EIF4E INHIBITING 4-OXO-3,4-DIHYDROPYRIDO[ ]PYRIMIDINE COMPOUNDS

FIELD

[001] The present invention generally relates to compounds having activity as inhibitors of eukaryotic initiation factor 4e (eIF4e), as well as to related compositions and methods for utilizing the inventive compounds as therapeutic agents for treatment of eIF4e dependent diseases, including the treatment of cancer.

BACKGROUND

[002] Eukaryotic initiation factor 4E (eIF4E) is a general translation factor, but it has the potential to enhance preferentially the translation of messenger RNAs (mRNAs) that lead to production of malignancy-associated proteins. This selectivity may relate to an increased requirement for eIF4E and its binding partners for the translation of mRNAs containing extensive secondary structure in their 5'-untranslated regions (5'-UTRs). These mRNAs include those encoding certain proteins that control cell cycle progression and tumorigenesis. Under normal cellular conditions the translation of these malignancy-associated mRNAs is suppressed as the availability of active eIF4E is limited; however, their levels can increase when eIF4E is over-expressed or hyperactivated. Elevated levels of eIF4E have been found in many types of tumors and cancer cell lines including cancers of the colon, breast, bladder, lung, prostate, gastrointestinal tract, head and neck, Hodgkin's lymphomas and neuroblastomas.

[003] Initiation of cap-dependent translation is thought to depend on the assembly of eIF4F, an initiation factor complex including eIF4E, the scaffold protein eIF4G, and the RNA helicase eIF4A. Because eIF4E is the only one of these proteins that binds directly to the mRNA cap structure, it is the key factor for the assembly of eIF4F at the 5' cap. The scaffold protein, eIF4G, also recruits the 40S ribosomal subunit to the mRNA via its interaction with eIF3 and binds eIF4B, a protein that aids the RNA-helicase function of eIF4A, thus facilitating the translation of mRNAs that contain structured 5'-UTRs. The availability of eIF4E as part of the eIF4F complex is a limiting factor in controlling the rate of translation, and therefore eIF4E is an important regulator of mRNA translation.

[004] Regulation of eIF4E activity forms a node of convergence of the PI3K/Akt/mTOR and Ras/Raf/MAPK signaling pathways. The PI3K (phosphoinositide 3-kinase)/PTEN (phosphatase and tensin homologue deleted on chromosome ten)/Akt/mTOR (mammalian target of rapamycin) pathway is often involved in tumorigenesis and in sensitivity and resistance to cancer therapy. Deregulated signaling through the PI3K/PTEN/Akt/mTOR pathway is often the result of genetic alterations in critical components of this pathway and/or mutations at upstream growth

factor receptors or signaling components. PI3K initiates a cascade of events when activated by, for example, extracellular growth factors, mitogens, cytokines and/or receptors, PDK1 activates Akt, which in turn phosphorylates and inactivates the tumor suppressor complex comprising TSC1 and 2 (tuberous sclerosis complex 1/2), resulting in the activation of mTORC1 (target of rapamycin complex 1) by Rheb-GTP. Activation of PDK1 and Akt by PI3Ks is negatively regulated by PTEN.

[005] PTEN is a critical tumor suppressor gene and is often mutated or silenced in human cancers. Its loss results in activation of Akt and increases downstream mTORC1 signaling. The involvement of mTOR complex1 (mTORC1) in neoplastic transformation appears to depend on its regulatory role toward the eIF4F complex; overexpression of eIF4E can confer resistance to rapamycin. mTORC1 regulates the eIF4F complex assembly that is critical for the translation of mRNAs associated with cell growth, prevention of apoptosis and transformation. mTORC1 achieves this by phosphorylation and inactivation of 4E-BPs and the subsequent dissociation of 4E-BPs from eIF4E. This then enables eIF4E to interact with the scaffold protein eIF4G, permitting assembly of the eIF4F complex for the translation of structured mRNAs. mTORC1 also promotes activation of the translational activator, S6K, which phosphorylates the ribosomal protein S6 and other substrates, including eIF4B. mTORC1 signaling is inhibited by rapamycin and its analogues (rapalogs), although these compounds act allosterically, rather than directly inhibiting mTOR kinase activity.

[006] Given the importance of the PI3K/Akt/mTOR pathway in regulating mRNA translation of genes that encode for pro-oncogenic proteins and activated mTORC1 signaling in a high proportion of cancers, these kinases have been actively pursued as oncology drug targets. A number of pharmacological inhibitors have been identified, some of which have reached advanced clinical stages. However, it has recently become clear that the mTOR pathway participates in a complicated feedback loop that can impair activation of Akt. It has been shown that prolonged treatment of cancer cells or patients with mTOR inhibitors causes elevated PI3K activity that leads to phosphorylation of Akt and eIF4E, and promotes cancer cell survival. eIF4E, acting downstream of Akt and mTOR, recapitulates Akt's action in tumorigenesis and drug resistance, and Akt signaling via eIF4E is an important mechanism of oncogenesis and drug resistance *in vivo*.

[007] In addition to the PI3K/Akt/mTOR pathway, eIF4E is also the target of the Ras/Raf/MAP signaling cascade which is activated by growth factors and for the stress-activated p38 MAP kinase pathway. Erk1/2 and p38 then phosphorylate MAP kinase-interacting kinase 1 (Mnk1)

and MAP kinase-interacting kinase 2 (Mnk2). The Erk pathway is also activated in many cancers, reflecting, for example, activating mutations in Ras (found in around 20% of tumors) or loss of function of the Ras GTPase-activator protein NF1. Mnk1 and Mnk2 are threonine/serine protein kinases and specifically phosphorylate serine 209 (Ser209) of eIF4E within the eIF4F complex, by virtue of the interaction between eIF4E and the Mnks, which serves to recruit Mnks to act on eIF4E. Mice with mutated eIF4E, in which Ser209 is replaced by alanine, show no eIF4E phosphorylation and significantly attenuated tumor growth. Significantly, while Mnk activity is necessary for eIF4E-mediated oncogenic transformation, it is dispensable for normal development. Pharmacologically inhibiting Mnks thus presents an attractive therapeutic strategy for cancer.

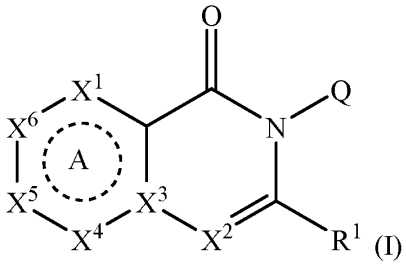
[008] Despite increased understanding of Mnk structure and function, little progress has been made with regard to the discovery of pharmacological Mnk inhibitors and relatively few Mnk inhibitors have been reported: CGP052088 (Tschopp *et al.*, *Mol Cell Biol Res Commun. 3*(4):205–211, 2000); CGP57380 (Rowlett *et al.*, *Am J Physiol Gastrointest Liver Physiol. 294*(2):G452–459, 2008); and Cercosporamide (Konicek *et al.*, *Cancer Res. 71*(5):1849–1857, 2011). These compounds, however, have mainly been used for the purpose of Mnk target validation. More recently, investigators have proposed further compounds for treating diseases influenced by the inhibition of kinase activity of Mnk1 and/or Mnk2, including, for example, the compounds disclosed in International Patent Application Publication WO 2014/044691 and the various patent documents cited therein, the 4-(dihydropyridinon-3-yl)amino-5-methylthieno[2,3,-d]pyrimidines disclosed by Yu *et al.*, *European Journal of Med. Chem.*, 95: 116-126, 2015, and the 6'-((6-aminopyrimidin-4-yl)amino)-8'-methyl-2'*H*-spiro[cyclohexane-1,3'-imidazo[1,5-*a*]pyridine]-1',5'-dione and the various compounds disclosed in International Patent Application Publication WO 2015/200481.

[009] Accordingly, while advances have been made in this field there remains a significant need in the art for compounds that specifically inhibit eFI4E activity, particularly with regard to eIF4E's role in regulation of cancer pathways, as well as for associated composition and methods. The present invention fulfils this need and provides further related advantages.

SUMMARY

[010] The present invention is directed to compounds that inhibit or modulate the activity of eIF4E, as well as stereoisomers, tautomers and pharmaceutically acceptable salts of such compounds. The present invention also is directed to pharmaceutically acceptable compositions containing such compounds and associated methods for treating conditions that would benefit from eIF4E inhibition, such as cancer.

[011] In one embodiment the invention is directed to compounds according to Formula I



(I)

or stereoisomers, tautomers, or pharmaceutically acceptable salts thereof, wherein:

X^1 is CR^2, -C-L^1-Y or N;

X^2, X^5 and X^6 are independently CR^2 or N,

wherein X^5 and X^6 together with 3 or 4 carbon or nitrogen atoms combine to form a 5- or 6-membered cycloalkyl or heterocyclyl,

or when X^2 is CR^2, R^1 and R^2 together with the atoms they attached to form a 6-membered aryl or heteroaryl;

X^3 is C, or X^3 is C or N when X^4 is a bond;

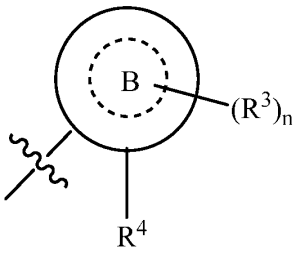
X^4 is a bond, CR^2 or N,

wherein X^4 and X^5 together with 3 or 4 carbon or nitrogen atoms combine to form a 5- or 6-membered heteroaryl;

Q is H or $–L^1$-Y;

L^1 is $–(CH_2)–$, $–(CH_2)_2–$, $–(CH_2)_3–$, $–CH((C_1\text{-}C_8)alkyl)(CH_2)–$, $–CH((C_1\text{-}C_8)alkyl)(CH_2)_2–$, $–(CH_2)_2\text{-}O–$, $–CH_2CH=CH–$, $–CH_2C\equiv C–$ or $–CH_2$(cyclopropyl)–;

Y is



, wherein

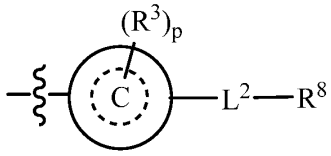
Ring B is a six-membered aryl, heteroaryl or heterocyclyl;

R^1 is H, OH, halo, CN, $(C_1$-$C_8)$alkyl, $(C_1$-$C_8)$haloalkyl, $(C_3$-$C_6)$cycloalkyl or NR^5R^5;

R^2 is independently H, halo, CN, NO, NO_2, C≡H, $(C_1$-$C_8)$alkyl, $(C_1$-$C_8)$haloalkyl, CH_2SR^5, OR^5, NHR^5, NR^5R^5, $[(C_1$-$C_8)$alkylene]heterocyclyl, $[(C_1$-$C_8)$alkylene]heteroaryl, $[(C_1$-$C_8)$alkylene]NHR^5, $[(C_1$-$C_8)$alkylene]NR^5R^5, $[(C_1$-$C_8)$alkylyne]NR^5R^5, $C(O)R^5$, $C(O)OR^5$, $C(O)NHR^5$, $C(O)NR^5R^5$, SR^5, $S(O)R^5$, SO_2R^5, SO_2NHR^5, $SO_2NR^5R^5$, $NH(CO)R^6$, $NR^5(CO)R^6$, aryl, heteroaryl, cycloalkyl or heterocyclyl;

R^3 is independently OH, halo, CN, NO_2, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$haloalkyl, $(C_1$-$C_6)$alkoxy, C≡H, NHR^7, NR^7R^7, CO_2H, CO_2R^7, $[(C_1$-$C_3)$alkylene] $(C_1$-$C_3)$alkoxy, $[(C_1$-$C_3)$alkylene]CO_2H, $(C_3$-$C_5)$cycloalkyl, =O. =S, SR^7, SO_2R^7, $NH(CO)R^7$ or $NR^7(CO)R^7$;

R^4 is H, OH, halo, CN, $(C_1$-$C_3)$alkyl, $(C_1$-$C_3)$haloalkyl, $(C_1$-$C_3)$alkoxy, SR^7 or Z, wherein Z is



;

Ring C is cycloalkyl, heterocyclyl, aryl or heteroaryl;

L^2 is $-C(R^6)(R^6)-$, $-C(R^6)(R^6)C(R^6)(R^6)-$, $-C(R^6)=C(R^6)-$, $-N(R^5)C(R^6)(R^6)-$, $-OC(R^6)(R^6)-$, -C(=O)-, $-C(=O)N(R^5)C(R^6)(R^6)-$ or a bond;

