), 4.26 (t, *J* = 5.2 Hz, 2H), 3.85 (t, *J* = 5.3 Hz, 2H), 3.72 (s, 3H), 3.33 (s, 3H).	DMSO	>98	G2/AQ3		
1392				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 9.67 (d, *J* = 1.7 Hz, 1H), 9.15 (d, *J* = 8.1 Hz, 1H), 8.99 (d, *J* = 4.1 Hz, 1H), 8.56 (s, 1H), 8.36 (d, *J* = 8.7 Hz, 1H), 8.17 (d, *J* = 8.7 Hz, 1H), 7.96 (dd, *J* = 8.1, 5.2 Hz, 1H), 7.86 – 7.70 (m, 1H), 7.55 – 7.40 (m, 1H), 7.30 (td, *J* = 8.5, 2.2 Hz, 1H), 4.36 – 4.18 (m, 2H), 3.88 – 3.77 (m, 2H), 3.72 (s, 3H), 3.33 (s, 3H).	DMSO	>98	G2/AQ3		

1393				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 9.70 (d, *J* = 1.7 Hz, 1H), 9.24 – 9.06 (m, 1H), 8.99 (dd, *J* = 5.1, 1.5 Hz, 1H), 8.52 (s, 1H), 8.40 (d, *J* = 8.7 Hz, 1H), 8.30 – 8.14 (m, 1H), 7.93 (dd, *J* = 8.0, 5.2 Hz, 1H), 7.63 – 7.46 (m, 2H), 7.46 – 7.25 (m, 1H), 4.22 – 4.11 (m, 2H), 3.73 (s, 3H), 3.59 (t, *J* = 5.9 Hz, 2H), 2.10 – 1.92 (m, 2H).	DMSO	>98	G2/AQ3		
1394				2 HCl	^{1}H NMR (300 MHz, DMSO) δ 9.68 (d, *J* = 1.7 Hz, 1H), 9.11 (d, *J* = 8.3 Hz, 1H), 8.97 (dd, *J* = 5.1, 1.5 Hz, 1H), 8.46 (s, 1H), 8.36 (d, *J* = 8.7 Hz, 1H), 8.17 (d, *J* = 8.8 Hz, 1H), 7.90 (dd, *J* = 8.1, 5.2 Hz, 1H), 7.80 (td, *J* = 8.9, 6.6 Hz, 1H), 7.47 (ddd, *J* = 11.6, 9.3, 2.6 Hz, 1H), 7.29 (td, *J* = 8.4, 2.1 Hz, 1H), 4.22 – 4.08 (m, 2H), 3.72 (s, 3H), 3.59 (t, *J* = 5.9 Hz, 2H), 2.10 – 1.94 (m, 2H).	DMSO	>98	G2/AQ3		
1395				HCl	^{1}H NMR (300 MHz, DMSO) δ 9.97 – 9.66 (m, 2H), 9.66 – 9.58 (m, 1H), 9.17 – 9.05 (m, 1H), 8.99 (dd, *J* = 5.2, 1.5 Hz, 1H), 8.66 (d, *J* = 8.6 Hz, 1H), 8.50 (s, 1H), 8.01 – 7.88 (m, 2H), 7.62 (ddd, *J* = 9.1, 6.1, 3.1 Hz, 1H), 7.58 – 7.36 (m, 2H).	DMSO	>98	G2/AQ3		
1396				HCl	^{1}H NMR (300 MHz, DMSO) δ 9.70 (d, *J* = 1.8 Hz, 1H), 9.16 (d, *J* = 8.3 Hz, 1H), 8.98 (d, *J* = 3.9 Hz, 1H), 8.58 – 8.42 (m, 2H), 8.00 – 7.82 (m, 2H), 7.69 – 7.38 (m, 3H), 3.69 (s, 6H).	DMSO	>98	G2/AQ3		

617

1397				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.47 (s, 1H), 9.68 (d, *J* = 1.8 Hz, 1H), 9.11 (d, *J* = 8.0 Hz, 1H), 9.04 (s, 1H), 8.96 (dd, *J* = 5.1, 1.4 Hz, 1H), 8.41 (dd, *J* = 8.8, 1.6 Hz, 1H), 8.30 (d, *J* = 8.7 Hz, 1H), 8.14 (d, *J* = 8.2 Hz, 2H), 7.90 (d, *J* = 8.4 Hz, 3H), 3.34 (t, *J* = 17.1 Hz, 3H).	DMSO	>98	AQ4		
1398				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.15 (s, 1H), 9.65 (d, *J* = 1.7 Hz, 1H), 9.06 (d, *J* = 7.9 Hz, 1H), 8.99 – 8.90 (m, 2H), 8.44 (d, *J* = 7.2 Hz, 1H), 8.28 – 8.17 (m, 3H), 7.94 – 7.76 (m, 3H), 3.32 (d, *J* = 4.5 Hz, 3H).	DMSO	>98	AQ4		
1399				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.05 (s, 1H), 9.65 (d, *J* = 2.1 Hz, 1H), 9.10 – 9.00 (m, 1H), 8.96 (dd, *J* = 5.1, 1.5 Hz, 1H), 8.65 (s, 1H), 8.26 – 8.17 (m, 1H), 8.16 – 8.07 (m, 1H), 7.90 (dd, *J* = 7.8, 5.3 Hz, 1H), 7.77 – 7.69 (m, 1H), 7.68 – 7.55 (m, 3H), 3.29 (d, *J* = 4.6 Hz, 3H).	DMSO	>98	AQ4		
1400				HCl	^{1}H NMR (400 MHz, DMSO) δ 9.77 (s, 1H), 9.63 (d, *J* = 1.7 Hz, 1H), 9.04 – 8.85 (m, 2H), 8.63 (s, 1H), 8.12 (q, *J* = 8.7 Hz, 2H), 7.83 (dd, *J* = 7.8, 4.9 Hz, 1H), 7.38 – 7.25 (m, 2H), 7.25 – 7.17 (m, 1H), 3.92 (s, 3H).	DMSO	>98	AQ4		

1401				HCl	^{1}H NMR (400 MHz, DMSO) δ 10.05 (s, 1H), 9.64 (d, *J* = 1.7 Hz, 1H), 9.04 (d, *J* = 7.6 Hz, 1H), 8.99 – 8.92 (m, 1H), 8.89 (s, 1H), 8.41 (d, *J* = 8.8 Hz, 1H), 8.33 – 8.20 (m, 2H), 8.16 (d, *J* = 8.6 Hz, 1H), 7.94 – 7.84 (m, 1H), 7.81 – 7.68 (m, 1H), 3.32 (d, *J* = 4.5 Hz, 3H).	DMSO	>98	AQ4		
1402				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.30 (s, 1H), 9.68 (d, *J* = 1.8 Hz, 1H), 9.15 – 9.05 (m, 1H), 8.97 (dd, *J* = 5.1, 1.4 Hz, 1H), 8.52 (s, 1H), 8.10 (s, 1H), 7.96 – 7.82 (m, 1H), 7.67 – 7.55 (m, 1H), 7.42 – 7.26 (m, 3H), 3.31 (d, *J* = 4.5 Hz, 3H), 2.40 (s, 3H).	DMSO	>98	AQ5		
1403				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 9.87 (s, 1H), 9.59 (d, *J* = 1.5 Hz, 1H), 9.00 – 8.89 (m, 2H), 8.42 (s, 1H), 7.93 – 7.80 (m, 2H), 7.62 – 7.54 (m, 1H), 7.49 – 7.36 (m, 3H), 3.30 (d, *J* = 4.6 Hz, 3H), 2.32 (s, 3H).	DMSO	>98	AQ5		
1404				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.19 (s, 1H), 9.68 – 9.61 (m, 1H), 9.05 – 8.98 (m, 1H), 8.94 (dd, *J* = 5.0, 1.6 Hz, 1H), 8.48 (d, *J* = 5.7 Hz, 1H), 8.02 (s, 1H), 7.91 – 7.82 (m, 1H), 7.59 – 7.50 (m, 2H), 7.43 – 7.36 (m, 2H), 3.31 (d, *J* = 4.6 Hz, 3H), 2.40 (s, 3H).	DMSO	>98	AQ5		

1405				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.11 (s, 1H), 9.69 – 9.61 (m, 1H), 9.11 – 9.02 (m, 1H), 8.95 (dd, *J* = 5.1, 1.5 Hz, 1H), 8.52 (s, 1H), 8.05 (s, 1H), 7.89 (dd, *J* = 8.1, 5.1 Hz, 1H), 7.68 – 7.56 (m, 1H), 7.48 – 7.38 (m, 1H), 7.33 – 7.25 (m, 1H), 3.31 (d, *J* = 4.6 Hz, 3H), 2.33 (s, 3H).	DMSO	>98	AQ5		
1406				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.03 (s, 1H), 9.63 (dd, *J* = 2.2, 0.7 Hz, 1H), 9.09 – 9.00 (m, 1H), 8.95 (dd, *J* = 5.1, 1.6 Hz, 1H), 8.48 (s, 1H), 8.00 (s, 1H), 7.89 (dd, *J* = 7.9, 5.2 Hz, 1H), 7.54 – 7.35 (m, 3H), 3.30 (d, *J* = 4.6 Hz, 3H), 2.33 (s, 3H).	DMSO	>98	AQ5		
1407				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.09 (s, 1H), 9.63 (d, *J* = 1.6 Hz, 1H), 9.08 – 8.98 (m, 1H), 8.95 (dd, *J* = 5.1, 1.5 Hz, 1H), 8.46 (s, 1H), 7.98 (s, 1H), 7.87 (dd, *J* = 8.1, 5.1 Hz, 1H), 7.64 (ddt, *J* = 16.8, 14.3, 5.3 Hz, 2H), 7.40 – 7.30 (m, 1H), 3.30 (d, *J* = 4.6 Hz, 3H), 2.41 (s, 3H).	DMSO	>98	AQ5		
1408				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 9.92 (s, 1H), 9.61 (d, *J* = 1.6 Hz, 1H), 9.03 – 8.97 (m, 1H), 8.94 (dd, *J* = 5.1, 1.5 Hz, 1H), 8.42 (s, 1H), 7.93 (s, 1H), 7.87 (dd, *J* = 8.1, 5.0 Hz, 1H), 7.44 – 7.36 (m, 1H), 7.33 – 7.23 (m, 2H), 3.29 (d, *J* = 4.6 Hz, 3H), 2.41 (s, 3H).	DMSO	>98	AQ5		

1409				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.11 (s, 1H), 9.64 (d, *J* = 2.2 Hz, 1H), 9.10 – 9.03 (m, 1H), 8.96 (dd, *J* = 5.1, 1.5 Hz, 1H), 8.49 (s, 1H), 8.05 – 7.94 (m, 3H), 7.94 – 7.88 (m, 1H), 7.88 – 7.82 (m, 1H), 7.77 (t, *J* = 7.7 Hz, 1H), 3.31 (d, *J* = 4.5 Hz, 3H), 2.40 (s, 3H).	DMSO	>98	AQ5		
1410				3 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.22 (s, 1H), 9.67 (d, *J* = 1.6 Hz, 1H), 9.14 – 9.07 (m, 1H), 8.97 (dd, *J* = 5.1, 1.5 Hz, 1H), 8.52 (s, 1H), 8.10 – 8.00 (m, 3H), 7.91 (dd, *J* = 7.9, 5.3 Hz, 1H), 7.75 – 7.67 (m, 2H), 3.31 (d, *J* = 4.5 Hz, 3H), 2.39 (s, 3H).	DMSO	>98	AQ5		
1411				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.20 – 9.85 (m, 1H), 9.58 (s, 1H), 8.94 – 8.85 (m, 2H), 8.38 (s, 1H), 7.88 – 7.76 (m, 2H), 7.54 – 7.44 (m, 1H), 7.24 – 7.16 (m, 2H), 7.12 (td, *J* = 7.4, 0.9 Hz, 1H), 3.76 (s, 3H), 3.31 (d, *J* = 4.5 Hz, 3H), 2.24 (s, 3H).	DMSO	>98%	AQ5		
1412				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.20 (s, 1H), 9.69 – 9.61 (m, 1H), 9.01 (d, *J* = 7.8 Hz, 1H), 8.93 (dd, *J* = 5.0, 1.6 Hz, 1H), 8.49 (s, 1H), 8.06 (s, 1H), 7.83 (dd, *J* = 8.0, 5.1 Hz, 1H), 7.51 – 7.41 (m, 1H), 7.13 – 7.05 (m, 1H), 7.05 – 6.95 (m, 2H), 3.81 (d, *J* = 10.8 Hz, 3H), 3.31 (d, *J* = 4.6 Hz, 3H), 2.41 (s, 3H).	DMSO	>98%	AQ5		

621

1413				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.09 (s, 1H), 9.60 (s, 1H), 9.00 – 8.88 (m, 2H), 8.42 (s, 1H), 7.94 (s, 1H), 7.86 – 7.78 (m, 1H), 7.48 – 7.39 (m, 2H), 7.16 – 7.06 (m, 2H), 3.85 (s, 3H), 3.31 (d, *J* = 4.6 Hz, 3H), 2.43 (s, 3H).	DMSO	>98%	AQ5		
1414				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.02 (s, 1H), 9.63 (s, 1H), 9.05 – 8.91 (m, 2H), 8.36 (s, 1H), 8.10 – 7.99 (m, 1H), 7.91 – 7.80 (m, 1H), 7.59 – 7.50 (m, 2H), 7.44 – 7.32 (m, 2H), 3.27 (d, *J* = 4.5 Hz, 3H), 2.45 (s, 3H).	DMSO	>98	AQ5		
1415				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.01 (s, 1H), 9.65 (s, 1H), 9.10 – 8.99 (m, 1H), 8.97 (d, *J* = 5.0 Hz, 1H), 8.41 (s, 1H), 8.09 (s, 1H), 7.97 – 7.83 (m, 1H), 7.61 – 7.41 (m, 2H), 7.31 (td, *J* = 8.4, 2.2 Hz, 1H), 3.26 (d, *J* = 4.5 Hz, 3H), 2.35 (s, 3H).	DMSO	>98	AQ5		
1416				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.01 – 9.69 (m, 1H), 9.61 (s, 1H), 8.94 (m, *J* = 5.0 Hz, 2H), 8.36 (s, 1H), 7.99 (s, 1H), 7.92 – 7.81 (m, 1H), 7.71 – 7.57 (m, 2H), 7.41 – 7.31 (m, 1H), 3.26 (d, *J* = 4.5 Hz, 3H), 2.47 (s, 3H).	DMSO	>98	AQ5		

622

1417				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 9.90 (s, 1H), 9.63 (d, *J* = 1.8 Hz, 1H), 9.08 – 8.89 (m, 2H), 8.40 (s, 1H), 8.02 (s, 1H), 7.92 – 7.81 (m, 1H), 7.44 – 7.25 (m, 3H), 3.27 (d, *J* = 4.5 Hz, 3H), 2.49 (s, 3H).	DMSO	>98	AQ5		
1418				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 9.99 (s, 1H), 9.62 (s, 1H), 8.95 (d, *J* = 5.0 Hz, 2H), 8.27 (s, 1H), 8.11 – 7.99 (m, 1H), 7.89 – 7.80 (m, 1H), 7.53 – 7.45 (m, 1H), 7.24 (dd, *J* = 7.4, 1.7 Hz, 1H), 7.19 (d, *J* = 8.0 Hz, 1H), 7.12 (td, *J* = 7.4, 0.9 Hz, 1H), 3.74 (d, *J* = 8.9 Hz, 3H), 3.26 (d, *J* = 4.6 Hz, 3H), 2.28 (s, 3H).	DMSO	>98	AQ5		
1419				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.30 (s, 1H), 9.72 (d, *J* = 1.6 Hz, 1H), 9.20 – 9.10 (m, 1H), 8.98 (dd, *J* = 5.1, 1.5 Hz, 1H), 8.45 (s, 1H), 8.21 (s, 1H), 7.91 (dd, *J* = 8.0, 5.1 Hz, 1H), 7.48 – 7.40 (m, 1H), 7.08 – 7.01 (m, 3H), 3.84 (s, 3H), 3.26 (d, *J* = 4.5 Hz, 3H), 2.45 (s, 3H).	DMSO	>98	AQ5		
1420				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.08 – 9.71 (m, 1H), 9.58 (d, *J* = 2.0 Hz, 1H), 8.96 – 8.83 (m, 2H), 8.31 (s, 1H), 7.94 (s, 1H), 7.87 – 7.79 (m, 1H), 7.47 – 7.39 (m, 2H), 7.10 (d, *J* = 8.8 Hz, 2H), 3.84 (s, 3H), 3.27 (d, *J* = 4.5 Hz, 3H), 2.47 (s, 3H).	DMSO	>98	AQ5		

1421				2 HCl	1H NMR (400 MHz, DMSO) δ 9.69 – 9.63 (m, 1H), 9.10 – 8.93 (m, 3H), 8.12 (d, J = 8.4 Hz, 1H), 7.90 – 7.82 (m, 2H), 7.68 – 7.58 (m, 1H), 7.56 – 7.48 (m, 1H), 7.30 – 7.22 (m, 1H), 3.35 (d, J = 4.6 Hz, 3H), 2.73 (s, 3H).	DMSO	>98	AQ4		
1422				2 HCl	1H NMR (400 MHz, DMSO) δ 9.62 (s, 1H), 8.95 (d, *J* = 5.0 Hz, 3H), 8.03 (s, 1H), 7.85 (t, *J* = 9.9 Hz, 2H), 7.44 – 7.34 (m, 1H), 7.17 (dd, *J* = 8.2, 2.2 Hz, 2H), 3.34 (d, *J* = 4.5 Hz, 3H), 2.73 (s, 3H).	DMSO	>98	AQ4		
1423				2 HCl	1H NMR (400 MHz, DMSO) δ 9.62 (d, *J* = 2.1 Hz, 1H), 9.00 – 8.75 (m, 3H), 8.08 – 7.99 (m, 1H), 7.99 – 7.93 (m, 1H), 7.93 – 7.79 (m, 3H), 7.79 – 7.73 (m, 2H), 3.34 (d, *J* = 4.5 Hz, 3H), 2.70 (s, 3H).	DMSO	>98	AQ4		
1424				2 HCl	1H NMR (400 MHz, DMSO) δ 9.61 (s, 1H), 8.99 – 8.63 (m, 3H), 8.07 – 7.98 (m, 3H), 7.89 – 7.78 (m, 2H), 7.65 – 7.59 (m, 2H), 3.33 (d, *J* = 4.5 Hz, 3H), 2.70 (s, 3H).	DMSO	>98	AQ4		

624

1425				3 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.49 (s, 1H), 9.56 (s, 1H), 9.19 (s, 1H), 8.95 (d, *J* = 5.3 Hz, 1H), 8.83 (d, *J* = 5.5 Hz, 1H), 8.73 (d, *J* = 6.4 Hz, 1H), 8.41 (d, *J* = 5.6 Hz, 1H), 8.26 (s, 1H), 8.09 (s, 1H), 8.02 – 7.91 (m, 2H), 7.85 (s, 1H), 7.78 – 7.68 (m, 1H), 7.61 – 7.51 (m, 1H), 7.48 – 7.36 (m, 2H), 5.36 (s, 2H).	DMSO	>98	Method AQ3		
1426				3 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.53 (s, 1H), 9.67 (d, *J* = 1.8 Hz, 1H), 9.32 (dd, *J* = 5.8, 4.1 Hz, 1H), 8.97 (dd, *J* = 5.4, 1.4 Hz, 1H), 8.75 (d, *J* = 8.7 Hz, 1H), 8.35 (t, *J* = 7.9 Hz, 1H), 8.24 (d, *J* = 13.5 Hz, 1H), 8.03 (dd, *J* = 8.1, 5.4 Hz, 1H), 7.92 (dd, *J* = 13.5, 4.8 Hz, 2H), 7.85 – 7.73 (m, 2H), 7.53 – 7.43 (m, 1H), 7.36 – 7.25 (m, 1H), 5.40 (d, *J* = 5.6 Hz, 2H), 2.85 (s, 3H).	DMSO	>98	Method AQ3		
1427				3 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.42 (s, 1H), 9.64 (d, *J* = 1.7 Hz, 1H), 9.26 (d, *J* = 8.1 Hz, 1H), 8.95 (dd, *J* = 5.3, 1.4 Hz, 1H), 8.71 (d, *J* = 8.7 Hz, 1H), 8.30 (d, *J* = 18.0 Hz, 2H), 8.04 – 7.84 (m, 3H), 7.74 (dd, *J* = 7.8, 6.0 Hz, 2H), 7.62 – 7.33 (m, 3H), 5.38 (d, *J* = 5.5 Hz, 2H), 2.84 (s, 3H).	DMSO	>98	Method AQ3		

625

1428				3 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.40 (s, 1H), 9.63 (d, *J* = 1.6 Hz, 1H), 9.24 (d, *J* = 8.1 Hz, 1H), 8.95 (dd, *J* = 5.3, 1.4 Hz, 1H), 8.69 (d, *J* = 8.7 Hz, 1H), 8.41 – 8.22 (m, 2H), 8.09 (dd, *J* = 8.7, 1.8 Hz, 1H), 8.01 – 7.84 (m, 4H), 7.74 (d, *J* = 7.8 Hz, 1H), 7.46 – 7.33 (m, 2H), 5.36 (d, *J* = 5.5 Hz, 2H), 2.83 (s, 3H).	DMSO	>98	Method AQ3		
1429				3 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.21 (s, 1H), 9.62 (s, 1H), 9.19 (d, *J* = 7.8 Hz, 1H), 8.93 (d, *J* = 4.6 Hz, 1H), 8.68 (d, *J* = 8.6 Hz, 1H), 8.26 (dd, *J* = 28.0, 20.1 Hz, 2H), 8.04 – 7.80 (m, 3H), 7.72 (d, *J* = 7.8 Hz, 1H), 7.64 – 7.50 (m, 2H), 7.46 – 7.33 (m, 1H), 5.33 (d, *J* = 5.3 Hz, 2H), 2.81 (s, 3H).	DMSO	>98	Method AQ3		
1430				3 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.40 (s, 1H), 9.66 (d, *J* = 1.8 Hz, 1H), 9.31 (d, *J* = 8.2 Hz, 1H), 8.96 (dd, *J* = 5.4, 1.4 Hz, 1H), 8.73 (d, *J* = 8.7 Hz, 1H), 8.33 (t, *J* = 7.9 Hz, 1H), 8.23 (s, 1H), 8.03 (dd, *J* = 8.1, 5.4 Hz, 1H), 7.93 (dd, *J* = 11.7, 8.3 Hz, 2H), 7.76 (d, *J* = 7.9 Hz, 1H), 7.70 – 7.60 (m, 1H), 7.54 – 7.35 (m, 2H), 5.38 (d, *J* = 5.5 Hz, 2H), 2.85 (s, 3H).	DMSO	>98	Method AQ3		

1431				3 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.15 (s, 1H), 9.61 (s, 1H), 9.22 (t, *J* = 7.3 Hz, 1H), 8.98 – 8.90 (m, 1H), 8.65 (dd, *J* = 8.6, 3.0 Hz, 1H), 8.36 – 8.26 (m, 2H), 8.13 (dd, *J* = 8.7, 1.9 Hz, 1H), 8.05 – 7.95 (m, 1H), 7.88 (d, *J* = 7.9 Hz, 1H), 7.76 – 7.64 (m, 3H), 7.43 – 7.33 (m, 1H), 5.33 (s, 2H), 2.82 (s, 3H).	DMSO	>98	Method AQ3		
1432				3 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.26 (s, 1H), 9.62 (d, *J* = 1.8 Hz, 1H), 9.23 (d, *J* = 8.2 Hz, 1H), 8.94 (dd, *J* = 5.4, 1.5 Hz, 1H), 8.78 (s, 1H), 8.30 (t, *J* = 7.9 Hz, 1H), 8.20 – 8.15 (m, 1H), 8.10 (d, *J* = 8.7 Hz, 1H), 8.00 (dd, *J* = 7.9, 5.3 Hz, 1H), 7.88 (d, *J* = 7.9 Hz, 1H), 7.80 – 7.71 (m, 2H), 7.59 – 7.50 (m, 1H), 7.47 – 7.35 (m, 2H), 5.35 (d, *J* = 5.5 Hz, 2H), 2.82 (s, 3H).	DMSO	>98	Method AQ3		
1433				3 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.39 (s, 1H), 9.61 (d, *J* = 1.7 Hz, 1H), 9.19 (d, *J* = 8.2 Hz, 1H), 9.01 (d, *J* = 1.8 Hz, 1H), 8.93 (dd, *J* = 5.3, 1.5 Hz, 1H), 8.38 (dd, *J* = 8.8, 1.9 Hz, 1H), 8.29 (t, *J* = 7.9 Hz, 1H), 8.09 (d, *J* = 8.7 Hz, 1H), 7.97 (dd, *J* = 8.1, 5.3 Hz, 1H), 7.92 – 7.80 (m, 3H), 7.72 (d, *J* = 7.8 Hz, 1H), 7.66 – 7.57 (m, 1H), 7.35 – 7.26 (m, 1H), 5.36 (d, *J* = 5.5 Hz, 2H), 2.81 (s, 3H).	DMSO	>98	Method AQ3		

627

1434				3 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.45 (s, 1H), 9.60 (d, *J* = 1.9 Hz, 1H), 9.19 (d, *J* = 8.2 Hz, 1H), 9.01 – 8.89 (m, 2H), 8.36 – 8.25 (m, 2H), 8.10 (d, *J* = 8.7 Hz, 1H), 8.05 – 7.94 (m, 3H), 7.88 (dd, *J* = 12.8, 5.4 Hz, 1H), 7.72 (d, *J* = 7.8 Hz, 1H), 7.46 – 7.35 (m, 2H), 5.36 (d, *J* = 5.5 Hz, 2H), 2.82 (s, 3H).	DMSO	>98	Method AQ3		
1435				3 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.28 (s, 1H), 9.63 (d, *J* = 1.8 Hz, 1H), 9.24 (d, *J* = 8.2 Hz, 1H), 8.95 (d, 1H), 8.83 (s, 1H), 8.30 (t, *J* = 7.9 Hz, 1H), 8.19 (dd, *J* = 8.7, 1.8 Hz, 1H), 8.11 (d, *J* = 8.7 Hz, 1H), 8.00 (dd, *J* = 8.1, 5.4 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.73 (d, *J* = 7.8 Hz, 1H), 7.64 – 7.51 (m, 2H), 7.46 – 7.37 (m, 1H), 5.36 (d, *J* = 5.5 Hz, 2H), 2.82 (s, 3H).	DMSO	>98	Method AQ3		
1436				3 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.02 (s, 1H), 9.56 (d, *J* = 1.6 Hz, 1H), 9.06 (d, *J* = 8.0 Hz, 1H), 8.88 (dd, *J* = 5.2, 1.5 Hz, 1H), 8.75 (s, 1H), 8.25 – 8.13 (m, 2H), 8.04 (d, *J* = 8.7 Hz, 1H), 7.89 (dd, *J* = 7.8, 5.3 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.70 – 7.60 (m, 2H), 7.53 – 7.44 (m, 1H), 7.38 (ddd, *J* = 12.2, 8.4, 3.5 Hz, 1H), 5.27 (d, *J* = 5.3 Hz, 2H), 2.77 (s, 3H).	DMSO	>98	Method AQ3		

628

1437				3 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.20 (s, 1H), 9.60 (d, *J* = 1.7 Hz, 1H), 9.19 (d, *J* = 8.1 Hz, 1H), 8.93 (dd, *J* = 5.4, 1.5 Hz, 1H), 8.75 (s, 1H), 8.29 (t, *J* = 7.9 Hz, 1H), 8.17 – 8.05 (m, 2H), 7.98 (dd, *J* = 8.0, 5.4 Hz, 1H), 7.83 (ddd, *J* = 15.5, 8.4, 6.0 Hz, 2H), 7.72 (d, *J* = 7.8 Hz, 1H), 7.54 – 7.44 (m, 1H), 7.38 – 7.28 (m, 1H), 5.33 (d, *J* = 5.5 Hz, 2H), 2.81 (s, 3H).	DMSO	>98	Method AQ3		
1438				4 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.45 (s, 1H), 9.62 (d, *J* = 1.7 Hz, 1H), 9.21 (d, *J* = 8.1 Hz, 1H), 9.03 (d, *J* = 1.7 Hz, 1H), 8.93 (dd, *J* = 5.3, 1.4 Hz, 1H), 8.39 – 8.26 (m, 2H), 8.15 – 8.04 (m, 2H), 8.00 – 7.81 (m, 3H), 7.76 – 7.59 (m, 2H), 5.36 (d, *J* = 5.5 Hz, 2H), 2.82 (s, 3H).	DMSO	>98	Method AQ3		
1439				3 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.29 (s, 1H), 9.53 (d, *J* = 1.8 Hz, 1H), 9.12 (d, *J* = 8.0 Hz, 1H), 8.93 (dd, *J* = 5.3, 1.4 Hz, 1H), 8.78 (d, *J* = 2.5 Hz, 2H), 8.31 (t, *J* = 7.8 Hz, 1H), 8.13 (q, *J* = 8.7 Hz, 2H), 8.04 – 7.89 (m, 2H), 7.87 – 7.68 (m, 2H), 7.50 (ddd, *J* = 11.6, 9.3, 2.6 Hz, 1H), 7.33 (td, *J* = 8.3, 1.9 Hz, 1H), 5.30 (d, *J* = 5.4 Hz, 2H).	DMSO	>98	Method AQ3		

629

1440				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.41 (s, 1H), 9.63 (d, *J* = 1.7 Hz, 1H), 9.15 (d, *J* = 8.1 Hz, 1H), 8.97 (dd, *J* = 5.2, 1.4 Hz, 1H), 8.83 (s, 1H), 8.20 (s, 2H), 7.97 (dd, *J* = 8.0, 5.3 Hz, 1H), 7.73 – 7.56 (m, 2H), 7.54 – 7.28 (m, 4H), 5.03 (d, *J* = 5.7 Hz, 2H).	DMSO	>98	Method AQ3		
1441				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 9.59 (d, *J* = 1.6 Hz, 1H), 9.07 – 8.94 (m, 2H), 8.84 (s, 1H), 8.76 (s, 1H), 8.22 – 8.13 (m, 2H), 7.96 (dd, *J* = 8.0, 5.3 Hz, 1H), 7.66 (ddd, *J* = 9.2, 6.1, 3.2 Hz, 1H), 7.53 – 7.32 (m, 2H), 1.69 (s, 9H).	DMSO	>98	Method AQ3		
1442				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 9.93 (s, 1H), 9.62 (d, *J* = 1.6 Hz, 1H), 9.06 – 8.87 (m, 2H), 8.39 (s, 1H), 8.06 – 7.98 (m, 3H), 7.87 (dd, *J* = 8.0, 5.1 Hz, 1H), 7.77 – 7.67 (m, 2H), 3.26 (d, *J* = 4.6 Hz, 3H), 2.45 (s, 3H).	DMSO	>98	Method AQ3		
1443				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 9.98 (s, 1H), 9.64 (s, 1H), 8.99 (dd, *J* = 27.3, 6.4 Hz, 2H), 8.41 (s, 1H), 8.10 – 7.93 (m, 3H), 7.88 (dd, *J* = 7.7, 6.0 Hz, 2H), 7.76 (t, *J* = 7.8 Hz, 1H), 3.27 (d, *J* = 4.5 Hz, 3H), 2.46 (s, 3H).	DMSO	>98	Method AQ3		

630

1444				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 9.76 – 9.69 (m, 1H), 9.37 (t, *J* = 5.4 Hz, 1H), 8.99 (dd, *J* = 11.7, 7.5 Hz, 1H), 8.81 (dt, *J* = 7.9, 4.0 Hz, 1H), 8.70 (t, *J* = 7.3 Hz, 1H), 8.52 (d, *J* = 9.2 Hz, 1H), 8.35 – 8.27 (m, 1H), 8.10 (dd, *J* = 12.8, 7.3 Hz, 1H), 8.01 – 7.90 (m, 2H), 7.77 – 7.71 (m, 1H), 7.50 – 7.37 (m, 3H), 7.06 – 7.01 (m, 1H), 5.19 (t, *J* = 17.9 Hz, 2H), 3.88 (s, 3H).	DMSO	>98	Method AQ3, F, G2 (reflux)		
1445				2 HCl	1H NMR (DMSO-d6) ppm 9.73 (s, 1H), 9.37 (brd, J = 8.08 Hz, 1H), 8.97 (brd, J = 5.24 Hz, 1H), 8.77 (brs, 1H), 8.20 (d, J =8.48 Hz, 1H), 8.10-8.07 (brm, 1H), 7.63-7.55 (brm, 2H), 7.47 (d, J =8.48 Hz, 1H), 7.32 (brm, 1H), 3.20 (d, J = 4.20 Hz, 3H), 2.65 (s, 3H). The 1H of 2HCl was not observed.	DMSO	>98	AQ6		
1446				3 HCl	1H NMR (DMSO-d6) ppm 9.73 (d, J = 1.76 Hz, 1H), 9.39 (brd, J = 8.16 Hz, 1H), 8.98 (dd, J = 5.44, 1.20 Hz, 1H), 8.80 'brs, 1H), 8.22 (d, J = 8.48 Hz, 1H), 8.12-8.08 (brm, 1H), 7.57-7.51 (m, 1H), 7.46-7.35 (m, 4H), 3.21 (d, J = 4.32 Hz, 3H), 2.55 (s, 3H) . The 1H of 3HCl was not observed.	DMSO	>98	AQ6		

631

1447				3 HCl	1H NMR (DMSO-d6) ppm 9.72 (d, J = 1.68 Hz, 1H), 9.26 (brd, J = 8.48 Hz, 1H), 8.91 (dd, J = 5.28, 1.40 Hz, 1H), 8.69 (brs, 1H), 8.18 (d, J = 8.56 Hz, 1H), 8.00-7.96 (brm, 1H), 7.53-7.49 (m, 2H), 7.44 (d,J = 8.56 Hz, 1H), 7.38-7.33 (m, 2H), 3.20 (d, J = 4.40 Hz, 3H), 2.63 (s, 3H) . The 1H of 3HCl was not observed.	DMSO	>98	AQ6		
1448				2 HCl	1H NMR (DMSO-d6) ppm 9.73 (d, J = 1.44 Hz, 1H), 9.36 (brd, J = 7.88 Hz, 1H), 8.96 (d, J = 5.04 Hz, 1H), 8.77 (brs, 1H), 8.21 (d, J = 8.56 Hz, 1H), 8.07 (brm, 1H), 7.48 (d, J = 8.56 Hz, 1H), 7.38-7.32 (m, 1H), 7.27- 7.22 (m, 2H), 3.20 (d, J = 4.4 Hz, 3H), 2.65 (s, 3H). The 1H of 2HCl was not observed.	DMSO	>98	AQ6		
1449				3 HCl	1H NMR (DMSO-d6) ppm 9.73 (d, J = 1.72 Hz, 1H), 9.32(brd, J =7.56 Hz, 1H), 8.94 (brd, J = 5.48 Hz, 1H), 8.74 (brs, 1H), 8.20 (d, J = 8.56 Hz, 1H), 8.08-8.02 (m, 1H) , 7.60-7.54 (m, 1H), 7.47 (d, J = 7.35-7.27 (m, 3H),3.20 (d, J = 4.4 Hz, 3H), 2.65 (s, 3H). The 1H of 3HCl was not observed.	DMSO	>98	AQ6		

632

1450				2 HCl	1H NMR (DMSO-d6) ppm 9.74 (d, J = 1.76 Hz, 1H), 9.37 (brd, J = 8.16 Hz, 1H), 8.97 (brdd, J = 5.44, 1.24 Hz, 1H), 8.79 (brs, 1H), 8.22 (d, J = 8.52 Hz, 1H), 8.10-8.06 (brm, 1H), 7.48- 7.35 (m, 4H), 3.21 (d, J = 4.36 Hz, 3H), 2.56 (brs, 3H). The 1H of 2HCl was not observed.	DMSO	>98	AQ6		
1451				3 HCl	1H NMR (DMSO-d6) ppm 9.74 (d, J = 1.52 Hz, 1H), 9.37 (d, J = 8.08 Hz, 1H), 8.97 (dd, J = 5.54, 1.16 Hz, 1H), 8.80 (brs, 1H), 8.23 (d, J = 8.52 Hz, 1H), 8.10-8.07 (m, 1H), 7.60-7.53 (m, 1H), 7.48 (d, J = 8.52 Hz, 1H), 7.41-7.36 (m, 1H), 7.30-7.26 (m,1H), 3.21 (d, J = 4.36 Hz, 3H), 2,56 (s, 3H) . The 1H of 3HCl was not observed.	DMSO	>98	AQ6		
1452				3 HCl	1H NMR (DMSO-d6) ppm 9.73 (d, J = 1.68 Hz, 1H), 9.26 (brd, J = 7.8 Hz, 1H), 8.91 (brdd, J = 5.28, 1.36 Hz, 1H), 8.71 (brs, 1H), 8.21 (d, J = 8.52 Hz, 1H), 8.00 (d, J = 8.4 Hz, 2H), 7.99-7.95 (m, 1H), 7.69 (d, 8.4 Hz, 2H),7.46 (d, J = 8.52Hz, 1H), 3.20 (d, J = 4.4 Hz, 3H), 2.63 (s, 3H). The 1H of 3HCl was not observed.	DMSO	>98	AQ6		

1453				2 HCl	1H NMR (DMSO-d6) ppm 9.73 (d, J = 1.72 Hz, 1H), 9.33 (brd, J = 7.64 Hz, 1H), 8.95 (brd, J = 5.28 Hz, 1H), 8.76 (brs, 1H), 8.22 (d, J = 8.48 Hz, 1H), 8.05 (brm, J = 7.64, 5.28 Hz, 1H), 7.98-7.93 (m, 2 H), 7.84- 7.81 (m, 1H), 7.74 (dd, J = 7.84, 7.76 Hz, 1H), 7.49 (d, J = 8.84 Hz, 1H), 3.21 (d, J = 4.4 Hz, 3H), 2.63 (s, 3H). The 1H of 2HCl was not observed.	DMSO	>98	AQ6		
1454				2 HCl	^{1}H NMR (DMSO-d_6) ppm 9.72 (d, J = 1.76 Hz, 1H), 9.42 (brd, J = 8.00 Hz, 1H), 9.00 (d, J = 5.52 Hz, 1H), 8.83 (bsr, 1H), 8.22 (d, J = 8.56 Hz, 1H), 8.13 (brm, 1H), 7.55- 7.51 (m, 2H), 7.48-7.43 (m, 4H), 3.21 (brd, J = 4.16 Hz, 3H), 2.64 (s, 3H). The 1H of 2HCl was not observed.	DMSO	>98	AQ6		
1455				2 HCl	^{1}H NMR (DMSO-d_6) ppm 9.72 (s, 1H), 9.33 (d, J = 8.24 Hz, 1H), 8.96 (d, J = 5.40 Hz, 1H), 8.75 (brs, 1H), 8.17 (d, J = 8.60 Hz, 1H), 8.06 (brm, 1H), 7.45 (d, J = 8.80 Hz, 1H), 7.40 (d, J = 8.64 Hz, 2H), 7.08 (d, J = 8.64 Hz, 2H), 3.84 (s, 3H), 3.20 (d, J = 4.20 Hz, 3H), 2.66 (s, 3H).The 1H of 2HCl was not observed.	DMSO	>98	AQ6		
1456				2 HCl	^{1}H NMR (DMSO-d_6) ppm 9.72 (d, J =1.64 Hz, 1H), 9.38 (d, J = 8.04 Hz, 1H), 8.98 (dd, J = 5.48, 1.24 Hz, 1H), 8.79 (brs, 1H), 8.20 (d, J = 8.52 Hz, 1H), 8.12-8.09 (m, 1H), 7.48-7.42 (m, 2H), 7.04-6.97 (m, 3H),3.82 (s, 3H), 3.21 (d, J = 4.28 Hz, 3H), 2.65 (s, 3H). The 1H of 2HCl was not observed.	DMSO	>98	AQ6		

634

1457				2 HCl	^{1}H NMR (DMSO-d_6) ppm 9.71 (d, J = 1.32 Hz, 1H), 9.40 (d, J =7.64 Hz, 1H), 8.99 (dd, J = 5.52, 1.16 Hz, 1H), 8.82 (brs, 1H), 8.17 (d, J = 8.48 Hz, 1H), 8.13 (m, 1H), 7.47-7.43 (m, 1H), 7.37 (d, J = 8.48 Hz, 1H), 7.22-7.16 (m, 2H), 7.11-7.07 (m, 1H), 3.73 (s, 3H), 3.21 (d, J = 4.12 Hz, 3H), 2.47 (s, 3H). The 1H of 2HCl was not observed.	DMSO	>98	AQ6		
1458				2 HCl	^{1}H NMR (DMSO-d_6) ppm 9.57 (d, J = 1.88 Hz, 1H), 8.93 (dd, J = 4.88, 1.56 Hz, 1H), 8.87 (brd, J = 6.52 Hz, 1H), 7.95 (d, J = 8.36 Hz, 1H), 7.84 (d, J = 8.36 Hz, 1H), 7.81 (m, 1H), 7.34 (d, J = 8.72 Hz, 2H), 7.11 (d, J = 8.72 Hz, 2H) ,3.84 (s, 3H), 3.34 (d, J = 4.56 Hz, 3H), 2.72 (s, 3H) . The 1H of 2HCl and NH- were not observed.	DMSO	>98	AQ6		
1459				2 HCl	^{1}H NMR (DMSO-d_6) ppm 9.59 (s, 1H), 8.94 (dd, J = 4.92, 1.48 Hz, 1H), 8.89 (br, 1H), 7.98 (d, J = 8.48 Hz, 1H), 7.86 (d, J = 8.48 Hz, 1H), 7.82 (m, 1H), 7.46 (t, J = 7.96 Hz, 1H), 7.06-7.03 (m, 1H), 6.98-6.94 (m, 2H), 3.83 (s, 3H), 3.34 (d, J = 4.56 Hz, 3H), 2.72 (s, 3H) . The 1H of 2HCl and NH- were not observed.	DMSO	>98	AQ6		

635

1460					^{1}H NMR (300 MHz, DMSO) δ 9.60 (s, 1H), 8.84 - 8.57 (m, 3H), 8.30 (d, J = 7.0 Hz, 1H), 8.18 (d, J = 8.8 Hz, 1H), 8.12 - 7.93 (m, 4H), 7.85 (dd, J = 8.7, 1.5 Hz, 1H), 7.60 - 7.46 (m, 1H), 4.85 - 4.58 (m, 1H), 1.37 (d, J = 6.5 Hz, 6H).	DMSO	100	AQ1	366 (M+1)	Method A (Formic acid)
1461				HCl	^{1}H NMR (300 MHz, DMSO) δ 9.81 (s, 1H), 9.60 (s, 1H), 8.95 (s, 3H), 8.39 (d, J = 8.9 Hz, 1H), 8.19 (s, 1H), 7.96 - 7.73 (m, 3H), 7.68 - 7.55 (m, 1H), 7.39 - 7.25 (m, 1H), 4.99 - 4.81 (m, 1H), 1.42 (d, J = 6.5 Hz, 6H).	DMSO	100	AQ1	359 (M+1)	Method A (Formic acid)
1462					^{1}H NMR (300 MHz, DMSO) δ 9.43 (s, 1H), 8.75 - 8.47 (m, 3H), 8.29 (d, J = 7.2 Hz, 1H), 7.79 (d, J = 7.1 Hz, 1H), 7.72 - 7.54 (m, 2H), 7.48 (dd, J = 7.8, 4.9 Hz, 1H), 7.44 - 7.32 (m, 1H), 7.30 - 7.12 (m, 1H), 3.32 (s, 3H), 3.16 (d, J = 4.3 Hz, 3H).	DMSO	100	AQ1	349 (M+1)	Method A (Formic acid)
1463					1H NMR (300 MHz, DMSO) δ 9.68 (dd, J = 2.1, 0.8 Hz, 1H), 8.86 - 8.78 (m, 1H), 8.74 (dd, J = 4.8, 1.7 Hz, 1H), 8.34 - 8.25 (m, 2H), 8.09 - 8.02 (m, 1H), 7.80 (d, J = 8.9 Hz, 2H), 7.60 (ddd, J = 8.0, 4.8, 0.8 Hz, 1H), 7.09 (d, J = 8.9 Hz, 2H), 4.31 (s, 3H), 3.83 (s, 3H).	DMSO	99	Method AQ2	344.0 (M+1)	Method C

636

1464					1H NMR (300 MHz, DMSO) δ 9.67 (d, J = 2.1 Hz, 1H), 8.82 (d, J = 7.9 Hz, 1H), 8.74 (dd, J = 4.8, 1.7 Hz, 1H), 8.46 (d, J = 1.7 Hz, 1H), 8.36 (dd, J = 8.8, 2.2 Hz, 1H), 8.15 - 7.94 (m, 5H), 7.60 (ddd, J = 8.0, 4.8, 0.8 Hz, 1H), 4.31 (s, 3H).	DMSO	99	Method AQ2	338.9 (M+1)	Method C
1465				2 HCl	1H NMR (300 MHz, DMSO) δ 9.71 (d, J = 1.8 Hz, 1H), 9.15 (d, J = 8.0 Hz, 1H), 8.90 (dd, J = 5.2, 1.4 Hz, 1H), 8.58 (s, J = 1.8 Hz, 1H), 8.48 (d, J = 1.6 Hz, 1H), 8.43 (dd, J = 8.7, 2.2 Hz, 1H), 8.32 (dd, J = 7.8, 0.9 Hz, 1H), 8.28 (dd, J = 8.2, 2.2 Hz, 1H), 8.14 (d, J = 8.7 Hz, 1H), 7.92 (dd, J = 8.0, 5.2 Hz, 1H), 7.81 (t, J = 8.0 Hz, 1H), 4.34 (s, 3H).	DMSO	99	Method AQ2	359.0 (M+1)	Method C
1466				2 HCl	1H NMR (300 MHz, DMSO) δ 9.71 (d, J = 2.0 Hz, 1H), 9.12 (dd, J = 8.0, 1.4 Hz, 1H), 8.89 (dd, J = 5.2, 1.5 Hz, 1H), 8.49 (d, J = 1.6 Hz, 1H), 8.42 (dd, J = 8.8, 2.2 Hz, 1H), 8.34 (d, J = 9.0 Hz, 2H), 8.14 (dd, J = 9.2, 2.4 Hz, 3H), 7.88 (dd, J = 7.8, 5.5 Hz, 1H), 4.34 (s, 3H).	DMSO	99	Method AQ2	359.0 (M+1)	Method C
1467				2 HCl	1H NMR (300 MHz, DMSO) δ 9.36 (s, 1H), 9.00 (d, J = 6.5 Hz, 2H), 8.78 (d, J = 4.5 Hz, 2H), 8.58 (s, 1H), 8.06 (s, 2H), 7.75 (dd, J = 15.6, 8.9 Hz, 1H), 7.47 (ddd, J = 11.7, 9.4, 2.6 Hz, 1H), 7.31 (td, J = 8.4, 2.7 Hz, 1H), 3.22 (d, J = 4.2 Hz, 3H).	DMSO	99	Method AQ2	349.6 (M+1)	Method C

637

1468				3 HCl	1H NMR (300 MHz, DMSO) δ 9.97 (s, 1H), 9.63 (d, J = 1.6 Hz, 1H), 9.04 (d, J = 7.0 Hz, 1H), 8.94 (dd, J = 5.1, 1.5 Hz, 1H), 8.76 (d, J = 0.7 Hz, 1H), 8.41 - 8.05 (m, 4H), 7.89 (dd, J = 7.1, 4.8 Hz, 1H), 7.59 (ddd, J = 7.1, 4.9, 1.8 Hz, 1H), 3.27 (d, J = 4.3 Hz, 3H).	DMSO	99	Method AQ2	332.4 (M+1)	Method C
1469				2 HCl	1H NMR (300 MHz, DMSO) δ 10.04 (s, 1H), 9.65 (d, J = 1.5 Hz, 1H), 9.06 (d, J = 7.3 Hz, 1H), 8.95 (dd, J = 5.1, 1.5 Hz, 1H), 8.71 (s, 1H), 8.19 (s, 2H), 7.89 (dd, J = 7.6, 5.1 Hz, 1H), 7.76 - 7.61 (m, 2H), 7.42 (td, J = 7.9, 0.9 Hz, 1H), 3.27 (d, J = 4.4 Hz, 3H).	DMSO	95	Method AQ2	365.3 (M+1)	Method C
1470				2 HCl	1H NMR (300 MHz, DMSO) δ 10.03 (s, 1H), 9.63 (d, J = 1.5 Hz, 1H), 9.04 (d, J = 7.9 Hz, 1H), 8.94 (dd, J = 5.1, 1.5 Hz, 1H), 8.68 (s, 1H), 8.16 (s, 2H), 7.88 (dd, J = 7.6, 5.1 Hz, 1H), 7.74 (t, J = 8.5 Hz, 1H), 7.67 (dd, J = 10.8, 2.0 Hz, 1H), 7.51 (dd, J = 8.3, 1.6 Hz, 1H), 3.27 (d, J = 4.4 Hz, 3H).	DMSO	94	Method AQ2	365.3 (M+1)	Method C
1471				2 HCl	1H NMR (300 MHz, DMSO) δ 9.95 (s, 1H), 9.64 (d, J = 1.6 Hz, 1H), 9.07 (d, J = 7.9 Hz, 1H), 8.94 (dd, J = 5.1, 1.5 Hz, 1H), 8.75 (s, 1H), 8.18 (s, 2H), 8.09 (d, J = 11.1 Hz, 1H), 7.92 (d, J = 4.0 Hz, 3H), 3.27 (d, J = 4.4 Hz, 3H).	DMSO	96	Method AQ2	356.4 (M+1)	Method C

638

1472				2 HCl	1H NMR (300 MHz, DMSO) δ 10.01 (s, 1H), 9.63 (d, J = 1.5 Hz, 1H), 9.03 (d, J = 7.8 Hz, 1H), 8.94 (dd, J = 5.1, 1.5 Hz, 1H), 8.73 (s, 1H), 8.25 - 8.12 (m, 3H), 7.93 - 7.76 (m, 4H), 7.63 (d, J = 0.8 Hz, 1H), 3.28 (d, J = 4.4 Hz, 3H).	DMSO	95	Method AQ2	374.4 (M+1)	Method C
1473				2 HCl	1H NMR (300 MHz, DMSO) δ 9.97 (s, 1H), 9.61 (d, J = 2.1 Hz, 1H), 8.98 (d, J = 4.6 Hz, 1H), 8.93 (dd, J = 5.1, 1.5 Hz, 1H), 8.68 - 8.60 (m, 1H), 8.13 (d, J = 6.1 Hz, 2H), 7.85 (dd, J = 7.7, 5.2 Hz, 1H), 7.63 (t, J = 8.3 Hz, 1H), 7.37 - 7.23 (m, 2H), 3.27 (d, J = 4.5 Hz, 3H), 2.56 (s, J = 5.2 Hz, 3H).	DMSO	95	Method AQ2	377.5 (M+1)	Method C
1474				2 HCl	1H NMR (300 MHz, DMSO) δ 9.98 (s, 1H), 9.64 (d, J = 1.6 Hz, 1H), 9.06 (d, J = 8.8 Hz, 1H), 8.94 (dd, J = 5.1, 1.5 Hz, 1H), 8.75 (s, 1H), 8.26 - 8.11 (m, 2H), 8.04 - 7.85 (m, 5H), 3.35 (s, 3H), 3.27 (d, J = 4.1 Hz, 3H).	DMSO	96	Method AQ2	409.5 (M+1)	Method C
1475				2 HCl	1H NMR (300 MHz, DMSO) δ 10.25 (s, 1H), 9.63 (d, J = 1.6 Hz, 1H), 9.00 (d, J = 7.1 Hz, 1H), 8.93 (dd, J = 5.0, 1.5 Hz, 1H), 8.79 (s, 1H), 8.31 (dd, J = 8.8, 1.5 Hz, 1H), 8.17 (d, J = 8.5 Hz, 1H), 7.84 (dd, J = 7.5, 4.8 Hz, 1H), 7.51 (d, J = 1.8 Hz, 1H), 7.40 (dd, J = 8.2, 1.9 Hz, 1H), 7.09 (d, J = 8.1 Hz, 1H), 6.10 (s, 2H), 3.29 (d, J = 4.3 Hz, 3H).	DMSO	99	Method AQ2	357.5 (M+1)	Method C

639

1476				2 HCl	1H NMR (300 MHz, DMSO) δ 10.26 (s, 1H), 9.63 (d, J = 1.6 Hz, 1H), 9.01 (d, J = 8.6 Hz, 1H), 8.93 (dd, J = 5.0, 1.5 Hz, 1H), 8.77 (s, 1H), 8.31 (dd, J = 8.8, 1.4 Hz, 1H), 8.18 (d, J = 8.6 Hz, 1H), 7.84 (dd, J = 6.9, 5.8 Hz, 1H), 7.44 (d, J = 2.2 Hz, 1H), 7.39 (dd, J = 8.4, 2.3 Hz, 1H), 7.01 (d, J = 8.4 Hz, 1H), 4.30 (s, 4H), 3.29 (d, J = 4.4 Hz, 3H).	DMSO	99	Method AQ2	371.5 (M+1)	Method C
1477				2 HCl	1H NMR (300 MHz, DMSO) δ 10.19 (s, 1H), 9.61 (d, J = 1.6 Hz, 1H), 8.98 (d, J = 8.8 Hz, 1H), 8.93 (dd, J = 5.0, 1.5 Hz, 1H), 8.82 (s, 1H), 8.35 (dd, J = 8.8, 1.3 Hz, 1H), 8.16 (d, J = 8.5 Hz, 1H), 7.85 (dd, J = 8.1, 5.2 Hz, 1H), 7.76 - 7.66 (m, 2H), 7.46 (t, J = 7.6 Hz, 1H), 7.31 (d, J = 7.7 Hz, 1H), 3.69 (t, J = 7.0 Hz, 2H), 3.31 (d, J = 4.4 Hz, 3H), 2.84 (t, J = 7.0 Hz, 2H).	DMSO	99	Method AQ2	357.5 (M+1)	Method C
1478				2 HCl	1H NMR (300 MHz, DMSO) δ 10.11 (s, 1H), 9.60 (d, J = 1.9 Hz, 1H), 8.93 (dd, J = 10.3, 5.4 Hz, 2H), 8.80 (d, J = 0.6 Hz, 1H), 8.34 (dd, J = 8.0, 0.5 Hz, 1H), 8.10 (d, J = 8.3 Hz, 1H), 7.88 - 7.75 (m, 3H), 7.40 (d, J = 8.3 Hz, 2H), 3.65 (t, J = 6.9 Hz, 2H), 3.30 (d, J = 4.4 Hz, 3H), 2.79 (t, J = 6.9 Hz, 2H).	DMSO	99	Method AQ2	357.5 (M+1)	Method C

1479				2 HCl	1H NMR (300 MHz, DMSO) δ 10.27 (s, 1H), 9.62 (d, J = 1.5 Hz, 1H), 8.99 (s, 1H), 8.96 - 8.88 (m, 2H), 8.37 (d, J = 8.9 Hz, 1H), 8.18 (d, J = 8.6 Hz, 1H), 7.96 (d, J = 8.5 Hz, 2H), 7.85 (s, 1H), 7.70 (d, J = 8.5 Hz, 2H), 3.30 (d, J = 4.3 Hz, 3H), 1.74 (s, 6H).	DMSO	99	Method AQ2	380.5 (M+1)	Method C
1480				2 HCl	1H NMR (300 MHz, DMSO) δ 10.23 (s, 1H), 9.62 (d, J = 1.8 Hz, 1H), 9.02 (d, J = 6.6 Hz, 1H), 8.93 (dd, J = 5.0, 1.5 Hz, 1H), 8.88 (d, J = 0.5 Hz, 1H), 8.33 (d, J = 8.5 Hz, 1H), 8.16 (d, J = 8.5 Hz, 1H), 7.99 (d, J = 1.7 Hz, 1H), 7.86 (dd, J = 7.4, 5.1 Hz, 1H), 7.75 (dd, J = 8.5, 1.8 Hz, 1H), 7.60 (d, J = 8.5 Hz, 1H), 3.29 (d, J = 4.3 Hz, 3H).	DMSO	99	Method AQ2	393.4 (M+1)	Method C
1481					1H NMR (300 MHz, DMSO) δ 9.63 (d, J = 1.4 Hz, 1H), 8.81 - 8.73 (m, 1H), 8.68 (dd, J = 4.7, 1.7 Hz, 1H), 8.61 (d, J = 4.3 Hz, 1H), 8.45 (s, 1H), 7.97 (d, J = 8.6 Hz, 1H), 7.86 (d, J = 8.7 Hz, 2H), 7.77 - 7.61 (m, 3H), 7.53 (dd, J = 7.9, 4.8 Hz, 1H), 7.40 (t, J = 7.6 Hz, 1H), 3.15 (d, J = 4.3 Hz, 3H).	DMSO	99	Method AQ2,followed by hydrolysis with 30% H_2O_2 and NaOH in ethanol	374.5 (M+1)	Method C

641

1482				2 HCl	1H NMR (300 MHz, DMSO) δ 10.60 (s, 1H), 10.29 (s, 1H), 9.62 (d, J = 1.5 Hz, 1H), 9.00 (d, J = 7.1 Hz 1H), 8.92 (dd, J = 4.9, 1.4 Hz, 1H), 8.76 (s, 1H), 8.29 (d, J = 8.9 Hz, 1H), 8.20 (d, J = 8.4 Hz, 1H), 7.84 (dd, J = 7.8, 4.8 Hz, 1H), 7.79 - 7.68 (m, 2H), 6.95 (d, J = 8.0 Hz, 1H), 3.57 (s, 2H), 3.29 (d, J = 4.3 Hz, 3H).	DMSO	94	Method AQ1, except that dioxane water was replaced with DME/water /EtOH in the microwave at 120°C for 10 min	368.5 (M+1)	Method C
1483				2 HCl	1H NMR (300 MHz, DMSO) δ 10.67 (s, 1H), 9.60 (d, J = 2.4 Hz, 1H), 8.99 - 8.88 (m, 2H), 8.73 (d, J = 1.0 Hz, 1H), 8.27 (d, J = 9.2 Hz, 1H), 8.10 (d, J = 7.5 Hz, 1H), 7.83 (dd, J = 6.9, 4.3 Hz, 1H), 7.40 (q, J = 8.3 Hz, 2H), 7.20 (s, 1H), 3.56 (s, 2H), 3.29 (d, J = 4.1 Hz, 3H).	DMSO	99	Method AQ1, except that dioxane water was replaced with DME/water /EtOH in the microwave at 120°C for 10 min	368.5 (M+1)	Method C
1484				2 HCl	1H NMR (300 MHz, DMSO) δ 10.12 (s, 1H), 9.61 (d, J = 1.9 Hz, 1H), 9.04 - 8.89 (m, 2H), 8.84 (d, J = 1.2 Hz, 1H), 8.36 (dd, J = 8.7, 1.3 Hz, 1H), 8.14 (d, J = 8.1 Hz, 1H), 7.94 - 7.78 (m, 3H), 7.50 (d, J = 8.3 Hz, 2H), 4.49 (s, 2H), 3.39 - 3.23 (m, 6H).	DMSO	99	Method AQ1, except that dioxane water was replaced with DME/water /EtOH in the microwave at 120°C for 10 min	357.5 (M+1)	Method C

642

1485					1H-NMR (400 MHz, DMSO-d6): δ 9.63 (s, 1H), 8.76 (td, J = 8.0, 1.6 Hz, 1H), 8.71 (dd, J = 4.8, 1.6 Hz, 1H), 8.37 (s, 1H), 7.81 (d, J = 8.8 Hz, 1H), 7.72 (d, J = 8.8 Hz, 1H), 7.59 – 7.54 (m, 1H), 7.43 (t, J = 8.0 Hz, 1H), 7.06 – 6.98 (m, 3H), 3.82 (s, 3H),	DMSO	95	Method G1,AQ1	377.0 379.0 (M+1)	Method B (NH_4HCO_3)
1486				2HCl	1H-NMR (400 MHz, DMSO-d6): δ 9.81 (s, 1H), 9.38 (d, J = 8.4 Hz, 1H), 9.15 (d, J = 5.2 Hz, 1H), 8.69 (d, J = 1.6 Hz, 1H), 8.41 (dd, J = 8.8, 2.0 Hz, 1H), 8.29 – 8.26 (m, 1H), 8.14 (d, J = 8.8 Hz, 1H), 7.50 – 7.41 (m, 3H), 7.11 – 7.08 (m, 1H), 4.80 – 4.76 (m, 1H), 3.66 – 3.57 (m, 2H), 3.50 (s, 3H), 3.44 (s, 3H), 1.35 (d, J = 6.4 Hz, 3H).	DMSO	95	Method G1,AQ1	401.1 (M+1)	Method B (NH_4HCO_3)
1487				2HCl	1H-NMR (400 MHz, CD3OD): δ 9.55 (s, 1H), 8.92 (d, J = 4.9 Hz, 1H), 8.89 (dt, J = 8.2, 1.8 Hz, 1H), 8.62 (s, 1H), 8.37 (d, J = 8.8 Hz, 1H), 8.03 (d, J = 8.7 Hz, 1H), 7.83 (dd, J = 8.0, 5.0 Hz, 1H), 7.49 (t, J = 8.1 Hz, 1H), 7.43 (s, 2H), 7.10 (d, J = 7.6 Hz, 1H), 4.01 (s, 2H), 3.46 (s, 3H), 3.35 (s, 3H), 1.37 (s, 6H).	MeOD	95	Method G1,AQ1	415.1 (M+1)	Method B (NH_4HCO_3)
1488				2HCl	1H-NMR (400 MHz, DMSO-d6): δ 10.34 (s, 1H), 9.65 (s, 1H), 9.04 (d, J = 6.9 Hz, 1H), 8.99 – 8.87 (m, 2H), 8.39 (d, J = 9.2 Hz, 1H), 8.24 (d, J = 8.2 Hz, 1H), 7.86 (s, 1H), 7.47 – 7.43 (m, 3H), 7.05 (d, J = 6.8 Hz, 1H), 4.26 – 4.22 (m, 2H), 3.77 – 3.73 (m, 2H), 3.56 – 3.50 (m, 2H), 3.32 (d, J = 4.3 Hz, 3H), 1.15 (t, J = 7.0 Hz, 3H).	DMSO	95	Method G1,AQ1	400.9 (M+1)	Method B (NH_4HCO_3)

643

1489					1H-NMR (400 MHz, DMSO-d6): δ 9.68 (s, 1H), 8.81 – 8.78 (m, 2H), 8.71 (d, *J* = 3.6 Hz, 1H), 8.54 (s, 1H), 8.32 (d, *J* = 1.2 Hz, 1H), 7.57 (dd, *J* = 7.6, 4.8 Hz, 1H), 7.46 – 7.42 (m, 3H), 7.04 – 7.01 (m, 1H), 3.88 (s, 3H), 3.19 (d, *J* = 4.0 Hz, 3H).	DMSO	95	Method G1,AQ1	377.1, 379.1 (M+1)	Method B (NH_4HCO_3)
1490				2HCl	1H-NMR (400 MHz, DMSO-d6): δ 10.50 (brs, 1H), 9.68 (d, J = 2.0 Hz, 1H), 9.09 (d, J = 8.0 Hz, 1H), 8.96 (dd, J = 5.2, 1.2 Hz, 1H), 8.94 (s, 1H), 8.40 (d, J = 9.2 Hz, 1H), 8.29 (d, J = 8.8 Hz, 1H), 7.89 (dd, J = 8.0, 1.6 Hz, 1H), 7.48 – 7.43 (m, 3H), 7.03 (d, J = 7.2 Hz, 1H), 4.06 – 4.05 (m, 2H), 3.92 (d, J = 11.6 Hz, 1H), 3.69 – 3.66 (m, 1H), 3.42 – 3.39 (m, 1H), 3.32 (d, J = 4.4 Hz, 3H), 1.86 – 1.83 (m, 1H), 1.69 (d, J = 12.4 Hz, 1H), 1.52 – 1.51 (m, 3H), 1.38 – 1.35 (m, 1H).	DMSO	95	Method G1,AQ1	427.2 (M+1)	Method B (NH_4HCO_3)
1492				3HCl	1H-NMR (400 MHz, DMSO-d6): δ 10.80 (s, 1H), 9.70 (s, 1H), 9.13 (d, J = 8.0 Hz, 1H), 9.07 (s, 1H), 8.97 (d, J = 4.4 Hz, 1H), 8.94 (s, 1H), 8.39 (d, J = 8.8 Hz, 1H), 8.32 (d, J = 8.8 Hz, 1H), 8.23 (d, J = 8.0 Hz, 1H), 7.98 (t, J = 8.0 Hz, 1H), 7.90 (t, J = 6.2 Hz, 1H), 7.68 (s, 1H), 7.53 (d, J = 8.0 Hz, 1H), 7.46 (d, J = 7.8 Hz, 1H), 7.12 (d, J = 8.0 Hz, 1H), 5.50 (s, 2H), 3.30 (d, J = 2.4 Hz, 3H).	DMSO	95	Method G1,AQ1	488.0 (M+1)	Method B (NH_4HCO_3)

644

1493				2HCl	1H-NMR (400 MHz, DMSO-d6): δ 10.58 (s, 1H), 9.71 (s, 1H), 9.14 (d, J = 7.6 Hz, 1H), 8.98 (d, J = 8.0 Hz, 2H), 8.40 (d, J = 8.8 Hz, 1H), 8.31 (d, J = 8.8 Hz, 1H), 7.92 (t, J = 6.2 Hz, 1H), 7.81 (t, J = 7.6 Hz, 1H), 7.47 – 7.43 (m, 3H), 7.02 (d, J = 7.2 Hz, 1H), 4.10 (t, J = 6.0 Hz, 2H), 3.53 (d, J = 6.4 Hz, 1H), 3.32 (d, J = 2.4 Hz, 3H), 2.26 (t, J = 7.0 Hz, 2H), 2.00 – 1.93 (m, 2H), 1.73 – 1.63 (m, 4H), 1.55 – 1.51 (m, 1H), 1.28 – 1.02 (m, 5H).	DMSO	95	Method G1,AQ1	496.2 (M+1)	Method B (NH_4HCO_3)
1494				2HCl	1H-NMR (400 MHz, DMSO-d6): δ 10.07 (s, 1H), 9.60 (s, 1H), 8.92 (d, J = 4.4 Hz, 2H), 8.76 (s, 1H), 8.32 (d, J = 8.4 Hz, 1H), 8.10 (d, J = 8.0 Hz, 1H), 7.85 – 7.83 (m, 4H), 7.11 (d, J = 8.8 Hz, 2H), 4.04 (t, J = 6.4 Hz, 2H), 3.30 (d, J = 4.0 Hz, 3H), 2.58 (d, J = 4.0 Hz, 3H), 2.26 (t, J = 7.4 Hz, 2H), 2.00 – 1.93 (m, 2H).	DMSO	95	Method G1,AQ1	428.1, 429.1, (M+1)	Method B (NH_4HCO_3)
1495				2HCl	1H-NMR (400 MHz, DMSO-d6): δ 10.63 (s, 1H), 9.73 (s, 1H), 9.17 (d, J = 7.6 Hz, 1H), 8.99 (s, 1H), 8.91 (s, 1H), 8.34 (s, 2H), 7.93 (t, J = 6.0 Hz, 1H), 7.88 (d, J = 7.2 Hz, 2H), 7.09 (d, J = 7.6 Hz, 2H), 4.08 – 4.06 (m, 2H), 3.32 (s, 3H), 2.98 (s, 3H), 2.84 (s, 3H), 2.47 – 2.46 (m, 2H), 1.98 – 1.94 (m, 2H).	DMSO	95	Method G1,AQ1	442.1, 443.1, (M+1)	Method B (NH_4HCO_3)

645

1496				2HCl	1H - NMR (400 MHz, DMSO-d6): δ 10.26 (s, 1H), 9.64 (s, 1H), 9.01 (d, J = 7.0 Hz, 1H), 8.94 (s, 1H), 8.89 (s, 1H), 8.39 (d, J = 8.2 Hz, 1H), 8.19 (d, J = 8.1 Hz, 1H), 7.85 (s, 1H), 7.47 (d, J = 5.8 Hz, 3H), 7.05 (d, J = 3.4 Hz, 1H), 4.21 (dt, J = 10.8, 5.5 Hz, 1H), 4.08 (qd, J = 10.1, 5.2 Hz, 2H), 3.82 (dd, J = 14.4, 7.0 Hz, 1H), 3.71 (dd, J = 14.1, 7.4 Hz, 1H), 3.31 (d, J = 4.2 Hz, 3H), 2.08 – 2.00 (m, 1H), 1.98 – 1.79 (m, 2H), 1.72 – 1.68 (m, 1H).	DMSO	95	Method G1,AQ1	413.1, 414.1 (M+1)	Method B (NH_4HCO_3)
1497				2HCl	1H-NMR (400 MHz, DMSO-d6): δ 10.53 (s, 1H), 9.68 (s, 1H), 9.09 (d, J = 7.7 Hz, 1H), 8.96 (d, J = 5.9 Hz, 2H), 8.39 (d, J = 8.7 Hz, 1H), 8.30 (d, J = 8.3 Hz, 1H), 7.94 – 7.79 (m, 1H), 7.48 – 7.45 (m, 3H), 7.04 (d, J = 7.5 Hz, 1H), 4.30 – 4.18 (m, 2H), 3.80– 3.70 (m, 2H), 3.44 (t, J = 6.6 Hz, 2H), 3.31 (d, J = 4.2 Hz, 3H), 1.56 – 1.54 (m, 2H), 0.89 (t, J = 7.4 Hz, 3H).	DMSO-d_6	95	Method G1,AQ1	415.1 (M+1)	Method B (NH_4HCO_3)
1498				2HCl	1H-NMR (400 MHz, DMSO-d6): δ 10.07 (s, 1H), 9.67 (s, 1H), 9.03 (d, J = 8.0 Hz, 1H), 8.95 (d, J = 4.5 Hz, 1H), 8.51 (s, 1H), 7.85 (s, 2H), 7.41 (t, J = 7.9 Hz, 1H), 7.18 (dd, J = 7.8, 5.1 Hz, 2H), 7.02 (dd, J = 8.2, 2.3 Hz, 1H), 3.97 (s, 3H), 3.84 (s, 3H),	DMSO	95	Method G1,AQ1	373.1 (M+1)	Method B (NH_4HCO_3)

646

1499				2HCl	1H-NMR (400 MHz, DMSO-d6): δ 10.06 (s, 1H), 9.66 (s, 1H), 9.02 (d, J = 7.5 Hz, 1H), 8.95 (s, 1H), 8.89 (s, 1H), 8.39 (d, J = 8.5 Hz, 1H), 8.22 (d, J = 8.6 Hz, 1H), 7.85 (dd, J = 7.0, 5.4 Hz, 1H), 7.52 – 7.43 (m, 3H), 7.09 – 7.01 (m, 1H), 4.17 – 4.15 (m, 2H), 3.32 – 3.30 (m, 4H), 3.25 (s, 3H), 1.98 – 1.82 (m, 2H), 1.17 (d, J = 6.1 Hz, 3H).	DMSO	95	Method G1,AQ1	415.1 (M+1)	Method B (NH_4HCO_3)
1500				2HCl	1H-NMR (400 MHz, CD3OD): δ 9.80 (s, 1H), 9.37 (d, J = 8.2 Hz, 1H), 9.13 (d, J = 5.3 Hz, 1H), 8.90 (s, 1H), 8.45 (d, J = 8.4 Hz, 1H), 8.25 (dd, J = 7.9, 5.6 Hz, 1H), 8.17 (d, J = 8.7 Hz, 1H), 7.64 (s, 1H), 7.54 (d, J = 5.1 Hz, 2H), 7.17 (dd, J = 7.5, 3.6 Hz, 1H), 4.70 – 4.62 (m, 2H), 4.42 (q, J = 9.0 Hz, 2H), 3.93 – 3.86 (m, 2H), 3.51 (s, 3H), 3.24 (s, 3H).	CD_3OD	95	Method G1,AQ1	468.1 (M+1)	Method B (NH_4HCO_3)
1501				2HCl	1H-NMR (400 MHz, DMSO): δ 10.45 (brs, 1H), 9.72 (s, 1H), 9.12 (d, J = 7.6 Hz, 1H), 8.97 (d, J = 4.0 Hz, 1H), 8.70 (s, 1H), 8.35 (d, J = 8.8 Hz, 1H), 8.23 (d, J = 8.4 Hz, 1H), 7.90 – 7.87 (m, 2H), 7.49 (d, J = 7.2 Hz, 1H), 7.43 (t, J = 7.2 Hz, 1H), 7.18 (d, J = 8.4 Hz, 1H), 7.11 (t, J = 7.2 Hz, 1H), 4.03 (t, J = 6.4 Hz, 2H), 3.30 (d, J = 4.4 Hz, 3H), 2.54 (d, J = 4.0 Hz, 3H), 2.19 (t, J = 7.4 Hz, 2H),1.93 – 1.86 (m, 2H).	DMSO	95	Method G1,AQ1	428.1 (M+1)	Method B (NH_4HCO_3)

647

1502					1H-NMR (400 MHz, DMSO-d6): δ 9.65 (s, 1H), 8.88 (s, 1H), 8.81 (d, J = 8 Hz,1H), 8.73 (s, 1H), 8.62 (s, 1H), 8.19 (d, J = 8 Hz, 1H), 7.88 (d, J = 9.2 Hz,1H), 7.61 – 7.58 (m, 1H), 7.47 – 7.44 (m, 3H), 7.06 – 7.04 (m, 1H), 4.56 – 4.54 (m, 1H), 3.87 (dd, J = 11.2, 2.0 Hz, 1H), 3.68 – 3.64 (m, 1H), 3.56 – 3.53 (m, 2H), 3.21 (d, J = 4.4 Hz, 3H), 2.09 – 2.05 (m, 1H), 1.83 – 1.72 (m, 2H), 1.61 – 1.55 (m, 1H).	DMSO	95	Method G1,AQ1	413.1 (M+1)	Method B (NH_4HCO_3)
1503				2HCl	1H-NMR (400 MHz, CD3OD): δ 9.77 (s, 1H), 9.43 (d, J = 8.1 Hz, 1H), 9.08 (d, J = 5.6 Hz, 1H), 8.46 (s, 1H), 8.34 – 8.25 (m, 1H), 8.20 (d, J = 8.7 Hz, 1H), 8.02 (d, J = 8.7 Hz, 1H), 7.37 (d, J = 7.5 Hz, 1H), 7.32 (t, J = 7.4 Hz, 1H), 7.05 (d, J = 8.3 Hz, 1H), 7.00 (t, J = 7.5 Hz, 1H), 3.98 (t, J = 6.1 Hz, 2H), 3.44 (t, J = 11.1 Hz, 1H), 3.35 (s, 3H), 2.17 (t, J = 7.3 Hz, 2H), 1.93 – 1.89 (m, 2H), 1.70 – 1.53 (m, 4H), 1.48 (d, J = 12.5 Hz, 1H), 1.22 – 1.12 (m, 2H), 1.08 – 1.02 (m, 3H).	CD_3OD	95	Method G1,AQ1	496.2 (M+1)	Method B (NH_4HCO_3)
1504					1H-NMR (400 MHz, DMSO-d6): δ 9.63 (s, 1H), 8.76 (d, *J* = 8.0 Hz, 1H), 8.67 (d, *J* = 3.6 Hz, 1H), 8.50 (d, *J* = 4.0 Hz, 1H), 8.10 (s, 1H), 7.56 – 7.53 (m, 2H), 7.46 – 7.42 (m, 3H), 7.03 – 7.01 (m, 1H), 4.07 (s, 3H), 3.88 (s, 3H), 3.17 (d, *J* = 4.0 Hz, 1H).	DMSO	95	Method G1,AQ1	372.9 (M+1)	Method B (NH_4HCO_3)

648

1505					1H-NMR (400 MHz, DMSO): δ 9.28 (s, 1H), 8.94 (t, *J* = 7.6 Hz, 1H), 8.62 (d, *J* = 4.2 Hz, 1H), 8.42 (s, 1H), 7.94 (d, *J* = 8.8 Hz, 1H), 7.84 (d, J = 8.8 Hz, 1H), 7.73 – 7.71 (m, 1H), 7.46 (t, J = 10.0 Hz, 1H), 7.33 – 7.27 (m, 2H), 3.16 (d, *J* = 4.4 Hz, 3H).	DMSO	95	Method G1,AQ1	367.0 (M+1)	Method B (NH_4HCO_3)
1506					1H-NMR (400 MHz, DMSO): δ 8.77 (s, 1H), 8.66 (t, *J* = 8.6 Hz, 1H), 8.52 (s, 1H), 8.44 - 8.31 (m, 1H), 8.03 (d, *J* = 8.6 Hz, 1H), 7.88 (d, *J* = 8.6 Hz, 1H), 7.62 – 7.49 (m, 3H), 7.42 – 7.37 (m, 1H), 3.12 (d, *J* = 3.0 Hz, 3H).	DMSO	95	Method G1,AQ1	366.9 (M+1)	Method B (NH_4HCO_3)
1507					1H-NMR (400 MHz, DMSO): δ 9.29 (d, *J* = 2.0 Hz, 1H), 8.95 (dt, *J* = 8.4, 2.4 Hz, 1H), 8.65 (d, *J* = 4.4 Hz, 1H), 8.49 (s, 1H), 7.94 – 7.93 (m, 2H), 7.60 - 7.26 (m, 4H), 3.16 (d, *J* = 4.4 Hz, 3H).	DMSO	95	Method G1,AQ1	367.1 (M+1)	Method B (NH_4HCO_3)
1508				2HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.46 (s, 1H), 8.77 (s, 1H), 8.65 (t, *J* = 8.5 Hz, 1H), 8.55 (s, 1H), 8.19 (d, *J* = 8.7 Hz, 1H), 8.07 (d, *J* = 8.6 Hz, 1H), 7.79 (dd, *J* = 15.8, 7.8 Hz, 1H), 7.71 – 7.66 (m, 1H), 7.51 (t, *J* = 10.2 Hz, 1H), 7.34 (t, *J* = 8.5 Hz, 1H), 3.23 (d, *J* = 3.3 Hz, 3H).	DMSO	95	Method G1,AQ1	367.0 (M+1)	Method B (NH_4HCO_3)