R^5 is independently H, $(C_1$-$C_3)$alkyl, $(C_1$-$C_3)$haloalkyl, $(C_3$-$C_5)$cycloalkyl, CO_2H, $[(C_1$-$C_3)$alkylene]heteroaryl, $[(C_1$-$C_3)$alkylene]aryl, $[(C_1$-$C_3)$alkylene]CO_2H, heterocyclyl, aryl or heteroaryl,

or wherein two R^5 substituents together with a nitrogen atom form a 4-, 5-, 6- or 7-membered heterocyclyl;

R^6 is independently H, OH, halo, CN, $(C_1$-$C_3)$alkyl, $(C_1$-$C_3)$haloalkyl, $(C_1$-$C_3)$alkoxy, NHR^7, NR^7R^7, CO_2H, $[(C_1$-$C_3)$alkylene]CO_2H, $(C_3$-$C_5)$cycloalkyl, SR^7, $NH(CO)R^7$ or $NR^7(CO)R^7$;

R^7 is independently H, $(C_1$-$C_8)$alkyl, $(C_1$-$C_8)$haloalkyl, cycloalkyl, heterocyclyl, aryl or heteroaryl;

R^8 is H, OH, CO_2H, CO_2R^7, $CF_2C(R^6)_2OH$, $C(R^6)_2OH$, $C(CF_3)_2OH$, SO_2H, SO_3H, $CF_2SO_2C(R^6)_3$, $CF_2SO_2N(H)R^5$, $SO_2N(H)R^5$, $SO_2N(H)C(O)R^6$, $C(O)N(H)SO_2R^5$, C(O)haloalkyl, $C(O)N(H)OR^5$, $C(O)N(R^5)OH$, $C(O)N(H)R^5$, $C(O)NR^5C(O)N(R^5)_2$, $P(O)(OR^5)OH$, $P(O)(O)N(H)R^5$, $P(O)(C(R^6)_3)C(R^6)_3$, $B(OH)_2$, heterocyclyl or heteroaryl;

n is 0, 1, 2 or 3;

p is 0, 1, 2 or 3;

wherein any alkyl, alkylene, cycloalkyl, heterocyclyl, heteroaryl or aryl is optionally substituted with 1, 2 or 3 groups selected from OH, CN, SH, SCH_3, SO_2CH_3, SO_2NH_2, $SO_2NH(C_1\text{-}C_4)$alkyl, halogen, NH_2, $NH(C_1\text{-}C_4)$alkyl, $N[(C_1\text{-}C_4)alkyl]_2$, NH(aryl), $C(O)NH_2$, C(O)NH(alkyl), $CH_2C(O)NH$(alkyl), COOH, COOMe, acetyl, $(C_1\text{-}C_8)$alkyl, $(C_1\text{-}C_8)$haloalkyl, $O(C_1\text{-}C_8)$alkyl, $O(C_1\text{-}C_8)$haloalkyl, $(C_2\text{-}C_8)$alkenyl, $(C_2\text{-}C_8)$alkynyl, thioalkyl, cyanomethylene, alkylaminyl, alkylene-$C(O)NH_2$, alkylene-C(O)-NH(Me), NHC(O)alkyl, CH_2-C(O)-$(C_1\text{-}C_8)$alkyl, C(O)-$(C_1\text{-}C_8)$alkyl and alkylcarbonylaminyl, or a cycloalkyl, heterocyclyl, aryl or heteroaryl optionally substituted with OH, halogen, $(C_1\text{-}C_8)$alkyl, $(C_1\text{-}C_8)$haloalkyl, $O(C_1\text{-}C_8)$alkyl or $O(C_1\text{-}C_8)$haloalkyl,

wherein when X^4 is a bond ring A forms a 5-membered heteroaryl wherein X^1, X^5 and X^6 can in addition to the above defined substituents be NR^2, and X^1 can in addition be -N-L^1-Y; and

wherein either Q is $-L^1$-Y, or X^1 is -C-L^1-Y or -N-L^1-Y.

[012] The present invention also provides a pharmaceutical composition comprising (i) a therapeutically effective amount of at least one compound according to Formula I, Formula II, Formula III, Formula IV, Formula V, or Formula VI or a stereoisomer, a tautomer or a pharmaceutically acceptable salt thereof; (ii) in combination with a pharmaceutically acceptable carrier, diluent or excipient.

[013] Also provided by the present invention is a method for attenuating or inhibiting the activity of eIF4E in at least one cell overexpressing eIF4E, comprising contacting the at least one cell with a compound according to Formula I or a stereoisomer, tautomer or pharmaceutically acceptable salt thereof.

[014] According to the inventive method at least one cell is a colon cancer cell, a gastric cancer cell, a thyroid cancer cell, a lung cancer cell, a leukemia cell, a B-cell lymphoma, a T-cell lymphoma, a hairy cell lymphoma, Hodgkin's lymphoma cell, non-Hodgkin's lymphoma cell, Burkitt's lymphoma cell, a pancreatic cancer cell, a melanoma cell, a multiple melanoma cell, a brain cancer cell, a CNS cancer cell, a renal cancer cell, a prostate cancer cell, an ovarian cancer cell, or a breast cancer cell.

[015] According to yet another embodiment the invention provides a method for treating a eIF4E dependent condition in a mammal in need thereof comprising administering to the mammal (i) a therapeutically effective amount of at least one compound according to Formula I, Formula II, Formula III, Formula IV, Formula V, or Formula VI or a stereoisomer, tautomer or

pharmaceutically acceptable salt thereof, or (ii) a pharmaceutical composition in accordance with the invention.

[016] Compounds and pharmaceutically acceptable formulations in accordance with the invention are useful for treating an eIF4E dependent condition such as colon cancer, gastric cancer, thyroid cancer, lung cancer, leukemia, B-cell lymphoma, T-cell lymphoma, hairy cell lymphoma, Hodgkin's lymphoma, non-Hodgkin's lymphoma, Burkitt's lymphoma, pancreatic cancer, melanoma, multiple melanoma, brain cancer, CNS cancer, renal cancer, prostate cancer, ovarian cancer, or breast cancer.

[017] The above embodiments and other aspects of the invention are readily apparent in the detailed description that follows. Various references are set forth herein which describe in more detail certain background information, procedures, compounds and/or compositions, and are each hereby incorporated by reference in their entirety.

BRIEF DESCRIPTION OF THE DRAWINGS

[018] Figure 1, graph showing the results of a cell proliferation assay using compound 1188.

[019] Figure 2, graph showing the results of a cell proliferation assay using compound 634.

[020] Figure 3, graph showing the results of a cell proliferation assay using compound 1141.

DETAILED DESCRIPTION

[021] In the following description certain specific details are set forth in order to provide a thorough understanding of various embodiments of the invention. However, one skilled in the art will understand that the invention may be practiced without these details. Unless the context requires otherwise, throughout the present specification and claims, the word "comprise" and variations thereof, such as, "comprises" and "comprising" are to be construed in an open, inclusive sense (*i.e.*, as "including, but not limited to").

[022] Reference throughout this specification to "one embodiment" or "an embodiment" means that a particular feature, structure or characteristic described in connection with the embodiment is included in at least one embodiment of the present invention. Thus, the appearances of the phrases "in one embodiment" or "in an embodiment" in various places throughout this specification are not necessarily all referring to the same embodiment. Furthermore, the particular features, structures, or characteristics may be combined in any suitable manner in one or more embodiments.

Definitions

[023] As used herein, and unless noted to the contrary, the following terms and phrases have the meaning noted below.

[024] "Amino" refers to the -NH_2 substituent.

[025] "Aminocarbonyl" refers to the –$C(O)NH_2$ substituent.

[026] "Carboxyl" refers to the –CO_2H substituent.

[027] "Carbonyl" refers to a –C(O)–, –(CO)– or –C(=O)– group. All notations are used interchangeably within the specification.

[028] "Cyano" refers to the –C≡N substituent.

[029] "Cyanoalkylene" refers to the -(alkylene)C≡N substituent.

[030] "Acetyl" refers to the –$C(O)CH_3$ substituent.

[031] "Hydroxy" or "hydroxyl" refers to the -OH substituent.

[032] "Hydroxyalkylene" refers to the -(alkylene)OH substituent.

[033] "Oxo" refers to a =O substituent.

[034] "Thio" or "thiol" refer to a –SH substituent.

[035] "Alkyl" refers to a saturated, straight or branched hydrocarbon chain radical consisting solely of carbon and hydrogen atoms, having from one to twelve carbon atoms (C_1-C_{12} alkyl), from one to eight carbon atoms (C_1-C_8 alkyl) or from one to six carbon atoms (C_1-C_6 alkyl), and which is attached to the rest of the molecule by a single bond. Exemplary alkyl groups include methyl, ethyl, n-propyl, 1-methylethyl (iso-propyl), n-butyl, n-pentyl, 1,1-dimethylethyl (t-butyl), 3-methylhexyl, 2-methylhexyl, and the like.

[036] "Lower alkyl" has the same meaning as alkyl defined above but having from one to four carbon atoms (C_1-C_4 alkyl).

[037] "Alkenyl" refers to an unsaturated alkyl group having at least one double bond and from two to twelve carbon atoms (C_2-C_{12} alkenyl), from two to eight carbon atoms (C_2-C_8 alkenyl) or from two to six carbon atoms (C_2-C_6 alkenyl), and which is attached to the rest of the molecule by a single bond, e.g., ethenyl, propenyl, butenyl, pentenyl, hexenyl, and the like.

[038] "Alkynyl" refers to an unsaturated alkyl group having at least one triple bond and from two to twelve carbon atoms (C_2-C_{12} alkynyl), from two to ten carbon atoms (C_2-C_{10} alkynyl)from two to eight carbon atoms (C_2-C_8 alkynyl) or from two to six carbon atoms (C_2-C_6 alkynyl), and which is attached to the rest of the molecule by a single bond, e.g., ethynyl, propynyl, butynyl, pentynyl, hexynyl, and the like.

[039] "Alkylene" or "alkylene chain" refers to a straight or branched divalent hydrocarbon (alkyl) chain linking the rest of the molecule to a radical group, consisting solely of carbon and hydrogen, respectively. Alkylenes can have from one to twelve carbon atoms, e.g., methylene, ethylene, propylene, n-butylene, and the like. The alkylene chain is attached to the rest of the molecule through a single or double bond. The points of attachment of the alkylene chain to the rest of the molecule can be through one carbon or any two carbons within the chain. "Optionally substituted alkylene" refers to alkylene or substituted alkylene.

[040] "Alkenylene" refers to divalent alkene. Examples of alkenylene include without limitation, ethenylene (-CH=CH-) and all stereoisomeric and conformational isomeric forms thereof. "Substituted alkenylene" refers to divalent substituted alkene. "Optionally substituted alkenylene" refers to alkenylene or substituted alkenylene.

[041] "Alkynylene" refers to divalent alkyne. Examples of alkynylene include without limitation, ethynylene, propynylene. "Substituted alkynylene" refers to divalent substituted alkyne.

[042] "Alkoxy" refers to a radical of the formula $-OR_a$ where R_a is an alkyl having the indicated number of carbon atoms as defined above. Examples of alkoxy groups include without limitation –O-methyl (methoxy), -O-ethyl (ethoxy), -O-propyl (propoxy), -O-isopropyl (iso propoxy) and the like.

[043] "Alkylaminyl" refers to a radical of the formula $-NHR_a$ or $-NR_aR_a$ where each R_a is, independently, an alkyl radical having the indicated number of carbon atoms as defined above.

[044] "Cycloalkylaminyl" refers to a radical of the formula $-NHR_a$ or $-NR_aR_a$ where R_a is a cycloalkyl radical as defined herein.

[045] "Alkylcarbonylaminyl" refers to a radical of the formula $-NHC(O)R_a$ or $-NR_aC(O)R_a$, where R_a is an alkyl radical having the indicated number of carbon atoms as defined herein.

[046] "Cycloalkylcarbonylaminyl" refers to a radical of the formula $-NHC(O)R_a$ or $-NR_aC(O)R_a$ where R_a is a cycloalkyl radical as defined herein.

[047] "Alkylaminocarbonyl" refers to a radical of the formula $-C(O)NHR_a$ or $-C(O)NR_aR_a$, where each R_a is independently, an alkyl radical having the indicated number of carbon atoms as defined herein.

[048] "Cyclolkylaminocarbonyl" refers to a radical of the formula $-C(O)NHR_a$, where R_a is a cycloalkyl radical as defined herein.

[049] "Aryl" refers to a hydrocarbon ring system radical comprising hydrogen, 6 to 18 carbon atoms and at least one aromatic ring. Exemplary aryls are hydrocarbon ring system radical comprising hydrogen and 6 to 9 carbon atoms and at least one aromatic ring; hydrocarbon ring system radical comprising hydrogen and 9 to 12 carbon atoms and at least one aromatic ring; hydrocarbon ring system radical comprising hydrogen and 12 to 15 carbon atoms and at least one aromatic ring; or hydrocarbon ring system radical comprising hydrogen and 15 to 18 carbon atoms and at least one aromatic ring. For purposes of this invention, the aryl radical may be a monocyclic, bicyclic, tricyclic or tetracyclic ring system, which may include fused or bridged ring systems. Aryl radicals include, but are not limited to, aryl radicals derived from aceanthrylene, acenaphthylene, acephenanthrylene, anthracene, azulene, benzene, chrysene, fluoranthene, fluorene, as-indacene, s-indacene, indane, indene, naphthalene, phenalene, phenanthrene, pleiadene, pyrene, and triphenylene. "Optionally substituted aryl" refers to an aryl group or a substituted aryl group.

[050] "Arylene" denotes divalent aryl, and "substituted arylene" refers to divalent substituted aryl.

[051] "Aralkyl" or "araalkylene" may be used interchangeably and refer to a radical of the formula $-R_b-R_c$ where R_b is an alkylene chain as defined herein and R_c is one or more aryl radicals as defined herein, for example, benzyl, diphenylmethyl and the like.

[052] "Cycloalkyl" refers to a stable non-aromatic monocyclic or polycyclic hydrocarbon radical consisting solely of carbon and hydrogen atoms, which may include fused or bridged ring systems, having from three to fifteen carbon atoms, preferably having from three to ten carbon atoms, three to nine carbon atoms, three to eight carbon atoms, three to seven carbon atoms, three to six carbon atoms, three to five carbon atoms, a ring with four carbon atoms, or a ring with three carbon atoms. The cycloalkyl ring may be saturated or unsaturated and attached to the rest of the molecule by a single bond. Monocyclic radicals include, for example, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, and cyclooctyl. Polycyclic radicals include, for example, adamantyl, norbornyl, decalinyl, 7,7-dimethyl-bicyclo[2.2.1]heptanyl, and the like.

[053] "Cycloalkylalkylene" or "cycloalkylalkyl" may be used interchangeably and refer to a radical of the formula $-R_bR_e$ where R_b is an alkylene chain as defined herein and R_e is a cycloalkyl radical as defined herein. In certain embodiments, R_b is further substituted with a cycloalkyl group, such that the cycloalkylalkylene comprises two cycloalkyl moieties. Cyclopropylalkylene and cyclobutylalkylene are exemplary cycloalkylalkylene groups, comprising at least one cyclopropyl or at least one cyclobutyl group, respectively.

[054] "Fused" refers to any ring structure described herein which is fused to an existing ring structure in the compounds of the invention. When the fused ring is a heterocyclyl ring or a heteroaryl ring, any carbon atom on the existing ring structure which becomes part of the fused heterocyclyl ring or the fused heteroaryl ring may be replaced with a nitrogen atom.

[055] "Halo" or "halogen" refers to bromo (bromine), chloro (chlorine), fluoro (fluorine), or iodo (iodine).

[056] "Haloalkyl" refers to an alkyl radical having the indicated number of carbon atoms, as defined herein, wherein one or more hydrogen atoms of the alkyl group are substituted with a halogen (halo radicals), as defined above. The halogen atoms can be the same or different. Exemplary haloalkyls are trifluoromethyl, difluoromethyl, trichloromethyl, 2,2,2-trifluoroethyl, 1,2-difluoroethyl, 3-bromo-2-fluoropropyl, 1,2-dibromoethyl, and the like.

[057] "Heterocyclyl", heterocycle", or "heterocyclic ring" refers to a stable 3- to 18-membered saturated or unsaturated radical which consists of two to twelve carbon atoms and from one to six heteroatoms, for example, one to five heteroatoms, one to four heteroatoms, one to three heteroatoms, or one to two heteroatoms selected from the group consisting of nitrogen, oxygen and sulfur. Exemplary heterocycles include without limitation stable 3-15 membered saturated or unsaturated radicals, stable 3-12 membered saturated or unsaturated radicals, stable 3-9 membered saturated or unsaturated radicals, stable 8-membered saturated or unsaturated radicals, stable 7-membered saturated or unsaturated radicals, stable 6-membered saturated or unsaturated radicals, or stable 5-membered saturated or unsaturated radicals.

[058] Unless stated otherwise specifically in the specification, the heterocyclyl radical may be a monocyclic, bicyclic, tricyclic or tetracyclic ring system, which may include fused, bridged or spiro ring systems; and the nitrogen, carbon or sulfur atoms in the heterocyclyl radical may be optionally oxidized; the nitrogen atom may be optionally quaternized; and the heterocyclyl radical may be partially or fully saturated. Examples of non-aromatic heterocyclyl radicals include, but are not limited to, oxirane, oxetane, azetidinyl, dioxolanyl, thienyl[1,3]dithianyl, decahydroisoquinolyl, imidazolinyl, imidazolidinyl, isothiazolidinyl, isoxazolidinyl, morpholinyl, octahydroindolyl, octahydroisoindolyl, 2-oxopiperazinyl, 2-oxopiperidinyl, 2-oxopyrrolidinyl, oxazolidinyl, piperidinyl, piperazinyl, 4-piperidonyl, pyrrolidinyl, pyrazolidinyl, quinuclidinyl, thiazolidinyl, tetrahydrofuryl, thietanyl, trithianyl, tetrahydropyranyl, thiomorpholinyl, thiamorpholinyl, 1-oxo-thiomorpholinyl, and 1,1-dioxo-thiomorpholinyl. Heterocyclyls include heteroaryls as defined herein, and examples of aromatic heterocyclyls are listed in the definition of heteroaryls below.

[059] "Heterocyclylalkyl" or "heterocyclylalkylene" refers to a radical of the formula -R_bR_f where R_b is an alkylene chain as defined herein and R_f is a heterocyclyl radical as defined above, and if the heterocyclyl is a nitrogen-containing heterocyclyl, the heterocyclyl may be attached to the alkyl radical at the nitrogen atom.

[060] "Heteroaryl" or "heteroarylene" refers to a 5- to 14-membered ring system radical comprising hydrogen atoms, one to thirteen carbon atoms, one to six heteroatoms selected from the group consisting of nitrogen, oxygen and sulfur, and at least one aromatic ring. For purposes of this invention, the heteroaryl radical may be a stable 5-12 membered ring, a stable 5-10 membered ring, a stable 5-9 membered ring, a stable 5-8 membered ring, a stable 5-7 membered ring, or a stable 6 membered ring that comprises at least 1 heteroatom, at least 2 heteroatoms, at least 3 heteroatoms, at least 4 heteroatoms, at least 5 heteroatoms or at least 6 heteroatoms. Heteroaryls may be a monocyclic, bicyclic, tricyclic or tetracyclic ring system, which may include fused or bridged ring systems; and the nitrogen, carbon or sulfur atoms in the heteroaryl radical may be optionally oxidized; the nitrogen atom may be optionally quaternized. The heteroatom may be a member of an aromatic or non-aromatic ring, provided at least one ring in the heteroaryl is aromatic. Examples include, but are not limited to, azepinyl, acridinyl, benzimidazolyl, benzothiazolyl, benzindolyl, benzodioxolyl, benzofuranyl, benzooxazolyl, benzothiazolyl, benzothiadiazolyl, benzo[b][1,4]dioxepinyl, 1,4-benzodioxanyl, benzonaphthofuranyl, benzoxazolyl, benzodioxolyl, benzodioxinyl, benzopyranyl, benzopyranonyl, benzofuranyl, benzofuranonyl, benzothienyl (benzothiophenyl), benzotriazolyl, benzo[4,6]imidazo[1,2-a]pyridinyl, carbazolyl, cinnolinyl, dibenzofuranyl, dibenzothiophenyl, furanyl, furanonyl, isothiazolyl, imidazolyl, indazolyl, indolyl, indazolyl, isoindolyl, indolinyl, isoindolinyl, isoquinolyl, indolizinyl, isoxazolyl, naphthyridinyl, oxadiazolyl, 2-oxoazepinyl, oxazolyl, oxiranyl, 1-oxidopyridinyl, 1-oxidopyrimidinyl, 1-oxidopyrazinyl, 1-oxidopyridazinyl, 1-phenyl-1H-pyrrolyl, phenazinyl, phenothiazinyl, phenoxazinyl, phthalazinyl, pteridinyl, purinyl, pyrrolyl, pyrazolyl, pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, quinazolinyl, quinoxalinyl, quinolinyl, quinuclidinyl, isoquinolinyl, tetrahydroquinolinyl, thiazolyl, thiadiazolyl, triazolyl, tetrazolyl, triazinyl, and thiophenyl (i.e. thienyl).

[061] "Heteroarylalkyl" or "heteroarylalkylene" refers to a radical of the formula -R_bR_g where R_b is an alkylene chain as defined above and R_g is a heteroaryl radical as defined above.

[062] "Thioalkyl" refers to a radical of the formula -SR_a where R_a is an alkyl radical as defined above containing one to twelve carbon atoms, at least 1-10 carbon atoms, at least 1-8 carbon atoms, at least 1-6 carbon atoms, or at least 1-4 carbon atoms.

[063] "Heterocyclylaminyl" refers to a radical of the formula $–NHR_f$ where R_f is a heterocyclyl radical as defined above.

[064] "Thione" refers to a =S group attached to a carbon atom of a saturated or unsaturated (C_3-C_8)cyclic or a (C_1-C_8)acyclic moiety.

[065] "Sulfoxide" refers to a –S(O)- group in which the sulfur atom is covalently attached to two carbon atoms.

[066] "Sulfone" refers to a $–S(O)_2–$ or $–(SO_2)–$ group in which a hexavalent sulfur is attached to each of the two oxygen atoms through double bonds and is further attached to two carbon atoms through single covalent bonds.

[067] The term "oxime" refers to a $–C(R_a)=N-OR_a$ radical where R_a is hydrogen, lower alkyl, an alkylene or arylene group as defined above.

[068] The compound of the invention can exist in various isomeric forms, as well as in one or more tautomeric forms, including both single tautomers and mixtures of tautomers. The term "isomer" is intended to encompass all isomeric forms of a compound of this invention, including tautomeric forms of the compound.

[069] Some compounds described here can have asymmetric centers and therefore exist in different enantiomeric and diastereomeric forms. A compound of the invention can be in the form of an optical isomer or a diastereomer. Accordingly, the invention encompasses compounds of the invention and their uses as described herein in the form of their optical isomers, diastereoisomers and mixtures thereof, including a racemic mixture. Optical isomers of the compounds of the invention can be obtained by known techniques such as asymmetric synthesis, chiral chromatography, or via chemical separation of stereoisomers through the employment of optically active resolving agents.

[070] Unless otherwise indicated "stereoisomer" means one stereoisomer of a compound that is substantially free of other stereoisomers of that compound. Thus, a stereomerically pure compound having one chiral center will be substantially free of the opposite enantiomer of the compound. A stereomerically pure compound having two chiral centers will be substantially free of other diastereomers of the compound. A typical stereomerically pure compound comprises greater than about 80% by weight of one stereoisomer of the compound and less than about 20% by weight of other stereoisomers of the compound, for example greater than about 90% by weight of one stereoisomer of the compound and less than about 10% by weight of the other stereoisomers of the compound, or greater than about 95% by weight of one stereoisomer of the compound and less than about 5% by weight of the other stereoisomers of the compound, or

greater than about 97% by weight of one stereoisomer of the compound and less than about 3% by weight of the other stereoisomers of the compound.

[071] If there is a discrepancy between a depicted structure and a name given to that structure, then the depicted structure controls. Additionally, if the stereochemistry of a structure or a portion of a structure is not indicated with, for example, bold or dashed lines, the structure or portion of the structure is to be interpreted as encompassing all stereoisomers of it. In some cases, however, where more than one chiral center exists, the structures and names may be represented as single enantiomers to help describe the relative stereochemistry. Those skilled in the art of organic synthesis will know if the compounds are prepared as single enantiomers from the methods used to prepare them.