649

1509				2HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.98 (s, 1H), 9.55 (d, *J* = 1.8 Hz, 1H), 9.07 (d, *J* = 7.2 Hz, 1H), 8.67 (s, 1H), 8.16 (dd, *J* = 18.0, 8.4 Hz, 2H), 7.84 (d, *J* = 8.3 Hz, 1H), 7.78 (td, *J* = 8.9, 6.6 Hz, 1H), 7.55 – 7.45 (m, 1H), 7.33 (td, *J* = 8.4, 2.0 Hz, 1H), 3.28 (d, *J* = 4.4 Hz, 3H), 2.74 (s, 3H).	DMSO	95	Method G1,AQ1	363.1 (M+1)	Method B (NH_4HCO_3)
1510				2HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.17 (s, 1H), 8.82 (dd, *J* = 7.9, 6.7 Hz, 2H), 8.65 (s, 1H), 8.21 (d, *J* = 8.5 Hz, 1H), 8.07 (d, *J* = 8.6 Hz, 1H), 7.80 (s, 1H), 7.65 – 7.50 (m, 2H), 7.42 (dd, *J* = 12.7, 7.6 Hz, 1H), 3.20 (d, *J* = 4.4 Hz, 3H), 2.94 (s, 3H).	DMSO	95	Method G1,AQ1	363.0 (M+1)	Method B (NH_4HCO_3)
1511				2HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.24 (s, 1H), 8.84 (d, *J* = 4.0 Hz, 1H), 8.77 (s, 1H), 8.64 (s, 1H), 8.18 (d, *J* = 8.6 Hz, 1H), 8.08 (d, *J* = 8.6 Hz, 1H), 7.79 (td, *J* = 8.9, 6.6 Hz, 2H), 7.57 – 7.46 (m, 1H), 7.34 (td, *J* = 8.5, 2.2 Hz, 1H), 3.20 (d, *J* = 4.5 Hz, 3H), 2.93 (s, 3H).	DMSO	95	Method G1,AQ1	362.9 (M+1)	Method B (NH_4HCO_3)
1512				2HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.57 (s,1H), 8.83 (dd, *J* = 8.0, 1.6 Hz, 1H), 8.63 (dd, *J* = 4.8, 2.0 Hz, 1H), 8.38 (s, 1H), 7.95 – 7.86 (m, 2H), 7.67 – 7.57 (m, 2H), 7.15 – 7.09 (m, 2H), 4.44 (brs, 1H), 2.17 (t, *J* = 7.6 Hz, 1H), 1.91 – 1.89 (m, 1H), 1.78 (d, *J* = 12.0 Hz, 1H), 1.56 – 1.48 (m, 4H), 1.32 – 1.28 (m, 1H).	DMSO	95	Method G1,AQ1	417.1 (M+1)	Method B (NH_4HCO_3)

650

1513				2HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.55 (s, 1H), 8.94 – 8.89 (m, 2H), 8.58 (s, 1H), 8.23 (d, *J* = 8.8 Hz, 1H), 8.04 (d, *J* = 8.8 Hz, 1H), 7.85 (t, *J* = 6.8 Hz, 1H), 7.73 (dd, *J* = 14.4, 8.0 Hz, 1H), 7.25 – 7.19 (m, 2H), 4.01 (q, *J* = 7.2 Hz, 2H), 1.48 (t, *J* =7.2 Hz, 3H).	DMSO	95	Method G1,AQ1	363.1 (M+1)	Method B (NH_4HCO_3)
1514				2HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.71 (s, 1H), 9.21 (d, *J* = 8.4 Hz, 1H), 9.08 (d, *J* = 4.4 Hz, 1H), 8.68 (s, 1H), 8.30 (d, *J* = 8.8 Hz, 1H), 8.15 – 8.12 (m, 2H), 7.50 – 7.38 (m, 3H), 4.04 (q, *J* = 7.2 Hz, 2H), 1.49 (t, *J* =7.2 Hz, 3H).	DMSO	95	Method G1,AQ1	363.1 (M+1)	Method B (NH_4HCO_3)
1515				2HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.67 (s, 1H), 9.25 (d, *J* = 8.0 Hz, 1H), 9.03 (d, *J* = 5.2 Hz, 1H), 8.60 (s, 1H), 8.21 – 8.14 (m, 2H), 8.06 (d, *J* = 8.4 Hz, 1H), 7.40 – 7.26 (m, 3H), 4.26 (brs, 4H), 2.14 (brs, 4H).	DMSO-d_6	95	Method G1,AQ1	389.1 (M+1)	Method B (NH_4HCO_3)
1516				2HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.60 (s, 1H), 9.14 (d, *J* = 8.0 Hz, 1H), 9.10 (d, *J* = 5.2 Hz, 1H), 8.69 (s, 1H), 8.19 (d, *J* = 8.4 Hz, 1H), 8.09 (dd, *J* = 8.0, 5.2 Hz, 1H), 8.03 (d, *J* = 8.8 Hz, 1H), 7.39 – 7.27 (m, 3H), 4.60 – 4.50 (m, 1H), 2.08 (d, *J* = 11.6 Hz, 2H), 1.84 (d, *J* = 12.0 Hz, 2H), 1.69 (d, *J* = 8.4 Hz, 1H), 1.57 – 1.45 (m, 4H), 1.18 – 1.10 (m, 1H).	DMSO	95	Method G1,AQ1	417.1 (M+1)	Method B (NH_4HCO_3)

651

1517					^{1}H-NMR (400 MHz, DMSO-d_6): δ 12.04 (brs, 1H), 9.58 (s, 1H), 9.38 (brs, 1H), 8.84 (d, *J* = 5.6 Hz, 2H), 8.72 (s, 1H), 8.28 (d, *J* = 9.2 Hz, 1H), 7.75 (t, *J* = 6.8 Hz, 1H), 7.51 – 7.41 (m, 3H), 7.07 – 7.03 (m, 1H), 3.88 (s, 3H), 3.80 (q, *J* = 5.6 Hz, 2H), 2.32 (t, *J* = 7.2 Hz, 2H), 1.86 – 1.74 (m, 2H), 1.73 – 1.64 (m, 2H).	DMSO	95	Method G1,AQ1	428.9 (M+1)	Method B (NH_4HCO_3)
1518					^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.61 (s, 1H), 8.74 (td, *J* = 8.0, 1.6 Hz, 1H), 8.71 – 8.66 (m, 1H), 8.31 (d, *J* = 1.6 Hz, 1H), 8.08 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.90 (d, *J* = 8.8 Hz, 1H), 7.87 – 7.81 (m, 2H), 7.58 – 7.49 (m, 1H), 7.39 – 7.30 (m, 2H), 3.49 (s, 6H).	DMSO	95	Method G1,AQ1	345.1 (M+1)	Method B (NH_4HCO_3)
1519					^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.61 (s, 1H), 8.74 (d, *J* = 7.2 Hz, 1H), 8.69 (d, *J* = 3.6 Hz, 1H), 8.32 (s, 1H), 8.08 (d, *J* = 8.4 Hz, 1H), 7.89 (d, *J* = 8.4 Hz, 1H), 7.82 (d, *J* = 7.6 Hz, 2H), 7.62 – 7.48 (m, 3H), 3.48 (s, 6H).	DMSO	95	Method G1,AQ1	361.1 363.1 (M+1)	Method B (NH_4HCO_3)
1520					^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.61 (s, 1H), 8.74 (td, *J* = 8.0, 1.6 Hz, 1H), 8.69 (dd, *J* = 4.8, 1.6 Hz, 1H), 8.42 (d, *J* = 2.0 Hz, 1H), 8.16 (dd, *J* = 8.8, 2.0 Hz, 1H), 8.04 – 7.89 (m, 5H), 7.54 (q, *J* = 5.2 Hz, 1H), 3.51 (s, 6H).	DMSO	95	Method G1,AQ1	352.1 (M+1)	Method B (NH_4HCO_3)

652

1521					^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.61 (s, 1H), 8.76 (d, *J* = 8.0 Hz, 1H), 8.68 – 8.60 (m, 2H), 8.15 (d, *J* = 8.8 Hz, 1H), 7.85 (d, *J* = 8.8 Hz, 1H), 7.56 (q, *J* = 4.8 Hz, 1H), 7.49 – 7.40 (m, 3H), 7.30 (s, 1H), 7.06 – 6.97 (m, 1H), 6.73 (s, 1H), 3.87 (s, 5H), 2.14 (t, *J* = 7.2 Hz, 2H), 1.80 – 1.71 (m, 2H), 1.71 – 1.62 (m, 2H).	DMSO	95	Method G1,AQ1	428.1 (M+1)	Method B (NH_4HCO_3)
1522				2 HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.67 (s, 1H), 9.39 (d, *J* = 8.2 Hz, 1H), 9.02 (d, *J* = 5.3 Hz, 1H), 8.31 (d, *J* = 9.3 Hz, 2H), 8.24 – 8.10 (m, 3H), 7.88 (d, *J* = 7.7 Hz, 1H), 7.72 (t, *J* = 7.8 Hz, 1H), 3.54 (s, 6H), 2.78 (s, 3H).	DMSO	95	Method G1,AQ1	366.1 (M+1)	Method B (NH_4HCO_3)
1523					^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.63 (d, *J* = 1.7 Hz, 1H), 8.88 – 8.32 (m, 4H), 8.16 (dd, *J* = 8.7, 1.8 Hz, 1H), 7.86 (t, *J* = 9.2 Hz, 1H), 7.55 (dd, *J* = 7.9, 4.8 Hz, 1H), 7.50 – 7.34 (m, 3H), 7.01 (dt, *J* = 7.3, 2.1 Hz, 1H), 3.96 – 3.84 (m, 5H), 2.78 (t, *J* = 6.9 Hz, 2H).	DMSO	95	Method G1,AQ1	400.9 (M+1)	Method B (NH_4HCO_3)
1524					^{1}H-NMR (400 MHz, DMSO-d_6): 9.63 (s, 1H), 8.77 (d, *J* = 8 Hz, 1H), 8.66 – 8.63 (m, 3H), 8.15 (d, *J* = 8.8 Hz, 1H), 7.85 (d, *J* = 8.8 Hz, 1H), 7.45 – 7.41 (m, 3H), 7.33 (s, 1H), 7.01 (d, *J* = 7.0 Hz, 1H), 6.79 (s, 1H), 3.88 (s, 3H), 3.72 (d, *J* = 6.0 Hz, 2H), 2.24 (t, *J* = 7.2 Hz, 2H), 2.04 – 1.94 (m, 2H).	DMSO	95	Method G1,AQ1	414.1 (M+1)	Method B (NH_4HCO_3)

653

1525					^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.58 (d, *J* = 1.2 Hz, 1H), 8.73 – 8.68 (m, 3H), 8.37 (s, 1H), 8.27 – 8.22 (m, 4H), 7.89 – 7.87 (m, 2H), 7.75 (t, *J* = 8.0 Hz, 1H), 7.55 (dd, *J* = 8.0, 5.2 Hz, 1H).	DMSO	95	Method G1,AQ1	324.1 (M+1)	Method B (NH_4HCO_3)
1526					^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.57 (d, *J* = 1.6 Hz, 1H), 8.72 – 8.66 (m, 2H), 8.57 (d, *J* = 1.6 Hz, 1H), 8.19 – 7.91 (m, 3H), 7.83 (d, *J* = 8.0 Hz, 3H), 7.54 (dd, *J* = 7.6, 4.8 Hz, 1H), 7.10 (d, *J* = 8.4 Hz, 2H), 3.83 (s, 3H).	DMSO	95	Method G1,AQ1	329.1 (M+1)	Method B (NH_4HCO_3)
1527					^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.58 (s, 1H), 8.72 – 8.66 (m, 3H), 8.16 (d, *J* = 8.4 Hz, 3H), 7.91 (d, *J* = 8.4 Hz, 2H), 7.85 (d, *J* = 8.8 Hz, 1H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.54 (dd, *J* = 7.6, 4.8 Hz, 1H).	DMSO	95	Method G1,AQ1	333.1, 335.0 (M+1)	Method B (NH_4HCO_3)
1528				2HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.59 (s, 1H), 9.28 (d, *J* = 8.0 Hz, 1H), 9.01 (d, *J* = 5.6 Hz, 1H), 8.65 (s, 2H), 8.37 (s, 2H), 8.25 (d, *J* = 8.0 Hz, 1H), 8.22 (s, 1H), 8.13 (t, *J* = 6.8 Hz, 1H), 7.88 (d, *J* = 7.6 Hz, 1H), 7.74 (t, *J* = 8.0 Hz, 1H), 2.77 (s, 3H).	DMSO	95	Method G1,AQ1	338.1 (M+1)	Method B (NH_4HCO_3)

654

1529				2HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.78 (s, 1H), 9.72 (d, *J* = 1.8 Hz, 1H), 9.18 (d, *J* = 8.1 Hz, 1H), 8.98 (dd, *J* = 5.1, 1.2 Hz, 1H), 8.78 (s, 1H), 8.29 (d, *J* = 8.6 Hz, 1H), 8.17 (d, *J* = 8.6 Hz, 1H), 7.95 (dd, *J* = 7.9, 5.3 Hz, 1H), 7.80 (td, *J* = 8.9, 6.6 Hz, 1H), 7.55 – 7.45 (m, 1H), 7.34 (td, *J* = 8.4, 2.3 Hz, 1H), 7.26 (s, 1H), 6.96 (s, 1H), 3.98 (d, *J* = 6.1 Hz, 2H), 1.24 (s, 6H).	DMSO	95	Method G1,AQ1	434.1 (M+1)	Method B (NH_4HCO_3)
1530				2HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.58 (s, 1H), 9.04 – 8.89 (m, 2H), 8.71 – 8.66 (m, 1H), 8.15 – 8.11(m, 2H), 7.82 –7.76 (m, 2H), 7.51 (t, *J* = 9.2 Hz, 1H), 7.34 (t, *J* = 8.8 Hz, 1H), 4.64 (s, 2H), 3.19 (s, 3H), 2.91 (s, 3H).	DMSO	95	Method G1,AQ1	420.1 (M+1)	Method B (NH_4HCO_3)
1531					^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.63 (s, 1H), 8.78 (d, *J* = 7.9 Hz, 1H), 8.72 (d, *J* = 3.2 Hz, 1H), 8.19 (s, 2H), 8.08 – 7.97 (m, 2H), 7.80 (dd, *J* = 15.5, 8.9 Hz, 1H), 7.58 (dd, *J* = 7.6, 4.9 Hz, 1H), 7.52 – 7.41 (m, 1H), 7.29 (td, *J* = 8.3, 1.9 Hz, 1H), 4.48 (s, 2H), 4.15 (s, 2H), 3.48 (s, 2H).	DMSO	95	Method G1,AQ1	418.1 (M+1)	Method B (NH_4HCO_3)
1532					^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.65 (s, 1H), 8.87 (s, 1H), 8.79 (d, *J* = 7.7 Hz, 1H), 8.70 (s, 1H), 8.59 (s, 1H), 8.23 (s, 1H), 8.05 – 7.89 (m, 3H), 7.75 (dd, *J* = 15.1, 7.6 Hz, 1H), 7.56 (s, 1H), 7.48 (t, *J* = 9.9 Hz, 1H), 7.32 (t, *J* = 8.1 Hz, 1H), 4.46 (t, *J* = 13.4 Hz, 2H).	DMSO	95	Method G1,AQ1	442.0 (M+1)	Method B (NH_4HCO_3)

655

1533				2HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.63 (s, 1H), 8.95 – 9.03 (m, 2H), 8.78 (s, 1H), 8.14 – 8.24 (m, 2H), 7.88 (t, *J* = 6.0 Hz, 1H), 7.79 (d, *J* = 8.8 Hz, 1H), 7.54 – 7.48 (m, 1H), 7.35 – 7.32 (m, 1H), 4.89 (m, 1H), 1.39 (d, *J* = 1.2 Hz, 6H).	DMSO	95	Method G1,AQ1	377.1 (M+1)	Method B (NH_4HCO_3)
1534				2HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.61 (s, 1H), 8.69 – 8.74 (m, 2H), 8.59 (s, 1H), 7.92 (d, J = 8.0 Hz, 1H), 7.84 (d, *J* = 8.4 Hz, 1H), 7.71 – 7.77 (m, 1H), 7.66 (s, 1H), 7.56 – 7.60 (m, 1H), 7.42 – 7.48 (m, 1H), 7.27 – 7.32 (m, 1H), 1.66 (s, 9H).	DMSO	95	Method G1,AQ1	391.1 (M+1)	Method B (NH_4HCO_3)
1535				2HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.74 (s, 1H), 9.66 (s, 1H), 9.22 (d, *J* = 7.6 Hz, 1H), 8.99 (d, *J* = 4.8 Hz, 1H), 8.83 (s, 1H), 8.33 (d, *J* = 8.4 Hz, 1H), 8.20 (d, *J* = 8.8 Hz, 1H), 7.95 (t, *J* = 6.2 Hz, 1H), 7.58 (q, *J* = 8.6 Hz, 1H), 7.51 (t, *J* = 7.0 Hz, 1H), 7.46 – 7.41 (m, 1H), 7.25 (s, 1H), 6.72 (s, 1H), 5.13 – 5.06 (m, 1H), 3.21 (q, *J* = 7.3 Hz, 1H), 2.22 – 1.92 (m, 5H), 1.68 – 1.57 (m, 1H).	DMSO	95	Method G1,AQ1	446.0 (M+1)	Method B (NH_4HCO_3)

656

1536				2HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.81 (s, 2H), 9.32 (d, *J* = 8.0 Hz, 1H), 9.02 (d, *J* = 5.2 Hz, 1H), 8.81 (s, 1H), 8.42 (d, *J* = 8.4 Hz, 1H), 8.18 (d, *J* = 8.4 Hz, 1H), 8.00 (dd, *J* = 7.8, 5.8 Hz, 1H), 7.76 (dd, *J* = 15.4, 8.6 Hz, 1H), 7.51 (t, *J* = 10.0 Hz, 1H), 7.35 (t, *J* = 8.2 Hz, 1H), 7.29 (s, 1H), 6.73 (s, 1H), 5.15 – 5.07 (m, 1H), 3.21 (q, *J* = 7.3 Hz, 1H), 2.23 – 1.87 (m, 5H), 1.68 – 1.57 (m, 1H).	DMSO	95	Method G1,AQ1	446.1 (M+1)	Method B (NH_4HCO_3)
1537					^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.66 (s, 1H), 8.79 (d, *J* = 7.6 Hz, 1H), 8.69 (dd, *J* = 4.4, 1.2 Hz, 1H), 8.61 (d, *J* = 1.6 Hz, 1H), 8.40 (d, *J* = 7.2 Hz, 1H), 8.13 (dd, *J* = 8.6, 1.4 Hz, 1H), 7.85 (d, *J* = 8.4 Hz, 1H), 7.55 (dd, *J* = 7.6, 4.8 Hz, 1H), 7.49 – 7.40 (m, 3H), 7.11 (s, 1H), 7.02 (d, *J* = 7.2 Hz, 1H), 6.69 (s, 1H), 5.03 – 4.96 (m, 1H), 3.87 (s, 3H), 3.20 (dd, *J* = 15.0, 7.4 Hz, 1H), 2.22 – 1.88 (m, 5H), 1.70 – 1.56 (m, 1H).	DMSO	95	Method G1,AQ1		Method B (NH_4HCO_3)
1538					^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.60 (s, 1H), 8.86 (d, *J* = 7.7 Hz, 1H), 8.74 (d, *J* = 8.0 Hz, 1H), 8.69 (d, *J* = 3.3 Hz, 1H), 8.65 (s, 1H), 8.19 (d, *J* = 7.4 Hz, 1H), 7.87 (d, *J* = 8.8 Hz, 2H), 7.54 (dd, *J* = 7.8, 4.8 Hz, 1H), 7.50 – 7.40 (m, 3H), 7.01 (dd, *J* = 7.3, 3.9 Hz, 1H), 4.85 (dd, *J* = 16.9, 8.7 Hz, 1H), 3.88 (s, 3H), 2.16 (s, 2H), 1.96 (s, 2H).	DMSO	95	Method G1,AQ1	426.1, 427.1 (M+1)	Method B (NH_4HCO_3)

657

1539				2HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.34 (s, 1H), 9.67 (s, 1H), 9.07 (s, 1H), 8.97 (d, *J* = 5.0 Hz, 1H), 8.92 (s, 1H), 8.39 (d, *J* = 8.8 Hz, 1H), 8.25 (d, *J* = 7.4 Hz, 1H), 7.99 (s, 1H), 7.90 (s, 1H), 7.48 (d, *J* = 5.8 Hz, 3H), 7.09 – 6.99 (m, 1H), 4.03 (d, *J* = 6.1 Hz, 2H), 3.89 (s, 3H), 2.65 (t, *J* = 6.8 Hz, 2H), 2.56 (d, *J* = 4.4 Hz, 3H).	DMSO	95	Method G1,AQ1	414.0, 415.0 (M+1)	Method B (NH_4HCO_3)
1540				2HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.48 (s, 1H), 9.64 (s, 1H), 9.05 (d, *J* = 7.9 Hz, 1H), 9.01 – 8.92 (m, 2H), 8.38 (d, *J* = 8.8 Hz, 1H), 8.28 (d, *J* = 8.6 Hz, 1H), 7.93 – 7.83 (m, 1H), 7.55 – 7.43 (m, 3H), 7.08 – 6.98 (m, 1H), 4.04 (dd, *J* = 12.4, 6.6 Hz, 2H), 3.89 (s, 3H), 2.98 (s, 3H), 2.89 (t, *J* = 7.0 Hz, 2H), 2.84 (s, 3H).	DMSO	95	Method G1,AQ1	428.1, 429.1 (M+1)	Method B (NH_4HCO_3)
1541				2HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.02 (brs, 1H), 9.75 (d, *J* = 1.6 Hz, 1H), 9.07 (dd, *J* = 8.0, 1.6 Hz, 1H), 8.83 (s, 1H), 8.35 (d, *J* = 9.2 Hz, 1H), 8.19 (d, *J* = 8.0 Hz, 1H), 8.14 (d, *J* = 8.8 Hz, 1H), 7.48 – 7.46(m, 3H), 7.06 – 7.03 (m, 1H), 3.89 (s, 3H), 3.30 (d, *J* = 4.0 Hz, 3H).	DMSO	95	Method G1,AQ1	411.1 (M+1)	Method B (NH_4HCO_3)

658

1542				2HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.22 (brs, 1H), 9.64 (s, 1H), 9.01 (d, *J* = 6.4 Hz, 1H), 8.95 (d, *J* = 4.0 Hz, 1H), 8.89 (s, 1H),8.39 (d, *J* = 8.4 Hz, 1H), 8.23 (d, *J* = 8.0 Hz, 1H), 7.85 (t, *J* = 5.2 Hz, 1H), 7.52 – 7.42 (m, 4H), 7.08 – 7.05 (m, 1H), 6.89 (s, 1H), 3.89 (s, 4H),3.83 – 3.76 (m, 2H), 2.83 – 2.79 (m, 1H), 1.65 – 1.56 (m, 7H), 1.24 – 1.07 (m, 6H), 0.89 – 0.81 (m, 2H).	DMSO	95	Method G1,AQ1	510.2 (M+1)	Method B (NH_4HCO_3)
1543					^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.67 (d, *J* = 1.6 Hz, 1H), 8.80 (dt, *J* = 8.0, 2.0 Hz, 1H), 8.70 (dd, *J* = 4.4, 2.0 Hz, 1H), 8.15 (s, 1H), 7.87 (s, 1H), 7.71 – 7.67 (m, 1H), 7.58 – 7.55 (m, 1H), 7.47 (d, *J* = 2.4 Hz, 1H), 7.34 (m, 2H), 3.45 (s, 6H), 2.76 (s, 3H).	DMSO	95	Method G1,AQ1	359.1 (M+1)	Method B (NH_4HCO_3)
1544					^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.66 (s, 1H), 8.82 – 8.79 (m, 1H), 8.70 (d, *J* = 4.0 Hz, 1H), 8.20 (d, *J* = 1.6 Hz, 1H), 8.02 (s, 1H), 7.86 – 7.84 (m, 2H), 7.58 – 7.55 (m, 3H), 3.48 (s, 6H), 2.77 (s, 3H).	DMSO	95	Method G1,AQ1	375.1 (M+1)	Method B (NH_4HCO_3)
1545					^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.68 (s, 1H), 9.01 (d, *J* = 8.0 Hz, 1H), 8.82 (d, *J* = 4.4 Hz, 1H), 8.18 (d, *J* = 1.6 Hz, 1H), 8.03 (s, 1H), 7.88 – 7.84 (m, 2H), 7.80 – 7.77 (m, 1H), 7.37 – 7.33 (m, 2H), 3.50 (s, 6H), 2.78 (s, 3H).	DMSO	95	Method G1,AQ1	359.1 (M+1)	Method B (NH_4HCO_3)

659

1546					^{1}H-NMR (400 MHz, CD_3OD): δ 9.51 (s, 1H), 8.81 (d, *J* = 7.8 Hz, 1H), 8.54 (s, 1H), 8.35 (s, 1H), 8.02 (d, *J* = 8.8 Hz, 1H), 7.83 (d, *J* = 8.8 Hz, 1H), 7.50 (d, *J* = 7.2 Hz, 1H), 7.29 (dt, *J* = 11.2, 4.8 Hz, 3H), 6.88 (d, *J* = 7.5 Hz, 1H), 4.43 (dd, *J* = 7.1, 4.0 Hz, 1H), 4.16 (dd, *J* = 13.8, 4.0 Hz, 1H), 3.86 (dd, *J* = 13.7, 7.4 Hz, 1H), 3.80 (s, 3H).	CD3OD	95	Method G1,AQ1	416.1 (M+1)	Method B (NH_4HCO_3)
1547				2HCl	^{1}H-NMR (400 MHz, CD_3OD): δ 9.74 (s, 1H), 9.44 (d, *J* = 8.2 Hz, 1H), 9.02 (d, *J* = 5.5 Hz, 1H), 8.50 (s, 1H), 8.24 (dd, *J* = 8.0, 5.9 Hz, 1H), 8.16 (q, *J* = 8.7 Hz, 2H), 7.70 – 7.58 (m, 1H), 7.12 – 7.00 (m, 2H), 6.13 (s, 1H), 4.44 – 4.41 (m, 1H), 4.29 – 4.27 (m, 1H), 2.37 – 2.16 (m, 3H), 2.09 – 2.07 (m, 1H).	CD_3OD	95	Method G1,AQ1	457.0 (M+1)	Method B (NH_4HCO_3)
1548				2HCl	^{1}H-NMR (400 MHz, CD_3OD): δ 9.85 (s, 1H), 9.57 (d, *J* = 8.0 Hz, 1H), 9.10 (d, *J* = 4.8 Hz, 1H), 8.64 (s, 1H), 8.34 – 8.22 (m, 3H), 7.51 (t, *J* = 6.9 Hz, 1H), 7.47 – 7.33 (m, 2H), 6.23 (s, 1H), 4.53 – 4.51 (m, 1H), 4.38 – 4.36 (m, 1H), 2.51 – 2.30 (m, 3H), 2.19 – 2.18 (m, 1H).	CD_3OD	95	Method G1,AQ1	457.1 (M+1)	Method B (NH_4HCO_3)

1549				2HCl	^{1}H-NMR (400 MHz, DMSO): δ 10.38 (brs, 1H), 9.63 (d, *J* = 1.6 Hz, 1H), 9.00 (d, *J* = 8.0 Hz, 1H), 8.95 – 8.94 (m, 2H), 8.39 (d, *J* = 9.2 Hz, 1H), 8.23 (d, *J* = 8.4 Hz, 1 H), 7.88 – 7.85 (m, 1 H), 7.49 – 7.48 (m, 3H), 7.07 – 7.04 (m, 1H), 3.94 – 3.89 (m, 5H), 3.60 – 3.57 (m, 2H), 1.96 – 1.93 (m, 2H).	DMSO	95	Method G1,AQ1	387.1 (M+1)	Method B (NH_4HCO_3)
1550					^{1}H-NMR (400 MHz, DMSO): δ 9.62 (s, 1H), 8.72 – 8.70 (m, 2H), 8.40 (s, 1H), 8.11 – 7.94 (m, 2H), 7.91 – 7.74 (m, 3H), 7.54 (dd, *J* = 7.6, 4.8 Hz, 1H), 7.09 (d, *J* = 8.6 Hz, 2H), 3.83 (s, 3H), 2.74 (s, 3H).	DMSO	95	Method G1,AQ1	343.1 (M+1)	Method B (NH_4HCO_3)
1551					^{1}H-NMR (400 MHz, DMSO): δ 9.64 (s, 1H), 8.76 (d, *J* = 8.0 Hz, 1H), 8.70 (d, *J* = 4.4 Hz, 1H), 8.46 (s, 1H), 8.12 – 7.83 (m, 5H), 7.57 (dd, *J* = 7.8, 4.8 Hz, 1H), 7.39 (t, *J* = 8.7 Hz, 2H), 2.84 (s, 3H).	DMSO	95	Method G1,AQ1	331.1 (M+1)	Method B (NH_4HCO_3)
1552					1H-NMR (400 MHz, DMSO): δ 9.62 (s, 1H), 8.77 (d, *J* = 8.0 Hz, 1H), 8.71 (d, *J* = 4.4 Hz, 1H), 8.23 (s, 1H), 8.20 (s, 1H), 8.07 – 8.00 (m, 2H), 7.60 – 7.50 (m, 3H), 7.40 – 7.37 (m, 1H), 4.48 (s, 2H), 4.12 – 4.10 (m, 2H), 3.48 – 3.46 (m, 2H).	DMSO	95	Method G1,AQ1	418.1 (M+1)	Method B (NH_4HCO_3)

1553				2HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.74 (s, 1H), 9.45(s, 1H), 9.27 (d, J =8.8 Hz, 1H), 8.97 (s, 1H), 8.69 (s, 1H), 8.12 – 8.00 (m, 3H), 7.83 – 7.76 (m, 1H), 7.51 – 7.32 (m, 2H), 480 – 4.64 (m, 2H).	DMSO	95	Method G1,AQ1	417.1 (M+1)	Method B (NH_4HCO_3)
1554				2HCl	^{1}H-NMR (400 MHz, CD3OD): δ 9.86 (s, 1H), 9.48 (d, J = 8.8 Hz, 1H), 9.18 (d, *J* = 5.2 Hz, 1H), 8.72 (s1H), 8.92 (s, 1H), 8.37-8.31 (m, 2H), 8.22 (d, *J* = 8.8 Hz, 1H), 7.80 – 7.55 (m, 1H), 7.26 – 7.20 (m, 2H), 4.92 (d, J =4.8 Hz, 1H) , 4.81 (t, *J* = 4.8 Hz, 1H), 4.39 – 4.30 (m, 2H).	CD3OD	95	Method G1,AQ1	380.9 (M+1)	Method B (NH_4HCO_3)
1555					^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.62 (s, 1H), 8.7 –8.68 (m, 2H), 8.32 (s, 1H), 7.97 –7.93 (m, 2H), 7.91 – 7.36 (m, 5H), 347 (s, 6H).	DMSO	95	Method G1,AQ1	345.1 (M+1)	Method B (NH_4HCO_3)
1556					^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.61 (s, 1H), 8.75 (d, *J* = 8.0 Hz, 1H), 8.67 (d, *J* = 3.6 Hz, 1H), 8.48 (s, 1H), 8.13 (d, *J* = 8.8 Hz, 1H), 7.91 (d, *J* = 8.8 Hz, 1H), 7.59 – 7.49 (m, 3H), 7.45 – 7.30 (m, 5H), 7.02 – 6.92 (m, 1H), 4.50 (q, *J* =3.2 Hz, 1H), 4.39 – 4.20 (m, 2H), 4.14 – 4.09 (m, 1H), 3.98 – 3.83 (m, 1H), 3.38 (s, 3H), 2.49 – 2.40 (m, 1H), 2.35 – 2.18 (m, 1H).	DMSO	95	Method G1,AQ1	493.0 495.0 (M+1)	Method B (NH_4HCO_3)

662

1557					^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.60 (s, 1H), 8.73 (dd, *J* = 7.6, 1.2 Hz, 1H), 8.67 (dd, J = 8.4, 1.2 Hz, 1H), 8.47 (s, 1H), 8.11 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.89 (d, *J* = 8.8 Hz, 1H), 7.54 – 7.50 (m, 1H), 7.42 (t, *J* = 8.0 Hz, 1H), 7.38 – 7.32 (m, 2H), 7.32 – 7.23 (m, 2H), 7.05 (d, *J* = 8.4 Hz, 1H), 7.00 – 6.92 (m, 2H), 4.45 (t, *J* = 8.4 Hz, 1H), 4.24 (s, 2H), 4.08 – 3.95 (m, 1H), 3.88 – 3.80 (m, 7H), 2.44 – 2.33 (m, 1H), 2.29 – 2.15 (m, 1H).	DMSO	95	Method G1,AQ1	489.1 (M+1)	Method B (NH_4HCO_3)
1558					^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.56 (s, 1H), 9.02 (s, 1H), 8.19 (d, *J* = 7.5 Hz, 1H), 7.86 (d, *J* = 8.7 Hz, 1H), 7.58 (dd, *J* = 7.7, 4.9 Hz, 1H), 7.52 – 7.37 (m, 3H), 7.37 – 7.24 (m, 3H), 7.12 (t, *J* = 8.8 Hz, 2H), 7.02 (d, *J* = 7.5 Hz, 1H), 6.84 (s, 1H), 3.89 – 3.78 (m, 4H), 3.72 – 3.66 (m, 1H), 3.13 (s, 1H), 2.97 – 2.90 (m, 1H), 2.86 – 2.78 (m, 1H).	DMSO	95	Method G1,AQ1	506.1 (M+1)	Method B (NH_4HCO_3)
1559				2 HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.48 – 10.00 (m, 1H), 9.70 (s, 1H), 9.12 – 8.77 (m, 3H), 8.42 – 8.32 (m, 1H), 8.30 – 8.17 (m, 1H), 7.95 – 7.79 (m, 1H), 7.55 – 7.44 (m, 6H), 7.26 (d, *J* = 7.2 Hz, 1H), 7.05 (s,1H), 6.94 (s, 1H), 3.89 (s, 5H), 3.22 (s, 1H), 2.97 – 2.81 (m, 2H).	DMSO	95	Method G1,AQ1	558.1 560.0 562.0 (M+1)	Method B (NH_4HCO_3)

1560				2HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.25 (s, 1H), 9.61 (d, *J* = 1.5 Hz, 1H), 8.96 (d, *J* = 4.0 Hz, 1H), 8.87 (s, 1H), 8.39 (d, *J* = 8.5 Hz, 1H), 8.25 (d, *J* = 7.7 Hz, 1H), 7.87 (s, 1H), 7.52 – 7.44 (m, 4H), 7.36 (t, *J* = 7.6 Hz, 1H), 7.28 (dd, *J* = 13.5, 6.0 Hz, 1H), 7.22 – 7.10 (m, 2H), 7.06 (d, *J* = 7.5 Hz, 1H), 6.89 (s, 1H), 3.95 – 3.81 (m, 5H), 3.21 (d, *J* = 9.0 Hz, 1H), 2.94 (d, *J* = 7.3 Hz, 2H).	DMSO	95	Method G1,AQ1	508.2 (M+1)	Method B (NH_4HCO_3)
1561					^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.64 (s, 1H), 8.74 (m, 2H), 8.69 (d, *J* = 3.5 Hz, 1H), 8.64 (s, 1H), 8.15 (d, *J* = 8.4 Hz, 1H), 7.85 (d, *J* = 8.7 Hz, 1H), 7.58 – 7.49 (m, 1H), 7.43 (m, 4H), 7.28 – 7.18 (m, 4H), 7.15 (m, 1H), 7.01 (d, *J* = 7.2 Hz, 1H), 6.94 (s, 1H), 3.82 – 3.73 (m, 5H), 2.90 – 2.87 (m. 1H), 2.68 – 2.65 (m, 2H), 1.89 – 1.86 (m, 2H).	DMSO	95	Method G1,AQ1	503.9 (M+1)	Method B (NH_4HCO_3)
1562					^{1}H-NMR (400 MHz, DMSO-d_6): 9.85 (s, 1H), 8.76 (s, 1H), 8.65 (d, *J* = 3.6 Hz, 1H), 8.64 (s, 1H), 8.53 (d, *J* = 8.0 Hz, 1H), 8.14 (d, *J* = 8.6 Hz, 1H), 7.83 (d, *J* = 8.7 Hz, 1H), 7.51 (dd, *J* = 8.0, 4.7 Hz, 1H), 7.45 (d, *J* = 6.7 Hz, 2H), 7.40 (s, 1H), 7.31 – 7.27 (m, 5H), 7.24 (d, *J* = 6.6 Hz, 1H), 7.00 (d, *J* = 6.9 Hz, 1H), 6.80 (s, 1H), 3.77 – 3.70 (m, 5H), 3.17 – 3.15 (m, 1H). 2.98 – 2.81 (m, 2H).	DMSO	95	Method G1,AQ1	489.9 (M+1)	Method B (NH_4HCO_3)

1563					^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.57 (s, 1H), 8.74 – 8.68 (m, 2H), 8.21 (s, 1H), 8.15 (dd, *J* = 8.7, 1.6 Hz, 1H), 7.95 (d, *J* = 8.7 Hz, 1H), 7.56 – 7.52 (m, 2H), 7.46 – 7.31 (m, 4H), 7.12 (d, *J* = 6.5 Hz, 2H), 6.95 – 6.93 (m, 1H), 5.16 (s, 2H), 3.78 (s, 3H), 3.53 (s, 3H).	DMSO	95	Method G1,AQ1	467.1, 469.1 (M+1)	Method B (NH_4HCO_3)
1564					^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.64 (d, *J* = 1.4 Hz, 1H), 8.75 (d, *J* = 7.9 Hz, 1H), 8.70 (d, *J* = 4.6 Hz, 1H), 8.32 (s, 1H), 8.12 (d, *J* = 8.7 Hz, 1H), 7.91 (d, *J* = 8.7 Hz, 1H), 7.55 (dd, *J* = 7.9, 4.8 Hz, 1H), 7.43 (t, *J* = 7.9 Hz, 1H), 7.36 – 7.29 (m, 2H), 7.01 – 6.98 (m, 1H), 6.88 (s, 1H), 6.83 (s, 2H), 4.12 – 4.03 (m, 2H), 3.85 (s, 3H), 3.69 (s, 3H), 3.62 (s, 3H), 3.56 (d, *J* = 8.0 Hz, 3H), 3.16 – 3.02 (m, 2H).	DMSO	95	Method G1,AQ1	507.2 (M+1)	Method B (NH_4HCO_3)
1565					^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.64 (d, *J* = 2.0 Hz, 1H), 8.77 – 8.69 (m, 2H), 8.68 (d, *J* = 1.6 Hz, 1H), 8.64 (d, *J* = 1.6 Hz, 1H), 8.16 (dd, *J* = 8.8, 1.6 Hz,1H), 7.85 (d, *J* = 8.8 Hz,1H), 7.55 – 7.52 (m, 1H), 7.46 – 7.41 (m, 4H), 7.29 (t, *J* = 7.2 Hz, 1H), 7.23 – 7.19 (m, 1H), 7.14 – 7.06 (m, 2H), 7.01 (dt, *J* = 9.2 , 2.0 Hz, 1H), 6.96 (s, 1H), 3.87 – 3.76 (m, 5H), 2.94 – 2.93 (m, 1H), 2.68 (t, *J* = 7.8 Hz, 2H), 1.89 – 1.83 (m, 2H).	DMSO	95	Method G1,AQ1	522.3 (M+1)	Method B (NH_4HCO_3)

1566					^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.59 (s, 1H), 8.76 (t, *J* = 5.2 Hz, 1H), 8.69 (dd, *J* = 4.4, 1.2 Hz, 1H), 8.63 (s, 1H), 8.56 (d, *J* = 8.4 Hz, 1H), 8.15 (dd, *J* = 8.8, 1.4 Hz, 1H), 7.84 (d, *J* = 8.4 Hz, 1H), 7.53 – 7.50 (m, 1H), 7.48 – 7.40 (m, 3H), 7.36 – 7.32 (m, 3H), 7.30 – 7.24 (m, 2H), 7.02 – 7.00 (m, 1H), 6.85 (s, 1H), 3.92 – 3.83 (m, 4H), 3.72 – 3.69 (m, 1H), 3.18 – 3.14 (m, 1H), 2.96 – 2.84 (m, 2H).	DMSO	95	Method G1,AQ1	524.2, 526.2 (M+1)	Method B (NH_4HCO_3)
1567					^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.64 (s, 1H), 9.08 (s, 1H), 8.79 – 8.69 (m, 2H), 8.51 (s, 1H), 8.31 (s, 1H), 8.00 – 7.89 (m, 2H), 7.85 – 7.69 (m, 1H), 7.67 – 7.42 (m, 2H), 7.30 – 7.21 (m, 2H), 5.00 (d, *J* = 5.1 Hz, 2H).	DMSO	95	Method G1,AQ1	416.0 (M+1)	Method B (NH_4HCO_3)
1568				2HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.58 (s, 1H), 10.09 (d, *J* = 4.4 Hz, 1H), 9.65 (s, 1H), 9.05 – 9.02 (m, 2H), 8.95 (d, *J* = 4.4 Hz, 1H), 8.37 (d, *J* = 8.4 Hz, 1H), 8.30 – 8.27 (m, 1H), 7.85 (t, *J* = 6.2 Hz, 1H), 7.59 (d, *J* = 8.0 Hz, 2H), 7.49 – 7.43 (m, 3H), 7.24 (t, *J* = 7.8 Hz, 2H), 7.03 – 6.97 (m, 2H), 3.89 (s, 3H), 3.86 – 3.84 (m, 2H), 2.44 (t, *J* = 7.0 Hz, 2H), 1.87 – 1.77 (m, 4H).	DMSO	95	Method G1,AQ1	504.1 (M+1)	Method B (NH_4HCO_3)