[072] In this description a "pharmaceutically acceptable salt" is a pharmaceutically acceptable, organic or inorganic acid or base salt of a compound of the invention. Representative pharmaceutically acceptable salts include, e.g., alkali metal salts, alkali earth salts, ammonium salts, water-soluble and water-insoluble salts, such as the acetate, amsonate (4,4-diaminostilbene-2,2-disulfonate), benzenesulfonate, benzonate, bicarbonate, bisulfate, bitartrate, borate, bromide, butyrate, calcium, calcium edetate, camsylate, carbonate, chloride, citrate, clavulariate, dihydrochloride, edetate, edisylate, estolate, esylate, fiunarate, gluceptate, gluconate, glutamate, glycollylarsanilate, hexafluorophosphate, hexylresorcinate, hydrabamine, hydrobromide, hydrochloride, hydroxynaphthoate, iodide, isothionate, lactate, lactobionate, laurate, malate, maleate, mandelate, mesylate, methylbromide, methylnitrate, methylsulfate, mucate, napsylate, nitrate, N-methylglucamine ammonium salt, 3-hydroxy-2-naphthoate, oleate, oxalate, palmitate, pamoate (1,1-methene-bis-2-hydroxy-3-naphthoate, einbonate), pantothenate, phosphate/diphosphate, picrate, polygalacturonate, propionate, p-toluenesulfonate, salicylate, stearate, subacetate, succinate, sulfate, sulfosaliculate, suramate, tannate, tartrate, teoclate, tosylate, triethiodide, and valerate salts. A pharmaceutically acceptable salt can have more than one charged atom in its structure. In this instance the pharmaceutically acceptable salt can have multiple counterions. Thus, a pharmaceutically acceptable salt can have one or more charged atoms and/or one or more counterions.

[073] The terms "treat", "treating" and "treatment" refer to the amelioration or eradication of a disease or symptoms associated with a disease. In certain embodiments, such terms refer to minimizing the spread or worsening of the disease resulting from the administration of one or more prophylactic or therapeutic agents to a patient with such a disease. In the context of the present invention the terms "treat", "treating" and "treatment" also refer to:

(i) preventing the disease or condition from occurring in a mammal, in particular, when such mammal is predisposed to the condition but has not yet been diagnosed as having it;

(ii) inhibiting the disease or condition, i.e., arresting its development;

(iii) relieving the disease or condition, i.e., causing regression of the disease or condition; or

(iv) relieving the symptoms resulting from the disease or condition, i.e., relieving pain without addressing the underlying disease or condition. As used herein, the terms “disease” and “condition” may be used interchangeably or may be different in that the particular malady or condition may not have a known causative agent (so that etiology has not yet been worked out) and it is therefore not yet recognized as a disease but only as an undesirable condition or syndrome, wherein a more or less specific set of symptoms have been identified by clinicians.

[074] The term “effective amount” refers to an amount of a compound of the invention or other active ingredient sufficient to provide a therapeutic or prophylactic benefit in the treatment or prevention of a disease or to delay or minimize symptoms associated with a disease. Further, a therapeutically effective amount with respect to a compound of the invention means that amount of therapeutic agent alone, or in combination with other therapies, that provides a therapeutic benefit in the treatment or prevention of a disease. Used in connection with a compound of the invention, the term can encompass an amount that improves overall therapy, reduces or avoids symptoms or causes of disease, or enhances the therapeutic efficacy or synergies with another therapeutic agent.

[075] The term "inhibit" or "inhibitor" refers to an alteration, interference, reduction, down regulation, blocking, suppression, abrogation or degradation, directly or indirectly, in the expression, amount or activity of a target gene, target protein, or signaling pathway relative to (1) a control, endogenous or reference target or pathway, or (2) the absence of a target or pathway, wherein the alteration, interference, reduction, down regulation, blocking, suppression, abrogation or degradation is statistically, biologically, or clinically significant. The term "inhibit" or "inhibitor" includes gene "knock out" and gene "knock down" methods, such as by chromosomal editing.

[076] The terms “modulate”, “modulation” and the like refer to the ability of a compound to increase or decrease the function, or activity of, for example, eukaryotic initiation factor 4E (eIF4E). “Modulation”, in its various forms, is intended to encompass inhibition, antagonism, partial antagonism, activation, agonism and/or partial agonism of the activity associated with eIF4E. eIF4E inhibitors are compounds that bind to, partially or totally block stimulation, decrease, prevent, delay activation, inactivate, desensitize, or down regulate signal transduction.

The ability of a compound to modulate eIF4E activity can be demonstrated in an enzymatic assay or a cell-based assay.

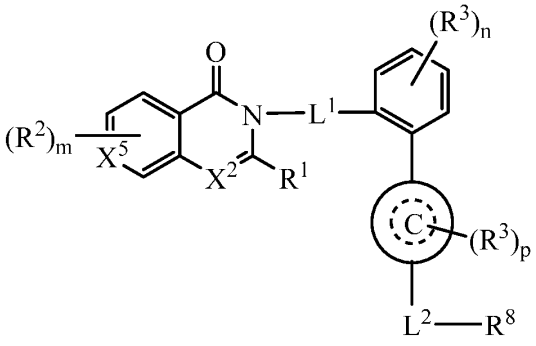
[077] A "patient" or subject" includes an animal, such as a human, cow, horse, sheep, lamb, pig, chicken, turkey, quail, cat, dog, mouse, rat, rabbit or guinea pig. The animal can be a mammal such as a non-primate and a primate (e.g., monkey and human). In one embodiment, a patient is a human, such as a human infant, child, adolescent or adult.

[078] The term "prodrug" refers to a precursor of a drug, a compound which upon administration to a patient, must undergo chemical conversion by metabolic processes before becoming an active pharmacological agent. Exemplary prodrugs of compounds in accordance with Formula I are esters, acetamides, and amides.

Compounds of the Invention

[079] The present invention generally is directed to compounds encompassed by the genus of Formula I, or stereoisomers, tautomers or pharmaceutically acceptable salts thereof.

[080] In one embodiment, the invention is directed to compounds according to Formula II



(II),

or stereoisomers, tautomers, or pharmaceutically acceptable salts thereof, wherein:

X^2 and X^5 are independently CR^2 or N,

or when X^2 is CR^2, R^1 and R^2 together with the atoms they attached to form a 6-membered aryl or heteroaryl;

L^1 is $–(CH_2)–$, $–(CH_2)_2–$, $–(CH_2)_3–$, $–CH((C_1\text{-}C_8)alkyl)(CH_2)–$, $–CH((C_1\text{-}C_8)alkyl)(CH_2)_2–$, $–(CH_2)_2\text{-}O–$, $–CH_2CH=CH–$, $–CH_2C\equiv C–$ or $–CH_2(cyclopropyl)–$;

L^2 is $-C(R^6)(R^6)-$, $-C(R^6)(R^6)C(R^6)(R^6)-$, $-C(R^6)=C(R^6)-$, $-N(R^5)C(R^6)(R^6)-$, $-OC(R^6)(R^6)-$, -C(=O)-, $-C(=O)N(R^5)C(R^6)(R^6)-$ or a bond;

Ring C is cycloalkyl, heterocyclyl, aryl or heteroaryl;

R^1 is H, OH, halo, CN, $(C_1\text{-}C_8)$alkyl, $(C_1\text{-}C_8)$haloalkyl, $(C_3\text{-}C_6)$cycloalkyl or NR^5R^5;

R^2 is independently H, halo, CN, NO, NO_2, C≡H, $(C_1\text{-}C_8)$alkyl, $(C_1\text{-}C_8)$haloalkyl, CH_2SR^5, OR^5, NHR^5, NR^5R^5, $[(C_1\text{-}C_8)$alkylene]heterocyclyl, $[(C_1\text{-}C_8)$alkylene]heteroaryl, $[(C_1\text{-}C_8)$alkylene]NHR^5, $[(C_1\text{-}C_8)$alkylene]NR^5R^5, $[(C_1\text{-}C_8)$alkylyne]NR^5R^5, $C(O)R^5$, $C(O)OR^5$, $C(O)NHR^5$, $C(O)NR^5R^5$, SR^5, $S(O)R^5$, SO_2R^5, SO_2NHR^5, $SO_2NR^5R^5$, $NH(CO)R^6$, $NR^5(CO)R^6$, aryl, heteroaryl, cycloalkyl or heterocyclyl;

R^3 is independently OH, halo, CN, NO_2, $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$haloalkyl, $(C_1\text{-}C_6)$alkoxy, C≡H, NHR^7, NR^7R^7, CO_2H, CO_2R^7, $[(C_1\text{-}C_3)$alkylene] $(C_1\text{-}C_3)$alkoxy, $[(C_1\text{-}C_3)$alkylene]CO_2H, $(C_3\text{-}C_5)$cycloalkyl, =O. =S, SR^7, SO_2R^7, $NH(CO)R^7$ or $NR^7(CO)R^7$;

R^5 is independently H, $(C_1\text{-}C_3)$alkyl, $(C_1\text{-}C_3)$haloalkyl, $(C_3\text{-}C_5)$cycloalkyl, CO_2H, $[(C_1\text{-}C_3)$alkylene]heteroaryl, $[(C_1\text{-}C_3)$alkylene]aryl, $[(C_1\text{-}C_3)$alkylene]CO_2H, heterocyclyl, aryl or heteroaryl,

or wherein two R^5 substituents together with a nitrogen atom form a 4-, 5-, 6-, or 7-membered heterocyclyl;

R^6 is independently H, OH, halo, CN, $(C_1\text{-}C_3)$alkyl, $(C_1\text{-}C_3)$haloalkyl, $(C_1\text{-}C_3)$alkoxy, NHR^7, NR^7R^7, CO_2H, $[(C_1\text{-}C_3)$alkylene]CO_2H, $(C_3\text{-}C_5)$cycloalkyl, SR^7, $NH(CO)R^7$ or $NR^7(CO)R^7$;

R^7 is independently H, $(C_1\text{-}C_8)$alkyl, $(C_1\text{-}C_8)$haloalkyl, cycloalkyl, heterocyclyl, aryl or heteroaryl;

R^8 is H, OH, CO_2H, CO_2R^7, $CF_2C(R^6)_2OH$, $C(R^6)_2OH$, $C(CF_3)_2OH$, SO_2H, SO_3H, $CF_2SO_2C(R^6)_3$, $CF_2SO_2N(H)R^5$, $SO_2N(H)R^5$, $SO_2N(H)C(O)R^6$, $C(O)N(H)SO_2R^5$, C(O)haloalkyl, $C(O)N(H)OR^5$, $C(O)N(R^5)OH$, $C(O)N(H)R^5$, $C(O)NR^5C(O)N(R^5)_2$, $P(O)(OR^5)OH$, $P(O)(O)N(H)R^5$, $P(O)(C(R^6)_3)C(R^6)_3$, $B(OH)_2$, heterocyclyl or heteroaryl;

m is 0, 1, 2 or 3;

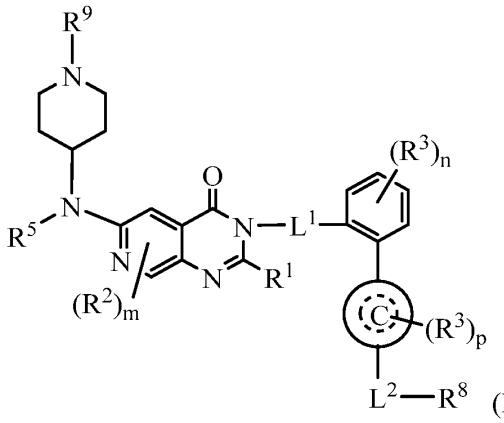
n is 0, 1, 2 or 3;

p is 0, 1, 2 or 3;

wherein any alkyl, alkylene, cycloalkyl, heterocyclyl, heteroaryl or aryl is optionally substituted with 1, 2 or 3 groups selected from OH, CN, SH, SCH_3, SO_2CH_3, SO_2NH_2, $SO_2NH(C_1\text{-}C_4)$alkyl, halogen, NH_2, $NH(C_1\text{-}C_4)$alkyl, $N[(C_1\text{-}C_4)alkyl]_2$, NH(aryl), $C(O)NH_2$, C(O)NH(alkyl), $CH_2C(O)NH(alkyl)$, COOH, COOMe, acetyl, $(C_1\text{-}C_8)$alkyl, $(C_1\text{-}C_8)$haloalkyl, $O(C_1\text{-}C_8)$alkyl, $O(C_1\text{-}C_8)$haloalkyl, $(C_2\text{-}C_8)$alkenyl, $(C_2\text{-}C_8)$alkynyl, thioalkyl, cyanomethylene, alkylaminyl, alkylene-$C(O)NH_2$, alkylene-C(O)-NH(Me), NHC(O)alkyl, CH_2-C(O)-$(C_1\text{-}C_8)$alkyl, C(O)-$(C_1\text{-}C_8)$alkyl and alkylcarbonylaminyl, or a cycloalkyl, heterocyclyl, aryl or

heteroaryl optionally substituted with OH, halogen, (C_1-C_8)alkyl, (C_1-C_8)haloalkyl, O(C_1-C_8)alkyl or O(C_1-C_8)haloalkyl.