1569				2HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.62 (s, 1H), 9.67 (s, 1H), 9.08 (d, *J* = 7.2 Hz, 1H), 9.03 (s, 1H), 8.97 (d, *J* = 5.2 Hz, 1H), 8.44 (t, *J* = 5.6 Hz, 1H), 8.40 (dd, *J* = 8.8, 0.8 Hz, 1H), 8.32 (dd, *J* = 9.2, 2.8 Hz, 1H), 7.89 (t, *J* = 6.4 Hz, 1H), 7.50 – 7.44 (m, 3H), 7.25 – 7.14 (m, 5H), 7.03 (d, *J* = 7.2 Hz, 1H), 4.24 (d, *J* = 6.0 Hz , 2H), 3.89 (s, 3H), 3.87 – 3.82 (m, 2H), 2.26 (t, *J* = 7.0 Hz, 2H), 1.84 – 1.69 (m, 4H).	DMSO	95	Method G1,AQ1	518.1 (M+1)	Method B (NH_4HCO_3)
1570					^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.55 (s, 1H), 8.69 (dd, *J* = 11.3, 6.2 Hz, 2H), 8.23 (s, 1H), 8.15 (d, *J* = 8.7 Hz, 1H), 7.95 (d, *J* = 8.7 Hz, 1H), 7.59 – 7.50 (m, 2H), 7.44 – 7.26 (m, 3H), 7.23 (t, *J* = 7.5 Hz, 1H), 7.15 (s, 1H), 7.12 (d, *J* = 7.7 Hz, 1H), 6.95 (d, *J* = 8.1 Hz, 1H), 5.18 (s, 2H), 3.79 (s, 3H), 3.54 (s, 3H).	DMSO	95	Method G1,AQ1	451.2, 452.2, 453.2 (M+1)	Method B (NH_4HCO_3)
1571				2HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.62 (s, 1H), 9.60 (s, 1H), 8.88 (d, *J* = 4.3 Hz, 1H), 8.82 (s, 1H), 8.78 (d, *J* = 8.1 Hz, 1H), 8.31 (d, *J* = 8.6 Hz, 1H), 8.12 (d, *J* = 7.9 Hz, 1H), 7.75 (dd, *J* = 7.8, 5.1 Hz, 1H), 7.53 – 7.39 (m, 4H), 7.33 (dd, *J* = 14.3, 7.9 Hz, 1H), 7.12 (t, *J* = 7.8 Hz, 2H), 7.03 (dd, *J* = 11.0, 6.3 Hz, 2H), 6.90 (s, 1H), 3.97 – 3.90 (m, 4H), 3.82 (dd, *J* = 18.0, 9.5 Hz, 1H), 3.19 (dd, *J* = 13.4, 7.5 Hz, 1H), 2.98 (dd, *J* = 13.6, 7.9 Hz, 1H), 2.87 (dd, *J* = 13.6, 6.7 Hz, 1H).	DMSO	95	Method G1,AQ1	508.1, 509.1, 510.1 (M+1)	Method B (NH_4HCO_3)

1572				2HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.20 (s, 1H), 9.61 (s, 1H), 8.94 (d, *J* = 4.8 Hz, 1H), 8.86 (s, 2H), 8.37 (d, *J* = 8.4 Hz, 1H), 8.22 (s, 1H), 7.83 (s, 1H), 7.56 – 7.32 (m, 6H), 7.31 – 7.19 (m, 2H), 7.06 (d, *J* = 7.2 Hz, 1H), 6.89 (s, 1H), 4.03 – 3.93 (m, 1H), 3.88 (s, 3H), 3.82 (dd, *J* = 14.4, 5.5 Hz, 1H), 3.22 (s, 1H), 3.02 (d, *J* = 7.2 Hz, 2H).	DMSO	95	Method G1,AQ1	524.1, 525.1, 526.0 (M+1)	Method B (NH_4HCO_3)
1573				2HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.31 (s, 1H), 9.63 (s, 1H), 8.96 (d, *J* = 4.4 Hz, 1H), 8.90 (s, 1H), 8.84 (d, *J* = 7.7 Hz, 1H), 8.39 (d, *J* = 8.7 Hz, 1H), 8.27 (d, *J* = 8.0 Hz, 1H), 7.91 – 7.80 (m, 1H), 7.48 (dd, *J* = 15.6, 7.7 Hz, 3H), 7.36 (s, 1H), 7.24 – 7.03 (m, 5H), 6.85 (s, 1H), 4.03 – 3.93 (m, 1H), 3.88 (s, 3H), 3.83 (dd, *J* = 14.7, 7.6 Hz, 1H), 3.15 (s, 1H), 2.94 (dd, *J* = 13.8, 8.0 Hz, 1H), 2.84 (dd, *J* = 13.8, 6.6 Hz, 1H), 2.29 (s, 3H).	DMSO	95	Method G1,AQ1	504.1, 505.2, 506.1 (M+1)	Method B (NH_4HCO_3)
1574				2HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.43 (s, 1H), 9.71 (s, 1H), 9.05 (d, *J* = 4.7 Hz, 1H), 9.01 (d, *J* = 7.6 Hz, 1H), 8.96 (s, 1H), 8.45 (d, *J* = 8.6 Hz, 1H), 8.38 (d, *J* = 8.4 Hz, 1H), 7.99 – 7.89 (m, 1H), 7.61 – 7.41 (m, 4H), 7.23 (d, *J* = 7.8 Hz, 2H), 7.13 (d, *J* = 7.6 Hz, 3H), 6.93 (s, 1H), 4.01 – 3.84 (m, 5H), 3.31 – 3.21 (m, 1H), 3.02 – 2.97 (m, 7.5 Hz, 1H), 2.87 – 2.81 (m, 1H), 2.29 (s, 3H).	DMSO	95	Method G1,AQ1	504.1 (M+1)	Method B (NH_4HCO_3)

1575					^{1}H-NMR (400 MHz, CD_3OD): δ 9.39 (s, 1H), 8.69 (d, *J* = 8.0 Hz, 1H), 8.65 (s, 1H), 8.38 (s, 1H), 8.07 (d, *J* = 7.9 Hz, 1H), 7.85 (d, *J* = 8.6 Hz, 1H), 7.60 – 7.53 (m, 1H), 7.35 – 7.25 (m, 5H), 7.18 (dd, *J* = 13.6, 7.2 Hz, 2H), 7.12 (s, 1H), 6.88 (dd, *J* = 7.9, 2.1 Hz, 1H), 4.49 (dd, *J* = 11.3, 7.9 Hz, 1H), 4.36 – 4.17 (m, 2H), 4.04 (t, *J* = 10.4 Hz, 1H), 3.74 (s, 3H), 3.60 – 3.49 (m, 1H), 2.50 – 2.39 (m, 1H), 2.27 – 2.14 (m, 1H).	CD3OD	95	Method G1,AQ1	459.0 (M+1)	Method B (NH_4HCO_3)
1576					^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.67 (d, *J* = 1.7 Hz, 1H), 9.05 (s, 1H), 8.94 (d, *J* = 3.7 Hz, 1H), 8.59 (s, 1H), 8.40 – 8.22 (m, 2H), 7.85 (s, 1H), 7.79 (d, *J* = 1.9 Hz, 1H), 7.66 (d, *J* = 8.3 Hz, 1H), 7.52 – 7.36 (m, 4H), 7.04 (d, *J* = 7.6 Hz, 1H), 4.74 – 4.72 (m, 2H), 4.48 – 4.43 (m, 3H), 3.85 (s, 3H), 3.74 – 3.60 (m, 1H), 2.25 – 2.23 (m, 1H).	DMSO	95	Method G1,AQ1	527.0, 529.0 (M+1)	Method B (NH_4HCO_3)
1577				2HCl	^{1}H-NMR (400 MHz, DMSO): δ 9.69 (d, *J* = 1.6 Hz, 1H), 8.89 (d, *J* = 8.0 Hz, 1H), 8.79 (d, *J* = 1.6 Hz, 1H), 8.73 (s, 1H), 8.21 (d, *J* = 9.2 Hz, 1H), 8.01 (d, *J* = 8.8 Hz, 1H), 7.67 (dd, *J* = 7.6, 4.8 Hz, 1H), 7.56 – 7.38 (m, 7H), 7.05 – 7.02 (m, 1H), 5.59 (s, 4H), 3.89 (s, 3H).	DMSO	95	Method G1,AQ1	431.1 (M+1)	Method B (NH_4HCO_3)

1578					^{1}H-NMR (400 MHz, DMSO): δ 9.59 (d, J = 1.6 Hz, 1H), 8.81 – 8.64 (m, 2H), 8.28 – 8.10 (m, 2H), 7.96 (d, *J* = 8.6 Hz, 1H), 7.55 (td, *J* = 8.5, 5.0 Hz, 3H), 7.40 – 7.06 (m, 5H), 6.94 (dd, *J* = 8.2, 2.0 Hz, 1H), 5.15 (s, 2H), 3.78 (s, 3H), 3.51 (s, 3H).	DMSO	95	Method G1,AQ1	451.2 (M+1)	Method B (NH_4HCO_3)
1579				2HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.61 (s, 1H), 9.66 (s, 1H), 9.00 (d, *J* = 13.5 Hz, 3H), 8.43 – 8.31 (m, 2H), 7.89 (s, 1H), 7.48 (dd, *J* = 14.6, 7.2 Hz, 3H), 7.33 – 7.22 (m, 4H), 7.21 – 7.14 (m, 1H), 7.05 (d, *J* = 7.2 Hz, 1H), 4.10 – 3.85 (m, 2H), 3.90 (s, 3H), 3.37 – 3.27 (m, 1H), 3.07 – 2.91 (m, 2H).	DMSO	95	Method G1,AQ1	491.2 (M+1)	Method B (NH_4HCO_3)
1580				2HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.91 (s, 1H), 9.60 (s, 1H), 9.11 (s, 1H), 8.95 (s, 1H), 8.66 (s, 1H), 8.20 – 8.02 (m, 3H), 7.97 (s, 1H), 7.78 (dd, *J* = 13.3, 6.5 Hz, 1H), 7.50 (t, *J* = 11.3 Hz, 1H), 7.33 (t, *J* = 8.1 Hz, 1H), 7.21 (s, 1H), 5.08 (d, *J* = 3.8 Hz, 2H).	DMSO	95	Method G1,AQ1	416.0 (M+1)	Method B (NH_4HCO_3)

670

1581				2HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.84 (s, 1H), 9.71 (s, 1H), 9.12 (d, *J* = 6.2 Hz, 1H), 8.96 (d, *J* = 4.8 Hz, 1H), 8.91 (s, 1H), 8.37 (d, *J* = 8.4 Hz, 1H), 8.30 (s, 1H), 7.88 (s, 1H), 7.57 – 7.38 (m, 3H), 7.24 (s, 1H), 7.08 (d, *J* = 7.9 Hz, 1H), 6.73 (s, 1H), 5.18 – 5.05 (m, 1H), 3.88 (s, 3H), 3.23 (dd, *J* = 14.8, 7.4 Hz, 1H), 2.31 – 2.17 (m, 1H), 2.15 – 1.89 (m, 4H), 1.71 – 1.57 (m, 1H).	DMSO	95	Method G1,AQ1	440.2 (M+1)	Method B (NH_4HCO_3)
1583				2HCl	1H-NMR (300 MHz, DMSO): δ 10.39 (s, 1H), 9.71 (s, 1H), 9.14 (d, *J* = 8.1 Hz, 1H), 8.98 (d, *J* = 4.0 Hz, 1H), 8.71 (s, 1H), 8.31 (d, *J* = 8.8 Hz, 1H), 8.25 – 8.19 (m, 1H), 7.96 – 7.89 (m, 1H), 7.38 (dd, *J* = 9.2, 3.0 Hz, 1H), 7.34 – 7.14 (m, 2H), 3.81 (s, 4H), 3.30 (d, *J* = 4.4 Hz, 4H).	DMSO	95	Method AQ2, AP	361.7 (M+1)	Method C
1584				2HCl	1H-NMR (300 MHz, DMSO): δ 10.84 (s, 1H), 9.01 (s, 1H), 8.95 (d, *J* = 3.9 Hz, 1H), 8.72 (d, *J* = 7.8 Hz, 1H), 8.50 – 8.40 (m, 1H), 8.33 (d, *J* = 8.8 Hz, 1H), 8.24 (td, *J* = 7.8, 1.7 Hz, 1H), 7.85 (dd, *J* = 6.5, 4.8 Hz, 1H), 7.57 – 7.43 (m, 3H), 7.09 – 7.02 (m, 1H), 3.90 (s, 3H), 3.38 (s, 3H)	DMSO	95	Method AQ2, AP	343.5 (M+1)	Method C

671

1585				2HCl	1H-NMR (300 MHz, DMSO): δ 10.44 – 10.13 (m, 1H), 9.66 (s, 1H), 9.08 (d, *J* = 10.1 Hz, 2H), 8.96 (d, *J* = 3.7 Hz, 1H), 8.44 (d, *J* = 8.9 Hz, 1H), 8.22 (d, *J* = 8.4 Hz, 1H), 8.13 (dd, *J* = 13.3, 5.3 Hz, 2H), 8.00 (d, *J* = 8.2 Hz, 1H), 7.91 (s, 1H), 3.30 (d, J = 4.4 Hz, 3H).	DMSO	95	Method AQ2, AP	356.4 (M+1)	Method C
1586					1H-NMR (300 MHz, DMSO): δ 9.64 (s, 1H), 8.78 (d, *J* = 8.0 Hz, 1H), 8.73 – 8.69 (m, 1H), 8.63 (s, 2H), 8.47 – 8.37 (m, 1H), 8.32 – 8.25 (m, 1H), 8.23 – 8.12 (m, 1H), 7.87 (d, *J* = 8.6 Hz, 1H), 7.73 (t, *J* = 9.0 Hz, 1H), 7.55 (dd, *J* = 7.9, 4.7 Hz, 1H), 3.20 (d, *J* = 4.3 Hz, 3H).	DMSO	95	Method AQ2, AP	356.4 (M+1)	Method C
1587					1H-NMR (300 MHz, DMSO): δ 9.65 (s, 1H), 8.79 (d, *J* = 8.0 Hz, 1H), 8.72 – 8.57 (m, 2H), 8.24 (d, *J* = 8.7 Hz, 1H), 7.88 (d, *J* = 8.7 Hz, 1H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.53 (t, *J* = 10.9 Hz, 2H), 7.45 – 7.36 (m, 1H), 3.99 (s, 3H), 3.94 (s, 3H), 3.21 (d, J = 4.1 Hz, 3H).	DMSO	95	Method AQ2, AP	401.5 (M+1)	Method C
1588				2HCl	1H-NMR (300 MHz, DMSO): δ 10.77 (s, 1H), 9.66 (s, 1H), 9.06 (s, 2H), 8.95 (d, *J* = 3.8 Hz, 1H), 8.38 (d, *J* = 8.8 Hz, 1H), 8.26 (d, *J* = 8.8 Hz, 1H), 7.87 (s, 1H), 7.71 (d, *J* = 8.1 Hz, 1H), 7.38 (dd, *J* = 22.8, 11.6 Hz, 2H), 4.03 (s, 3H), 3.31 (d, *J* = 4.1 Hz, 3H).	DMSO	95	Method AQ2, AP	361.5 (M+1)	Method C

1589				2HCl	1H-NMR (300 MHz, DMSO): δ 10.23 – 10.05 (m, 1H), 9.64 (s, 1H), 9.00 (s, 1H), 8.94 (s, 1H), 8.89 (s, 1H), 8.38 (d, *J* = 8.6 Hz, 1H), 8.14 (d, *J* = 8.5 Hz, 1H), 7.85 (s, 1H), 7.36 (d, *J* = 8.7 Hz, 2H), 6.95 (d, *J* = 10.9 Hz, 1H), 3.90 (s, 1H), 3.30 (d, *J* = 4.3 Hz, 3H).	DMSO	95	Method AQ2, AP	361.5 (M+1)	Method C
1590				2HCl	1H-NMR (300 MHz, DMSO): δ 10.34 (s, 1H), 9.70 (s, 1H), 9.14 (d, *J* = 7.4 Hz, 1H), 8.98 (d, *J* = 3.9 Hz, 1H), 8.75 (s, 1H), 8.32 (d, *J* = 8.8 Hz, 1H), 8.17 (d, *J* = 8.8 Hz, 1H), 7.93 (d, *J* = 4.8 Hz, 1H), 7.27 (dd, *J* = 19.5, 6.3 Hz, 3H), 3.88 (s, 3H), 3.28 (d, *J* = 4.1 Hz, 3H).	DMSO	95	Method AQ2, AP	361.3 (M+1)	Method C
1591				2HCl	1H-NMR (300 MHz, DMSO): δ 10.21 (s, 1H), 9.66 (d, *J* = 1.6 Hz, 1H), 9.04 (d, *J* = 7.3 Hz, 1H), 8.96 (d, *J* = 3.5 Hz, 1H), 8.67 (s, 1H), 8.28 – 8.12 (m, 2H), 7.88 (s, 1H), 7.66 (t, *J* = 8.8 Hz, 1H), 7.11 – 6.97 (m, 2H), 3.86 (s, 3H), 3.30 (d, *J* = 4.4 Hz, 3H).	DMSO	95	Method AQ2, AP	361.3 (M+1)	Method C
1592				3HCl	1H-NMR (300 MHz, DMSO): δ 10.77 (s, 1H), 9.69 (s, 1H), 9.39 (s, 1H), 9.16 (d, *J* = 7.8 Hz, 1H), 9.04 (s, 1H), 8.97 (d, *J* = 3.6 Hz, 1H), 8.63 (d, *J* = 2.5 Hz, 1H), 8.53 (s, 2H), 8.31 (d, *J* = 8.5 Hz, 1H), 7.91 (d, *J* = 5.4 Hz, 1H), 4.11 (s, 3H), 3.30 (d, *J* = 4.4 Hz, 3H).	DMSO	95	Method AQ2, AP	343.1 (M+1)	Method C

673

1593				2HCl		DMSO	95	Method AQ2, AP	359.1 (M+1)	Method C
1594					1H-NMR (300 MHz, DMSO): δ 9.64 (d, *J* = 1.3 Hz, 1H), 8.82 – 8.75 (m, 1H), 8.68 (dd, *J* = 4.8, 1.7 Hz,1H), 8.60 (s, 1H), 8.53 (d, *J* = 1.7 Hz, 1H), 8.10 (dd, *J* = 8.7, 1.9 Hz, 1H), 7.86 – 7.77 (m, 4H), 7.58 – 7.48 (m, 2H), 7.09 (d, *J* = 8.8 Hz, 2H), 6.97 (d, *J* = 8.8 Hz, 1H), 3.99 (d, *J* = 6.0 Hz, 2H), 3.18 (d, *J* = 4.4 Hz, 3H), 1.82 – 1.69 (m, 2H), 1.07 (d, *J* = 6.7 Hz, 3H).	DMSO	95	Method AQ2, AP	371.1 (M+1)	Method C
1595				2HCl	1H-NMR (300 MHz, DMSO): δ 10.24 – 10.10 (bs, 1H), 9.65 (s, 1H), 9.02 (s, 1H), 8.96 (d, *J* = 3.8 Hz, 1H), 8.90 (s, 1H), 8.39 (s, 1H), 8.20 (s, 1H), 8.07 (s, 1H), 7.98 (s, 1H), 7.89 (s, 1H), 7.54 (t, *J* = 9.1 Hz, 1H), 3.70 (bs, 4H), 3.59 (bs, 4H), 3.32 (d, J = 4.4 Hz, 3H).	DMSO	95	Method AQ2, AP	443.5 (M+1)	Method C
1596				2HCl	1H-NMR (300 MHz, DMSO): δ 10.37 (s, 1H), 9.69 (d, *J* = 1.7 Hz, 1H), 9.10 (d, *J* = 7.0 Hz, 1H), 9.03 – 8.93 (m, 2H), 8.42 (d, *J* = 8.6 Hz, 1H), 8.28 (d, *J* = 9.3 Hz, 1H), 8.05 (d, *J* = 3.5 Hz, 1H), 7.99 (dd, *J* = 6.2, 2.4 Hz, 2H), 7.52 (t, *J* = 9.1 Hz, 1H), 3.54 – 3.43 (m, 4H), 3.30 (t, *J* = 10.4 Hz, 3H), 1.98 – 1.81 (m, 4H).	DMSO	95	Method AQ2, AP	428.5 (M+1)	Method C

674

1597				2HCl	1H-NMR (300 MHz, DMSO): δ 10.71 (s, 1H), 8.96 (d, *J* = 3.9 Hz, 1H), 8.81 (s, 1H), 8.74 (d, *J* = 7.9 Hz, 1H), 8.36 (d, *J* = 8.7 Hz, 1H), 8.29 – 8.19 (m, 2H), 7.87 (dd, *J* = 6.5, 4.7 Hz, 1H), 7.80 (dd, *J* = 15.5, 8.9 Hz, 1H), 7.61 – 7.50 (m, 1H), 7.36 (d, *J* = 8.1 Hz, 1H), 3.37 (d, *J* = 4.5 Hz, 3H).	DMSO	95	Method AQ2, AP	349.4 (M+1)	Method C
1598					1H-NMR (300 MHz, DMSO): δ 9.27 (d, *J* = 1.5 Hz, 1H), 8.61 (dd, *J* = 12.6, 3.0 Hz, 2H), 8.41 (d, *J* = 2.9 Hz, 1H), 8.34 – 8.27 (m, 1H), 8.16 (dd, *J* = 8.7, 1.9 Hz, 1H), 7.86 (d, *J* = 8.7 Hz, 1H), 7.45 (dd, J = 16.0, 9.2 Hz, 3H), 7.05 – 6.97 (m, 1H), 3.96 (s, 3H), 3.87 (s, 3H), 3.19 (d, *J* = 4.3 Hz, 3H).	DMSO	95	Method AQ2, AP	373.4 (M+1)	Method C
1599				2HCl	1H-NMR (300 MHz, DMSO): δ 10.44 – 10.13 (m, 1H), 9.65 (s, 1H), 9.02 (s, 1H), 8.96 (d, *J* = 3.5 Hz, 1H), 8.87 (s, 1H), 8.37 (d, *J* = 9.1 Hz, 1H), 8.24 (s, 1H), 7.86 (s, 2H), 7.78 (d, *J* = 7.9 Hz, 1H), 7.54 (d, *J* = 7.6 Hz, 1H), 7.43 (d, *J* = 7.5 Hz, 1H), 4.64 (s, 2H), 3.33 (d, *J* = 4.2 Hz, 3H), 3.17 (s, 1H).	DMSO	95	Method AQ2, AP	343.5 (M+1)	Method C

675

1600				MSA	1H-NMR (300 MHz, DMSO): δ 9.90 (s, 1H), 9.57 (d, J = 1.6 Hz, 1H), 8.93 (dd, J = 5.0, 1.5 Hz, 2H), 8.73 (s, 1H), 8.32 (d, J = 8.7 Hz, 1H), 8.01 (d, J = 8.8 Hz, 1H), 7.85 (dd, J = 10.1, 7.0 Hz, 2H), 7.73 (d, J = 7.5 Hz, 1H), 7.52 (t, J = 7.6 Hz, 1H), 7.42 (d, J = 7.5 Hz, 1H), 4.63 (s, 2H), 3.30 (d, J = 4.3 Hz, 3H), 2.32 (s, 3H).	DMSO	95	Method AQ2, AP	343.5 (M+1)	Method C
1601				MsOH	^{1}H NMR (300 MHz, DMSO) δ 9.72 (brs, 1H), 9.58 (d, *J* = 1.6 Hz, 1H), 9.03 – 8.89 (m, 2H), 8.45 (d, *J* = 8.7 Hz, 1H), 8.11 (s, 1H), 7.99 – 7.84 (m, 2H), 7.64 (ddd, *J* = 9.2, 6.1, 3.1 Hz, 1H), 7.58 – 7.31 (m, 2H), 3.28 (d, *J* = 4.5 Hz, 3H), 2.39 (s, 3H).	DMSO	>98	G2/AQ3		
1602					^{1}H NMR (300 MHz, DMSO) δ 9.59 (d, *J* = 2.0 Hz, 1H), 9.33 (s, 2H), 9.24 (s, 1H), 8.79 (d, *J* = 1.5 Hz, 1H), 8.76 – 8.64 (m, 2H), 8.30 (dd, *J* = 8.7, 1.5 Hz, 1H), 8.12 (brs, 2H), 7.91 (d, *J* = 8.7 Hz, 1H), 7.55 (dd, *J* = 7.9, 4.8 Hz, 1H).	DMSO	>98	G2/AQ3		
1603					^{1}H NMR (300 MHz, DMSO) δ 9.64 – 9.53 (m, 1H), 8.77 – 8.58 (m, 2H), 8.53 (s, 1H), 8.43 (d, *J* = 1.5 Hz, 1H), 8.11 – 7.90 (m, 3H), 7.82 (d, *J* = 8.7 Hz, 1H), 7.54 (dd, *J* = 7.9, 4.8 Hz, 1H), 4.00 (s, 3H), 3.98 (s, 3H).	DMSO	>98	G2/AQ3		

1604					^{1}H NMR (300 MHz, DMSO) δ 9.59 (d, *J* = 2.0 Hz, 1H), 8.83 – 8.66 (m, 2H), 8.55 (s, 1H), 8.27 – 7.99 (m, 4H), 7.99 – 7.82 (m, 2H), 7.77 (d, *J* = 7.7 Hz, 1H), 7.66 (t, *J* = 7.6 Hz, 1H), 7.56 (dd, *J* = 7.9, 4.8 Hz, 1H).	DMSO	>98	G2/AQ3		
1605					^{1}H NMR (300 MHz, DMSO) δ 9.58 (d, *J* = 2.1 Hz, 1H), 8.80 – 8.64 (m, 2H), 8.25 (dd, *J* = 8.7, 1.6 Hz, 1H), 8.10 (d, *J* = 8.3 Hz, 2H), 8.02 (d, *J* = 8.3 Hz, 2H), 7.88 (d, *J* = 8.7 Hz, 1H), 7.55 (dd, *J* = 7.9, 4.8 Hz, 1H).	DMSO	>98	G2/AQ3		
1606				2HCl	^{1}H NMR (300 MHz, DMSO) δ 9.95 – 9.43 (m, 3H), 9.05 (d, *J* = 8.2 Hz, 1H), 8.99 (dd, *J* = 5.1, 1.5 Hz, 1H), 8.74 (s, 1H), 8.33 (d, *J* = 8.7 Hz, 1H), 8.21 (d, *J* = 8.7 Hz, 1H), 7.93 (dd, *J* = 8.0, 5.1 Hz, 1H), 7.79 (td, *J* = 8.9, 6.6 Hz, 1H), 7.51 (ddd, *J* = 11.5, 9.3, 2.6 Hz, 1H), 7.33 (td, *J* = 8.3, 1.9 Hz, 1H).	DMSO	>98	G2/AQ3		

677

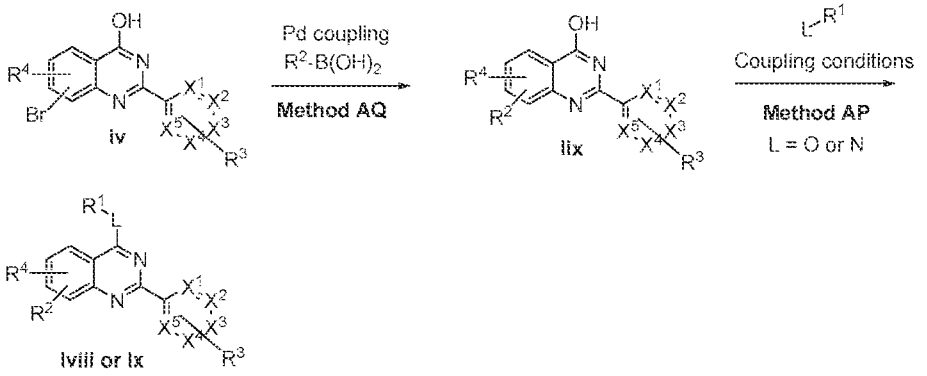
1607				3HCl	^{1}H NMR (300 MHz, DMSO) δ 11.88 (s, 1H), 9.77 (d, *J* = 1.7 Hz, 1H), 9.56 – 9.28 (m, 1H), 9.19 – 9.01 (m, 1H), 8.31 – 8.11 (m, 4H), 7.75 – 7.47 (m, 2H), 7.47 – 7.23 (m, 1H), 4.83 – 4.67 (m, 2H), 3.96 (t, *J* = 12.2 Hz, 2H), 3.57 (d, *J* = 11.9 Hz, 2H), 3.46 – 3.19 (m, 2H), 2.83 (d, *J* = 3.1 Hz, 3H).	DMSO	>98	G2/AQ3		
1608				HCl	^{1}H NMR (300 MHz, DMSO) δ 14.45 (s, 1H), 10.36 (s, 1H), 9.31 (d, J = 2.2 Hz, 1H), 8.82 (s, 1H), 8.73 (ddd, J = 8.8, 2.5, 0.9 Hz, 1H), 8.36 (d, J = 9.0 Hz, 1H), 8.16 (d, J = 8.4 Hz, 1H), 7.56 - 7.36 (m, 3H), 7.11 (d, J = 8.4 Hz, 1H), 7.03 (d, J = 7.1 Hz, 1H), 3.99 (s, 3H), 3.87 (s, 3H), 3.30 (d, J = 3.9 Hz, 3H).	DMSO	100	Method AQ2/BF		
1609				HCl	^{1}H NMR (300 MHz, DMSO) δ 10.97 (s, 1H), 9.56 - 9.35 (m, 2H), 9.04 - 8.81 (m, 2H), 8.66 (t, J = 7.7 Hz, 1H), 8.61 - 8.45 (m, 2H), 8.15 (d, J = 8.6 Hz, 1H), 8.10 - 7.96 (m, 1H), 7.77 - 7.58 (m, 1H), 3.25 (d, J = 4.1 Hz, 3H).	DMSO	100	Method AQ2/BF		

1610				2 MsOH	^{1}H NMR (300 MHz, $CDCl_3$) δ 9.93 (brs, 1H), 9.61 (d, *J* = 1.8 Hz, 1H), 9.10 – 8.96 (m, 2H), 8.64 (s, 1H), 8.21 (d, *J* = 8.7 Hz, 1H), 8.06 (d, *J* = 8.7 Hz, 1H), 7.99 (dd, *J* = 8.0, 5.3 Hz, 1H), 7.69 – 7.47 (m, 2H), 7.47 – 7.34 (m, 1H), 3.30 (d, *J* = 4.5 Hz, 3H), 2.42 (s, 6H).	DMSO	>98	G2/AQ3	Method 3	
1611				2HCl	^{1}H NMR (300 MHz, $CDCl_3$) δ 10.42 (brs, 1H), 9.71 (d, *J* = 1.9 Hz, 1H), 9.17 (d, *J* = 8.1 Hz, 1H), 8.99 (dd, *J* = 5.1, 1.3 Hz, 1H), 8.78 (s, 1H), 8.33 (d, *J* = 8.7 Hz, 1H), 8.17 (d, *J* = 8.7 Hz, 1H), 7.94 (dd, *J* = 8.1, 5.2 Hz, 1H), 7.79 (td, *J* = 8.9, 6.7 Hz, 1H), 7.55 – 7.37 (m, 1H), 7.31 (td, *J* = 8.4, 2.2 Hz, 1H), 3.29 (d, *J* = 4.4 Hz, 3H).	DMSO	>98	G2/AQ3		
1612				HCl	^{1}H NMR (300 MHz, DMSO) δ 9.95 (brs, 1H), 9.65 (s, 1H), 9.18 – 9.02 (m, 1H), 8.95 (d, *J* = 4.7 Hz, 1H), 8.58 (d, *J* = 8.7 Hz, 1H), 8.28 (s, 1H), 8.09 – 7.70 (m, 4H), 3.29 (d, *J* = 4.4 Hz, 3H).	DMSO	>98	G2/AQ3		
1613					^{1}H NMR (300 MHz, DMSO) δ 9.64 (d, *J* = 1.5 Hz, 1H), 8.77 (dt, *J* = 7.9, 1.9 Hz, 1H), 8.69 (dd, *J* = 4.8, 1.7 Hz, 1H), 8.61 – 8.48 (m, 1H), 8.31 (d, *J* = 8.7 Hz, 1H), 8.11 (d, *J* = 1.8 Hz, 1H), 8.00 – 7.83 (m, 3H), 7.55 (dd, *J* = 7.9, 4.8 Hz, 1H), 3.17 (d, *J* = 4.4 Hz, 3H).	DMSO	>98	G2/AQ3		

1614					^{1}H NMR (300 MHz, DMSO) δ 9.65 (dd, *J* = 2.1, 0.8 Hz, 1H), 8.78 (dt, *J* = 8.0, 1.9 Hz, 1H), 8.69 (dd, *J* = 4.8, 1.7 Hz, 1H), 8.65 – 8.50 (m, 1H), 8.33 (d, *J* = 8.6 Hz, 1H), 8.04 – 7.85 (m, 1H), 7.69 (dt, *J* = 8.5, 1.8 Hz, 1H), 7.65 – 7.37 (m, 3H), 3.18 (d, *J* = 4.5 Hz, 3H).	DMSO	>98	G2/AQ3	Method 3	
1615					^{1}H NMR (300 MHz, DMSO) δ 9.65 (d, *J* = 1.7 Hz, 1H), 8.84 – 8.74 (m, 1H), 8.69 (dd, *J* = 4.7, 1.5 Hz, 1H), 8.65 – 8.52 (m, 1H), 8.34 (d, *J* = 8.6 Hz, 1H), 7.98 (s, 1H), 7.72 (d, *J* = 8.5 Hz, 1H), 7.69 – 7.43 (m, 3H), 3.18 (d, *J* = 4.3 Hz, 3H).	DMSO	>98	G2/AQ3	Method 3	
1760				2 HCl	^{1}H NMR (400 MHz, DMSO) δ 10.04 (s, 1H), 9.65 (s, 1H), 9.11 – 8.99 (m, 1H), 8.96 (dd, *J* = 5.0, 1.4 Hz, 1H), 8.41 (s, 1H), 8.13 – 8.05 (m, 1H), 7.92 – 7.82 (m, 1H), 7.64 – 7.55 (m, 1H), 7.44 – 7.26 (m, 3H), 3.27 (d, *J* = 4.6 Hz, 3H), 2.47 (s, 3H).	DMSO	>98	AQ5	ND	4

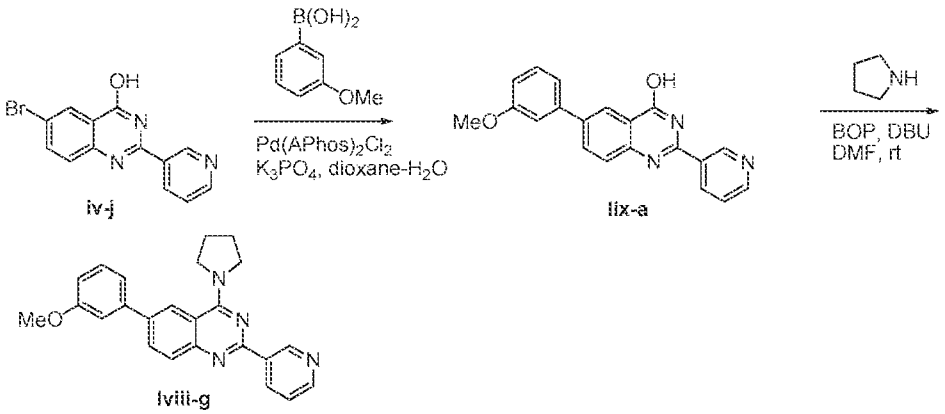
680

Scheme 76: General route for the synthesis of compounds with general formula lviii and lx



X^1, X^2, X^3, X^4 or X^5 = CH or N, at least one X^1, X^2, X^3, X^4 or X^5 must be N

Scheme 77: Representative synthesis of compounds of formula lviii (see Scheme 76)



6-(3-methoxyphenyl)-2-(pyridine-3-yl)quinazoline-4-ol (lix-a) 6-(3-methoxyphenyl)-2-(pyridine-3-yl)quinazoline-4-ol was prepared from 6-bromo-2-(pyridin-3-yl)quinazolin-4-ol **(synthesized following Scheme 70 substituting 2-amino-5-bromobenzamide for 2-amino-5-bromo-3-methylbenzamide)** and 3-methoxylphenylboronic acid as described in **Scheme 72** using **method AQ2**. The

resultant product, 6-(6-methoxypyridin-3-yl)-*N*-methyl-2-(pyridine-3-yl)quinazoline-4-amine, was a pale yellow solid (19.1 mg, 51%). LCMS m/z = 344 (M +1) (Method C) (retention time = 2.01 min). ^{1}H NMR (300 MHz, DMSO) δ 9.64 (d, *J* = 1.3 Hz, 1H), 8.84 – 8.74 (m, 1H), 8.68 (dd, *J* = 6.2, 1.7 Hz, 2H), 8.57 (d, *J* = 1.6 Hz, 2H), 8.16 (ddd, *J* = 14.4, 8.7, 2.2 Hz, 2H), 7.85 (d, *J* = 8.7 Hz, 1H), 7.54 (dd, *J* = 7.9, 4.8 Hz, 1H), 7.00 (d, *J* = 8.7 Hz, 1H), 3.93 (s, 3H), 3.18 (d, *J* = 4.3 Hz, 3H).

Method AP: 6-(3-methoxyphenyl)-2-(pyridine-3-yl)-4-(pyrrolidin-1-yl)quinazoline (lviii-g) 6-(3-methoxyphenyl)-2-(pyridine-3-yl)-4-(pyrrolidin-1-yl)quinazoline was prepared from 6-(3-methoxyphenyl)-2-(pyridine-3-yl)quinazoline-4-ol and pyrrolidine in a manner analogous to that described for 6-bromo-*N*-methyl-2-(pyridine-3-yl)quinazoline-4-amine using **Method AP** in **Scheme 72**. 6-(3-methoxyphenyl)-2-(pyridine-3-yl)-4-(pyrrolidin-1-yl)quinazoline was a pale yellow solid (43 mg, 31%). LCMS m/z = 383 (M +1) (Method C) (retention time = 2.49 min). ^{1}H NMR (300 MHz, DMSO) δ 9.62 (s, 1H), 8.94 (d, *J* = 5.0 Hz, 2H), 8.56 (s, 1H), 8.32 (dd, *J* = 19.9, 8.5 Hz, 2H), 7.83 (s, 1H), 7.56 – 7.30 (m, 3H), 7.04 (d, *J* = 6.8 Hz, 1H), 4.27 (s, 4H), 3.86 (s, 3H), 2.08 (s, 4H).