[081] In another embodiment the invention is directed to compounds of Formula III



(III),

or stereoisomers, tautomers, or pharmaceutically acceptable salts thereof, wherein:

L^1 is –(CH_2)–, –(CH_2)$_2$–, –(CH_2)$_3$–, –CH((C_1-C_8)alkyl)(CH_2)–, –CH((C_1-C_8)alkyl)(CH_2)$_2$–, –(CH_2)$_2$-O–, –CH_2CH=CH–, –CH_2C≡C– or –CH_2(cyclopropyl)–;

L^2 is -C(R^6)(R^6)-, -C(R^6)(R^6)C(R^6)(R^6)-, -C(R^6)=C(R^6)-, -N(R^5)C(R^6)(R^6)-, -OC(R^6)(R^6)-, -C(=O)-, -C(=O)N(R^5)C(R^6)(R^6)- or a bond;

Ring C is a heteroaryl;

R^1 is H, OH, halo, CN, (C_1-C_8)alkyl, (C_1-C_8)haloalkyl, (C_3-C_6)cycloalkyl or NR^5R^5;

R^2 is independently H, halo, CN, NO, NO_2, C≡H, (C_1-C_8)alkyl, (C_1-C_8)haloalkyl, CH_2SR^5, OR^5, NHR^5, NR^5R^5, [(C_1-C_8)alkylene]heterocyclyl, [(C_1-C_8)alkylene]heteroaryl, [(C_1-C_8)alkylene]NHR^5, [(C_1-C_8)alkylene]NR^5R^5, [(C_1-C_8)alkylyne]NR^5R^5, C(O)R^5, C(O)OR^5, C(O)NHR^5, C(O)NR^5R^5, SR^5, S(O)R^5, SO_2R^5, SO_2NHR^5, $SO_2NR^5R^5$, NH(CO)R^6, NR^5(CO)R^6, aryl, heteroaryl, cycloalkyl or heterocyclyl;

R^3 is independently OH, halo, CN, NO_2, (C_1-C_6)alkyl, (C_1-C_6)haloalkyl, (C_1-C_6)alkoxy, C≡H, NHR^7, NR^7R^7, CO_2H, CO_2R^7, [(C_1-C_3)alkylene] (C_1-C_3)alkoxy, [(C_1-C_3)alkylene]CO_2H, (C_3-C_5)cycloalkyl, =O. =S, SR^7, SO_2R^7, NH(CO)R^7 or NR^7(CO)R^7;

R^5 is independently H, (C_1-C_3)alkyl, (C_1-C_3)haloalkyl, (C_3-C_5)cycloalkyl or heterocyclyl;

R^6 is independently H, OH, halo, CN, (C_1-C_3)alkyl, (C_1-C_3)haloalkyl, (C_1-C_3)alkoxy, NHR^7, NR^7R^7, CO_2H, [(C_1-C_3)alkylene]CO_2H, (C_3-C_5)cycloalkyl, SR^7, NH(CO)R^7 or NR^7(CO)R^7;

R^7 is independently H, (C_1-C_8)alkyl, (C_1-C_8)haloalkyl, cycloalkyl, heterocyclyl, aryl or heteroaryl;

R^8 is H, OH, CO_2H, CO_2R^7, $CF_2C(R^6)_2OH$, $C(R^6)_2OH$, $C(CF_3)_2OH$, SO_2H, SO_3H, $CF_2SO_2C(R^6)_3$, $CF_2SO_2N(H)R^5$, $SO_2N(H)R^5$, $SO_2N(H)C(O)R^6$, $C(O)N(H)SO_2R^5$, C(O)haloalkyl, $C(O)N(H)OR^5$, $C(O)N(R^5)OH$, $C(O)N(H)R^5$, $C(O)NR^5C(O)N(R^5)_2$, $P(O)(OR^5)OH$, $P(O)(O)N(H)R^5$, $P(O)(C(R^6)_3)C(R^6)_3$, $B(OH)_2$, heterocyclyl or heteroaryl;

R^9 is H, $(C_1\text{-}C_8)$alkyl, $(C_1\text{-}C_8)$haloalkyl, cycloalkyl or heterocyclyl;

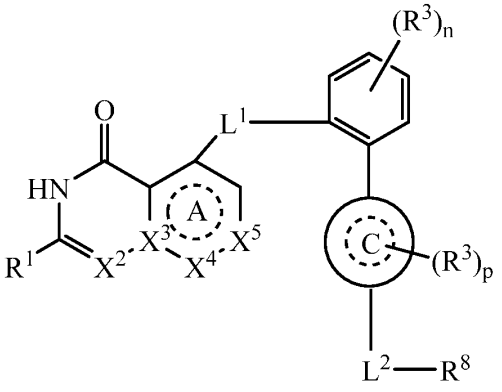
m is 0, 1, or 2;

n is 0, 1, 2 or 3;

p is 0, 1, 2 or 3;

wherein any alkyl, alkylene, cycloalkyl, heterocyclyl, heteroaryl or aryl is optionally substituted with 1, 2 or 3 groups selected from OH, CN, SH, SCH_3, SO_2CH_3, SO_2NH_2, $SO_2NH(C_1\text{-}C_4)$alkyl, halogen, NH_2, $NH(C_1\text{-}C_4)$alkyl, $N[(C_1\text{-}C_4)alkyl]_2$, NH(aryl), $C(O)NH_2$, C(O)NH(alkyl), $CH_2C(O)NH(alkyl)$, COOH, COOMe, acetyl, $(C_1\text{-}C_8)$alkyl, $(C_1\text{-}C_8)$haloalkyl, $O(C_1\text{-}C_8)$alkyl, $O(C_1\text{-}C_8)$haloalkyl, $(C_2\text{-}C_8)$alkenyl, $(C_2\text{-}C_8)$alkynyl, thioalkyl, cyanomethylene, alkylaminyl, alkylene-$C(O)NH_2$, alkylene-C(O)-NH(Me), NHC(O)alkyl, CH_2-C(O)-$(C_1\text{-}C_8)$alkyl, C(O)-$(C_1\text{-}C_8)$alkyl and alkylcarbonylaminyl.

[082] In one embodiment, the invention is directed to compounds according to Formula IV



(IV),

or stereoisomers, tautomers, or pharmaceutically acceptable salts thereof, wherein:

X^2 and X^5 are independently CR^2 or N,

or when X^2 is CR^2, R^1 and R^2 together with the atoms they attached to form a 6-membered aryl or heteroaryl;

X^3 is C, or X^3 is C or N when X^4 is a bond;

X^4 is a bond, CR^2 or N,

wherein X^4 and X^5 together with 3 or 4 carbon or nitrogen atoms combine to form a 5- or 6-membered heteroaryl;

L^1 is $–(CH_2)–$, $–(CH_2)_2–$, $–(CH_2)_3–$, $–CH((C_1\text{-}C_8)alkyl)(CH_2)–$, $–CH((C_1\text{-}C_8)alkyl)(CH_2)_2–$, $–(CH_2)_2\text{-}O–$, $–CH_2CH=CH–$, $–CH_2C\equiv C–$ or $–CH_2(cyclopropyl)–$;

L^2 is $-C(R^6)(R^6)-$, $-C(R^6)(R^6)C(R^6)(R^6)-$, $-C(R^6)=C(R^6)-$, $-N(R^5)C(R^6)(R^6)-$, $-OC(R^6)(R^6)-$, $-C(=O)-$, $-C(=O)N(R^5)C(R^6)(R^6)-$;

Ring C is cycloalkyl, heterocyclyl, aryl or heteroaryl;

R^1 is H, OH, halo, CN, $(C_1\text{-}C_8)$alkyl, $(C_1\text{-}C_8)$haloalkyl, $(C_3\text{-}C_6)$cycloalkyl or NR^5R^5;

R^2 is independently H, halo, CN, NO, NO_2, $C\equiv H$, $(C_1\text{-}C_8)$alkyl, $(C_1\text{-}C_8)$haloalkyl, CH_2SR^5, OR^5, NHR^5, NR^5R^5, $[(C_1\text{-}C_8)alkylene]$heterocyclyl, $[(C_1\text{-}C_8)alkylene]$heteroaryl, $[(C_1\text{-}C_8)alkylene]NHR^5$, $[(C_1\text{-}C_8)alkylene]NR^5R^5$, $[(C_1\text{-}C_8)alkylyne]NR^5R^5$, $C(O)R^5$, $C(O)OR^5$, $C(O)NHR^5$, $C(O)NR^5R^5$, SR^5, $S(O)R^5$, SO_2R^5, SO_2NHR^5, $SO_2NR^5R^5$, $NH(CO)R^6$, $NR^5(CO)R^6$, aryl, heteroaryl, cycloalkyl or heterocyclyl;

R^3 is independently OH, halo, CN, NO_2, $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$haloalkyl, $(C_1\text{-}C_6)$alkoxy, $C\equiv H$, NHR^7, NR^7R^7, CO_2H, CO_2R^7, $[(C_1\text{-}C_3)alkylene]$ $(C_1\text{-}C_3)$alkoxy, $[(C_1\text{-}C_3)alkylene]CO_2H$, $(C_3\text{-}C_5)$cycloalkyl, =O. =S, SR^7, SO_2R^7, $NH(CO)R^7$ or $NR^7(CO)R^7$;

R^5 is independently H, $(C_1\text{-}C_3)$alkyl, $(C_1\text{-}C_3)$haloalkyl, $(C_3\text{-}C_5)$cycloalkyl, CO_2H, $[(C_1\text{-}C_3)alkylene]$heteroaryl, $[(C_1\text{-}C_3)alkylene]$aryl, $[(C_1\text{-}C_3)alkylene]CO_2H$, heterocyclyl, aryl or heteroaryl,

or wherein two R^5 substituents together with a nitrogen atom form a 4-, 5-, 6- or 7-membered heterocyclyl;

R^6 is independently H, OH, halo, CN, $(C_1\text{-}C_3)$alkyl, $(C_1\text{-}C_3)$haloalkyl, $(C_1\text{-}C_3)$alkoxy, NHR^7, NR^7R^7, CO_2H, $[(C_1\text{-}C_3)alkylene]CO_2H$, $(C_3\text{-}C_5)$cycloalkyl, SR^7, $NH(CO)R^7$ or $NR^7(CO)R^7$;

R^7 is independently H, $(C_1\text{-}C_8)$alkyl, $(C_1\text{-}C_8)$haloalkyl, cycloalkyl, heterocyclyl, aryl or heteroaryl;

R^8 is H, OH, CO_2H, CO_2R^7, $CF_2C(R^6)_2OH$, $C(R^6)_2OH$, $C(CF_3)_2OH$, SO_2H, SO_3H, $CF_2SO_2C(R^6)_3$, $CF_2SO_2N(H)R^5$, $SO_2N(H)R^5$, $SO_2N(H)C(O)R^6$, $C(O)N(H)SO_2R^5$, C(O)haloalkyl, $C(O)N(H)OR^5$, $C(O)N(R^5)OH$, $C(O)N(H)R^5$, $C(O)NR^5C(O)N(R^5)_2$, $P(O)(OR^5)OH$, $P(O)(O)N(H)R^5$, $P(O)(C(R^6)_3)C(R^6)_3$, $B(OH)_2$, heterocyclyl or heteroaryl;

n is 0, 1, 2 or 3;

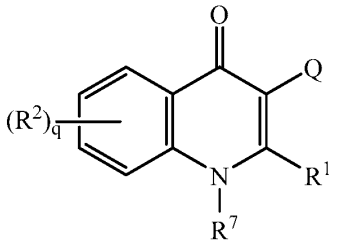
p is 0, 1, 2 or 3;

wherein any alkyl, alkylene, cycloalkyl, heterocyclyl, heteroaryl or aryl is optionally substituted with 1, 2 or 3 groups selected from OH, CN, SH, SCH_3, SO_2CH_3, SO_2NH_2, $SO_2NH(C_1\text{-}C_4)$alkyl, halogen, NH_2, $NH(C_1\text{-}C_4)$alkyl, $N[(C_1\text{-}C_4)alkyl]_2$, NH(aryl), $C(O)NH_2$,

C(O)NH(alkyl), $CH_2C(O)NH$(alkyl), COOH, COOMe, acetyl, (C_1-C_8)alkyl, (C_1-C_8)haloalkyl, O(C_1-C_8)alkyl, O(C_1-C_8)haloalkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, thioalkyl, cyanomethylene, alkylaminyl, alkylene-$C(O)NH_2$, alkylene-C(O)-NH(Me), NHC(O)alkyl, CH_2-C(O)-(C_1-C_8)alkyl, C(O)-(C_1-C_8)alkyl and alkylcarbonylaminyl, or a cycloalkyl, heterocyclyl, aryl or heteroaryl optionally substituted with OH, halogen, (C_1-C_8)alkyl, (C_1-C_8)haloalkyl, O(C_1-C_8)alkyl or O(C_1-C_8)haloalkyl,

wherein when X^4 is a bond, ring A forms a 5-membered heteroaryl wherein $X^1$and X^5 can in addition to C be N.

[083] In another embodiment the invention is directed to compounds of Formula V



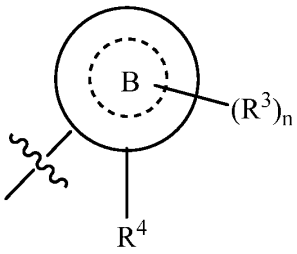
(V),

or stereoisomers, tautomers, or pharmaceutically acceptable salts thereof, wherein:

Q is $-L^1$-Y;

L^1 is $-(CH_2)-$, $-(CH_2)_2-$, $-(CH_2)_3-$, –CH(((C_1-C_8)alkyl)$(CH_2)-$, –CH(((C_1-C_8)alkyl)$(CH_2)_2-$, $-(CH_2)_2$-O–, $-CH_2CH=CH-$, $-CH_2C\equiv C-$ or $-CH_2$(cyclopropyl)–;

Y is



, wherein

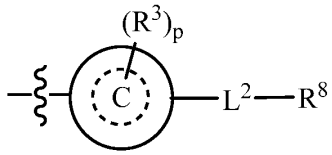
Ring B is a six-membered aryl, heteroaryl or heterocyclyl;

R^1 is H, OH, halo, CN, (C_1-C_8)alkyl, (C_1-C_8)haloalkyl, (C_3-C_6)cycloalkyl or NR^5R^5;

R^2 is independently H, halo, CN, NO, NO_2, C≡H, (C_1-C_8)alkyl, (C_1-C_8)haloalkyl, CH_2SR^5, OR^5, NHR^5, NR^5R^5, [(C_1-C_8)alkylene]heterocyclyl, [(C_1-C_8)alkylene]heteroaryl, [(C_1-C_8)alkylene]NHR^5, [(C_1-C_8)alkylene]NR^5R^5, [(C_1-C_8)alkylyne]NR^5R^5, $C(O)R^5$, $C(O)OR^5$, $C(O)NHR^5$, $C(O)NR^5R^5$, SR^5, $S(O)R^5$, SO_2R^5, SO_2NHR^5, $SO_2NR^5R^5$, $NH(CO)R^6$, $NR^5(CO)R^6$, aryl, heteroaryl, cycloalkyl or heterocyclyl;

R^3 is independently OH, halo, CN, NO_2, (C_1-C_6)alkyl, (C_1-C_6)haloalkyl, (C_1-C_6)alkoxy, C≡H, NHR^7, NR^7R^7, CO_2H, CO_2R^7, [(C_1-C_3)alkylene] (C_1-C_3)alkoxy, [(C_1-C_3)alkylene]CO_2H, (C_3-C_5)cycloalkyl, =O. =S, SR^7, SO_2R^7, $NH(CO)R^7$ or $NR^7(CO)R^7$;

R^4 is H, OH, halo, CN, (C_1-C_3)alkyl, (C_1-C_3)haloalkyl, (C_1-C_3)alkoxy, SR^7 or Z, wherein Z is



;

Ring C is cycloalkyl, heterocyclyl, aryl or heteroaryl;

L^2 is $-C(R^6)(R^6)-$, $-C(R^6)(R^6)C(R^6)(R^6)-$, $-C(R^6)=C(R^6)-$, $-N(R^5)C(R^6)(R^6)-$, $-OC(R^6)(R^6)-$, $-C(=O)-$, $-C(=O)N(R^5)C(R^6)(R^6)-$ or a bond;

R^5 is independently H, (C_1-C_3)alkyl, (C_1-C_3)haloalkyl, (C_3-C_5)cycloalkyl, CO_2H, [(C_1-C_3)alkylene]heteroaryl, [(C_1-C_3)alkylene]aryl, [(C_1-C_3)alkylene]CO_2H, heterocyclyl, aryl or heteroaryl,

or wherein two R^5 substituents together with a nitrogen atom form a 4-, 5-, or 6-membered heterocyclyl;

R^6 is independently H, OH, halo, CN, (C_1-C_3)alkyl, (C_1-C_3)haloalkyl, (C_1-C_3)alkoxy, NHR^7, NR^7R^7, CO_2H, [(C_1-C_3)alkylene]CO_2H, (C_3-C_5)cycloalkyl, SR^7, $NH(CO)R^7$ or $NR^7(CO)R^7$;

R^7 is independently H, (C_1-C_8)alkyl, (C_1-C_8)haloalkyl, cycloalkyl, heterocyclyl, aryl or heteroaryl;

R^8 is H, OH, CO_2H, CO_2R^7, $CF_2C(R^6)_2OH$, $C(R^6)_2OH$, $C(CF_3)_2OH$, SO_2H, SO_3H, $CF_2SO_2C(R^6)_3$, $CF_2SO_2N(H)R^5$, $SO_2N(H)R^5$, $SO_2N(H)C(O)R^6$, $C(O)N(H)SO_2R^5$, C(O)haloalkyl, $C(O)N(H)OR^5$, $C(O)N(R^5)OH$, $C(O)N(H)R^5$, $P(O)(OR^5)OH$, $P(O)(O)N(H)R^5$, $P(O)(C(R^6)_3)C(R^6)_3$, $B(OH)_2$, heterocyclyl or heteroaryl;

n is 0, 1, 2 or 3;

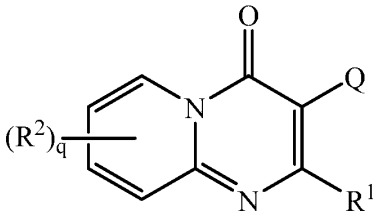
p is 0, 1, 2 or 3;

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

wherein any alkyl, alkylene, cycloalkyl, heterocyclyl, heteroaryl or aryl is optionally substituted with 1, 2 or 3 groups selected from OH, CN, SH, SCH_3, SO_2CH_3, SO_2NH_2, $SO_2NH(C_1$-$C_4)$alkyl, halogen, NH_2, $NH(C_1$-$C_4)$alkyl, $N[(C_1$-$C_4)alkyl]_2$, NH(aryl), $C(O)NH_2$, C(O)NH(alkyl), $CH_2C(O)NH$(alkyl), COOH, COOMe, acetyl, (C_1-C_8)alkyl, (C_1-C_8)haloalkyl, $O(C_1$-$C_8)$alkyl, $O(C_1$-$C_8)$haloalkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, thioalkyl, cyanomethylene,

alkylaminyl, alkylene-C(O)NH_2, alkylene-C(O)-NH(Me), NHC(O)alkyl, CH_2-C(O)-(C_1-C_8)alkyl, C(O)-(C_1-C_8)alkyl and alkylcarbonylaminyl, or a cycloalkyl, heterocyclyl, aryl or heteroaryl optionally substituted with OH, halogen, (C_1-C_8)alkyl, (C_1-C_8)haloalkyl, O(C_1-C_8)alkyl or O(C_1-C_8)haloalkyl.

[084] In another embodiment the invention is directed to compounds of Formula VI



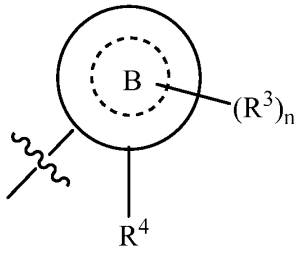
(VI),

or stereoisomers, tautomers, or pharmaceutically acceptable salts thereof, wherein:

Q is $-L^1$-Y;

L^1 is $-(CH_2)-$, $-(CH_2)_2-$, $-(CH_2)_3-$, $-CH((C_1$-$C_8)alkyl)(CH_2)-$, $-CH((C_1$-$C_8)alkyl)$(CH_2)_2-$, $-(CH_2)_2$-O–, $-CH_2CH=CH-$, $-CH_2C\equiv C-$ or $-CH_2$(cyclopropyl)–;

Y is



, wherein

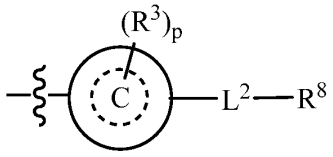
Ring B is a six-membered aryl, heteroaryl or heterocyclyl;

R^1 is H, OH, halo, CN, (C_1-C_8)alkyl, (C_1-C_8)haloalkyl, (C_3-C_6)cycloalkyl or NR^5R^5;

R^2 is independently H, halo, CN, NO, NO_2, C≡H, (C_1-C_8)alkyl, (C_1-C_8)haloalkyl, CH_2SR^5, OR^5, NHR^5, NR^5R^5, [(C_1-C_8)alkylene]heterocyclyl, [(C_1-C_8)alkylene]heteroaryl, [(C_1-C_8)alkylene]NHR^5, [(C_1-C_8)alkylene]NR^5R^5, [(C_1-C_8)alkylyne]NR^5R^5, $C(O)R^5$, $C(O)OR^5$, $C(O)NHR^5$, $C(O)NR^5R^5$, SR^5, $S(O)R^5$, SO_2R^5, SO_2NHR^5, $SO_2NR^5R^5$, $NH(CO)R^6$, $NR^5(CO)R^6$, aryl, heteroaryl, cycloalkyl or heterocyclyl;

R^3 is independently OH, halo, CN, NO_2, (C_1-C_6)alkyl, (C_1-C_6)haloalkyl, (C_1-C_6)alkoxy, C≡H, NHR^7, NR^7R^7, CO_2H, CO_2R^7, [(C_1-C_3)alkylene] (C_1-C_3)alkoxy, [(C_1-C_3)alkylene]CO_2H, (C_3-C_5)cycloalkyl, =O. =S, SR^7, SO_2R^7, $NH(CO)R^7$ or $NR^7(CO)R^7$;

R^4 is H, OH, halo, CN, (C_1-C_3)alkyl, (C_1-C_3)haloalkyl, (C_1-C_3)alkoxy, SR^7 or Z, wherein Z is



;

Ring C is cycloalkyl, heterocyclyl, aryl or heteroaryl;

L^2 is $-C(R^6)(R^6)-$, $-C(R^6)(R^6)C(R^6)(R^6)-$, $-C(R^6)=C(R^6)-$, $-N(R^5)C(R^6)(R^6)-$, $-OC(R^6)(R^6)-$, $-C(=O)-$, $-C(=O)N(R^5)C(R^6)(R^6)-$ or a bond;

R^5 is independently H, $(C_1\text{-}C_3)$alkyl, $(C_1\text{-}C_3)$haloalkyl, $(C_3\text{-}C_5)$cycloalkyl, CO_2H, [$(C_1\text{-}C_3)$alkylene]heteroaryl, [$(C_1\text{-}C_3)$alkylene]aryl, [$(C_1\text{-}C_3)$alkylene]CO_2H, heterocyclyl, aryl or heteroaryl,

or wherein two R^5 substituents together with a nitrogen atom form a 4-, 5-, or 6-membered heterocyclyl;

R^6 is independently H, OH, halo, CN, $(C_1\text{-}C_3)$alkyl, $(C_1\text{-}C_3)$haloalkyl, $(C_1\text{-}C_3)$alkoxy, NHR^7, NR^7R^7, CO_2H, [$(C_1\text{-}C_3)$alkylene]CO_2H, $(C_3\text{-}C_5)$cycloalkyl, SR^7, $NH(CO)R^7$ or $NR^7(CO)R^7$;