The compounds in the following table were prepared in a manner analogous to that described in **Scheme 76**, replacing pyrrolidine with the appropriate amine and 3-methoxyphenylboronic acid with the appropriate boronic acid.

Table 25:

Number	Product	Salt	^{1}H-NMR	H-NMR Solvent	LCMS	Retention Time	LCMS Protocol	Purity Percent	Method for Coupling
1616		HCl	1H NMR (300 MHz, DMSO) δ 9.82 (s, 1H), 9.59 (s, 1H), 9.08 – 8.81 (m, 3H), 8.36 (d, J = 6.8 Hz, 1H), 6.17 (d, J = 8.6 Hz, 1H), 7.95 – 7.77 (m, 1H), 7.58 – 7.37 (m, 3H), 7.05 (d, J = 6.5 Hz, 1H), 5.01 – 4.79 (m, 1H), 3.87 (s, 3H), 1.42 (d, J = 6.5 Hz, 6H).	DMSO	371 (M+1)	2.36	Method C	100	Method AP
1617		HCl	1H NMR (300 MHz, DMSO) δ 10.38 (s, 1H), 9.64 (s, 1H), 9.43 (s, 1H), 9.28 (s, 1H), 9.07 (d, J = 7.9 Hz, 1H), 9.00 – 8.76 (m, 3H), 8.48 (d, J = 7.5 Hz, 1H), 8.27 (d, J = 8.4 Hz, 1H), 8.08 – 7.95 (m, 1H), 7.94 – 7.81 (m, 1H), 3.97 – 3.74 (m, 2H), 1.38 (t, J = 7.2 Hz, 3H).	DMSO	328 (M+1)	1.82	Method C	100	Method AP
1618		HCl	1H NMR (300 MHz, DMSO) δ 10.11 (s, 1H), 9.58 (s, 1H), 9.03 – 8.79 (m, 3H), 8.35 (d, J = 8.7 Hz, 1H), 8.23 – 8.09 (m, 1H), 7.90 – 7.75 (m, 1H), 7.58 – 7.36 (m, 3H), 7.04 (d, J = 3.3 Hz, 1H), 3.88 (s, 3H), 3.65 (t, J = 6.0 Hz, 2H), 2.29 – 2.09 (m, 1H), 1.02 (d, J = 6.7 Hz, 6H).	DMSO	385 (M+1)	1.76	Method D	100	Method AP
1619		HCl	1H NMR (300 MHz, DMSO) δ 9.83 – 9.52 (m, 2H), 9.27 (d, J = 7.1 Hz, 1H), 8.95 (d, J = 5.1 Hz, 1H), 8.87 (s, 1H), 8.32 (d, J = 8.9 Hz, 1H), 8.15 – 7.92 (m, 2H), 7.59 – 7.33 (m, 3H), 7.04 (d, J = 3.4 Hz, 1H), 4.86 – 4.57 (m, 2H), 3.88 (s, 3H).	DMSO	411 (M+1)	1.99	Method D	100	Method AP
1620		HCl	1H NMR (300 MHz, DMSO) δ 10.50 (s, 1H), 9.64 (d, J = 1.4 Hz, 1H), 9.12 – 8.85 (m, 3H), 8.46 – 8.33 (m, 1H), 8.27 (d, J = 8.9 Hz, 1H), 7.88 (dd, J = 7.9, 5.1 Hz, 1H), 7.57 – 7.37 (m, 3H), 7.11 – 6.94 (m, 1H), 4.00 – 3.76 (m, 5H), 1.37 (t, J = 7.2 Hz, 3H).	DMSO	MS not work	1.56	Method D	100	Method AP

683

1621			1H NMR (300 MHz, DMSO) δ 9.57 (s, 1H), 8.78 – 8.50 (m, 3H), 8.33 – 7.89 (m, 3H), 7.63 (d, J = 8.7 Hz, 1H), 7.53 (dd, J = 7.9, 4.8 Hz, 1H), 7.47 – 7.32 (m, 3H), 7.04 – 6.91 (m, 1H), 3.66 (s, 3H).	DMSO	329 (M+1)	1.47	Method D	100	Method AP
1622		HCl	1H NMR (300 MHz, DMSO) δ 9.65 (s, 1H), 9.14 – 8.87 (m, 2H), 8.50 (s, 1H), 8.33 (s, 2H), 7.94 – 7.77 (m, 1H), 7.52 – 7.25 (m, 3H), 7.02 (d, J = 7.9 Hz, 1H), 3.84 (s, 3H), 3.71 (s, 6H).	DMSO	357 (M+1)	1.55	Method D	100	Method AP
1623			1H NMR (300 MHz, DMSO) δ 9.60 (d, J = 1.4 Hz, 1H), 8.81 – 8.55 (m, 3H), 8.42 (d, J = 1.8 Hz, 1H), 8.11 (ddd, J = 18.8, 8.7, 2.2 Hz, 2H), 7.86 (d, J = 8.7 Hz, 1H), 7.52 (dd, J = 7.9, 4.8 Hz, 1H), 6.95 (d, J = 8.6 Hz, 1H), 4.27 (s, 4H), 3.92 (s, 3H), 2.08 (s, 4H).	DMSO	384.1 (M+1)	2.33	Method C	100	Method AP
1624		2HCl	1H NMR (300 MHz, DMSO) δ 9.62 (s, 1H), 8.94 (d, J = 5.0 Hz, 2H), 8.56 (s, 1H), 8.32 (dd, J = 19.9, 8.5 Hz, 2H), 7.83 (s, 1H), 7.56 – 7.30 (m, 3H), 7.04 (d, J = 6.8 Hz, 1H), 4.27 (s, 4H), 3.86 (s, 3H), 2.08 (s, 4H).	DMSO	383.2 (M+1)	2.47	Method C	95	Method AP
1625			1H NMR (300 MHz, DMSO) δ 9.70 (d, J = 1.4 Hz, 1H), 8.85 (d, J = 7.9 Hz, 1H), 8.80 – 8.72 (m, 2H), 8.45 (d, J = 8.7 Hz, 1H), 8.27 (dd, J = 14.9, 5.9 Hz, 3H), 7.63 (dd, J = 7.3, 4.8 Hz, 1H), 7.52 – 7.33 (m, 4H), 7.04 (d, J = 7.1 Hz, 1H), 3.88 (s, 3H).	DMSO	380.1 (M+1)	2.01	Method C	100	Method AP

1626		HCl	1H NMR (300 MHz, DMSO) δ 9.61 (s, 1H), 8.75 (d, J = 7.7 Hz, 1H), 8.68 (d, J = 4.6 Hz, 1H), 8.30 (s, 1H), 8.08 (d, J = 8.6 Hz, 1H), 7.89 (d, J = 8.8 Hz, 1H), 7.75 (d, J = 8.7 Hz, 2H), 7.54 (dd, J = 7.6, 5.0 Hz, 1H), 7.07 (d, J = 8.7 Hz, 2H), 3.82 (s, 4H), 3.49 (s, 7H).	DMSO	358.6 (M+1)	2.25	Method C	100	Method AP
1627		HCl	1H NMR (300 MHz, DMSO) δ 9.62 (s, 1H), 8.76 (d, J = 7.9 Hz, 1H), 8.73 – 8.66 (m, 1H), 8.19 – 8.09 (m, 2H), 7.97 (d, J = 8.6 Hz, 1H), 7.82 – 7.73 (m, 2H), 7.61 – 7.52 (m, 1H), 7.14 – 7.05 (m, 2H), 3.94 (s, 5H), 3.89 – 3.80 (m, 9H).	DMSO	399.2 (M+1)	2.19	Method C	100	Method AP
1628			1H NMR (300 MHz, DMSO) δ 9.55 (dd, J = 2.1, 0.8 Hz, 1H), 8.76 – 8.62 (m, 3H), 8.60 (d, J = 1.7 Hz, 1H), 8.24 – 8.10 (m, 2H), 8.02 (s, 2H), 7.83 (d, J = 8.7 Hz, 1H), 7.56 – 7.46 (m, 1H), 6.98 (d, J = 9.2 Hz, 1H), 3.91 (s, 3H).	DMSO	330.1 (M+1)	1.72	Method C	100	Method AP
1629			1H NMR (300 MHz, DMSO) δ 9.65 (d, J = 2.1 Hz, 1H), 8.79 (d, J = 6.0 Hz, 1H), 8.73 (dd, J = 4.7, 1.6 Hz, 1H), 8.36 – 8.25 (m, 2H), 8.06 (d, J = 8.7 Hz, 1H), 7.59 (dd, J = 7.6, 4.4 Hz, 1H), 7.48 – 7.40 (m, 1H), 7.41 – 7.29 (m, 2H), 7.01 (dd, J = 8.0, 2.4 Hz, 1H), 4.80 (q, J = 7.1 Hz, 2H), 3.85 (s, 3H), 1.53 (t, J = 7.0Hz, 3H).	DMSO	358 (M+1)		Method C	99	Method AP
1630		2 HCl	1H NMR (300 MHz, DMSO) δ 9.68 (d, J = 1.8 Hz, 1H), 9.07 (d, J = 5.5 Hz, 1H), 8.96 (d, J = 3.5 Hz, 1H), 8.90 (s, 1H), 8.37 (d, J = 7.5 Hz, 1H), 8.22 (d, J = 8.3 Hz, 1H), 7.94 - 7.83 (m, 1H), 7.57 - 7.39 (m, 3H), 7.22 (d, J = 1.0 Hz, 1H), 7.08 (d, J = 7.3 Hz, 1H), 6.72 (s, 1H), 5.16 - 5.04 (m, 1H), 3.68 (s, J = 2.7 Hz, 3H), 3.23 (dd, J = 13.7, 6.1 Hz, 1H), 2.31 - 2.17 (m, 1H), 2.17 - 1.88 (m, 4H), 1.74 - 1.55 (m, 1H).	DMSO	440.6 (M+1)		Method C	99	Method AP

685

1631		2 HCl	1H NMR (300 MHz, DMSO) δ 9.70 (d, J = 1.6 Hz, 1H), 9.24 (d, J = 7.4 Hz, 1H), 8.99 (dd, J = 5.3, 1.4 Hz, 1H), 8.34 (dd, J = 15.7, 6.1 Hz, 3H), 8.21 (d, J = 8.4 Hz, 1H), 8.01 (dd, J = 7.7, 5.1 Hz, 1H), 7.51 - 7.33 (m, 3H), 7.04 (dd, J = 7.8, 2.4 Hz, 1H), 4.67 (s, 2H), 4.33 (s, 2H), 3.87 (s, J = 3.6 Hz, 3H), 3.50 (s, 2H).	DMSO	412.4 (M+1)		Method C	99	Method AP
1632		2 HCl	1H NMR (300 MHz, DMSO) δ 9.00 (d, J = 6.5 Hz, 2H), 8.78 (d, J = 6.5 Hz, 2H), 8.46 - 8.32 (m, 2H), 8.15 (d, J = 8.4 Hz, 1H), 7.53 - 7.30 (m, 3H), 7.02 (d, J = 7.8 Hz, 1H), 4.34 (s, J = 2.4 Hz, 3H), 3.86 (s, J = 2.5 Hz, 3H).	DMSO	344.4 (M+1)		Method C	99	Method AP
1633			1H NMR (300 MHz, DMSO) δ 9.55 (dd, J = 2.1, 0.8 Hz, 1H), 8.76 – 8.62 (m, 3H), 8.60 (d, J = 1.7 Hz, 1H), 8.24 – 8.10 (m, 2H), 8.02 (s, 2H), 7.83 (d, J = 8.7 Hz, 1H), 7.56 – 7.46 (m, 1H), 6.98 (d, J = 9.2 Hz, 1H), 3.91 (s, 3H).	DMSO	330.1 (M+1)		Method C	99	Method AP

lumber	Starting Material R[1]	Starting Material R[3]	Product	Salt Type	^{1}H NMR	^{1}H NMR Solvent	Purity percent	Method of Coupling
1634					^{1}H NMR (DMSO-d_6) ppm 3.87 (s, 3H), 4.78 (d, 2H, J = 5.4 Hz), 6.58 (d, 1H, J = 1.1 Hz), 7.00-7.75 (m, 8H), 7.85 (d, 1H, J = 8.6 Hz), 8.64-8.97 (m, 4H), 9.64 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)
1635					^{1}H NMR (DMSO-d_6) ppm 3.84-3.95 (m, 11H), 7.01 (d, 1H, J = 8.1 Hz), 7.32-7.46 (m, 3H), 7.56 (dd, 1H, J = 6.1, 8.1 Hz), 7.97 (d, 1H, J = 8.2 Hz), 8.16-8.76 (m, 4H), 9.61 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)
1636					^{1}H NMR (DMSO-d_6) ppm 2.23 (m, 2H), 3.85 (s, 3H), 4.71 (br s, 4H), 6.98 (dd, 1H, J = 2.1, 8.0 Hz), 7.31-7.55 (m, 4H), 7.87 (d, 1H, J = 8.2 Hz), 8.12-8.74 (m, 4H), 9.59 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)

1637					1H NMR (DMSO-d6) ppm 1.77 (br s, 6H), 3.66-3.89 (br m, 7H), 6.99 (dd, 1H, J = 1.4, 8.6 Hz), 7.31-7.57 (m, 4H), 7.93 (d, 1H, J = 1.4, 8.6 Hz), 8.11-8.16 (m, 2H), 8.69-8.76 (m, 2H), 9.61 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)
1638					1H NMR (DMSO-d6) ppm 2.18-2.22 (m, 1H), 3.00-3.09 (m, 1H), 3.11-3.22 (m, 2H), 3.31-3.34 (m, 1H), 3.86 (s, 3H), 6.29-6.31 (m, 1H), 7.17-8.82 (m, 14H), 9.63 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)
1639					1H NMR (DMSO-d6) ppm 3.87 (s, 3H), 4.10-4.13 (m, 2H), 4.35-4.38 (m, 2H), 6.92-7.46 (m, 10H), 7.85 (d, 1H, *J* = 8.6 Hz), 8.16 (d, 1H, *J* = 8.6 Hz), 8.66-8.75 (m, 4H), 9.61 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)
1640					1H NMR (DMSO-d6) ppm 3.07 (t, 2H, J = 6.9 Hz), 3.87 (s, 3H), 3.92-3.96 (m, 2H), 7.00-7.58 (m, 10H), 7.84 (d, 1H, J = 8.6 Hz), 8.14 (d, 1H, J = 8.6 Hz), 8.59-8.78 (m, 4H), 9.64 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)

688

1641					1H NMR (DMSO-d6) ppm 3.87 (s, 3H), 4.95 (d, 2H, J = 5.6 Hz), 7.01-7.51 (m, 10H), 7.85 (d, 1H, J = 8.6 Hz), 8.16 (d, 1H, J = 8.6 Hz), 8.65-8.73 (m, 4H), 9.56 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)
1642					1H NMR (DMSO-d6) ppm 1.66-1.781 (m, 6H), 2.16-2.19 (m, 2H), 3.87 (s, 3H), 4.78 (br s, 1H), 7.00-7.55 (m, 5H), 7.63 (d, 1H, J = 8.6 Hz), 8.12 (d, 1H, J = 8.6 Hz), 8.29 (s, 1H), 8.67-8.77 (m, 3H), 9.62 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)
1643				HCl	1H NMR (DMSO-d6) ppm 0.81 (t, 3H, *J* =7.4 Hz), 1.47-1.54 (m, 2H), 2.00-2.05 (m, 2H), 3.32-3.37 (m, 4H), 3.86-3.91 (m, 5H), 7.03-7.80 (m, 5H), 8.16 (d, 1H, J = 8.7 Hz), 8.34 (d, 1H, J = 8.7 Hz), 8.86-8.96 (m, 3H), 9.61 (s, 1H), 10.03 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)
1644					1H NMR (DMSO-d6) ppm 0.36-0.54 (m, 4H), 1.30-1.32 (m, 1H), 3.58-3.62 (m, 2H), 3.87 (s, 3H), 7.00-7.54 (m, 5H), 7.66 (d, 1H, J = 8.6 Hz), 8.14 (d, 1H, J = 8.6 Hz), 8.64-8.76 (m, 4H), 9.62 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)
1645					1H NMR (DMSO-d6) ppm 1.83-1.88 (m, 2H), 2.21-2.27 (m, 2H), 2.49 (br s, 2H), 3.87 (s, 3H), 4.88-4.91 (m, 1H), 7.03-7.57 (m, 5H), 7.63 (d, 1H, J = 8.6 Hz), 8.13 (d, 1H, J = 8.6 Hz), 8.62-8.77 (m, 4H), 9.63 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)

1646					1H NMR (DMSO-d6) ppm 3.21 (s, 1H), 3.88 (s, 3H), 4.52 (dd, 2H, *J* = 2.2, 5.2 Hz), 7.01-7.56 (m, 5H), 7.88 (d, 1H, J = 8.7 Hz), 8.19 (d, 1H, J = 8.6 Hz), 8.64-9.01 (m, 4H), 9.66 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)
1647					1H NMR (DMSO-d6) ppm 3.87 (s, 3H), 4.37 (br s, 2H), 5.19 (dd, 1H, J = 1.5, 10.2 Hz), 5.31 (dd, 1H, J = 1.5, 17.2 Hz), 6.01-6.22 (m, 1H), 7.00-7.56 (m, 5H), 7.85 (d, 1H, J = 8.6 Hz), 8.16 (d, 1H, J = 8.6 Hz), 8.67-8.82 (m, 4H), 9.61 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)
1648					1H NMR (DMSO-d6) ppm 0.94-0.99 (t, 6H, *J* = 7.4 Hz), 1.68-1.80 (m, 4H), 3.87 (s, 3H), 4.49-4.52 (m, 1H), 7.01-7.47 (m, 5H), 7.83 (d, 1H, J = 8.6 Hz), 8.11-8.15 (m, 2H), 8.67-8.75 (m, 3H), 9.63 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)
1649					1H NMR (DMSO-d6) ppm 1.68 (s, 9H), 3.87 (s, 3H), 7.01-7.70 (m, 6H), 7.82 (d, 1H, J = 8.6 Hz), 8.11 (d, 1H, J = 8.6 Hz), 8.67-8.74 (m, 3H), 9.60 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)
1650					1H NMR (DMSO-d6) ppm 0.97 (t, 3H, *J* = 7.2 Hz), 1.44-1.48 (m, 2H), 1.74-1.78 (m, 2H), 3.71-3.75 (m, 2H), 3.89 (s, 3H), 7.00-7.56 (m, 5H), 7.83 (d, 1H, J = 8.6 Hz), 8.15 (d, 1H, J = 8.6 Hz), 8.59-8.76 (m, 4H), 9.62 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)

1651					1H NMR (DMSO-d6) ppm 3.87 (s, 3H), 4.98 (d, 2H, *J* = 5.6 Hz), 7.02-7.46 (m, 7H), 7.87 (d, 1H, J = 8.7 Hz), 8.51 (dd, 1H, J = 1.5, 4.5 Hz), 8.50-8.71 (m, 5H), 9.26 (s, 1H), 9.46 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)
1652					1H NMR (DMSO-d6) ppm 3.87 (s, 3H), 4.98 (d, 2H, *J* = 5.5 Hz), 7.00-7.46 (m, 6H), 7.86-7.90 (m, 2H), 8.16 (d, 1H, J = 1.7 Hz), 8.46 (d, 1H, J = 1.7 Hz), 8.66-8.76 (m, 4H), 9.22 (s, 1H), 9.56 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)
1653					1H NMR (DMSO-d6) ppm 3.22-3.27 (m, 2H), 3.87 (s, 3H), 4.04-4.11 (m, 2H), 7.02-7.46 (m, 8H), 7.83 (d, 1H, J = 8.6 Hz), 8.13 (d, 1H, J = 1.6 Hz), 8.67-8.78 (m, 5H), 9.64 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)
1654					1H NMR (DMSO-d6) ppm 1.76-1.88 (m, 4H), 2.66 (br s, 1H), 3.37-3.48 (m, 2H), 3.86 (s, 3H), 4.39-4.47 (m, 2H), 6.95-7.57 (m, 7H), 7.95 (d, 1H, J = 8.7 Hz), 8.15-8.19 (m, 2H), 8.69-8.76 (m, 2H), 9 61 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)

1655					^{1}H NMR (DMSO-d_6) ppm 3.87 (s, 3H), 4.97 (d, 2H, J = 5.6 Hz), 7.00-7.50 (m, 8H), 7.85 (d, 1H, J = 8.7 Hz), 8.16 (s, 1H), 8.66-8.77 (m, 3H), 9.11 (s, 1H), 9.61 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)
1656					^{1}H NMR (DMSO-d_6) ppm 2.28 (s, 3H), 3.87 (s, 3H), 4.91 (d, 2H, J = 5.5 Hz), 7.00-7.52 (m, 9H), 7.86 (d, 1H, J = 8.6 Hz), 8.17 (dd, 1H, J = 8.6, 1.8 Hz), 8.66-9.16 (m, 3H), 9.18-9.16 (m, 1H), 9.57 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)
1657					^{1}H NMR (DMSO-d_6) ppm 3.71 (s, 3H), 3.87 (s, 3H), 4.91 (d, 2H, J = 5.7 Hz), 6.82-7.52 (m, 9H), 7.86 (d, 1H, J = 8.7 Hz), 8.17 (dd, 1H, J = 8.7, 1.8 Hz), 8.66-9.15 (m, 3H), 9.17-9.19 (m, 1H), 9.57 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)
1658					^{1}H NMR (DMSO-d_6) ppm 2.25 (s, 3H), 3.87 (s, 3H), 4.91 (d, 2H, J = 5.7 Hz), 7.00-7.53 (m, 9H), 7.86 (d, 1H, J = 8.6 Hz), 8.17 (dd, 1H, J = 8.6, 1.8 Hz), 8.66-9.15 (m, 3H), 9.17-9.19 (m, 1H), 9.57 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)
1659					^{1}H NMR (DMSO-d_6) ppm 2.44 (s, 3H), 3.86 (s, 3H), 4 95 (d, 2H, J = 5.7 Hz), 7.01-7.53 (m, 9H), 7.86 (d, 1H, J = 8.6 Hz), 8.17 (dd, 1H, J = 8.6, 1.8 Hz), 8.65-9 02 (m, 3H), 9.50-9 52 (m, 1H), 9.54 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)

692

1660					^{1}H NMR (DMSO-d_6) ppm 3.87 (s, 3H), 7.03 (s, 1H), 7.44-7.94 (m, 10H), 8.07-8.70 (m, 4H), 9.41 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)
1661					^{1}H NMR (DMSO-d_6) ppm 3.87 (s, 3H), 4.91 (d, 2H, J = 5.5 Hz), 7.00-7.04 (m, 1H), 7.04-7.55 (m, 7H), 7.87 (d, 1H, *J* = 8.6 Hz), 8 18 (dd, 1H, J = 8.6, 1.8 Hz), 8 66-9.18 (m, 3H), 9.18-9.21 (m, 1H), 9.55 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)
1662					^{1}H NMR (DMSO-d_6) ppm 3.87 (s, 3H), 4.99 (d, 2H, J = 5 5 Hz), 7.01-7.05 (m, 2H), 7.15-7.56 (m, 6H), 7.88 (d, 1H, *J* = 8.6 Hz), 8.20 (dd, 1H, J = 8.6, 1.8 Hz), 8.64-9.18 (m, 3H), 9.19-9.21 (m, 1H), 9 50 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)
1663					^{1}H NMR (DMSO-d_6) ppm 3.49 (s, 3H), 3.74 (s, 3H), 5.15 (s, 2H), 6.90 (d, *J* = 8.2 Hz, 1H), 7.04-7.29 (m, 2H), 7 33-7.54 (m, 7H), 7.93 (d, 1H, *J* = 8.6 Hz), 8.15 (dd, 1H, J = 8.6, 1.8 Hz), 8.21 (s, 1H), 8 68-8 75 (m, 2H), 9 59 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)
1664					^{1}H NMR (DMSO-d_6) ppm 3.87 (s, 3H), 4.94 (d, 2H, J = 5 5 Hz), 7.01-7.03 (m, 1H), 7.35-7.57 (m, 7H), 7.88 (d, 1H, *J* = 8.6 Hz), 8.20 (dd, 1H, J = 8.6, 1.8 Hz), 8.66-9.22 (m, 3H), 9.19-9.21 (m, 1H), 9.50 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)

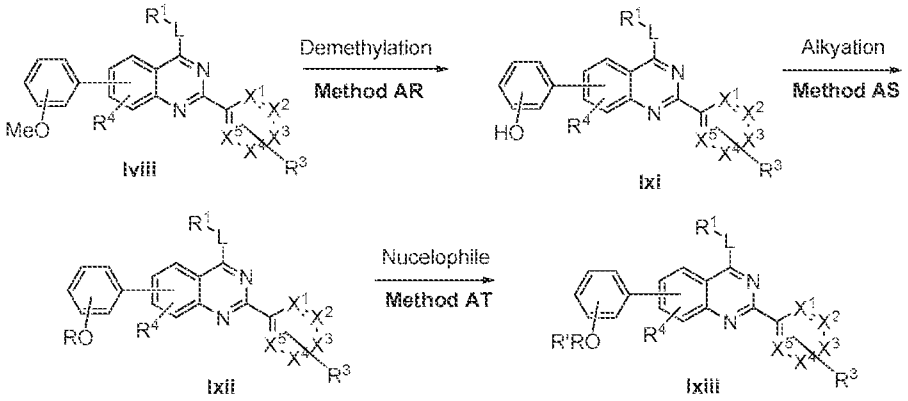
1665					^{1}H NMR (DMSO-d_6) ppm 3.87 (s, 3H), 4.96 (d, 2H, J = 5.5 Hz), 7.00-7.03 (m, 2H), 7.33-7.52 (m, 7H), 7.88 (d, 1H, *J* = 8.6 Hz), 8.19 (dd, 1H, J = 8.6, 1.8 Hz), 8.65-9.20 (m, 3H), 9.19-9.21 (m, 1H), 9.54 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)
1666					^{1}H NMR (DMSO-d_6) ppm 3.87 (s, 3H), 4.93 (d, 2H, J = 5.5 Hz), 7.00-7.19 (m, 3H), 7.41-7.55 (m, 6H), 7.88 (d, 1H, *J* = 8.6 Hz), 8.17 (dd, 1H, J = 8.6, 1.8 Hz), 8.65-9.18 (m, 3H), 9.19-9.21 (m, 1H), 9.57 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)
1667					^{1}H NMR (DMSO-d_6) ppm 3.87 (s, 3H), 4.92 (d, 2H, J = 5.5 Hz), 7.01-7.03 (d, 1H, *J* = 7.0 Hz), 7.37-7.53 (m, 6H), 7.72 (d, 1H, *J* = 8.6 Hz), 8.18 (dd, 1H, J = 8.6, 1.8 Hz), 8.66-9.19 (m, 3H), 9.20-9.23 (m, 1H), 9.56 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)
1668					^{1}H NMR (DMSO-d_6) ppm 1.68 (d, 3H, *J* = 7.0 Hz), 3.87 (s, 3H), 4.92 (d, 2H, J = 5.5 Hz), 5.75-5.76 (m, 1H), 7.02 (d, 1H, *J* = 7.0 Hz), 7.32-7.56 (m, 9H), 7.64 (d, 1H, *J* = 8.6 Hz), 8.15 (dd, 1H, J = 8.6, 1.8 Hz), 8.64-8.84 (m, 4H), 9.51 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)
1669					^{1}H NMR (DMSO-d_6) ppm 3.70 (s, 3H), 3.86 (s, 3H), 4.92 (d, *J* = 5.1 Hz, 2H), 6.89-7.01 (m, 3H), 7.41-7.54 (m, 6H), 7.85 (d, J = 8.6 Hz, 1H), 7.85 (d, J = 8.6 Hz, 1H), 8.67-8.75 (m, 3H), 9.19 (s, 1H), 9.56 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)

1670					^{1}H NMR (DMSO-d_6) ppm 3.87 (s, 3H), 3.91 (s, 3H), 4.92 (d, J = 5.0 Hz, 2H), 6.87-7.52 (m, 9H), 7.85 (d, J = 8.5 Hz, 1H), 8.17 (d, J = 8.5 Hz, 1H), 8.64-8.73 (m, 3H), 9.05 (s, 1H), 9.52 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)
1671					^{1}H NMR (DMSO-d_6) ppm 3.87 (s, 3H), 4.93 (d, J = 5.6 Hz, 2H), 7.02 (s, 1H), 7.41-7.61 (m, 7H), 7.83 (d, J = 8.9 Hz, 1H), 8.18 (d, J = 8.9 Hz, 1H), 8.66-8.71 (m, 3H), 9.21 (s, 1H), 9.54 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)
1672					^{1}H NMR (DMSO-d_6) ppm 3.69 (s, 6H), 3.87 (s, 3H), 4.93 (d, J = 5.6 Hz, 2H), 6.90 (s, 1H), 7.00-7.54 (m, 7H), 7.85 (d, J = 8.6 Hz, 1H), 8.17 (d, J = 8.6 Hz, 1H), 8.66-8.78 (m, 3H), 9.14 (s, 1H), 9.63 (s, 1H)	DMSO	>98	Method AQ3, F5, G2 (reflux)
1673					-	DMSO	95	Method AQ3, AP
1674				2HCl	1H-NMR (300 MHz, DMSO): δ 9.71 (d, J = 1.6 Hz, 1H), 9.16 (d, J = 8.2 Hz, 1H), 8.98 (dd, J = 5.1, 1.5 Hz, 1H), 8.58 (s, 1H), 8.48 – 8.34 (m, 3H), 8.20 (d, J = 8.0 Hz, 1H), 7.98 – 7.87 (m, 2H), 7.75 (t, J = 7.8 Hz, 1H), 3.73 (s, 6H).	DMSO	95	Method AQ3, AP

695

1675					1H-NMR (300 MHz, DMSO): δ 9.59 (s, 1H), 8.78 – 8.62 (m, 2H), 8.38 (s, 1H), 8.05 (dd, *J* = 8.6, 1.8 Hz,1H), 7.84 (d, *J* = 8.7 Hz, 1H), 7.73 (d, *J* = 8.7 Hz, 2H), 7.52 (dd, *J* = 7.8, 4.7 Hz, 1H), 7.07 (d, *J* = 8.8 Hz, 2H), 4.04 (s, 4H), 3.82 (s, 3H), 2.02 (s, 4H).	DMSO	95	Method AQ3, AP
1676				3HCl	1H-NMR (300 MHz, DMSO): δ 10.40 (s, 1H), 9.48 (d, *J* = 2.0 Hz, 1H), 8.95 (s, 2H), 8.88 (d, *J* = 5.2 Hz, 1H), 8.72 (d, *J* = 4.3 Hz, 1H), 8.35 (d, *J* = 8.9 Hz, 1H), 8.18 (s, 1H), 8.08 (d, *J* = 8.8 Hz, 1H), 7.94 – 7.81 (m, 2H), 7.64 (s, 1H), 7.54 – 7.45 (m, 3H), 7.06 – 7.00 (m, 1H), 5.25 (d, *J* = 5.1 Hz, 2H), 3.88 (s, 3H).	DMSO	95	Method AQ3, AP
1677					1H-NMR (300 MHz, DMSO): δ 12.83 (s, 1H), 9.32 (d, J = 2.2 Hz, 1H), 8.77 (dd, J = 4.8, 1.5 Hz, 1H), 8.63 (d, J = 2.5 Hz, 1H), 8.56 – 8.49 (m, 1H), 8.37 (d, J = 2.2 Hz, 1H), 8.23 – 8.14 (m, 2H), 7.85 (d, J = 8.5 Hz, 1H), 7.60 (dd, J = 8.0, 4.8 Hz, 1H), 6.96 (d, J = 8.7 Hz, 1H), 3.92 (s, 3H).	DMSO	95	Method AQ3, AP
1678	NH3			2HCl	^{1}H NMR (300 MHz, DMSO) δ 9.79 (brs, 1H), 9.60 (s, 2H), 9.07 (d, *J* = 7.4 Hz, 1H), 9.00 (d, *J* = 4.5 Hz, 1H), 8.80 (s, 1H), 8.35 (d, *J* = 8.7 Hz, 1H), 8.26 (d, *J* = 8.6 Hz, 1H), 8.02 – 7.88 (m, 1H), 7.67 – 7.48 (m, 2H), 7.49 – 7.37 (m, 1H).	DMSO	>98	Method AQ3, F5, G2 (reflux)

Scheme 78: General route for the synthesis of compounds with general formula lxiii

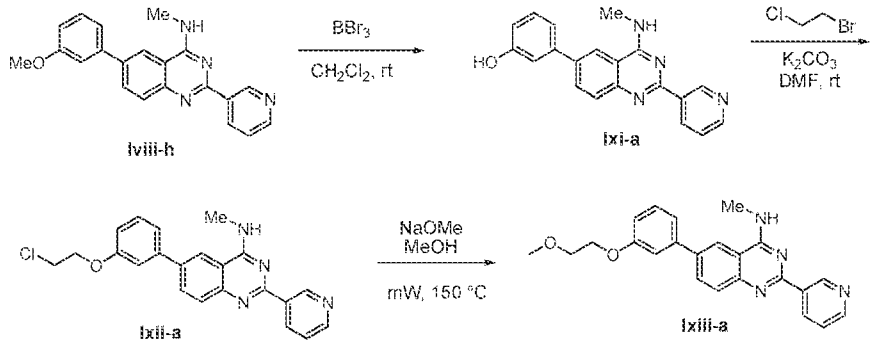


X^1, X^2, X^3, X^4 or X^5 = CH or N, at least one X^1, X^2, X^3, X^4 or X^5 must be N

Method AT for alkylation:

Method AT1: NaOMe/MeOH/microwave/150 °C
Method AT2: MeOH/microwave/150 °C
Method AT3: DIPEA/KI/DMF/microwave/150 °C

Scheme 79: Representative synthesis of compounds of formula lxiii (see Scheme 76)



Method AR: 3-(4-(methylamino)-2-(pyridin-3-yl)quinazolin-6-yl)phenol (lxi-a) To a suspension of 6-(3-methoxyphenyl)-N-methyl-2-(pyridin-3-yl)quinazolin-4-amine **(prepared in a similar method described for 6-(3-methoxyphenyl)-2-(pyridine-3-yl)-4-(pyrrolidin-1-yl)quinazoline using Scheme 74, substituting N-**

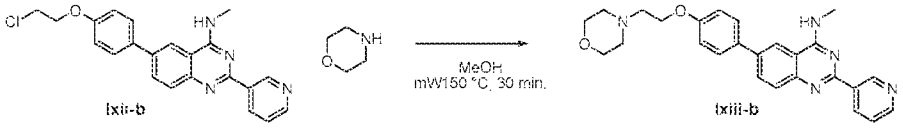
methylamine for pyrrolidine) (1.00 g, 2.9 mmol) in CH_2Cl_2 (15 mL) and boron tribromide 1M solution in dichloromethane (8.76 ml, 8.76 mmol) was added at 0 °C. The reaction mixture was stirred overnight at room temperature after which it was carefully poured into a vigorously stirring mixture of ice and saturated aqueous solution of $NaHCO_3$. The resultant solid was collected by filtration, dried and then dissolved in a mixture of K_2CO_3 (2 g) and methanol (50 mL). The solution was then acidified using aqueous NH_4Cl solution. (50 mL) and the precipitate which formed was collected by filtration and dried to give 0.95 g of 3-(4-(methylamino)-2-(pyridin-3-yl)quinazolin-6-yl)phenol as pale yellow solid (99 %). LCMS m/z = 329 (M +1) (Method D) (retention time = 1.30 min). ^{1}H NMR (300 MHz, DMSO) δ 9.63 (s, 1H), 9.60 (s, 1H), 8.77 (d, J = 8.0 Hz, 1H), 8.74 – 8.59 (m, 2H), 8.54 (s, 1H), 8.05 (d, J = 8.7 Hz, 1H), 7.83 (d, J = 8.7 Hz, 1H), 7.54 (dd, J = 7.9, 4.8 Hz, 1H), 7.38 – 7.12 (m, 3H), 6.82 (d, J = 7.8 Hz, 1H), 3.17 (d, J = 4.3 Hz, 3H).

Method AS: 6-(3-(2-chloroethoxy)phenyl)-N-methyl-2-(pyridin-3-yl)quinazolin-4-amine (lxii-a) A suspension of 3-(4-(methylamino)-2-(pyridin-3-yl)quinazolin-6-yl)phenol (0.30 g, 0.914 mmol), 1-bromo-2-chloroethane (0.38 ml, 4.57 mmol), and potassium carbonate (0.38 g, 2.74 mmol) in DMF (10 mL) was stirred for 2 days at room temperature. Water (10 mL) and ethyl acetate (10 mL) were added to the mixture and extracted. The organic layer was separated and concentrated *in vacuo* to leave a solid, which was collected by filtration and washed with hexane and dried to give 0.30 g of 6-(3-(2-chloroethoxy)phenyl)-N-methyl-2-(pyridin-3-yl)quinazolin-4-amine as brown solid (83 %). The product was used without further purification.

Method AT1: 6-(3-(2-methoxyethoxy)phenyl)-N-methyl-2-(pyridin-3-yl)quinazolin-4-amine (lxiii-a) A solution of 6-(3-(2-chloroethoxy)phenyl)-N-methyl-2-(pyridin-3-yl)quinazolin-4-amine (70 mg, 0.18 mmol) and sodium methoxide (97 mg, 1.8 mmol) in methanol (3 mL) was placed in a microwave reaction vial. The mixture was heated under microwave irradiation conditions at 150°C for 30 minutes after which the solvent was removed *in vacuo*. The crude product was obtained, which was purified by column chromatography on basic silica gel (eluted

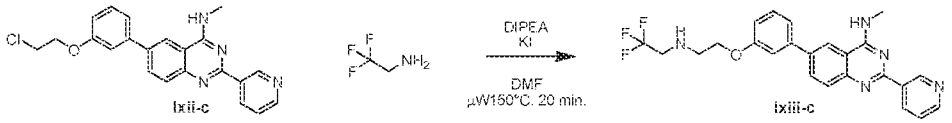
with hexane/ethyl acetate 3:1→1:4) to give 20 mg of 6-(3-(2-methoxyethoxy)phenyl)-N-methyl-2-(pyridin-3-yl)quinazolin-4-amine as an off-white powder (29 %). LCMS m/z = 387 (M +1) (Method D) (retention time = 1.49 min). ^{1}H NMR (300 MHz, DMSO) δ 9.64 (s, 1H), 8.77 (d, J = 8.2 Hz, 1H), 8.73 – 8.51 (m, 3H), 8.16 (d, J = 8.7 Hz, 1H), 7.84 (d, J = 8.3 Hz, 1H), 7.60 – 7.32 (m, 4H), 7.01 (s, 1H), 4.21 (s, 2H), 3.70 (s, 2H), 3.33 (s, 3H), 3.19 (s, 3H).

Method AT2: N-Methyl-6-(4-(2-morpholinoethoxy)phenyl)-2-(pyridin-3-yl)quinazolin-4-amine (lxiii-b)



In a 10 mL microwave vial 6-(4-(2-chloroethoxy)phenyl)-N-methyl-2-(pyridin-3-yl)quinazolin-4-amine (70.0 mg, 0.179 mmol) and morpholine (0.155 ml, 1.791 mmol) were added in methanol (3 mL) to give a yellow suspension. The vial was irradiated at 150 °C in the microwave for 30 min. The volatiles were evaporated *in vacuo*. Water (10 mL) was added to the reaction mixture and extracted with ethyl acetate (2 x 10 mL). The organic layers were combined and washed with brine (1 x 20 mL), then dried over $MgSO_4$, filtered and concentrated. The residue was purified by column chromatography on basic silica gel (eluted with hexane/ethyl acetate 3:2 to 0:1). The product was obtained as the parent and converted to the HCl salt by addition of 4 M HCl-dioxane, then crystallized from EtOH-H2O to give 55 mg of N-methyl-6-(4-(2-morpholinoethoxy)phenyl)-2-(pyridin-3-yl)quinazolin-4-amine as a yellow powder (60 % yield). LCMS m/z = 442 (M +1) (Method D) (retention time = 1.12 min). ^{1}H NMR (300 MHz, DMSO) δ 11.31 (s, 1H), 10.41 (s, 1H), 9.63 (s, 1H), 9.10 - 8.79 (m, 3H), 8.34 (d, J = 8.2 Hz, 1H), 8.28 - 8.12 (m, 1H), 7.92 (d, J = 8.0 Hz, 2H), 7.87 - 7.74 (m, 1H), 7.18 (d, J = 8.0 Hz, 2H), 4.60 - 4.46 (m, 2H), 4.06 - 3.91 (m, 2H), 3.91 - 3.74 (m, 2H), 3.67 - 3.41 (m, 4H), 3.38 - 3.09 (m, J = 10.1 Hz, 5H).