R^7 is independently H, $(C_1\text{-}C_8)$alkyl, $(C_1\text{-}C_8)$haloalkyl, cycloalkyl, heterocyclyl, aryl or heteroaryl;

R^8 is H, OH, CO_2H, CO_2R^7, $CF_2C(R^6)_2OH$, $C(R^6)_2OH$, $C(CF_3)_2OH$, SO_2H, SO_3H, $CF_2SO_2C(R^6)_3$, $CF_2SO_2N(H)R^5$, $SO_2N(H)R^5$, $SO_2N(H)C(O)R^6$, $C(O)N(H)SO_2R^5$, C(O)haloalkyl, $C(O)N(H)OR^5$, $C(O)N(R^5)OH$, $C(O)N(H)R^5$, $C(O)NR^5C(O)N(R^5)_2$, $P(O)(OR^5)OH$, $P(O)(O)N(H)R^5$, $P(O)(C(R^6)_3)C(R^6)_3$, $B(OH)_2$, heterocyclyl or heteroaryl;

n is 0, 1, 2 or 3;

p is 0, 1, 2 or 3;

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

wherein any alkyl, alkylene, cycloalkyl, heterocyclyl, heteroaryl or aryl is optionally substituted with 1, 2 or 3 groups selected from OH, CN, SH, SCH_3, SO_2CH_3, SO_2NH_2, $SO_2NH(C_1\text{-}C_4)$alkyl, halogen, NH_2, $NH(C_1\text{-}C_4)$alkyl, $N[(C_1\text{-}C_4)alkyl]_2$, NH(aryl), $C(O)NH_2$, C(O)NH(alkyl), $CH_2C(O)NH$(alkyl), COOH, COOMe, acetyl, $(C_1\text{-}C_8)$alkyl, $(C_1\text{-}C_8)$haloalkyl, $O(C_1\text{-}C_8)$alkyl, $O(C_1\text{-}C_8)$haloalkyl, $(C_2\text{-}C_8)$alkenyl, $(C_2\text{-}C_8)$alkynyl, thioalkyl, cyanomethylene, alkylaminyl, alkylene-$C(O)NH_2$, alkylene-C(O)-NH(Me), NHC(O)alkyl, CH_2-C(O)-$(C_1\text{-}C_8)$alkyl, C(O)-$(C_1\text{-}C_8)$alkyl and alkylcarbonylaminyl, or a cycloalkyl, heterocyclyl, aryl or heteroaryl optionally substituted with OH, halogen, $(C_1\text{-}C_8)$alkyl, $(C_1\text{-}C_8)$haloalkyl, $O(C_1\text{-}C_8)$alkyl or $O(C_1\text{-}C_8)$haloalkyl.

[085] In one embodiment X^2 of Formulae I, II, and IV is N.

[086] In one embodiment X^3 of Formulae I and IV is C.

[087] In one embodiment X^4 of Formulae I and IV is CR^2 or N.

[088] In one embodiment X^5 of Formulae I and IV is CR^2.

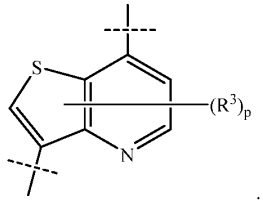
[089] In one embodiment L^1 of Formulae I, II, III, IV, V and VI is $–(CH_2)_2–O–$, $–CH_2CH=CH–$ or $–CH_2C\equiv C–$. In another embodiment L^1 is $–(CH_2)_2–O–$.

[090] In one embodiment L^2 of Formulae I, II, III, IV, V and VI is a bond.

[091] In one embodiment Ring B of Formulae I, V and VI is aryl.

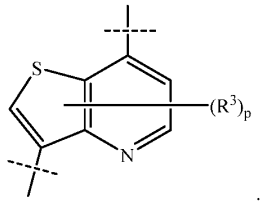
[092] In one embodiment Ring C of Formulae I, II, III, IV, V and VI is heteroaryl.

[093] In one embodiment Ring C of Formulae I, II, III, IV, V and VI is



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[094] In one embodiment Ring C of Formula III is



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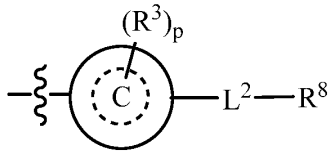
[095] In one embodiment R^1 of Formulae I, II, III, IV, V and VI is H, $(C_1\text{-}C_8)$alkyl or $(C_1\text{-}C_8)$haloalkyl.

[096] In one embodiment R^1 of Formula IV is NHR^5 or $N[(C_1\text{-}C_3)\text{alkyl}](R^5)$.

[097] In one embodiment R^2 of Formulae I, II, III, IV, V and VI is halo, CN, $(C_1\text{-}C_8)$alkyl, $(C_1\text{-}C_8)$haloalkyl or OR^5. In another embodiment R^2 is halo, CN or $(C_1\text{-}C_8)$haloalkyl.

[098] In one embodiment R^3 of Formulae I, II, III, IV, V and VI is halo, CN, $(C_1\text{-}C_3)$alkyl or $(C_1\text{-}C_3)$haloalkyl.

[099] In one embodiment R^4 of Formulae I, V and VI is Z, wherein Z is



;

[0100] In one embodiment R^5 of Formulae I, II, III, V and VI is H, $(C_1\text{-}C_3)$alkyl or $(C_1\text{-}C_3)$haloalkyl. In another embodiment R^5 of Formula IV is aryl. In another embodiment R^5 of Formulae I, II, III, IV, V, and VI is H, $(C_1\text{-}C_3)$alkyl or $(C_1\text{-}C_3)$haloalkyl.

[0101] In one embodiment R^6 of Formulae I, II, III, IV, V and VI is H, OH, halo, CN, (C_1-C_3)alkyl, (C_1-C_3)haloalkyl or (C_1-C_3)alkoxy.

[0102] In one embodiment R^7 of Formulae I, II, III, IV, V and VI is H, (C_1-C_8)alkyl or (C_1-C_8)haloalkyl.

[0103] In one embodiment R^8 of Formulae I, II, III, IV, V and VI is CO_2H or $C(O)N(H)SO_2R^5$.

[0104] In one embodiment R^9 of Formula III is (C_1-C_8)alkyl or (C_1-C_8)haloalkyl.

[0105] In one embodiment R^9 of Formula III is cycloalkyl or heterocyclyl.

[0106] In one embodiment "m" of Formulae I and II = 2 or 3. In another embodiment "n" of Formulae I, II, IV, V and VI = 1 or 2. In yet another embodiment "p" of Formulae I, II, III, IV, V and VI = 0 or 1.

[0107] In one embodiment the optional substituents of alkyl, cycloalkyl, heterocyclyl, heteroaryl or aryl are OH, CN, halogen, (C_1-C_8)alkyl, O(C_1-C_8)alkyl, haloalkyl, alkylene-$C(O)NH_2$ or alkylene-C(O)-NH(Me).

[0108] In one embodiment the optional substituents of alkyl, cycloalkyl, heterocyclyl, heteroaryl or aryl are cycloalkyl, heterocyclyl, aryl or heteroaryl optionally substituted with OH, halogen, (C_1-C_8)alkyl, (C_1-C_8)haloalkyl, O(C_1-C_8)alkyl or O(C_1-C_8)haloalkyl.

[0109] In one embodiment, the compounds according to Formulae I, II, III, IV, V and VI are selected from compounds 1-1250.

[0110] The inventive compounds according to Formulae I, II, III, IV, V and VI may be isotopically-labeled by having one or more atoms replaced by an atom having a different atomic mass or mass number. Examples of isotopes that can be incorporated into compounds according to Formulae I, II, III, IV, V and VI include isotopes of hydrogen, carbon, nitrogen, oxygen, phosphorous, fluorine, chlorine, or iodine. Illustrative of such isotopes are ^{2}H, ^{3}H, ^{11}C, ^{13}C, ^{14}C, ^{13}N, ^{15}N, ^{15}O, ^{17}O, ^{18}O, ^{31}P, ^{32}P, ^{35}S, ^{18}F, ^{36}Cl, ^{123}I, and ^{125}I, respectively. These radiolabeled compounds can be used to measure the biodistribution, tissue concentration and the kinetics of transport and excretion from biological tissues including a subject to which such a labeled compound is administered. Labeled compounds are also used to determine therapeutic effectiveness, the site or mode of action, and the binding affinity of a candidate therapeutic to a pharmacologically important target. Certain radioactive-labeled compounds according to Formulae I, II, III, IV, V and VI, therefore, are useful in drug and/or tissue distribution studies. The radioactive isotopes tritium, i.e. ^{3}H, and carbon-14, i.e. ^{14}C, are particularly useful for this purpose in view of their ease of incorporation and ready means of detection.

[0111] Substitution with heavier isotopes such as deuterium, i.e. ^{2}H, affords certain therapeutic advantages resulting from the greater metabolic stability, for example, increased *in vivo* half-life of compounds containing deuterium. Substitution of hydrogen with deuterium may reduce dose required for therapeutic effect, and hence may be preferred in a discovery or clinical setting.

[0112] Substitution with positron emitting isotopes, such as ^{11}C, ^{18}F, ^{15}O and ^{13}N, provides labeled analogs of the inventive compounds that are useful in Positron Emission Tomography (PET) studies, *e.g.,* for examining substrate receptor occupancy. Isotopically-labeled compounds according to Formulae I, II, III, IV, V and VI can generally be prepared by conventional techniques known to those skilled in the art or by processes analogous to those described in the Preparations and Examples section as set out below using an appropriate isotopic-labeling reagent.

[0113] Embodiments of the invention disclosed herein are also meant to encompass the *in vivo* metabolic products of compounds according to Formulae I, II, III, IV, V and VI. Such products may result from, for example, the oxidation, reduction, hydrolysis, amidation, esterification, and like processes primarily due to enzymatic activity upon administration of a compound of the invention. Accordingly, the invention includes compounds that are produced as by-products of enzymatic or non-enzymatic activity on an inventive compound following the administration of such a compound to a mammal for a period of time sufficient to yield a metabolic product. Metabolic products, particularly pharmaceutically active metabolites are typically identified by administering a radiolabeled compound of the invention in a detectable dose to a subject, such as rat, mouse, guinea pig, monkey, or human, for a sufficient period of time during which metabolism occurs, and isolating the metabolic products from urine, blood or other biological samples that are obtained from the subject receiving the radiolabeled compound.

[0114] The invention also provides pharmaceutically acceptable salt forms of compounds in Formulae I, II, III, IV, V and VI. Encompassed within the scope of the invention are both acid and base addition salts that are formed by contacting a pharmaceutically suitable acid or a pharmaceutically suitable base with a compound of the invention.

[0115] To this end, a "pharmaceutically acceptable acid addition salt" refers to those salts which retain the biological effectiveness and properties of the free bases, which are not biologically or otherwise undesirable, and which are formed with inorganic acids such as, but are not limited to, hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid and the like, and organic acids such as, but not limited to, acetic acid, 2,2-dichloroacetic acid, adipic acid, alginic acid, ascorbic acid, aspartic acid, benzenesulfonic acid, benzoic acid, 4-acetamidobenzoic acid,

camphoric acid, camphor-10-sulfonic acid, capric acid, caproic acid, caprylic acid, carbonic acid, cinnamic acid, citric acid, cyclamic acid, dodecylsulfuric acid, ethane-1,2-disulfonic acid, ethanesulfonic acid, 2-hydroxyethanesulfonic acid, formic acid, fumaric acid, galactaric acid, gentisic acid, glucoheptonic acid, gluconic acid, glucuronic acid, glutamic acid, glutaric acid, 2-oxo-glutaric acid, glycerophosphoric acid, glycolic acid, hippuric acid, isobutyric acid, lactic acid, lactobionic acid, lauric acid, maleic acid, malic acid, malonic acid, mandelic acid, methanesulfonic acid, mucic acid, naphthalene-1,5-disulfonic acid, naphthalene-2-sulfonic acid, 1-hydroxy-2-naphthoic acid, nicotinic acid, oleic acid, orotic acid, oxalic acid, palmitic acid, pamoic acid, propionic acid, pyroglutamic acid, pyruvic acid, salicylic acid, 4-aminosalicylic acid, sebacic acid, stearic acid, succinic acid, tartaric acid, thiocyanic acid, p-toluenesulfonic acid, trifluoroacetic acid, undecylenic acid, and the like.