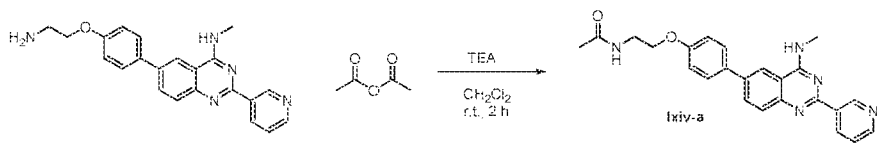
Method AT3: N-methyl-2-(pyridin-3-yl)-6-(3-(2-(2,2,2 trifluoroethylamino)ethoxy) phenyl)quinazolin-4-amine (lxiii-c)



lxii-c lxiii-c

In a 10 mL microwave vial was added 6-(3-(2-chloroethoxy)phenyl)-N-methyl-2-(pyridin-3-yl)quinazolin-4-amine (50.0 mg, 0.128 mmol), 2,2,2-trifluoroethylamine (0.100 ml, 1.279 mmol), potassium iodide (42.5 mg, 0.256 mmol), and N,N'-diisopropylethylamine (0.045 ml, 0.256 mmol) in DMF (3 mL) to give a yellow suspension. The vial was irradiated at 150 °C in the microwave for 20 min. Water (10 mL) was added to the mixture and extracted with ethyl acetate (2 x 20 mL). The organic layers were combined and washed with water (1 x 20 mL) and brine (1 x 20 mL), dried over $MgSO_4$, filtered and concentrated. The residue was purified by column chromatography on silica gel (eluted with CH_2Cl_2/CH_2Cl_2-MeOH-NH_4OH=100:20:1 1:0 to 0:1). The product was converted to the HCl salt by addition of 4 M HCl-dioxane, then crystallization from IPA-H2O to give 30 mg of N-methyl-2-(pyridin-3-yl)-6-(3-(2-(2,2,2-trifluoroethylamino)ethoxy)phenyl)quinazolin-4-amine as a yellow powder (42 %). LCMS m/z = 454 (M +1) (Method C) (retention time = 2.26 min). ^{1}H NMR (300 MHz, DMSO) δ 10.73 - 10.36 (m, 1H), 9.65 (s, 1H), 9.13 - 8.98 (m, 2H), 8.93 (d, J = 5.0 Hz, 1H), 8.38 (d, J = 8.4 Hz, 1H), 8.24 (d, J = 7.7 Hz, 1H), 7.94 - 7.75 (m, 1H), 7.69 - 7.41 (m, 3H), 7.09 (d, J = 8.1 Hz, 1H), 4.61 - 4.43 (m, 2H), 4.28 - 4.07 (m, 2H), 3.59 - 3.39 (m, 2H), 3.30 (d, J = 2.8 Hz, 3H).

Scheme 80: Method AU: N-(2-(4-(4-(methylamino)-2-(pyridin-3-yl)quinazolin-6-yl)phenoxy)ethyl)acetamide (lxiv-a)



lxiv-a

In a 50 mL round-bottomed flask was added 6-(4-(2-aminoethoxy)phenyl)-N-methyl-2-(pyridin-3-yl)quinazolin-4-amine (15.0 mg, 0.040 mmol) and triethylamine (0.017

ml, 0.121 mmol) in CH_2Cl_2 (5 mL) to give a yellow solution. Acetic anhydride (4.58 µl, 0.048 mmol) was added and the mixture was stirred for 2 h at room temperature. Water (10 mL) was added to the mixture and extracted with ethyl acetate (2 x 10 mL). The organic layers were combined and washed with brine (1 x 20 mL), dried over Mg_2SO4, filtered and concentrated. The residue was purified by column chromatography on silica gel (eluted with CH_2Cl_2/MeOH 1:0 to 9:1). The product was converted to the HCl salt by addition of 4 M HCl-dioxane, then dissolved in a small amount of methanol, followed by ethyl acetate. The resulting solid was filtered and dried to give 10 mg of N-(2-(4-(4-(methylamino)-2-(pyridin-3-yl)quinazolin-6-yl)phenoxy)ethyl)acetamide as a HCl salt as a yellow solid in a 51% yield. LCMS m/z = 414 (M +1) (Method C) (retention time = 1.28 min). ^{1}H NMR (300 MHz, DMSO) δ 10.26 (s, 1H), 9.62 (s, 1H), 9.06 - 8.90 (m, 2H), 8.81 (s, 1H), 8.34 (d, J = 9.0 Hz, 1H), 8.17 (d, J = 6.6 Hz, 2H), 7.86 (d, J = 8.0 Hz, 3H), 7.13 (d, J = 7.9 Hz, 2H), 4.06 (t, J = 5.4 Hz, 2H), 3.52 - 3.38 (m, 2H), 3.30 (d, J = 4.1 Hz, 3H), 1.84 (s, 3H).

The compounds in the following table were prepared in a manner analogous to that described in **Scheme 78**, replacing 1-bromo-2-chloroethane with the corresponding alkyl halide.

Table 26:

Number	PRODUCT	Salt	^{1}H-NMR	^{1}H-NMR Solvent	LCMS	Retention Time	LCMS Protocol	Purity percent	Method for Coupling
1679		HCl	1H NMR (300 MHz, DMSO) δ 10.36 (s, 1H), 9.65 (s, 1H), 9.13 – 8.99 (m, 1H), 8.99 – 8.83 (m, 2H), 8.38 (d, J = 8.8 Hz, 1H), 8.30 – 8.16 (m, 1H), 7.94 – 7.80 (m, 1H), 7.55 – 7.35 (m, 3H), 7.09 – 6.97 (m, 1H), 4.16 (q, J = 7.0 Hz, 2H), 3.31 (d, J = 4.3 Hz, 3H), 1.37 (t, J = 6.9 Hz, 3H).	DMSO	357 (M+1)	1.62	Method D	100	Method AR/AS/AT1
1680			1H NMR (300 MHz, DMSO) δ 9.64 (s, 1H), 8.77 (d, J = 8.2 Hz, 1H), 8.73 – 8.51 (m, 3H), 8.16 (d, J = 8.7 Hz, 1H), 7.84 (d, J = 8.3 Hz, 1H), 7.60 – 7.32 (m, 4H), 7.01 (s, 1H), 4.21 (s, 2H), 3.70 (s, 2H), 3.33 (s, 3H), 3.19 (s, 3H).	DMSO	387 (M+1)	1.49	Method D	100	Method AR/AS/AT1
1681			1H NMR (300 MHz, DMSO) δ 9.64 (s, 1H), 8.78 (d, J = 7.9 Hz, 1H), 8.72 – 8.49 (m, 3H), 8.22 – 8.01 (m, 2H), 7.85 (d, J = 8.6 Hz, 1H), 7.62 – 7.36 (m, 4H), 7.01 (s, 1H), 4.59 (s, 2H), 3.19 (d, J = 4.0 Hz, 3H), 2.68 (d, J = 4.5 Hz, 3H).	DMSO	400 (M+1)	1.31	Method D	100	Method AR/W with KI
1682		2HCl	1H NMR (300 MHz, DMSO) d 10.47 (s, 1H), 9.65 (d, J = 1.7 Hz, 1H), 9.05 (d, J = 7.9 Hz, 1H), 9.01 - 8.88 (m, 2H), 8.39 (m, 1H), 8.23 (d, J = 8.8 Hz, 1H), 7.87 (dd, J = 8.0, 5.3 Hz, 1H), 7.65 - 7.39 (m, 3H), 7.09 (m, 1H), 6.44 (m, 1H), 4.47 (td, J = 14.7, 3.4 Hz, 2H), 3.29 (d, J = 4.5 Hz, 3H).	DMSO	393.4 (M+1)		Method C (NH4HCO3)	100	Method AR/AS (K2CO3, DMF-THF (1 : 1), 60 °C) then Method AT
1683		HCl	^{1}H NMR (300 MHz, DMSO) δ 10.12 (s, 1H), 9.60 (s, 1H), 9.03 - 8.87 (m, 2H), 8.77 (s, 1H), 8.32 (d, J = 8.5 Hz, 1H), 8.21 - 8.02 (m, 1H), 7.92 - 7.69 (m, 3H), 7.20 - 7.02 (m, 2H), 4.93 (s, 2H), 3.70 - 3.40 (m, 8H), 3.29 (d, J = 3.5 Hz, 3H).	DMSO	456 (M+1)	1.73	Method B (Ammonium formate)	100	Method AR/W with KI

702

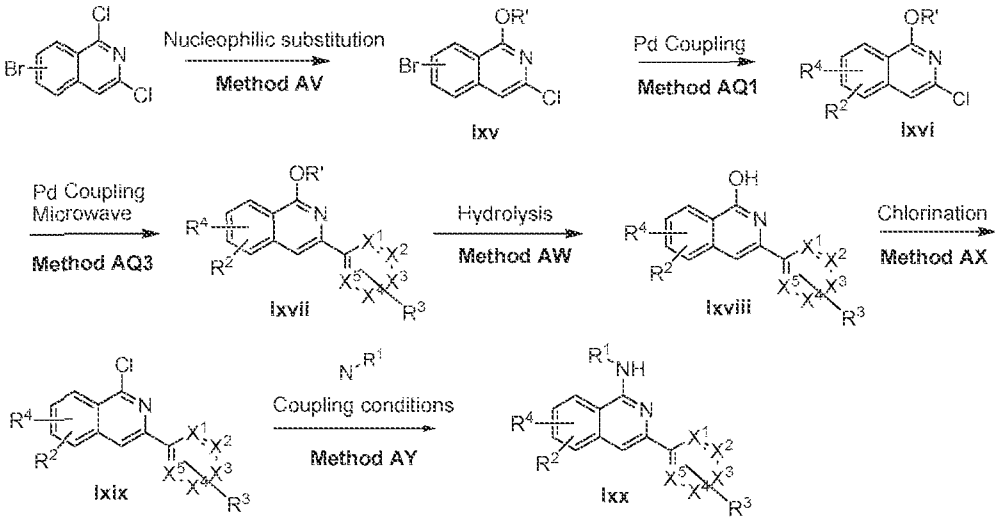
1684		HCl	^{1}H NMR (300 MHz, DMSO) δ 10.38 (s, 1H), 9.64 (s, 1H), 9.02 (d, J = 6.7 Hz, 1H), 8.93 (d, J = 4.9 Hz, 1H), 8.84 (s, 1H), 8.34 (d, J = 9.0 Hz, 1H), 8.22 (d, J = 8.7 Hz, 1H), 7.98 - 7.70 (m, 3H), 7.11 (d, J = 7.3 Hz, 2H), 4.26 - 4.05 (m, 2H), 3.78 - 3.57 (m, 2H), 3.45 - 3.19 (m, 6H).	DMSO	387 (M+1)	1.47	Method A (Formic acid)	100	Method AR/AS/AT1
1685		HCl	^{1}H NMR (300 MHz, DMSO) δ 11.31 (s, 1H), 10.41 (s, 1H), 9.63 (s, 1H), 9.10 - 8.79 (m, 3H), 8.34 (d, J = 8.2 Hz, 1H), 8.28 - 8.12 (m, 1H), 7.92 (d, J = 8.0 Hz, 2H), 7.87 - 7.74 (m, 1H), 7.18 (d, J = 8.0 Hz, 2H), 4.60 - 4.46 (m, 2H), 4.06 - 3.91 (m, 2H), 3.91 - 3.74 (m, 2H), 3.67 - 3.41 (m, 4H), 3.38 - 3.09 (m, J = 10.1 Hz, 5H).	DMSO	442 (M+1)	1.22	Method A (Formic acid)	100	Method AR/AS/AT2
1686		HCl	^{1}H NMR (300 MHz, DMSO) δ 10.32 - 9.70 (m, 1H), 9.61 (s, 1H), 9.13 - 8.70 (m, 5H), 8.29 (d, J = 8.5 Hz, 1H), 8.20 - 8.01 (m, 1H), 7.89 (d, J = 8.6 Hz, 2H), 7.83 - 7.67 (m, 1H), 7.16 (d, J = 8.8 Hz, 2H), 4.38 - 4.27 (m, 2H), 3.43 - 3.32 (m, 2H), 3.27 (d, J = 3.7 Hz, 3H), 2.63 (t, J = 4.8 Hz, 3H).	DMSO	386 (M+1)	1.46	Method B (Ammonium formate)	100	Method AR/AS/AT2
1687		HCl	^{1}H NMR (300 MHz, DMSO) δ 9.95 (s, 1H), 9.62 (s, 1H), 9.13 - 8.86 (m, J = 5.2 Hz, 3H), 8.39 (d, J = 8.7 Hz, 1H), 8.26 (s, 1H), 7.97 - 7.80 (m, 1H), 7.61 - 7.37 (m, 3H), 7.14 - 6.98 (m, 1H), 5.01 - 4.81 (m, 1H), 4.31 - 4.13 (m, 2H), 3.79 - 3.63 (m, 2H), 1.42 (d, J = 6.5 Hz, 6H).	DMSO	415 (M+1)	1.65	Method A (Formic acid)	100	Method AR/AS/AT1
1688		HCl	^{1}H NMR (300 MHz, DMSO) δ 10.12 (s, 1H), 9.63 (s, 1H), 9.10 - 8.88 (m, 2H), 8.72 (s, 1H), 8.44 (d, J = 8.3 Hz, 1H), 8.14 (d, J = 8.3 Hz, 1H), 7.85 (dd, J = 7.6, 4.8 Hz, 1H), 7.52 (d, J = 6.3 Hz, 1H), 7.39 (t, J = 7.9 Hz, 1H), 7.22 - 7.04 (m, 2H), 4.97 (s, 2H), 3.30 (d, J = 4.1 Hz, 3H), 2.97 (s, 3H), 2.85 (s, 3H).	DMSO	414 (M+1)	1.28	Method A (Formic acid)	100	Method AR/W with KI
1689		HCl	^{1}H NMR (300 MHz, DMSO) δ 10.22 (s, 1H), 9.63 (s, 1H), 9.10 - 8.87 (m, 2H), 8.75 (s, 1H), 8.35 (d, J = 8.8 Hz, 1H), 8.15 (d, J = 8.7 Hz, 1H), 8.01 (d, J = 4.2 Hz, 1H), 7.93 - 7.77 (m, 1H), 7.51 (d, J = 7.3 Hz, 1H), 7.43 (t, J = 7.8 Hz, 1H), 7.16 (t, J = 7.5 Hz, 1H), 7.07 (d, J = 8.5 Hz, 1H), 4.54 (s, 2H), 3.29 (d, J = 3.9 Hz, 3H), 2.64 (d, J = 4.4 Hz, 3H).	DMSO	400 (M+1)	1.33	Method A (Formic acid)	100	Method AR/W with KI

703

1690		HCl	^{1}H NMR (300 MHz, DMSO) δ 10.09 (s, 1H), 9.62 (s, 1H), 9.05 - 8.87 (m, 2H), 8.60 (s, 1H), 8.26 (d, J = 8.6 Hz, 1H), 8.13 (d, J = 8.8 Hz, 1H), 7.90 - 7.77 (m, 1H), 7.54 - 7.36 (m, 2H), 7.26 - 7.06 (m, 2H), 4.23 - 4.11 (m, 2H), 3.70 - 3.58 (m, 2H), 3.29 (d, J = 4.4 Hz, 3H), 3.24 (s, 3H).	DMSO	387 (M+1)	1.51	Method A (Formic acid)	100	Method AR/AS/AT1
1691		HCl	^{1}H NMR (300 MHz, DMSO) δ 9.65 (s, 1H), 9.04 (d, J = 7.8 Hz, 1H), 8.94 (d, J = 5.0 Hz, 1H), 8.50 (s,1H), 8.39 - 8.22 (m, 2H), 7.97 - 7.80 (m, 1H), 7.53 - 7.31 (m, 3H), 7.03 (d, J = 6.8 Hz, 1H), 4.26 - 4.13 (m, 2H), 3.82 - 3.59 (m, 8H), 3.32 (s, 3H).	DMSO	401 (M+1)	1.47	Method A (Formic acid)	100	Method AR/AS/AT1
1692		HCl	^{1}H NMR (300 MHz, DMSO) δ 9.83 - 9.26 (m, 3H), 9.00 - 8.76 (m, 3H), 8.40 (d, J = 8.8 Hz, 1H), 8.18 (d, J = 8.6 Hz, 1H), 7.89 - 7.72 (m, 1H), 7.58 - 7.36 (m, 3H), 7.04 (d, J = 3.4 Hz, 1H), 4.30 - 4.18 (m, 2H), 3.79 - 3.66 (m, 2H), 3.33 (s, 3H).	DMSO	373 (M+1)	1.42	Method A (Formic acid)	100	Method AR/AS/AT1
1693		HCl	^{1}H NMR (300 MHz, DMSO) δ 10.73 - 10.36 (m, 1H), 9.65 (s, 1H), 9.13 - 8.98 (m, 2H), 8.93 (d, J = 5.0 Hz, 1H), 8.38 (d, J = 8.4 Hz, 1H), 8.24 (d, J = 7.7 Hz, 1H), 7.94 - 7.75 (m, 1H), 7.69 - 7.41 (m, 3H), 7.09 (d, J = 8.1 Hz, 1H), 4.61 - 4.43 (m, 2H), 4.28 - 4.07 (m, 2H), 3.59 - 3.39 (m, 2H), 3.30 (d, J = 2.8 Hz, 3H).	DMSO	454 (M+1)	2.26	Method B (Ammonium formate)	100	Method AR/AS/AT3
1694		HCl	^{1}H NMR (300 MHz, DMSO) δ 10.35 (s, 1H), 9.67 (s, 1H), 9.04 (d, J = 7.3 Hz, 1H), 8.94 (d, J = 5.0 Hz, 1H), 8.78 (s, 1H), 8.24 (s, 2H), 7.96 - 7.77 (m, 1H), 7.60 - 7.40 (m, 2H), 7.33 - 7.10 (m, 2H), 4.50 - 4.36 (m, 2H), 4.05 - 3.85 (m, 2H), 3.53 - 3.37 (m, 2H), 3.28 (d, J = 3.6 Hz, 3H).	DMSO	454 (M+1)	2.11	Method B (Ammonium formate)	100	Method AR/AS/AT3
1695			^{1}H NMR (300 MHz, DMSO) δ 9.64 (s, 1H), 8.77 (d, J = 8.0 Hz, 1H), 8.73 - 8.50 (m, 3H), 8.14 (d, J = 8.7 Hz, 1H), 7.84 (d, J = 8.7 Hz, 1H), 7.54 (dd, J = 7.9, 4.8 Hz, 1H), 7.48 - 7.34 (m, 3H), 6.96 (d, J = 3.2 Hz, 1H), 4.91 (s, 2H), 3.18 (d, J = 4.3 Hz, 3H), 3.03 (s, 3H), 2.86 (s, 3H).	DMSO	414 (M+1)	1.30	Method A (Formic acid)	100	Method AR/W with KI

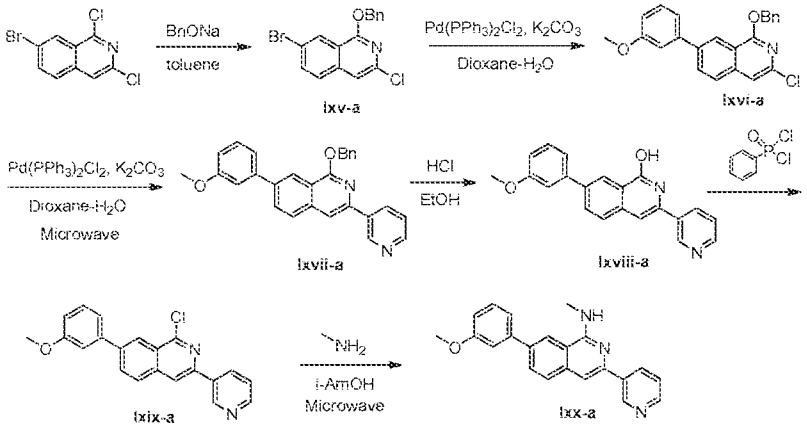
704

Scheme 81: General route for the synthesis of compounds with general formula lxx



X^1, X^2, X^3, X^4 or X^5 = CH or N, at least one X^1, X^2, X^3, X^4 or X^5 must be N

Scheme 82: Representative synthesis of compounds of formula lxx-a: (see Scheme 81)



Method AV: 1-(Benzyloxy)-7-bromo-3-chloroisoquinoline (lxv-a) To 20 mL of benzylalcohol was slowly added Na (2.00 g, 86.9 mmol) at 0°C, the mixture was then stirred at room temperature for 4h. 7-bromo-1,3-dichloroisoquinoline (2.00 g, 7.2 mmol) in toluene (50 mL) was added to the mixture with stirring. The reaction

mixture was heated at 80°C overnight. The solvent was removed under reduced pressure, the residue was purified with chromatography on silica gel (petroleum ether) to give 2.00 g **xiv-a** as a white solid (yield 80%). LCMS m/z = 257.9, 259.9 (M +1) (Method B) (retention time = 1.62 min).

Method AQ1: 1-(Benzyloxy)-3-chloro-7-(3-methoxyphenyl) isoquinoline (lxvi-a) To a mixture of 1-(benzyloxy)-7-bromo-3-chloroisoquinoline (1.00 g, 2.86 mmol, 1.0 eq), 3-methoxyphenylboronic acid (435 mg, 2.86 mmol, 1.0 eq), K_2CO_3 (2.13 g, 15.4 mmol, 5.4 eq) in dioxane (10 mL) and H_2O (5 mL) was added $Pd(PPh_3)_2Cl_2$ (100 mg, 0.15 mmol, 0.05 eq) under N_2 atmosphere. The resulting mixture was stirred at 110℃ under N_2 atmosphere overnight. The solvent was removed *in vacuo* and the residue was purified with chromatography on silica gel (hexane/ ethyl acetate 250:1) to give 550 mg of **lxvi-a** as white solid (yield 37%). LCMS m/z = 376.0 (M +1) (Method B) (retention time = 2.43 min).

Method AQ3: 1-(Benzyloxy)-7-(3-methoxyphenyl)-3-(pyridin-3-yl)isoquinoline (lxvii-a) To a mixture of 1-(benzyloxy)-3-chloro-7-(3-methoxyphenyl)isoquinoline (150 mg, 0.40 mmol, 1.0 eq), pyridin-3-ylboronic acid (74 mg, 0.60 mmol, 1.5 eq), K_2CO_3 (166 mg, 1.20 mmol, 3.0 eq) in dioxane (2 mL) and H_2O (1 mL) was added $Pd(PPh_3)_2Cl_2$ (14 mg, 0.02 mmol, 0.05 eq) under N_2 atmosphere. The sealed tube was irradiated in the CEM microwave at 130°C for 1h. After the reaction was completed, the volatiles were removed *in vacuo* and the residue was purified with chromatography on silica gel (hexane/ ethyl acetate 50:1) to give 200 mg of crude **lxvii-a** as a brown oil, which was used directly in the next step without purification. LCMS m/z = 419.0 (M +1) (Method B) (retention time = 2.25 min).

Method AW: 7-(3-Methoxyphenyl)-3-(pyridin-3-yl)isoquinolin-1-ol (lxviii-a) A mixture of 1-(benzyloxy)-7-(3-methoxyphenyl)-3-(pyridin-3-yl)isoquinoline (200 mg, 0.48 mmol), and concentrated HCl (10 mL) in ethanol (20 mL) was stirred at room temperature overnight. After the reaction was completed, the mixture was filtered and

concentrated to afford 130 mg of **lxviii-a** as a yellow solid (yield 90% for two steps). LCMS m/z = 329.0 (M +1) (Method B) (retention time = 1.66 min).

Method AX: 1-Chloro-7-(3-methoxyphenyl)-3-(pyridin-3-yl)isoquinoline (lxix-a) To a mixture of 7-(3-methoxyphenyl)-3-(pyridin-3-yl)isoquinolin-1-ol (130 mg, 0.395 mmol) in phenylphosphonic dichloride (5 mL) was stirred at 120°C overnight. After the reaction was completed, the mixture was added to ice-water slowly. The pH was adjusted to 7 by slow addition of $NH_3 \cdot H_2O$ at 0°C. Then the mixture was extracted with dichloromethane (100 mL x 3). The combined organic layer were dried over $MgSO_4$, filtered and concentrated *in vacuo* to give 130 mg of crude **lxix-a** as a white solid, which was used directly in the next step without purification. LCMS m/z = 346.9 (M +1) (Method B) (retention time = 1.80 min).

Method AY: 7-(3-Methoxyphenyl)-N-methyl-3-(pyridin-3-yl)isoquinolin-1-amine (lxx-a) A mixture of 1-chloro-7-(3-methoxyphenyl)-3-(pyridin-3-yl)isoquinoline (90 mg, 0.26 mmol), methylamine hydrochloride (200 mg, 2.96 mmol, 10.0 eq) and Et_3N (0.5 mL) was added to a sealed tube with i-AmOH (2 mL). The sealed tube was irradiated in the CEM microwave at 160 °C for 1 h. After the reaction was completed, the i-AmOH was removed *in vacuo* and the residue was dissolved in 10 mL of water and dichloromethane, the mixture was extracted with dichloromethane (3x 50 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo* and the residue was washed with MeOH to give 5 mg of **lxx-a** as a brown solid (yield 6%). LCMS m/z = 342.1 (M+1) (Method B) (retention time = 2.02 min). ^1H NMR (400 MHz, DMSO-d_6): δ 9.40 (d, J = 0.9 Hz, 1H), 8.67 – 8.47 (m, 3H), 8.08 – 7.95 (m, 1H), 7.89 – 7.84 (m, 2H), 7.66 (s, 1H), 7.57 – 7.49 (m, 1H), 7.46 – 7.42 (m, 3H), 7.08 – 6.95 (m, 1H), 3.88 (s, 3H), 3.14 (d, J = 4.3 Hz, 3H).

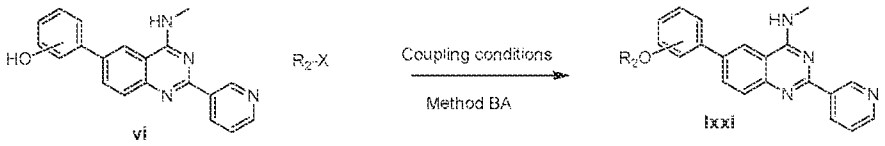
The compounds in the following table were prepared in a manner analogous to that described in **Scheme 81**, replacing with the appropriate isoquinoline and aniline.

Table 27:

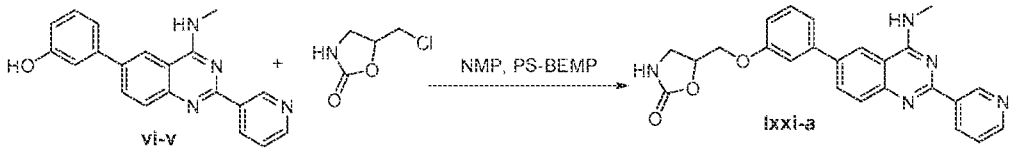
Number	PRODUCT	Salt type	Molecular Mass	^{1}H-NMR	^{1}H-NMR Solvent	LCMS	LCMS Protocol	Purity percent	Method for Coupling
1697			341.41	1H-NMR (400 MHz, DMSO-d6):δ 9.40 (d, J = 0.9 Hz, 1H), 8.67 - 8.47 (m, 3H), 8.08 - 7.95 (m, 1H), 7.89 - 7.84 (m, 2H), 7.66 (s, 1H), 7.57 - 7.49 (m, 1H), 7.46 - 7.42 (m, 3H), 7.08 - 6.95 (m, 1H), 3.88 (s, 3H), 3.14 (d, J = 4.3 Hz, 3H).	DMSO	342.1 (M+1)	Method B (NH4HCO3)	95	Method AX, H1
1698			312.37	1H-NMR (400 MHz, DMSO-d6): δ 9.40 (d, J = 1.8 Hz, 1H), 9.12 (d, J = 2.1 Hz, 1H), 8.66 (s, 1H), 8.60 (m, 2H), 8.54 (dt, J = 8.0, 1.9 Hz, 1H), 8.29 – 8.23 (m, 1H), 8.08 (dd, J = 8.5, 1.6 Hz, 1H), 7.92 (d, J = 8.5 Hz, 1H), 7.87 (d, J = 4.5 Hz, 1H), 7.68 (s, 1H), 7.56 (dd, J = 7.8, 4.8 Hz, 1H), 7.51 (dd, J = 7.8, 4.8 Hz, 1H), 3.14 (d, J = 4.4 Hz, 3H).	DMSO	312.9 (M+1)	Method B (NH4HCO3)	95	Method AX, H1

708

Scheme 83: General route for the synthesis of compounds with general formula lxxi



Scheme 84: Representative synthesis of compounds of formula lxxi-a (see Scheme 81)



Method BA: Synthesis of 5-[3-(4-Methylamino-2-pyridin-3-yl-quinazolin-6-yl)-phenoxymethyl]-oxazolidin-2-one (lxxi-a) To 5-(chloromethyl)oxazolidin-2-one (45 µmol) was added the solution of 3-(4-(methylamino)-2-(pyridin-3-yl)quinazolin-6-yl)phenol (30 µmol) in NMP (200 µL). PS-BEMP (90 µmol) was added to the vials by resin dispenser. After the reaction mixture was heated at 90^{0}C for 12 h, the residue was diluted with methanol and purified by **PREP-HPLC Condition D.** The target fraction was lyophilized to afford the titled compound whose structure was finally confirmed by LCMS using LCMS **Method E.**

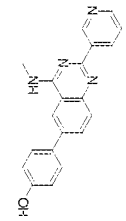
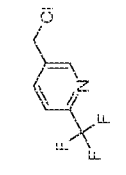
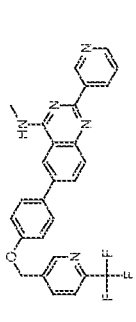
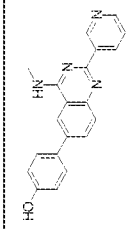
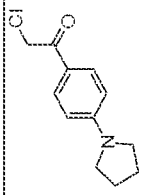
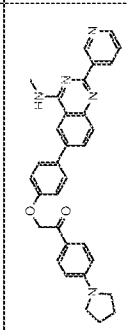
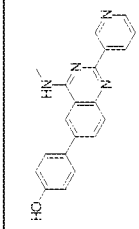
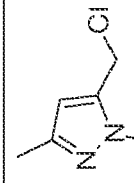
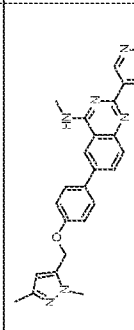
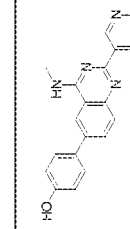
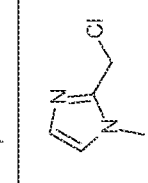
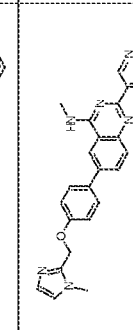
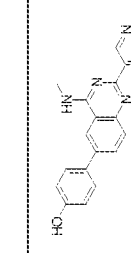
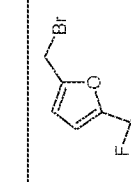
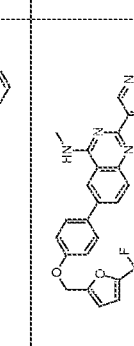
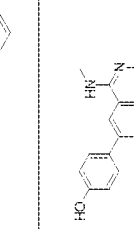
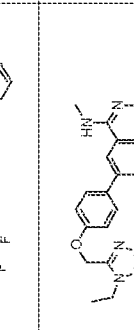
The compounds in the following table were prepared in a manner analogous to that described in **Scheme 80**, replacing 5-(chloromethyl)oxazolidin-2-one with the appropriate alkyl halide.

Table 28:

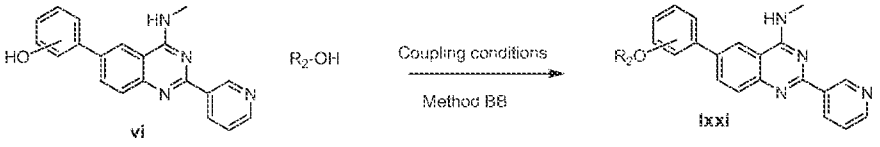
Number	Starting Material 1	Starting Material 2	Product	Salt Type	Exact Mass	Mass Found (M+1)	Purity (%)
1699					427	428	98
1700					421	422	98
1701				TFA	467	468	98
1702					515	516	98
1703				2TFA	468	469	98

710

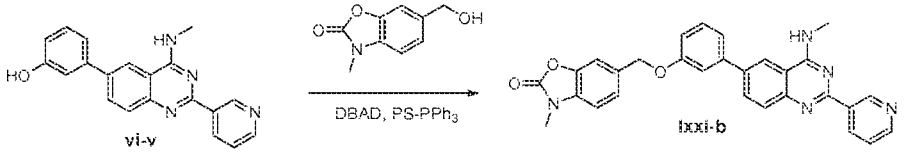
1704			TFA	436	437	98
1705				455	456	98
1706				438	439	98
1707				421	422	98
1708				453	454	98
1709			TFA	467	468	98

1710					487	488	98
1711				TFA	515	516	98
1712				TFA	436	437	98
1713				TFA	422	423	98
1714				TFA	476	477	98
1715				2TFA	438	439	98

Scheme 85: General route for the synthesis of compounds with general formula lxxi



Scheme 86: Representative synthesis of compounds of formula lxxi (see Scheme 85)



Method BB: Synthesis of 3-methyl-6-((3-(4-(methylamino)-2-(pyridin-3-yl)quinazolin-6-yl)phenoxy)methyl)benzo[d]oxazol-2(3H)-one (lxxi-b) To 6-(hydroxymethyl)-3-methylbenzo[d]oxazol-2(3H)-one (45 μmol) was added the solution of 3-(4-(methylamino)-2-(pyridin-3-yl)quinazolin-6-yl)phenol (30 μmol) in THF (400 μL). After PS-triphenylphosphine (60 μmol) was added, the solution of DBAD (di-*tert*-butyl azodicarboxylate, 66 μmol) in THF was dispensed to the vials. The mixture was heated at 50°C for 8 h. After the solvent was removed, the residue was diluted with methanol and purified by Mass triggered **PREP-HPLC Condition D.** The target fraction was lyophilized to afford the titled compound whose structure was finally confirmed by LCMS using LCMS **Method E.**

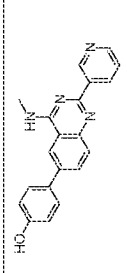
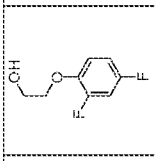
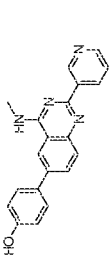
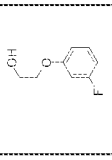
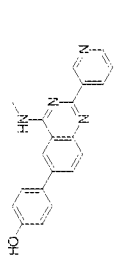
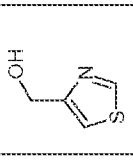
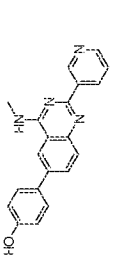
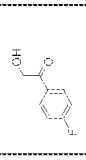
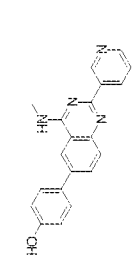
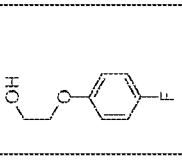
The compounds in the following table were prepared in a manner analogous to that described in **Scheme 85**, replacing 6-(hydroxymethyl)-3-methylbenzo[d]oxazol-2(3H)-one with the appropriate alkyl alcohol.

Table 29:

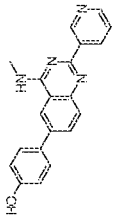
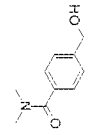
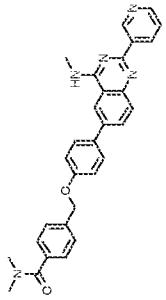
Number	Starting Material 1	Starting Material 2	Product	Salt Type	Exact Mass	Mass Found (M+1)	Purity (%)
1716				TFA	489	490	100
1717				TFA	448	449	100
1718				TFA	422	423	100
1719				TFA	422	423	100
1720				TFA	472	473	100

1721				TFA	489	490	100
1722				TFA	489	490	100
1723				TFA	466	467	100
1724				TFA	425	426	94
1725				TFA	453	454	100
1726				TFA	489	490	100

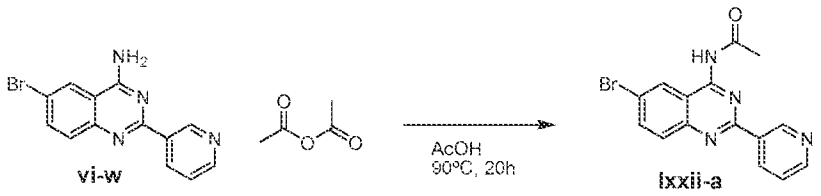
1727			TFA	489	490	100
1728			TFA	448	449	100
1729			TFA	422	423	100
1730			TFA	504	505	100
1731			TFA	424	425	100
1732			TFA	433	434	100

1733			TFA	484	485	100
1734			TFA	466	467	100
1735			TFA	425	426	100
1736			TFA	464	465	95
1737			TFA	466	467	100

718

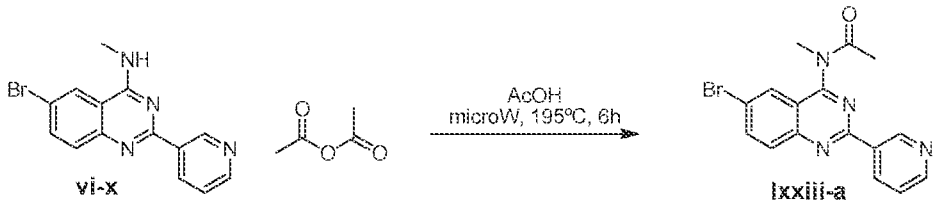
1738				TFA	489	490	100

Scheme 87: Synthesis of N-(6-bromo-2-(pyridin-3-yl)quinazolin-4-yl)acetamide with formula lxxii (Compound 1739)



Synthesis of N-(6-bromo-2-(pyridin-3-yl)quinazolin-4-yl)acetamide (lxxii-a) A 100 mL round bottom flask was fitted with a reflux condenser and charged with 6-bromo-2-(pyridin-3-yl)quinazolin-4-amine (2.45 g, 8.14 mmol), acetic anhydride (5.81 g, 57.0 mmol) and acetic acid (30 mL). The reaction mixture was stirred at 90 °C for 20 min and then cooled to room temperature. A precipitate formed during the reaction and was collected by filtration and washed with water (100 mL). The solid was dried at 60 °C to give N-(6-bromo-2-(pyridin-3-yl)quinazolin-4-yl)acetamide as a white powder (1.83 g, 66%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.72 (s, 1H), 8.84 – 8.69 (m, 3H), 8.22 (s, 1H), 8.02 – 7.90 (m, 2H), 7.53 – 7.41 (m, 1H), 2.83 (s, 3H).

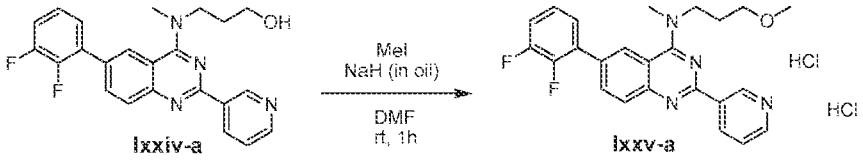
Scheme 88: Synthesis of N-(6-bromo-2-(pyridin-3-yl)quinazolin-4-yl)-N-methylacetamide with formula lxxiii (Compound 1740)



Synthesis of N-(6-bromo-2-(pyridin-3-yl)quinazolin-4-yl)-N-methylacetamide (lxxiii-a) To a solution of 6-bromo-N-methyl-2-(pyridin-3-yl)quinazolin-4-amine (1.20 g, 3.81 mmol) in acetic acid (10 mL) was added acetic anhydride (1.94 g, 19.0 mmol) and stirred at 195 °C using microwave for 6h. The reaction mixture was checked by LC-MS, no starting material was observed, ice was added into the reaction. The precipitate was collected by filtration and washed with water. The

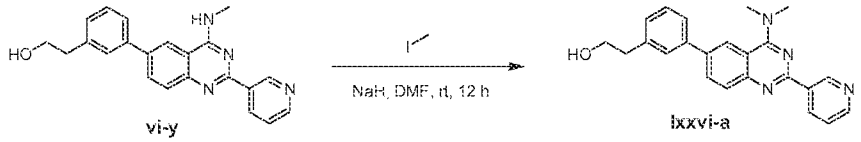
product was dried at 60 °C to give N-(6-bromo-2-(pyridin-3-yl)quinazolin-4-yl)-N-methylacetamide (711 mg, 52%) as a light brown powder. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.76 (dd, J = 2.2, 0.8 Hz, 1H), 8.85 – 8.79 (m, 1H), 8.76 (dd, J = 4.8, 1.7 Hz, 1H), 8.09 (dd, J = 1.8, 0.8 Hz, 1H), 8.05 – 8.01 (m, 2H), 7.46 (ddd, J = 8.0, 4.8, 0.8 Hz, 1H), 3.52 (s, 3H), 2.11 (s, 3H).

Scheme 89: Synthesis of compounds of formula lxxv



Method BC : Synthesis of 6-(2,3-difluorophenyl)-N-(3-methoxypropyl)-N-methyl-2-(pyridin-3-yl)quinazolin-4-amine dihydrochloride (lxxv-a) (Compound 1742) To a solution of the hydroxyl derivative (520 mg, 1.27 mmol) in DMF (20 mL) was added methyl iodide (262 mg, 1.84 mmol) and NaH (55% in oil; 69 mg, 1.9 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 1h and the ice water was added into the reaction mixture. The resulting solution was extracted with ethyl acetate (3 times), dried over Na_2SO_4, concentrated and purified by column chromatography (NH-silica gel, 50% hexane/50% ethyl acetate). The resulting product was dissolved in isopropyl alcohol and 1N-HCl (5 mL) was added and a precipitate formed which was collected by filtration and dried at 60 °C to give 6-(2,3-difluorophenyl)-N-(3-methoxypropyl)-N-methyl-2-(pyridin-3-yl)quinazolin-4-amine dihydrochloride as an orange powder (130 mg, 21%). ^{1}H NMR (300 MHz, DMSO) δ 9.66 (d, *J* = 1.6 Hz, 1H), 9.09 (d, *J* = 8.1 Hz, 1H), 8.96 (dd, *J* = 5.1, 1.5 Hz, 1H), 8.51 (s, 1H), 8.33 (d, *J* = 8.7 Hz, 1H), 8.20 (d, *J* = 8.8 Hz, 1H), 7.90 (dd, *J* = 8.1, 5.1 Hz, 1H), 7.66 – 7.47 (m, 2H), 7.47 – 7.32 (m, 1H), 4.22 – 4.07 (m, 2H), 3.70 (s, 3H), 3.48 (t, *J* = 5.8 Hz, 2H), 3.22 (s, 3H), 2.19 – 2.01 (m, 2H).

Scheme 90: Synthesis of 2-(3-(4-(dimethylamino)-2-(pyridin-3-yl)quinazolin-6-yl)phenyl)ethanol of formula lxxvi (Compound 1743)

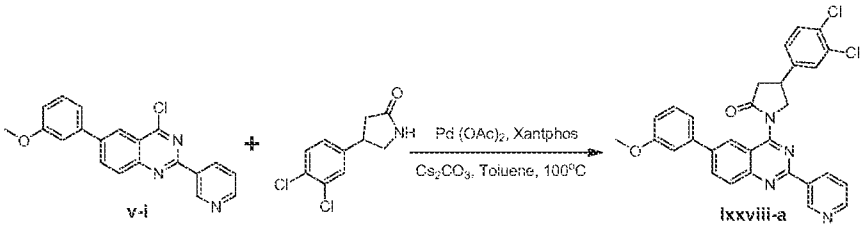


Method BD: 2-(3-(4-(dimethylamino)-2-(pyridin-3-yl)quinazolin-6-yl)phenyl)ethanol, 2HCl (lxxvi-a) To a reaction vial containing 2-(3-(4-(methylamino)-2-(pyridin-3-yl)quinazolin-6-yl)phenyl)ethanol (89.0 mg, 0.25 mmol) in DMF (1 mL) was added 60% sodium hydride (13 mg, 0.325 mmol) and iodomethane (0.02 mL, 0.325 mmol). The reaction mixture was allowed to stir at ambient temperature for 12 h. Water (20 mL) was added to the reaction mixture, and the crude product was extracted with ethyl acetate (4 x 15 mL). The crude material was purified via ISCO (silica, 4 g column, 95% CH_2Cl_2 – 5% MeOH – 0.1% NH_4OH) to give the product as an off-white solid. The free base was then converted to the HCl salt to yield the final product as a yellow solid (24.6 mg, 0.055 mmol, 22%). LC-MS m/z = 371.5 (M+1) (retention time = 1.86) ^{1}H NMR (300 MHz, DMSO) δ 9.61 (d, J = 2.1 Hz, 1H), 8.99 (d, J = 7.5 Hz, 1H), 8.93 (dd, J = 5.0, 1.5 Hz, 1H), 8.48 (d, J = 1.0 Hz, 1H), 8.28 (dd, J = 17.4, 9.4 Hz, 2H), 7.84 (dd, J = 7.7, 5.1 Hz, 1H), 7.69 - 7.60 (m, 2H), 7.44 (t, J = 7.5 Hz, 1H), 7.30 (d, J = 7.3 Hz, 1H), 3.78 - 3.61 (m, 9H), 2.82 (t, J = 7.0 Hz, 2H).

Synthesis of 6-(2,4-difluorophenyl)-N-(3-methoxypropyl)-N-methyl-2-(pyridin-3-yl)quinazolin-4-amine dihydrochloride (lxxvii-a) (Compound 1744) 6-(2,4-difluorophenyl)-N-(3-methoxypropyl)-N-methyl-2-(pyridin-3-yl)quinazolin-4-amine dihydrochloride was synthesized in a similar manner to that described for 6-(2,3-difluorophenyl)-N-(3-methoxypropyl)-N-methyl-2-(pyridin-3-yl)quinazolin-4-amine dihydrochloride substituting the appropriate hydroxyl derivative. 6-(2,4-difluorophenyl)-N-(3-methoxypropyl)-N-methyl-2-(pyridin-3-yl)quinazolin-4-amine was obtained as the dihydrochloride salt ^{1}H NMR (300 MHz, DMSO) δ 9.69 (d, *J* = 2.0 Hz, 1H), 9.14 (d, *J* = 8.3 Hz, 1H), 8.97 (dd, *J* = 5.1, 1.2 Hz, 1H), 8.45 (s, 1H), 8.39 (d, *J* = 8.6 Hz, 1H), 8.17 (d, *J* = 8.8 Hz, 1H), 7.92 (dd, *J* = 8.0, 5.2 Hz, 1H), 7.86 –

7.73 (m, 1H), 7.57 – 7.38 (m, 1H), 7.36 – 7.23 (m, 1H), 4.19 – 4.04 (m, 2H), 3.71 (s, 3H), 3.48 (t, *J* = 5.7 Hz, 2H), 3.23 (s, 3H), 2.21 – 1.96 (m, 2H).

Scheme 91: Synthesis of compounds of formula lxxviii



Method BE: 4-(3,4-dichlorophenyl)-1-(6-(3-methoxyphenyl)-2-(pyridin-3-yl)quinazolin-4-yl)pyrrolidin-2-one (lxxviii-a) To a mixture of 4-chloro-6-(3-methoxyphenyl)-2-(pyridin-3-yl)quinazoline (40 mg, 0.12 mmol), 4-(3,4-dichlorophenyl)pyrrolidin-2-one (100 mg, 0.437 mmol) and Cs_2CO_3 (42 mg, 0.127 mmol) in dry toluene (6 mL) was added $Pd(OAc)_2$ (3 mg, 0.01 mmol) and Xantphos (10 mg, 0.02 mmol) under a nitrogen atmosphere. The resulting mixture was stirred at 100 °C for 12h. After cooling, the mixture was filtered through a pad of celite. The residue was purified by silica gel chromatography, eluted with petroleum ether/ethyl acetate (5:4) to give the desired product as a yellow solid. 14 mg of the desired product was obtained in a 22.5%. yield, LCMS: retention time = 1.802 min, $[MH]^+$ = 541.0, 543.0. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.73 (s, 1H), 9.05 – 9.04 (m, 1H), 8.86 – 8.85 (m, 1H), 8.42 – 8.38 (m, 2H), 8.19 (d, *J* = 8.8 Hz, 1H), 7.89 (d, *J* = 1.6 Hz, 1H), 7.82 – 7.81 (m, 1H), 7.69 (d, *J* = 8.0 Hz, 1H), 7.58 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.50 (t, *J* = 8.0 Hz, 1H), 7.41 – 7.36 (m, 2H), 7.07 (dd, *J* = 8.0, 2.0 Hz, 1H), 4.57 – 4.46 (m, 2H), 4.06 – 4.03 (m, 1H), 3.20 – 3.01 (m, 2H), 3.88 (s, 3H).

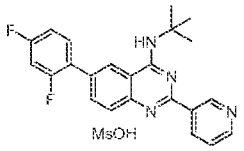
The compounds in the following table were prepared in a manner analogous to that described in **Scheme 91**, replacing 4-(3,4-dichlorophenyl)pyrrolidin-2-one with the appropriate amide

Table 30:

Number	Product	Salt type	^{1}H NMR	^{1}H NMR Solvent	Purity percent	Method of Coupling	LCMS	LCMS Method
1745			^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.75 (s, 1H), 8.90 (d, J = 8.0 Hz, 1H), 8.78 (d, J = 4.0 Hz, 1H), 8.35 (s, 1H), 8.28 – 8.19 (m, 2H), 7.92 (d, J = 7.6 Hz, 1H), 7.82 (d, J = 5.0 Hz, 2H), 7.73 – 7.70 (m, 1H), 7.68 – 7.61 (m, 2H), 7.52 – 7.42 (m, 1H), 7.29 (t, J = 8.4 Hz, 1H), 5.61 (s, 2H).	DMSO	95	Method BE	451.0 (M+1)	Method B (NH_4HCO_3)
1746			^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.74 (s, 1H), 8.89 (d, J = 8.0 Hz, 1H), 8.77 (d, J = 3.8 Hz, 1H), 8.45 (s, 1H), 8.39 (d, J = 8.7 Hz, 1H), 8.18 (d, J = 8.7 Hz, 1H), 7.94 (d, J = 7.6 Hz, 1H), 7.83 (s, 2H), 7.72 – 7.56 (m, 2H), 7.52 – 7.27 (m, 3H), 7.03 (d, J = 7.9 Hz, 1H), 5.60 (s, 2H), 3.85 (s, 3H).	DMSO	95	Method BE	445.1 (M+1)	Method B (NH_4HCO_3)
1747			^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.76 (s, 1H), 8.91 (d, J = 6.4 Hz, 1H), 8.79 (s, 1H), 8.41 (s, 1H), 8.30 – 8.23 (m, 2H), 7.92 (d, J = 8.0 Hz, 1H), 7.83 (s, 2H), 7.65 (d, J = 3.6 Hz, 2H), 7.55 – 7.49 (m, 2H), 7.40 (s, 1H), 5.61 (s, 2H).	DMSO	95	Method BE	451.0, 452.0, (M+1)	Method B (NH_4HCO_3)
1748		2HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.73 (s, 1H), 9.05 – 9.04 (m, 1H), 8.86 – 8.85 (m, 1H), 8.42 – 8.38 (m, 2H), 8.19 (d, J = 8.8 Hz, 1H), 7.89 (d, J = 1.6 Hz, 1H), 7.82 – 7.81 (m, 1H), 7.69 (d, J = 8.0 Hz, 1H), 7.58 (dd, J = 8.0, 1.6 Hz, 1H), 7.50 (t, J = 8.0 Hz, 1H), 7.41 – 7.36 (m, 2H), 7.07 (dd, J = 8.0, 2.0 Hz, 1H), 4.57 – 4.46 (m, 2H), 4.06 – 4.03 (m, 1H), 3.20 – 3.01 (m, 2H), 3.88 (s, 3H).	DMSO	95	Method BE	541.0, 543.0 (M+1)	Method B (NH_4HCO_3)

1749		2HCl	^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.68 (s, 1H), 8.83 (d, *J* = 8.0 Hz, 1H), 8.76 (s, 1H), 8.39 – 8.37 (m, 2H), 8.17 (d, *J* = 10.0 Hz, 1H), 7.63 – 7.31 (m, 9H), 7.06 (dd, *J* = 8.4, 2.0 Hz, 1H), 4.56 – 4.45 (m, 2H), 4.03 – 3.99 (m, 1H), 3.88 (s, 3H), 3.19 – 2.97 (m, 2H).	DMSO	95	Method BE	472.9 (M+1)	Method B (NH_4HCO_3)
1750			^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.74 (d, *J* = 8.4 Hz, 1H), 8.89 (dt, *J* = 8.4, 1.6 Hz, 1H), 8.78 (dd, *J* = 4.4,1.2 Hz, 1H), 8.46 (d, *J* = 1.6 Hz, 1H), 8.41 (dd, *J* = 8.8, 1.6 Hz, 1H), 8.20 (d, *J* = 8.4 Hz, 1H), 7.97 (s, 1H), 7.88 (s, 2H), 7.65 – 7.62 (m, 1H), 7.48 – 7.44 (m, 1H),7.41 – 7.37 (m, 2H), 7.04 (dd, *J* = 8.0, 1.6 Hz, 1H), 5.59 (s, 2H), 3.86 (s, 3H).	DMSO	95	Method BE	479.0 (M+1)	Method B (NH_4HCO_3)
1751			^{1}H-NMR (400 MHz, DMSO-d_6): δ 9.74 (s, 1H), 8.89 (d, *J* = 8.4 Hz, 1H), 8.78 (d, *J* = 4.4 Hz, 1H), 8.46 (s, 1H), 8.41 (d, *J* = 9.2 Hz, 1H), 8.20 (d, *J* = 8.8 Hz, 1H), 7.91 – 7.87 (m, 1H), 7.77 – 7.62 (m, 3H), 7.48 – 7.37 (m, 3H), 7.03 (d, *J* = 6.4 Hz, 1H), 5.58 (s, 2H), 3.86 (s, 3H).	DMSO	95	Method BE	463.1 (M+1)	Method B (NH_4HCO_3)

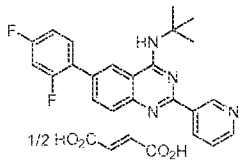
Scheme 91: Synthesis of N-tert-butyl-6-(2,4-difluorophenyl)-2-(pyridin-3-yl)quinazolin-4-amine methanesulfonate (lxxix-a) (Compound 1752)



lxxix-a
(Compound 1752)

N-tert-butyl-6-(2,4-difluorophenyl)-2-(pyridin-3-yl)quinazolin-4-amine (1.51 g, 3.87 mmol) was dissolved in CH_2Cl_2/MeOH (20 mL/20 mL). Methanesulfonic acid (0.251 mL, 3.87 mmol) was added to the solution. The volatiles were evaporated *in vacuo*. The resultant residue was crystallized from EtOH (30 mL) to give 1.35 g of N-tert-butyl-6-(2,4-difluorophenyl)-2-(pyridin-3-yl)quinazolin-4-amine methanesulfonate as a light yellow powder (72 %). LCMS m/z = 391 (M +1) (Method D) (Retention time = 1.91 min). ^{1}H NMR (300 MHz, DMSO) δ 9.52 (s, 1H), 9.01 - 8.83 (m, 2H), 8.75 (s, 1H), 8.58 (s, 1H), 8.09 (d, *J* = 7.2 Hz, 1H), 8.03 - 7.85 (m, 2H), 7.83 - 7.68 (m, 1H), 7.59 - 7.43 (m, 1H), 7.33 (t, *J* = 7.9 Hz, 1H), 2.31 (s, 3H), 1.66 (s, 9H).

Scheme 92: Synthesis of N-tert-butyl-6-(2,4-difluorophenyl)-2-(pyridin-3-yl)quinazolin-4-amine fumarate (lxxx) (Compound 1753)

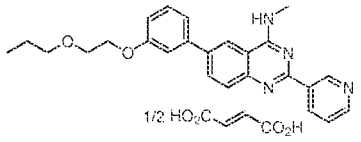


lxxx-a
(Compound 1753)

N-tert-butyl-6-(2,4-difluorophenyl)-2-(pyridin-3-yl)quinazolin-4-amine (1.22 g, 3.12 mmol) was dissolved in CH_2Cl_2/MeOH (20 mL/20 mL). Fumaric acid (0.363 g, 3.12 mmol) was added to the solution. The mixture was sonicated until fumaric acid was dissolved. Then, the volatiles were evaporated *in vacuo*. The resultant solid was

washed with MeOH and dried to give 1.28 g of N-tert-butyl-6-(2,4-difluorophenyl)-2-(pyridin-3-yl)quinazolin-4-amine ½ fumarate as a light yellow powder (91 %). LCMS m/z = 391 (M +1) (Method D) (Retention time = 1.95 min). ^{1}H NMR (300 MHz, DMSO) δ 13.14 (s, 1H), 9.59 (s, 1H), 8.82 - 8.65 (m, 2H), 8.57 (s, 1H), 7.89 (d, *J* = 8.7 Hz, 1H), 7.82 (d, *J* = 8.7 Hz, 1H), 7.79 - 7.62 (m, 2H), 7.61 - 7.52 (m, 1H), 7.51 - 7.38 (m, 1H), 7.28 (t, *J* = 8.6 Hz, 1H), 6.61 (s, 1H), 1.64 (s, 9H).

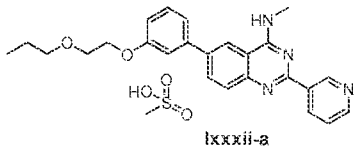
Scheme 93: Synthesis of N-methyl-6-(3-(2-propoxyethoxy)phenyl)-2-(pyridin-3-yl)quinazolin-4-amine fumarate (lxxxi) (Compound 1754)



lxxxi-a
(Compound 1754)

N-methyl-6-(3-(2-propoxyethoxy)phenyl)-2-(pyridin-3-yl)quinazolin-4-amine fumarate was synthesized in a similar manner to that described N-tert-butyl-6-(2,4-difluorophenyl)-2-(pyridin-3-yl)quinazolin-4-amine fumarate. LCMS m/z = 415.5 (M +1) (Method C (NH_4HCO_3) (Retention time = 2.43 min). ^{1}H NMR (300 MHz, CD_3OD) δ 9.57 (s, 1H), 8.84 (m, 1H), 8.63 (s, 1H), 8.35 (m, 1H), 8.07 (m, 1H), 7.88 (d, *J* = 8.7 Hz, 1H), 7.58 (m, 1H), 7.48 – 7.24 (m, 4H), 7.00 (m, 1H), 6.74 (s, 1H), 4.36 – 4.05 (m, 2H), 4.00 – 3.70 (m, 2H), 3.53 (t, *J* = 6.6 Hz, 2H), 3.29 – 3.13 (m, 3H), 1.75 – 1.51 (m, 2H), 0.95 (t, *J* = 7.4 Hz, 3H).

Scheme 94: Synthesis of N-methyl-6-(3-(2-propoxyethoxy)phenyl)-2-(pyridin-3-yl)quinazolin-4-amine methanesulfonate (lxxxii-a) (Compound 1755)



lxxxii-a
(Compound 1755)

N-methyl-6-(3-(2-propoxyethoxy)phenyl)-2-(pyridin-3-yl)quinazolin-4-amine methanesulfonate was synthesized in a similar manner to that described N-tert-butyl-6-(2,4-difluorophenyl)-2-(pyridin-3-yl)quinazolin-4-amine methanesulfonate. LCMS m/z = 415.5 (M +1) (Method C (NH_4HCO_3) (Retention time = 2.43 min). ^{1}H NMR (300 MHz, CD_3OD) δ 9.49 (s, 1H), 9.00 – 8.72 (m, 1H), 8.53 (s, 1H), 8.29 (m, 1H), 7.99 (d, *J* = 8.7 Hz, 1H), 7.80 (dd, *J* = 8.0, 5.1 Hz, 1H), 7.52 – 7.25 (m, 3H), 7.02 (m, 1H), 4.38-4.06 (m, 2H), 3.98-3.72 (m, 2H), 3.61 – 3.48 (m, 2H), 3.42 (d, *J* = 0.6 Hz, 3H), 3.34 – 3.26 (m, 2H), 2.71 (s, 3H), 1.80-1.47 (m, 2H), 0.96 (t, *J* = 7.4 Hz, 3H).

Biological Testing:

STEP46 biochemical assays

Serial dilutions of compounds were performed in 100% DMSO and 1 uL of compounds were dispensed into 384-well black polystyrene plates (Corning, NY). Compounds were incubated with 24 uL of buffer containing 50 mM Hepes, 1 mM DTT, 0.02% Brij35, 1 ng/well purified STEP46 enzyme for 30 min at room temperature. The reaction was initiated by addition of 25 uL of DiFMUP (6, 8-difluoro-4-methylumbelliferyl phosphate) (InVitrogen, CA) with a final concentration of 10 μM and incubated at 27 °C for 90 min. Final DMSO concentration is 2%. Plates were read with florescence intensity at excitation/emission of 360/460nm using a PheraStar plate reader (BMG Labtech, NC).

Data analysis

Data were expressed as percentage (%) inhibition of enzyme activity. 0% inhibition is defined as the RFUs (relative fluorescence units) in the absence of compounds and 100% inhibition is defined as RFUs in the absence of STEP46 enzyme. IC_{50} values of compounds with inhibitory activity against STEP46 were determined by GraphPad Prism (version 4.03) using four parameter logistic equation. Some compounds act as

activators. For compounds showing STEP46 enzymatic activation, data are represented as percentage of inhibition but with negative values at three representative concentrations (25, 50 and 100 uM).

Compounds **1 – 1760** show either inhibition or activation > 50% at 100 uM, 50 or 25 uM.

Number	STEP IC50 (μM)		Number	STEP IC50 (μM)		Number	STEP IC50 (μM)		Number	STEP IC50 (μM)	
73	++		327	++		391	++		427	++	
296	++		329	+++		392	++		428	++	
297	+		330	++		393	++		429	+++	
300	+		332	+++		396	++		430	+++	
303	++		333	+++		399	+++		431	+++	
306	+		334	++		400	++		433	++	
309	++		335	+++		403	++		434	++	
312	+++		336	+++		407	++		435	+++	
313	+++		337	+++		412	+++		436	++	
314	++		339	++		415	++		437	++	
315	++		341	++		416	+++		439	+++	
316	+++		342	++		418	++		440	++	
317	++		343	+		419	+++		441	++	
318	++		344	++		421	+		442	+++	
320	++		346	++		423	++		443	+++	
322	+		348	++		424	++		444	+++	
325	+++		352	++		425	++		445	+++	
326	++		390	++		426	+		446	++	

Number	STEP IC50 (μM)	Number	STEP IC50 (μM)	Number	STEP IC50 (μM)	Number	STEP IC50 (μM)
447	++	470	++	642	+++	663	+++
448	+++	471	++	643	+++	664	++
449	++	472	++	644	++	665	++
451	+++	473	++	645	++	666	+++
452	+++	474	++	647	++	667	+++
453	+++	629	++	648	++	668	+++
454	++	630	++	649	++	669	+++
455	++	631	++	650	+++	670	+++
456	+++	632	+++	651	+++	671	++
457	++	633	++	652	+++	672	++
458	+++	634	++	653	+++	673	++
459	+++	635	+++	655	+++	674	++
460	++	636	+	656	+++	675	+++
461	++	637	++	657	+++	676	+++
463	++	638	++	658	++	677	+
466	++	639	+++	660	+++	678	++
467	++	640	++	661	+++	679	+++
468	+++	641	+++	662	+++	680	++

Number	STEP IC50 (μM)	Number	STEP IC50 (μM)	Number	STEP IC50 (μM)	Number	STEP IC50 (μM)
681	++	699	+++	900	++	1150	+
682	++	700	+++	901	++	1151	++
683	++	701	++	923	++	1152	++
684	++	702	+++	932	++	1153	++
685	+++	703	+++	933	++	1155	++
686	+++	704	+++	934	+++	1157	++
687	+++	705	+++	962	+++	1158	++
688	+++	706	+++	1124	+++	1159	++
689	+++	707	+++	1125	++	1160	++
690	++	708	++	1126	++	1161	++
691	+++	709	+++	1140	+++	1165	+++
692	+++	846	++	1141	+++	1167	++
693	+++	847	+++	1142	++	1168	++
694	+++	884	+	1143	++	1171	++
695	+++	888	+	1144	++	1172	++
696	+++	889	++	1145	++	1173	+
697	++	898	+	1146	++	1176	++
698	+++	899	++	1148	++	1178	++

Number	STEP IC50 (μM)	Number	STEP IC50 (μM)	Number	STEP IC50 (μM)	Number	STEP IC50 (μM)
1180	++	1204	+	1226	++	1324	++
1181	++	1205	++	1227	++	1327	+
1182	++	1206	++	1228	++	1328	+
1183	++	1208	+	1229	++	1330	+
1184	++	1211	+	1230	++	1332	++
1185	++	1212	++	1234	++	1333	+
1186	++	1213	++	1237	++	1334	+
1187	+++	1214	++	1238	++	1335	++
1188	++	1215	+++	1239	++	1336	++
1191	++	1216	+++	1248	++	1337	++
1192	++	1217	++	1279	++	1339	++
1193	++	1218	++	1280	++	1340	++
1194	+++	1219	++	1281	+++	1341	++
1198	++	1220	+	1282	++	1346	++
1200	++	1221	+	1283	+	1348	+
1201	++	1222	++	1284	++	1350	++
1202	++	1223	+++	1285	+	1351	++
1203	++	1225	++	1286	++	1352	+

Number	STEP IC50 (μM)	Number	STEP IC50 (μM)	Number	STEP IC50 (μM)	Number	STEP IC50 (μM)
1353	++	1374	++	1410	++	1448	++
1354	++	1375	++	1411	+	1449	+
1356	++	1376	++	1412	++	1450	++
1357	++	1380	++	1413	++	1451	++
1358	++	1381	++	1414	++	1452	+++
1359	++	1382	+++	1415	+	1453	++
1360	++	1391	+	1416	++	1454	+
1361	+	1395	++	1419	++	1455	++
1362	++	1396	++	1420	++	1456	++
1363	++	1400	++	1422	++	1458	+
1364	++	1401	++	1423	+	1467	++
1365	++	1402	++	1424	+	1497	++
1366	++	1403	+	1425	++	1516	+
1369	++	1404	+	1430	++	1601	++
1370	++	1406	++	1437	++	1611	++
1371	++	1407	++	1445	++	1680	++
1372	++	1408	++	1446	++		
1373	++	1409	++	1447	+		

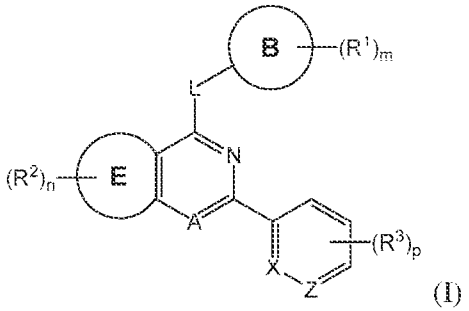
Key	
+	IC_{50} > 10 uM
++	IC_{50} 1-10 uM
+++	IC_{50} < 1 uM

Having thus described several aspects of at least one embodiment of this invention, it is to be appreciated various alterations, modifications, and improvements will readily occur to those skilled in the art. Such alterations, modifications, and improvements are intended to be part of this disclosure, and are intended to be within

the spirit and scope of the invention. Accordingly, the foregoing description and drawings are by way of example only.

CLAIMS

1. A compound of formula (I):



(I)

or a salt thereof,

wherein:

A is CR^4 or N;

B is aryl, cyclyl or a 5- or 6-membered heteroaryl;

m is 0, 1, 2, 3, 4 or 5;

E is aryl or a 5-membered heteroaryl;

n is 0, 1, 2, 3 or 4;

when E is aryl, n is 0, 1, 2, 3 or 4; and when E is a 5-membered heteroaryl, n is 0, 1, 2 or 3;

L is NR^5, S, O or a direct bond;

one of X and Z is N and the other is CH;

p is 0, 1, 2, 3 or 4;

each R^1, R^2 and R^3 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silyloxyalkynyl, silylalkoxy, silylalkoxyalkyl, –CN, oxo, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^6; wherein two R^1, together with the atoms to which they are attached, may form an optionally substituted cyclyl, heterocyclyl, aryl or heteroaryl ring;

R^4 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^6;

R^5 is hydrogen; or when m is not 0, R^5 and one R^1 may be taken together with the atoms to which they are attached to form an optionally substituted heteroaryl or heterocyclyl ring;

each R^6 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thioxo, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$,$–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^7;

each R^7 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thioxo, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^9;

each R^9 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy,

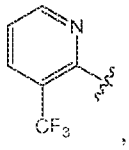
silylalkoxyalkyl, oxo, thioxo, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$;

Y is O or S;

q is 1 or 2 and

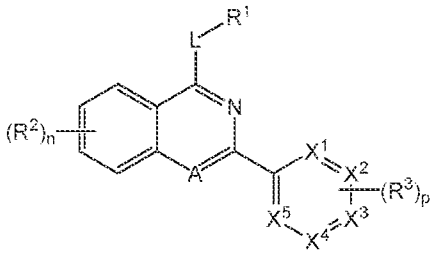
each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, acyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy or silylalkoxyalkyl;

wherein when B is phenyl, two R^1 are not taken together to form a pyrazole ring; and

when B is phenyl, R^2 is not 

,

a compound of formula (II):



(II)

or a salt thereof,

wherein:

L is CR^4R^5, O, C(O), $NR^6C(O)$ or NR^7;

A is N;

each X^1, X^2, X^3, X^4 and X^5 is independently CH or N, provided that at least two of X^1, X^2, X^3, X^4 and X^5 are N;

n is 0, 1, 2, 3 or 4;

p is 0, 1, 2 or 3;

R^1 is C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl or heterocyclylalkyl, each of which is optionally substituted with 1-5 R^9; wherein R^1 or R^9 is optionally taken together with one of R^4, R^5, R^6 or R^7, and the atoms to which they are attached, to form a cyclyl, heterocyclyl, aryl or heteroaryl ring that is optionally substituted with 1-3 R^{10};

each R^2 and R^3 is independently hydrogen,C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$; each of which is optionally substituted with 1-3 R^{11};

each R^4, R^5, R^6 and R^7 is independently hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$;

each R^9, R^{10} and R^{11} is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thioxo, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$,$–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{12};

wherein, two R^9, two R^{10} or two R^{11} is optionally taken together with the atoms to which they are attached to form an optionally substituted cyclyl, heterocyclyl, aryl or heteroaryl ring;

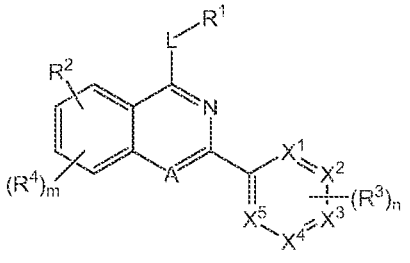
R^{12} is $-OR^d$;

Y is O or S;

q is 1 or 2 and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e, $R^{e'}$ and R^f is independently hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, acyl, cyclyl, heterocyclyl, aryl, heteroaryl, cyclylalkyl, heterocyclylalkyl, arylalkyl or heteroarylalkyl and

a compound of formula (III):



(III)

or a salt thereof,

wherein:

A is CH or N;

L is O, a direct bond or NR^6;

one of X^1, X^2, X^3, X^4 and X^5 is N and the others are CH;

m is 1, 2 or 3;

n is 1, 2, 3 or 4;

R^1 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, alkoxyalkyl, hydroxyalkyl, heteroaryl , heteroarylalkyl,arylalkyl, $-C(Y)R^e$, cyclyl ,cyclylalkyl or heterocyclyl, each of which is optionally substituted with 1-3 R^7;

R^2 is aryl or heteroaryl, each of which is optionally substituted with 1-5 R^9;

each R^3 or R^4 is independently hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy,

silylalkoxyalkyl, –CN, –NO_2, –C(O)OR^a, –C(Y)$NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^cSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$, –OR^d, –$SR^{d'}$, –C(Y)R^e or -$S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{10};

R^6 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, cyclyl or heterocyclyl, each of which is optionally substituted with 1-3 R^{11};

each R^7, R^9 and R^{10} is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thioxo, –CN, –NO_2, –C(O)OR^a, –C(Y)$NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^cSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$,–OR^d, –$SR^{d'}$, –C(Y)R^e or -$S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{12}; wherein two R^7, two R^9 or two R^{10} are optionally be taken together with the atoms to which they are attached to form an optionally substituted cyclyl, heterocyclyl, aryl or heteroaryl ring;

each R^{11} and R^{12} is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thioxo, –CN, –NO_2, –C(O)OR^a, –C(Y)$NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^cSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$,–OR^d, –$SR^{d'}$, –C(Y)R^e or -$S(O)_qR^f$,each of which is optionally substituted with 1-3 R^{13};

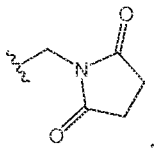
R^{13} is independently C_1-C_8 alkyl, haloalkyl ,halo, heterocyclyl, cyclyl,oxo or –C(Y)$NR^bR^{b'}$;

Y is independently O or S;

q is 1 or 2 ;and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, acyl, haloalkyl alkoxyalkyl, alkylaminoalkyl,

dialkylaminoalkyl, cyclyl, heterocyclyl, aryl, heteroaryl, cyclylalkyl, heterocyclylalkyl, arylalkyl or heteroarylalkyl;

with proviso R^9 is not .

2. The compound according to claim 1 represented by general formula (I) or a salt thereof,

wherein:

A is CR^4 or N;

B is aryl ,cyclyl or a 5- or 6-membered heteroaryl;

m is 0, 1, 2, 3, 4 or 5;

n is 0, 1, 2, 3 or 4;

E is aryl or a 5-membered heteroaryl;

when E is aryl, n is 0,1, 2, 3 or 4; and when E is a 5-membered heteroaryl, n is 0, 1, 2 or 3;

L is NR^5 ,S,O or a direct bond;

one of X and Z is N and the other is CH;

p is 0, 1, 2, 3 or 4;

each R^1, R^2 and R^3 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silyloxyalkynyl, silylalkoxy, silylalkoxyalkyl, –CN, oxo,–NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^cSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$, –OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$, each of which is optionally substituted with 1-3 R^6; wherein two R^1, together with the atoms to which they are attached, may form an optionally substituted cyclyl, heterocyclyl, aryl or heteroaryl ring;

R^4 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^6;

R^5 is hydrogen; or when m is not 0, R^5 and one R^1 may be taken together with the atoms to which they are attached to form an optionally substituted heteroaryl or heterocyclyl ring;

each R^6 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thioxo, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$,$–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^7;

each R^7 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thioxo, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$,$–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$,each of which is optionally substituted with 1-3 R^9;

each R^9 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy,

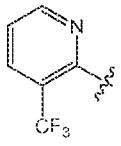
silylalkoxyalkyl, oxo, thioxo, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$;

Y is O or S;

q is 1 or 2; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, acyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy or silylalkoxyalkyl;

wherein when B is phenyl, two R^1 are not taken together to form a pyrazole ring; and

when B is phenyl, R^2 is not 

.

3. The compound according to claim 2 represented by general formula (I) or a salt thereof,

wherein:

A is CH or N;

B is aryl, cyclyl or a 5- or 6-membered heteroaryl;

m is 0, 1, 2, 3 or 4;

E is aryl or a 5-membered heteroaryl;

n is 0, 1 or 2;

when E is aryl, n is 0, 1 or 2 and when E is a 5-membered heteroaryl, n is 0 or 1;

p is 0, 1 or 2;

each R^1, R^2 and R^3 is independently C_1-C_8 alkyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silyloxyalkynyl, –CN, oxo, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^bR^{b'}$,

$-OC(O)NR^bR^{b'}$, $-NR^cC(Y)R^{c'}$, $-SO_2NR^bR^{b'}$, $-OR^d$, $-SR^{d'}$, $-C(Y)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^6; wherein two R^1, together with the atoms to which they are attached, may form an optionally substituted cyclyl, heterocyclyl, aryl or heteroaryl ring;

each R^6 is independently C_1-C_8 alkyl, heterocyclyl, heterocyclylalkyl, hydroxyalkyl, halo, haloalkyl, haloalkoxy, alkoxyalkyl, oxo, $-CN$, $-NO_2$, $-C(O)OR^a$, $-C(Y)NR^bR^{b'}$, $-NR^cC(Y)R^{c'}$, $-NR^bR^{b'}$, $-OR^d$ or $-C(Y)R^e$, each of which is optionally substituted with 1-3 R^7;

each R^7 is oxo; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, acyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, haloalkyl, dialkylaminoalkyl, hydroxyalkyl or alkoxyalkyl.

4. The compound according to claim 3 represented by general formula (I) or a salt thereof,

wherein:

B or two R^1 and B are taken together to form a group is phenyl, dihydroindenyl, dihydrobenzoxazinyl, dihydrobenzodioxinyl, chromenyl, tetrahydroquinoxalinyl, tetrahydroisoquinolinyl, tetrahydroquinolinyl, dihydroquinolinyl, quinolyl, isoquinolinyl, tetrahydroquinazolinyl, indolinyl, dihydrobenzothiazolyl, dihydrobenzimidazolyl, dihydrobenzoxazolyl, isoindolinyl, dihydroisobenzofuranyl, benzofuryl, benzothienyl, benzodioxolyl, indolyl, indazolyl, benzoimidazolyl, benzotriazolyl, benzisoxazolyl, benzoxazolyl, benzothiazolyl, benzoxadiazolyl, dihydrocyclopentathiophenyl, tetrahydrobenzothiophenyl, thienyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, thiadiazolyl, pyrrolyl or pyridyl;

E is phenyl, thienyl or pyrrolyl ;

when E is phenyl , n is 1 or 2; and when E is thienyl, n is 0 or 1;

each R^1, R^2 and R^3 is independently C_1-C_8 alkyl ,C_2-C_8 alkynyl, phenyl, thienyl, pyrrolyl, oxadiazolyl, pyridyl, benzodioxolyl, furyl, pyrimidinyl, oxazolyl, isoxazolyl,

pyrazolyl, C_3-C_8 cycloalkyl, piperidyl, pyrrolidinyl, morpholinyl, dioxolanyl, phenylalkyl, thiomorpholinylalkyl, pyrrolidinylalkyl, morpholinylalkyl, piperidylalkyl, piperazinylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxyalkyl, silyloxyalkynyl, –CN, –NO_2, oxo, $-C(O)OR^a$, $-C(Y)NR^bR^{b'}$, $-NR^cC(Y)R^{c'}$, $-NR^bR^{b'}$, $-OC(O)NR^bR^{b'}$, $-SO_2NR^bR^{b'}$, $-OR^d$, $-SR^{d'}$, $-C(Y)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^6;

each R^6 is independently C_1-C_8 alkyl, tetrahydropyranyl, morpholinyl, thiomorpholinyl, morpholinylalkyl, dialkylaminoalkyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, oxo, –CN, $–NO_2$, $-C(O)OR^a$, $-NR^cC(Y)R^{c'}$, $-C(Y)NR^bR^{b'}$, $-NR^bR^{b'}$, alkoxyalkyl, $-OR^d$ or $-C(Y)R^e$; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 cycloalkyl, phenyl, pyridyl, dihydroindenyl, morpholinyl, tetrahydropyranyl, piperidyl, pyrrolidinyl, piperazinyl, thiomorpholinyl, phenylalkyl, thienylalkyl, furylalkyl, pyridylalkyl, tetrahydropyranylalkyl, dihydroindenylalkyl, tetrahydrofurylalkyl, hydroxyalkyl, thiazolylalkyl, pyrazolylalkyl, morpholinylalkyl, pyrrolidinylalkyl, dialkylaminoalkyl, piperidylalkyl, benzodioxolylalkyl, dihydrobenzodioxinylalkyl, benzothienylalkyl, C_3-C_8 cycloalkylalkyl, oxazolidinylalkyl, haloalkyl or alkoxyalkyl.

5. The compound according to claim 3 represented by general formula (I) or a salt thereof,

wherein:

B or two R^1 and B are taken together to form a group is phenyl, dihydroindenyl, dihydrobenzoxazinyl, dihydrobenzodioxinyl, chromenyl, tetrahydroquinoxalinyl, tetrahydroisoquinolyl, tetrahydroquinolinyl, dihydroquinolyl, quinolyl, isoquinolyl, tetrahydroquinazolinyl, indolinyl, dihydrobenzothiazolyl, dihydrobenzimidazolyl, dihydrobenzoxazolyl, isoindolinyl, dihydroisobenzofuranyl, benzofuryl, benzothienyl, benzodioxolyl, indolyl, indazolyl, benzoimidazolyl, benzotriazolyl, benzisoxazolyl, benzoxazolyl, benzothiazolyl, benzoxadiazolyl, dihydrocyclopentathiophenyl,

tetrahydrobenzothienyl, thienyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, thiadiazolyl, pyrrolyl or pyridyl;

E is phenyl, thienyl or pyrrolyl ;

when E is phenyl , n is 0, 1or 2; and when E is thienyl, n is 0 or 1;

each R^1, R^2 and R^3 is independently C_1-C_8 alkyl, C_2-C_8 alkynyl, phenyl, thienyl, pyrrolyl, oxazolyl, oxadiazolyl, pyridyl, benzodioxolyl, furyl, pyrimidinyl, isoxazolyl, pyrazolyl, C_3-C_8 cycloalkyl, piperidyl, pyrrolidinyl, morpholinyl, dioxolanyl, phenylalkyl, thiomorpholinylalkyl, pyrrolidinylalkyl, morpholinylalkyl, piperidylalkyl, piperazinylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxyalkyl, silyloxyalkynyl, –CN, –NO_2, oxo, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$OC(O)NR^bR^{b'}$, –$SO_2NR^bR^{b'}$, –OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$, each of which is optionally substituted with 1-3 R^6;

each R^6 is independently C_1-C_8 alkyl, tetrahydropyranyl, morpholinyl, thiomorpholinyl, morpholinylalkyl, dialkylaminoalkyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, oxo, –CN, –NO_2, –$C(O)OR^a$, –$NR^cC(Y)R^{c'}$, –$C(Y)NR^bR^{b'}$, –$NR^bR^{b'}$, alkoxyalkyl, –OR^d or –$C(Y)R^e$, each of which is optionally substituted with 1-3 R^7;

R^7 is oxo; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 cycloalkyl, phenyl, pyridyl, dihydroindenyl, morpholinyl, tetrahydropyranyl, piperidyl, pyrrolidinyl, piperazinyl, thiomorpholinyl, phenylalkyl, thienylalkyl, furylalkyl, pyridylalkyl, tetrahydropyranylalkyl, dihydroindenylalkyl, tetrahydrofurylalkyl, hydroxyalkyl, thiazolylalkyl, pyrazolylalkyl, morpholinylalkyl, pyrrolidinylalkyl, dialkylaminoalkyl, piperidylalkyl, benzodioxolilalkyl, dihydrobenzodioxinylalkyl, benzothienylalkyl, C_3-C_8 cycloalkylalkyl, oxazolidinylalkyl, haloalkyl or alkoxyalkyl.

6. The compound according to claim 5 represented by general formula (I) or a salt thereof,

wherein:

R^1 is C_1-C_8 alkyl, phenyl, thienyl, pyrrolyl, oxazolyl, C_3-C_8 cycloalkyl, dioxolanyl, phenylalkyl, halo, haloalkyl, haloalkoxy, alkoxyalkyl, –CN, oxo, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$SO_2NR^bR^{b'}$, –OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$, each of which is optionally substituted with 1-3 R^6;

R^2 is C_1-C_8 alkyl, C_2-C_8 alkynyl, phenyl, thienyl, pyridyl, benzodioxolyl, furyl, pyrimidinyl, isoxazolyl, pyrazolyl, C_3-C_8 cycloalkyl, pyrrolidinyl, morpholinyl , thiomorpholinylalkyl, pyrrolidinylalkyl, morpholinylalkyl, piperiridylalkyl, piperazinylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxyalkyl, silyloxyalkynyl, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$,–$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –OR^d or –$C(Y)R^e$, each of which is optionally substituted with 1-3 R^6;

R^3 is C_1-C_8 alkyl, halo, haloalkyl ,–$NR^bR^{b'}$ or –OR^d, each of which is optionally substituted with 1-3 R^6.

7. The compound according to claim 4 or 6 represented by general formula (I) or a salt thereof,

wherein:

R^1 is C_1-C_8 alkyl, phenyl, thienyl, pyrrolyl, oxazolyl, C_3-C_8 cycloalkyl, dioxolanyl, phenylalkyl, halo, haloalkyl, haloalkoxy, alkoxyalkyl, –CN, oxo, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$SO_2NR^bR^{b'}$, –OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$;

R^2 is C_1-C_8 alkyl, C_2-C_8 alkynyl, phenyl, thienyl, pyridyl, benzodioxolyl, furyl, pyrimidinyl, isoxazolyl, pyrazolyl, C_3-C_8 cycloalkyl, piperidinyl, pyrrolidinyl, morpholinyl, thiomorpholinylalkyl, pyrrolidinylalkyl, morpholinylalkyl, piperiridinylalkyl, piperazinylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxyalkyl, silyloxyalkynyl, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$,–$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –OR^d, –$C(Y)R^e$ or -$S(O)_qR^f$;

R^3 is C_1-C_8 alkyl, halo, haloalkyl ,–$NR^bR^{b'}$ or –OR^d.

8. The compound according to claim 7 represented by general formula (I) or a salt thereof,

wherein:

B or two R^1 and B are taken together to form a group is phenyl, dihydroindenyl, dihydrobenzoxazinyl, dihydrobenzodioxinyl, chromenyl, tetrahydroisoquinolyl, tetrahydroquinolinyl, dihydroquinolyl, quinolyl, tetrahydroquinazolinyl, indolinyl, dihydrobenzothiazolyl, dihydrobenzimidazolyl, dihydrobenzoxazolyl, isoindolinyl, benzofuryl, benzothienyl, benzodioxolyl, indolyl, indazolyl, benzoimidazolyl, benzotriazolyl, benzisoxazolyl, benzoxazolyl, benzothiazolyl, benzoxadiazolyl, tetrahydrobenzothienyl, thienyl, thiazolyl, imidazolyl, pyrazolyl, thiadiazolyl or pyridyl;

m is 1, 2, 3 or 4;

R^1 is C_1-C_8 alkyl, halo, haloalkyl, haloalkoxy, alkoxyalkyl, –CN, oxo, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$SO_2NR^bR^{b'}$, –OR^d, or -$S(O)_qR^f$;

R^2 is C_1-C_8 alkyl, C_3-C_8 cycloalkyl, thiomorpholinylalkyl, pyrrolidinylalkyl, morpholinylalkyl, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxyalkyl, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$,–$NR^bR^{b'}$, –OR^d, –$C(Y)R^e$ or -$S(O)_qR^f$;

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 cycloalkyl, phenyl, dihydroindenyl, morpholinyl, tetrahydropyranyl, piperidyl, pyrrolidinyl, thiomorpholinyl, phenylalkyl, thienylalkyl, pyridylalkyl, tetrahydropyranylalkyl, dihydroindenylalkyl, tetrahydrofurylalkyl, hydroxyalkyl, morpholinylalkyl, pyrrolidinylalkyl, dialkylaminoalkyl, piperidylalkyl, benzodioxolilalkyl, dihydrobenzodioxinylalkyl, C_3-C_8 cycloalkylalkyl, haloalkyl or alkoxyalkyl.

9. The compound according to claim 1 represented by general formula (II) or a salt thereof,

wherein:

L is CR^4R^5, O, C(O), $NR^6C(O)$ or NR^7;

A is N;

each X^1, X^2, X^3, X^4 and X^5 is independently CH or N, provided that at least two of X^1, X^2, X^3, X^4 and X^5 are N;

n is 0, 1, 2, 3 or 4;

p is 0, 1, 2 or 3;

R^1 is C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl or heterocyclylalkyl, each of which is optionally substituted with 1-5 R^9; wherein R^1 or R^9 is optionally taken together with one of R^4, R^5, R^6 or R^7, and the atoms to which they are attached to form a cyclyl, heterocyclyl, aryl or heteroaryl ring that is optionally substituted with 1-3 R^{10};

each R^2 and R^3 is independently hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{11};

each R^4, R^5, R^6 and R^7 is independently hydrogen , C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$,$–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$;

each R^9, R^{10} and R^{11} is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thioxo, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, –

$NR^bR^{b'}$, $-OC(O)NR^bR^{b'}$, $-NR^cC(O)OR^{c'}$, $-SO_2NR^bR^{b'}$, $-NR^cSO_2R^{c'}$, $-NR^cC(Y)NR^bR^{b'}$, $-OR^d$, $-SR^{d'}$, $-C(Y)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{12};wherein two R^8, two R^9, two R^{10} or two R^{11} is optionally taken together with the atoms to which they are attached to form an optionally substituted cyclyl, heterocyclyl, aryl or heteroaryl ring;

R^{12} is $-OR^d$;

Y is O or S;

q is 1 or 2; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e, $R^{e'}$ and R^f is independently hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, acyl, cyclyl, heterocyclyl, aryl, heteroaryl, cyclylalkyl, heterocyclylalkyl, arylalkyl or heteroarylalkyl.

10. The compound according to claim 9 represented by general formula (II) or a salt thereof,

L is NR^7;

n is 0, 1 or 2;

p is 0;

R^1 is C_1-C_8 alkyl, aryl or heteroaryl;

each R^2 and R^3 is independently hydrogen, C_1-C_8 alkyl, aryl, halo, heterocyclylalkyl, $-NR^cC(Y)R^c$, $-NR^bR^{b'}$ or $-OR^d$, each of which is optionally substituted with 1-3 R^{11};

R^7 is hydrogen; and

each R^9, R^{10} and R^{11} is independently C_1-C_8 alkyl, heterocyclyl, halo, haloalkyl, haloalkoxy, $-CN$, $-C(O)OR^a$, $-C(Y)NR^bR^{b'}$, $-OR^d$ or $-C(Y)R^e$;

Y is O;

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e, $R^{e'}$ and R^f is independently hydrogen, C_1-C_8 alkyl, cyclyl, heterocyclyl, aryl or heteroaryl.

11 .The compound according to claim 10 represented by general formula (II) or a salt thereof,

wherein:

R^1 is C_1-C_8 alkyl, phenyl or benzodioxolyl;

each R^2 and R^3 is independently hydrogen, C_1-C_8 alkyl, phenyl, halo, morholinylalkyl, $-NR^cC(Y)R^c$, $-NR^bR^{b'}$ or $-OR^d$;

R^9 is independently C_1-C_8 alkyl, morpholinyl, tetrahydropyranyl, halo, haloalkyl, haloalkoxy, –CN, $-C(O)OR^a$, $-C(Y)NR^bR^{b'}$, $-OR^d$ or $-C(Y)R^e$; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e, $R^{e'}$ and R^f is independently hydrogen, C_1-C_8 alkyl, C_3-C_8 cycloalkyl, tetrahydropyranyl, phenyl or pyridyl.

12. The compound according to claim 10 represented by general formula (II) or a salt thereof,

wherein:

R^1 is C_1-C_8 alkyl, phenyl or benzodioxolyl;

each R^2 and R^3 is independently hydrogen, C_1-C_8 alkyl, phenyl, halo, morholinylalkyl, $-NR^cC(Y)R^c$, $-NR^bR^{b'}$ or $-OR^d$, each of which is optionally substituted with 1-3 R^{11};

each R^9, R^{10} and R^{11} is independently C_1-C_8 alkyl, morpholinyl, tetrahydropyranyl, halo, haloalkyl, haloalkoxy, –CN, $-C(O)OR^a$, $-C(Y)NR^bR^{b'}$,$-OR^d$ or $-C(Y)R^e$; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e, $R^{e'}$ and R^f is independently hydrogen, C_1-C_8 alkyl, C_3-C_8 cycloalkyl, tetrahydropyranyl, phenyl or pyridyl.

13. The compoundaccording to claim 12 represented by general formula (II) or a salt thereof, wherein:

R^2 is C_1-C_8 alkyl, phenyl, halo, morholinylalkyl, $-NR^cC(Y)R^{c'}$, $-NR^bR^{b'}$ or $-OR^d$, each of which is optionally substituted with 1-3 R^{11};

R^3 is hydrogen;

R^9 is halo, haloalkoxy, –CN, $-C(O)OR^a$ or $-C(Y)NR^bR^{b'}$; and

R^{11} is C_1-C_8 alkyl, morpholinyl, tetrahydropyranyl, halo, –CN, $-OR^d$ or $-C(Y)R^e$;

14. The compound according to claim 11 or 13 represented by general formula (II) or a salt thereof, wherein:

R^2 is C_1-C_8 alkyl, phenyl, halo, morholinylalkyl, $-NR^cC(Y)R^{c'}$, $-NR^bR^{b'}$ or $-OR^d$;

R^3 is hydrogen; and

R^9 is halo, haloalkoxy, –CN, $-C(O)OR^a$ or $-C(Y)NR^bR^{b'}$.

15. The compound according to claim 1 represented by general formula (III) or a salt thereof,

wherein:

A is CH or N;

L is O, a direct bond or NH;

one of X^1, X^2, X^3, X^4 and X^5 is N and the others are CH;

m is 1, 2 or 3;

n is 1, 2, 3 or 4;

R^1 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, alkoxyalkyl, hydroxyalkyl, heteroaryl, heteroarylalkyl, arylalkyl, $-C(Y)R^e$, cyclyl, cyclylalkyl or heterocyclyl, each of which is optionally substituted with 1-3 R^7;

R^2 is aryl or heteroaryl, each of which is optionally substituted with 1-5 R^9;

each R^3 or R^4 is independently hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, $-NO_2$, $-C(O)OR^a$, $-C(Y)NR^bR^{b'}$, $-NR^cC(Y)R^{c'}$, $-NR^bR^{b'}$, $-OC(O)NR^bR^{b'}$, $-NR^cC(O)OR^{c'}$, $-SO_2NR^bR^{b'}$, $-NR^cSO_2R^{c'}$, $-NR^cC(Y)NR^bR^{b'}$, $-OR^d$, $-SR^{d'}$, $-C(Y)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{10};

each R^7, R^9 and R^{10} is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thioxo, –CN, $-NO_2$, $-C(O)OR^a$, $-C(Y)NR^bR^{b'}$, $-NR^cC(Y)R^{c'}$, –

$NR^bR^{b'}$, $-OC(O)NR^bR^{b'}$, $-NR^cC(O)OR^{c'}$, $-SO_2NR^bR^{b'}$, $-NR^cSO_2R^{c'}$, $-NR^cC(Y)NR^bR^{b'}$, $-OR^d$, $-SR^{d'}$, $-C(Y)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{12}; wherein two R^7 or two R^9 are optionally be taken together with the atoms to which they are attached to form an optionally substituted cyclyl, heterocyclyl, aryl or heteroaryl ring;

R^{12} is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, arylalkyl, heteroarylalkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thioxo, –CN, $-NO_2$, $-C(O)OR^a$, $-C(Y)NR^bR^{b'}$, $-NR^cC(Y)R^{c'}$, $-NR^bR^{b'}$, $-OC(O)NR^bR^{b'}$, $-NR^cC(O)OR^{c'}$, $-SO_2NR^bR^{b'}$, $-NR^cSO_2R^{c'}$, $-NR^cC(Y)NR^bR^{b'}$, $-OR^d$, $-SR^{d'}$, $-C(Y)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{13};

R^{13} is independently C_1-C_8 alkyl, haloalkyl, halo, heterocyclyl, cyclyl, oxo or $-C(Y)NR^bR^{b'}$;

Y is O or S;

q is 1 or 2; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, acyl, cyclyl, heterocyclyl, aryl, haloalkyl, alkoxyalkyl, alkylaminoalkyl, dialkylaminoalkyl, heteroaryl, cyclylalkyl, heterocyclylalkyl, arylalkyl or heteroarylalkyl..

16. The compound according to claim 15 represented by general formula (III) or a salt thereof,

wherein:

m is 1;

n is 1;

R^1 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, heteroaryl, heterocyclyl, arylalkyl, cyclylalkyl, heteroarylalkyl, alkoxyalkyl, hydroxyalkyl or $-C(O)R^e$, each of which is optionally substituted with 1-3 R^7;

R^2 is aryl, heteroaryl or benzofuryl, each of which is optionally substituted with 1-5 R^9;

each R^3 or R^4 is independently hydrogen, C_1-C_8 alkyl, halo, haloalkyl or $-OR^d$;

R^6 is hydrogen or C_1-C_8 alkyl;

each R^7 and R^9 is independently C_1-C_8 alkyl, aryl, heteroaryl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, alkoxyalkyl, oxo, –CN, –NO_2, $-C(O)OR^a$, $-C(O)NR^bR^{b'}$, $-NR^bR^{b'}$, $-OR^d$, $-C(O)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{12};

R^{12} is independently C_1-C_8 alkyl, oxo, halo, haloalkyl, –CN, $-C(O)NR^bR^{b'}$ or $-C(O)R^e$ each of which is optionally substituted with 1-3 R^{13};

R^{13} is independently C_1-C_8 alkyl, halo or heterocyclyl ; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, cyclyl, heterocyclyl, arylalkyl, alkoxyalkyl, heterocyclylalkyl, heteroarylalkyl, alkylaminoalkyl, dialkylaminoalkyl or phenyl.

17. The compound according to claim 16 represented by general formula (III) or a salt thereof,

wherein:

R^1 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, alkoxyalkyl, hydroxyalkyl, imidazolyl, pyridylalkyl, phenylalkyl, oxazolylalkyl, thienylalkyl, thiazolidinyl isoindolyl, $-C(O)R^e$, dihydroindenyl, C_3-C_8 cycloalkyl, C_3-C_8 cycloalkylalkyl, piperidyl, morpholinyl, pyrrolidinyl, azetidinyl or piperazinyl, each of which is optionally substituted with 1-3 R^7;

R^2 is phenyl, naphthyl, benzofuryl, indazolyl, benzothienyl, pyridyl, pyrimidinyl, dihydrobenzodioxinyl, benzodioxolyl, benzoimidazolyl, isoxazolyl, pyrazolyl, indolinyl or benzoisoxazolyl, each of which is optionally substituted with 1-5 R^9;

each R^3 or R^4 is independently hydrogen, C_1-C_8 alkyl, halo, haloalkyl or $-OR^d$;

R^6 is hydrogen or C_1-C_8 alkyl;

each R^7 and R^9 is independently C_1-C_8 alkyl, phenyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, alkoxyalkyl, oxo, –CN, –NO_2, –$C(O)OR^a$, –$C(O)NR^bR^{b'}$, –$NR^bR^{b'}$, –OR^d, –$C(O)R^e$ or -$S(O)_qR^f$; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, C_3-C_8 cycloalkyl, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, tetrahydropyranyl, phenylalkyl, alkoxyalkyl, morholinylalkyl, oxazolidinylalkyl, imidazolylalkyl, tetrahydropyranylalkyl, pyridylalkyl, pyrazolylalkyl, tetrazolylalkyl, thiazolylalkyl, pyrrolylalkyl, benzoxazolylalkyl, indazolylalkyl, dihydrobenzoxazinylalkyl, tetrahydrofurylalkyl, tetrahydrofuryl, alkylaminoalkyl, dialkylaminoalkyl or phenyl.

18. The compound according to claim 16 represented by general formula (III) or a salt thereof,

wherein:

R^1 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, alkoxyalkyl, hydroxyalkyl, imidazolyl, furylalkyl, pyridylalkyl, phenylalkyl, oxazolylalkyl, thienylalkyl, thiazolidinyl, isoindolyl, –$C(O)R^e$, dihydroindenyl, C_3-C_8 cycloalkyl, C_3-C_8 cycloalkylalkyl, piperidyl, morpholinyl, pyrrolidinyl, azetidinyl or piperazinyl, each of which is optionally substituted with 1-3 R^7;

R^2 is phenyl, naphthyl, benzofuryl, indazolyl, benzothienyl, pyridyl, pyrimidinyl, dihydrobenzodioxinyl, benzodioxolyl, benzoimidazolyl, isoxazolyl, pyrazolyl, indolinyl or benzisoxazolyl, each of which is optionally substituted with 1-5 R^9;

each R^3 or R^4 is independently hydrogen, C_1-C_8 alkyl, halo, haloalkyl or –OR^d;

R^6 is hydrogen or C_1-C_8 alkyl;

each R^7 and R^9 is independently C_1-C_8 alkyl, phenyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, alkoxyalkyl, oxo, –CN, –NO_2, –$C(O)OR^a$, –$C(O)NR^bR^{b'}$, –$NR^bR^{b'}$, –OR^d, –$C(O)R^e$ or -$S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{12};

R^{12} is independently C_1-C_8 alkyl, oxo, halo, haloalkyl, –CN, –$C(O)NR^bR^{b'}$ or –$C(O)R^e$, each of which is optionally substituted with 1-3 R^{13};

R^{13} is independently C_1-C_8 alkyl, halo or pyrrolidinyl; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, C_3-C_8 cycloalkyl, pyrrolidinyl, piperidyl, morpholinyl, piperazinyl, tetrahydropyranyl, phenylalkyl, alkoxyalkyl, morpholinylalkyl, oxazolidinylalkyl, imidazolylalkyl, tetrahydropyranylalkyl, pyridylalkyl, pyrazolylalkyl, tetrazolylalkyl, thiazolylalkyl, pyrrolylalkyl, benzoxazolylalkyl, indazolylalkyl, dihydrobenzoxazinylalkyl, tetrahydrofurylalkyl, tetrahydrofuryl, alkylaminoalkyl, dialkylaminoalkyl or phenyl.

19. The compound according to claim 18 represented by general formula (III) or a salt thereof,

wherein:

A is N;

R^3 is hydrogen, C_1-C_8 alkyl, halo, haloalkyl, or $-OR^d$;

R^4 is hydrogen, C_1-C_8 alkyl, halo, or $-OR^d$;

R^7 is C_1-C_8 alkyl, phenyl, halo, haloalkyl, oxo, $-C(O)OR^a$, $-C(O)NR^bR^{b'}$ or $-OR^d$ each of which is optionally substituted with 1-3 R^{12};

R^9 is C_1-C_8 alkyl, phenyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, alkoxyalkyl, $-CN$, $-NO_2$, $-C(O)NR^bR^{b'}$, $-C(O)OR^a$, $-NR^bR^{b'}$, $-OR^d$, $-C(O)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{12}; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, C_3-C_8 cycloalkyl, pyrrolidinyl, piperidyl, morpholinyl, piperazinyl, tetrahydropyranyl, phenylalkyl, alkoxyalkyl, morpholinylalkyl, oxazolidinylalkyl, imidazolylalkyl, tetrahydropyranylalkyl, pyridylalkyl, pyrazolylalkyl, tetrazolylalkyl, thiazolylalkyl, pyrrolylalkyl, benzoxazolylalkyl, indazolylalkyl, tetrahydrofurylalkyl, dihydrobenzoxazinylalkyl, tetrahydrofuryl, alkylaminoalkyl, dialkylaminoalkyl or phenyl;.

20. The compound according to claim 17 or 19 represented by general formula (III) or a salt thereof,

wherein:

A is N;

R^3 is hydrogen, C_1-C_8 alkyl, halo, haloalkyl, or $-OR^d$;

R^4 is hydrogen, C_1-C_8 alkyl, halo, or $-OR^d$;

R^7 is C_1-C_8 alkyl, phenyl, halo, haloalkyl, oxo, $-C(O)OR^a$, $-C(O)NR^bR^{b'}$ or $-OR^d$;

R^9 is C_1-C_8 alkyl, phenyl, halo, haloalkyl, haloalkoxy, hydroxyalkyl, alkoxyalkyl, –CN, $-NO_2$, $-C(O)NR^bR^{b'}$, $-C(O)OR^a$, $-NR^bR^{b'}$, $-OR^d$, $-C(O)R^e$ or $-S(O)_qR^f$; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, C_3-C_8 cycloalkyl, pyrrolidinyl, piperidyl, morpholinyl, piperazinyl, tetrahydropyranyl, phenylalkyl, alkoxyalkyl, morpholinylalkyl, oxazolidinylalkyl, imidazolylalkyl, tetrahydropyranylalkyl, pyridylalkyl, pyrazolylalkyl, tetrazolylalkyl, thiazolylalkyl, pyrrolylalkyl, benzoxazolylalkyl, indazolylalkyl, tetrahydrofurylalkyl, tetrahydrofuryl, dihydrobenzoxazinylalkyl, alkylaminoalkyl, dialkylaminoalkyl or phenyl.

21. The compound according to claim 20 represented by general formula (III) or a salt thereof,

wherein:

R^1 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, alkoxyalkyl, hydroxyalkyl, imidazolyl, furylalkyl, pyridylalkyl, phenylalkyl, oxazolylalkyl, thienylalkyl, isoindolyl, $-C(O)R^e$, dihydroindenyl, C_3-C_8 cycloalkyl, C_3-C_8 cycloalkylalkyl, piperidyl, morpholinyl, pyrrolidinyl, azetidinyl or piperazinyl, each of which is optionally substituted with 1-3 R^7;

R^2 is phenyl, which is optionally substituted with 1-5 R^9; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e and R^f is independently hydrogen, C_1-C_8 alkyl, pyrrolidinyl, morpholinyl, tetrahydropyranyl, alkoxyalkyl, morpholinylalkyl, tetrahydropyranylalkyl, pyridylalkyl, thiazolylalkyl, pyrrolylalkyl, tetrahydrofuryl, alkylaminoalkyl or phenyl.

22. A pharmaceutical composition comprising the compound according to any one of claims 1 to 21 or a salt thereof as an active ingredient and a pharmaceutically acceptable carrier.

23. The pharmaceutical composition according to claim 22 for preventing or treating central nervous system diseases.

24. The pharmaceutical composition according to claim 23 for treating or preventing central nervous system disorders selected from the group consisting of schizophrenia; refractory, intractable or chronic schizophrenia; emotional disturbance; psychotic disorder; mood disorder; bipolar I type disorder; bipolar II type disorder; depression; endogenous depression; major depression; melancholy and refractory depression; dysthymic disorder; cyclothymic disorder; panic attack; panic disorder; agoraphobia; social phobia; obsessive-compulsive disorder; post-traumatic stress disorder; generalized anxiety disorder; acute stress disorder; hysteria; somatization disorder; conversion disorder; pain disorder; hypochondriasis; factitious disorder; dissociative disorder; sexual dysfunction; sexual desire disorder; sexual arousal disorder; erectile dysfunction; anorexia nervosa; bulimia nervosa; sleep disorder; adjustment disorder; alcohol abuse; alcohol intoxication; drug addiction; stimulant intoxication; narcotism; anhedonia; iatrogenic anhedonia; anhedonia of a psychic or mental cause; anhedonia associated with depression; anhedonia associated with schizophrenia; delirium; cognitive impairment; cognitive impairment associated with Alzheimer's disease, Parkinson's disease and other neurodegenerative diseases; cognitive impairment caused by Alzheimer's disease; Parkinson's disease and associated neurodegenerative diseases; cognitive impairment of schizophrenia; cognitive impairment caused by refractory, intractable or chronic schizophrenia; vomiting; motion sickness; obesity; migraine; pain (ache) ; mental retardation; autism disorder (autism); Tourette's disorder; tic disorder; attention-deficit/hyperactivity disorder; conduct disorder; and Down's syndrome.

25. A process for producing a pharmaceutical composition comprising mixing a compound of the formula (I), (II), or (III) or a salt thereof according to any one of claims 1 to 21 with a pharmaceutically acceptable carrier.

26. Use of a compound of the formula (I), (II) or (III) or a salt thereof according to any one of claims 1 to 21 as a drug.

27. Use of the compound according to any one of claims 1 to 21 represented by general formula(I), (II) or (III) or a salt thereof as a STEP inhibitor.

28. A method of treating a disorder that would benefit by the modulation of STEP (e.g., by activation of inhibition of STEP) in a subject, the method comprising administering to a compound of formula (I), (II) or (III) or a salt thereof according to any one of claims 1 to 21.

29. The method of claim 28, wherein the disorder is schizophrenia.

30. The method of claim 28, wherein the disorder is cognitive deficit.

31. The method of claim 28, wherein the compound of formula (I), (II) or (III) is administered in combination with an additional therapeutic agent.

32. The method of claim 28, wherein the additional therapeutic agent is an atypical antipsychotic.

33. The method of claim 28, wherein the additional therapeutic agent is selected from the group consisting of aripiprazole, clozapine, ziprasidone, risperidone, quetiapine, olanzapine, amisulpride, asenapine, iloperidone, melperone, paliperidone, perospirone, sertindole and sulpiride.

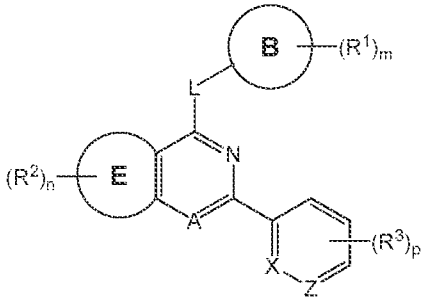
34. The method of claim 28, wherein the additional therapeutic agent is a typical antipsychotic.

35. The method of claim 28, wherein the additional therapeutic agent is selected from the group consisting of haloperidol, molindone, loxapine, thioridazine, molindone, thiothixene, pimozide, fluphenazine, trifluoperazine, mesoridazine, chlorprothixene, chlorpromazine, perphenazine, triflupromazine and zuclopenthixol.

36. A kit comprising a composition comprising a compound of formula (I), (II), or (III) or a salt thereof according to any one of claims 1 to 21 and an acceptable carrier.

37. A kit comprising a pharmaceutical composition comprising a compound of formula (I), (II), or (III) or a salt thereof according to any one of claims 1 to 21 and a pharmaceutically acceptable carrier.

38. A compound of formula (IV):



(IV)

wherein:

A is CH, CR^4 or N;

B is aryl or a 5- or 6-membered heteroaryl;

m is 0, 1, 2, 3, 4 or 5;

E is aryl or a 5-membered heteroaryl;

when E is aryl, n is 1, 2, 3 or 4; and when E is a 5-membered heteroaryl, n is 0, 1, 2 or 3;

L is NR^5 or O;

one of X and Z is N and the other is CH;

p is 0, 1, 2, 3 or 4;

each R^1, R^2 and R^3 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^cSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$,–OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$, each of which may be optionally substituted with 1-3 R^6; wherein two R^1, together with the atoms to which they are attached, may form an optionally substituted cyclyl, heterocyclyl, aryl or heteroaryl ring;

R^4 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^cSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$,–OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$, each of which may be optionally substituted with 1-3 R^6;

R^5 is hydrogen; or when m is not 0, R^5 and 1 R^1 may be taken together with the atoms to which they are attached to form an optionally substituted heteroaryl or heterocyclyl ring;

each R^6 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thiono, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^cSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$,–OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$, each of which may be optionally substituted with 1-3 R^7;

each R^7 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl,

hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thiono, –CN, –NO_2, –$C(O)OR^a$, –$C(Y)NR^bR^{b'}$, –$NR^cC(Y)R^{c'}$, –$NR^bR^{b'}$, –$OC(O)NR^bR^{b'}$, –$NR^cC(O)OR^{c'}$, –$SO_2NR^bR^{b'}$, –$NR^cSO_2R^{c'}$, –$NR^cC(Y)NR^bR^{b'}$,–OR^d, –$SR^{d'}$, –$C(Y)R^e$ or -$S(O)_qR^f$;

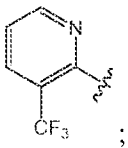
each Y is independently O or S;

q is 1 or 2; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e, $R^{e'}$ and R^f is independently selected from hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, acyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy and silylalkoxyalkyl, each of which may be optionally substituted with 1-3 R^6, wherein R^b and $R^{b'}$, together with the atoms to which they are attached, may form an optionally substituted cyclyl or heterocyclyl ring;

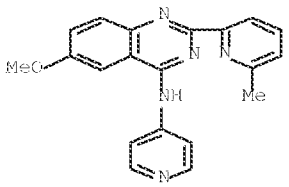
or a pharmaceutically acceptable derivative or prodrug thereof,

wherein when B is phenyl, two R^1 are not taken together to form a pyrazole ring;

when B is phenyl, R^2 is not 

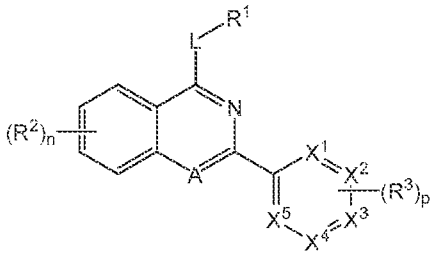
;

and where in the compound is not:



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39. A compound of formula (V):



(V)

wherein:

L is CR^4R^5, O, C(O), $NR^6C(O)$, or NR^7;

A is CR^8, CH or N;

each X^1, X^2, X^3, X^4 and X^5 is independently CH or N, provided that at least two of X^1, X^2, X^3, X^4 and X^5 are N;

n is 0, 1, 2, 3 or 4;

p is 0, 1, 2 or 3;

R^1 is C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl or heterocyclylalkyl, each of which may be optionally substituted with 1-5 R^9; wherein R^1 or R^9 may optionally be taken together with one of R^4, R^5, R^6 or R^7, and the atoms to which they are attached, to form a cyclyl, heterocyclyl, aryl or heteroaryl ring that is optionally substituted with 1-3 R^{10};

each R^2 and R^3 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$; each of which is optionally substituted with 1-3 R^{11};

each R^4, R^5, R^6 and R^7 is independently H, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl,–CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, –

$OC(O)NR^bR^{b'}$, $-NR^cC(O)OR^{c'}$, $-SO_2NR^bR^{b'}$, $-NR^cSO_2R^{c'}$, $-NR^cC(Y)NR^bR^{b'}$, $-OR^d$, $-SR^{d'}$, $-C(Y)R^e$ or $-S(O)_qR^f$;

each R^8, R^9, R^{10} and R^{11} is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thiono, $-CN$, $-NO_2$, $-C(O)OR^a$, $-C(Y)NR^bR^{b'}$, $-NR^cC(Y)R^{c'}$, $-NR^bR^{b'}$, $-OC(O)NR^bR^{b'}$, $-NR^cC(O)OR^{c'}$, $-SO_2NR^bR^{b'}$, $-NR^cSO_2R^{c'}$, $-NR^cC(Y)NR^bR^{b'}$, $-OR^d$, $-SR^{d'}$, $-C(Y)R^e$ or $-S(O)_qR^f$, each of which may be optionally further substituted; wherein two R^8, two R^9, two R^{10} or two R^{11} may optionally be taken together with the atoms to which they are attached to form an optionally substituted cyclyl, heterocyclyl, aryl or heteroaryl ring;

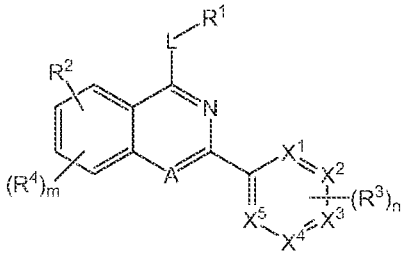
each Y is independently O or S;

q is 1 or 2; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e, $R^{e'}$ and R^f is independently selected from hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, acyl, cyclyl, heterocyclyl, aryl, heteroaryl, cyclylalkyl, heterocyclylalkyl, aralkyl and heteroaralkyl, each of which may be optionally substituted with 1-3 R^8,

or a pharmaceutically acceptable derivative or prodrug thereof.

40. A compound of formula (VI):



(VI)

wherein:

A is CR^5, CH or N;

L is O or NR^6;

1, 2 or 3 of X^1, X^2, X^3, X^4 and X^5 are N and the others are CH;

m is 0, 1, 2 or 3;

n is 0, 1, 2, 3 or 4;

R^1 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, cyclyl or heterocyclyl, each of which is optionally substituted with 1-3 R^7; or when L is NR^6, R^1 or R^7 may be taken together with R^6 and the atoms to which they are attached to form a heterocyclyl or heteroaryl ring that is optionally substituted with 1-3 R^8;

R^2 is aryl or heteroaryl, each of which is optionally substituted with 1-5 R^9;

each R^3, R^4 and R^5 is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{10};

R^6 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, cyclyl or heterocyclyl, each of which is optionally substituted with 1-3 R^{11};

each R^7, R^8, R^9 and R^{10} is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy, silylalkoxyalkyl, oxo, thiono, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$, each of which is optionally substituted with 1-3 R^{12}; wherein two R^7, two R^8, two R^9 or two R^{10} may optionally be taken together with the atoms to which they are attached to form an optionally substituted cyclyl, heterocyclyl, aryl or heteroaryl ring;

each R^{11} and R^{12} is independently C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, aralkyl, heteroaralkyl, cyclylalkyl, heterocyclylalkyl, halo, haloalkyl, haloalkoxy, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, alkoxyalkyl, silyloxy, silyloxyalkyl, silylalkoxy,

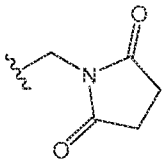
silylalkoxyalkyl, oxo, thiono, –CN, $–NO_2$, $–C(O)OR^a$, $–C(Y)NR^bR^{b'}$, $–NR^cC(Y)R^{c'}$, $–NR^bR^{b'}$, $–OC(O)NR^bR^{b'}$, $–NR^cC(O)OR^{c'}$, $–SO_2NR^bR^{b'}$, $–NR^cSO_2R^{c'}$, $–NR^cC(Y)NR^bR^{b'}$, $–OR^d$, $–SR^{d'}$, $–C(Y)R^e$ or $-S(O)_qR^f$;

each Y is independently O or S;

q is 1 or 2; and

each R^a, R^b, $R^{b'}$, R^c, $R^{c'}$, R^d, $R^{d'}$, R^e, $R^{e'}$ and R^f is independently selected from hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, acyl, cyclyl, heterocyclyl, aryl, heteroaryl, cyclylalkyl, heterocyclylalkyl, aralkyl and heteroaralkyl, each of which may be optionally substituted with 1-3 R^7;

or a pharmaceutically acceptable derivative or prodrug thereof,

wherein when R^1 is cyclopropyl, R^9 is not: 

41. A compound described herein.