[0116] Similarly, a "pharmaceutically acceptable base addition salt" refers to those salts which retain the biological effectiveness and properties of the free acids, which are not biologically or otherwise undesirable. These salts are prepared by addition of an inorganic base or an organic base to the free acid. Salts derived from inorganic bases include, but are not limited to, the sodium, potassium, lithium, ammonium, calcium, magnesium, iron, zinc, copper, manganese, aluminum salts and the like. Preferred inorganic salts are the ammonium, sodium, potassium, calcium, and magnesium salts. Salts derived from organic bases include, but are not limited to, salts of primary, secondary, and tertiary amines, substituted amines including naturally occurring substituted amines, cyclic amines and basic ion exchange resins, such as ammonia, isopropylamine, trimethylamine, diethylamine, triethylamine, tripropylamine, diethanolamine, ethanolamine, deanol, 2-dimethylaminoethanol, 2-diethylaminoethanol, dicyclohexylamine, lysine, arginine, histidine, caffeine, procaine, hydrabamine, choline, betaine, benethamine, benzathine, ethylenediamine, glucosamine, methylglucamine, theobromine, triethanolamine, tromethamine, purines, piperazine, piperidine, N-ethylpiperidine, polyamine resins and the like. Particularly preferred organic bases are isopropylamine, diethylamine, ethanolamine, trimethylamine, dicyclohexylamine, choline and caffeine.

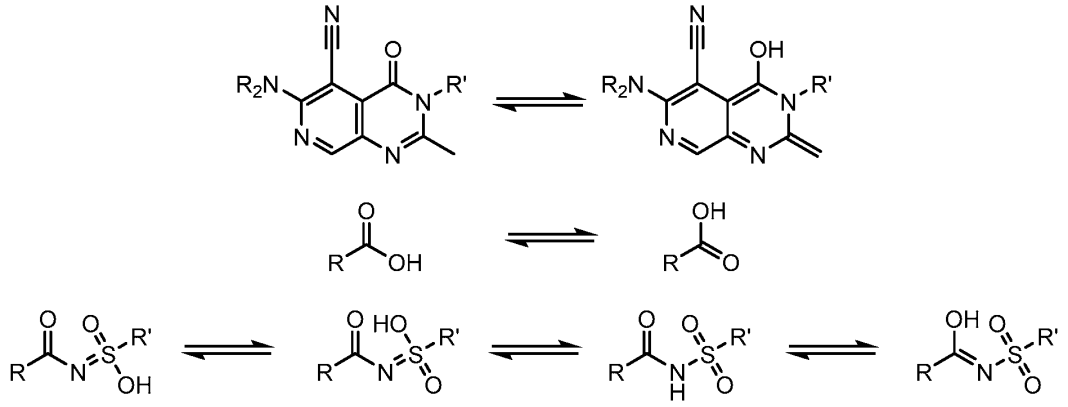
[0117] Often crystallizations produce a solvate of the compound of the invention. As used herein, the term "solvate" refers to an aggregate that comprises one or more molecules of a compound of the invention with one or more molecules of solvent. The solvent may be water, in which case the solvate may be a hydrate. Alternatively, the solvent may be an organic solvent. Thus, the compounds of the present invention may exist as a hydrate, including a monohydrate, dihydrate, hemihydrate, sesquihydrate, trihydrate, tetrahydrate and the like, as well as the

corresponding solvated forms. The compound of the invention may be true solvates, while in other cases the compound of the invention may merely retain adventitious water or be a mixture of water plus some adventitious solvent.

[0118] A "stereoisomer" refers to a compound made up of the same atoms bonded by the same bonds but having different three-dimensional structures, which are not interchangeable. The present invention contemplates various stereoisomers and mixtures thereof and includes "enantiomers", which refers to two stereoisomers whose molecules are nonsuperimposeable mirror images of one another.

[0119] Compounds of the invention or their pharmaceutically acceptable salts may contain one or more asymmetric centers and may thus give rise to enantiomers, diastereomers, and other stereoisomeric forms that may be defined, in terms of absolute stereochemistry, as (R)- or (S)- or, as (D)- or (L)- for amino acids. The present invention is meant to include all such possible isomers, as well as their racemic and optically pure forms. Optically active (+) and (-), (R)- and (S)-, or (D)- and (L)- isomers may be prepared using chiral synthons or chiral reagents, or resolved using conventional techniques, for example, chromatography and fractional crystallization. Conventional techniques for the preparation/isolation of individual enantiomers include chiral synthesis from a suitable optically pure precursor or resolution of the racemate (or the racemate of a salt or derivative) using, for example, chiral high pressure liquid chromatography (HPLC). When the compounds described herein contain olefinic double bonds or other centers of geometric asymmetry, and unless specified otherwise, it is intended that the compounds include both E and Z geometric isomers. Likewise, all tautomeric forms are also intended to be included.

[0120] The term "tautomer" refers to a proton shift from one atom of a molecule to another atom of the same molecule. For example:



[0121] The compounds provided in this disclosure may be depicted as different tautomers, and when compounds have tautomeric forms, all tautomeric forms are intended to be within the scope of the invention, and the naming of a compound does not exclude any tautomer of that compound.

[0122] The inventive compounds are synthesized using conventional synthetic methods, and more specifically using the general methods noted below.

Pharmaceutical Formulations

[0123] In one embodiment compounds according to Formulae I, II, III, IV, V and VI are formulated as pharmaceutically acceptable compositions that contain compounds of Formulae I, II, III, IV, V and VI in an amount effective to treat a particular disease or condition of interest upon administration of the pharmaceutical composition to a mammal. Pharmaceutical compositions in accordance with the present invention can comprise compounds of Formulae I, II, III, IV, V and VI in combination with a pharmaceutically acceptable carrier, diluent or excipient.

[0124] In this regard, a "pharmaceutically acceptable carrier, diluent or excipient" includes without limitation any adjuvant, carrier, excipient, glidant, sweetening agent, diluent, preservative, dye/colorant, flavor enhancer, surfactant, wetting agent, dispersing agent, suspending agent, stabilizer, isotonic agent, solvent, or emulsifier which has been approved by the United States Food and Drug Administration as being acceptable for use in humans or domestic animals.

[0125] Further, a "mammal" includes humans and both domestic animals such as laboratory animals and household pets (e.g., cats, dogs, swine, cattle, sheep, goats, horses, rabbits), and non-domestic animals such as wildlife and the like.

[0126] The pharmaceutical compositions of the invention can be prepared by combining a compound of the invention with an appropriate pharmaceutically acceptable carrier, diluent or excipient, and may be formulated into preparations in solid, semi-solid, liquid or gaseous forms, such as tablets, capsules, powders, granules, ointments, solutions, suppositories, injections, inhalants, gels, microspheres, and aerosols. Typical routes of administering such pharmaceutical compositions include, without limitation, oral, topical, transdermal, inhalation, parenteral, sublingual, buccal, rectal, vaginal, and intranasal. The term parenteral as used herein includes subcutaneous injections, intravenous, intramuscular, intrasternal injection or infusion techniques. Pharmaceutical compositions of the invention are formulated so as to allow the active ingredients contained therein to be bioavailable upon administration of the composition to a patient.

Compositions that will be administered to a subject or patient take the form of one or more dosage units, where for example, a tablet may be a single dosage unit, and a container of a compound of the invention in aerosol form may hold a plurality of dosage units. Actual methods of preparing such dosage forms are known, or will be apparent, to those skilled in this art; for example, see Remington: The Science and Practice of Pharmacy, 20th Edition (Philadelphia College of Pharmacy and Science, 2000). The composition to be administered will, in any event, contain a therapeutically effective amount of a compound of the invention, or a pharmaceutically acceptable salt thereof, for treatment of a disease or condition of interest in accordance with the teachings of this invention.

[0127] A pharmaceutical composition of the invention may be in the form of a solid or liquid. In one aspect, the carrier(s) are particulate, so that the compositions are, for example, in tablet or powder form. The carrier(s) may be liquid, with the compositions being, for example, an oral syrup, injectable liquid or an aerosol, which is useful in, for example, inhalatory administration. When intended for oral administration, the pharmaceutical composition is preferably in either solid or liquid form, where semi-solid, semi-liquid, suspension and gel forms are included within the forms considered herein as either solid or liquid.

[0128] As a solid composition for oral administration the pharmaceutical composition may be formulated into a powder, granule, compressed tablet, pill, capsule, chewing gum, wafer or the like form. Such a solid composition will typically contain one or more inert diluents or edible carriers. In addition, one or more of the following may be present: binders such as carboxymethylcellulose, ethyl cellulose, microcrystalline cellulose, gum tragacanth or gelatin; excipients such as starch, lactose or dextrins, disintegrating agents such as alginic acid, sodium alginate, Primogel, corn starch and the like; lubricants such as magnesium stearate or Sterotex; glidants such as colloidal silicon dioxide; sweetening agents such as sucrose or saccharin; a flavoring agent such as peppermint, methyl salicylate or orange flavoring; and a coloring agent.

[0129] When the pharmaceutical composition is in the form of a capsule, for example, a gelatin capsule, it may contain, in addition to materials of the above type, a liquid carrier such as polyethylene glycol or oil.

[0130] The pharmaceutical composition may be in the form of a liquid, for example, an elixir, syrup, solution, emulsion or suspension. The liquid may be for oral administration or for delivery by injection, as two examples. When intended for oral administration, preferred composition contain, in addition to the present compounds, one or more of a sweetening agent, preservatives, dye/colorant and flavor enhancer. In a composition intended to be administered by injection, one

or more of a surfactant, preservative, wetting agent, dispersing agent, suspending agent, buffer, stabilizer and isotonic agent may be included.

[0131] The liquid pharmaceutical compositions of the invention, whether they be solutions, suspensions or other like form, may include one or more of the following adjuvants: sterile diluents such as water for injection, saline solution, preferably physiological saline, Ringer's solution, isotonic sodium chloride, fixed oils such as synthetic mono or diglycerides which may serve as the solvent or suspending medium, polyethylene glycols, glycerin, propylene glycol or other solvents; antibacterial agents such as benzyl alcohol or methyl paraben; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid; buffers such as acetates, citrates or phosphates and agents for the adjustment of tonicity such as sodium chloride or dextrose. The parenteral preparation can be enclosed in ampoules, disposable syringes or multiple dose vials made of glass or plastic. Physiological saline is a preferred adjuvant. An injectable pharmaceutical composition is preferably sterile.

[0132] A liquid pharmaceutical composition of the invention intended for either parenteral or oral administration should contain an amount of a compound of the invention such that a suitable dosage will be obtained.

[0133] The pharmaceutical composition of the invention may be intended for topical administration, in which case the carrier may suitably comprise a solution, emulsion, ointment or gel base. The base, for example, may comprise one or more of the following: petrolatum, lanolin, polyethylene glycols, bee wax, mineral oil, diluents such as water and alcohol, and emulsifiers and stabilizers. Thickening agents may be present in a pharmaceutical composition for topical administration. If intended for transdermal administration, the composition may include a transdermal patch or iontophoresis device.

[0134] The pharmaceutical composition of the invention may be intended for rectal administration, in the form, for example, of a suppository, which will melt in the rectum and release the drug. The composition for rectal administration may contain an oleaginous base as a suitable nonirritating excipient. Such bases include, without limitation, lanolin, cocoa butter and polyethylene glycol.

[0135] The pharmaceutical composition of the invention may include various materials, which modify the physical form of a solid or liquid dosage unit. For example, the composition may include materials that form a coating shell around the active ingredients. The materials that form the coating shell are typically inert, and may be selected from, for example, sugar, shellac, and

other enteric coating agents. Alternatively, the active ingredients may be encased in a gelatin capsule.

[0136] The pharmaceutical composition of the invention in solid or liquid form may include an agent that binds to the compound of the invention and thereby assists in the delivery of the compound. Suitable agents that may act in this capacity include a monoclonal or polyclonal antibody, a protein or a liposome.

[0137] The pharmaceutical composition of the invention may consist of dosage units that can be administered as an aerosol. The term aerosol is used to denote a variety of systems ranging from those of colloidal nature to systems consisting of pressurized packages. Delivery may be by a liquefied or compressed gas or by a suitable pump system that dispenses the active ingredients. Aerosols of compounds of the invention may be delivered in single phase, bi-phasic, or tri-phasic systems in order to deliver the active ingredient(s). Delivery of the aerosol includes the necessary container, activators, valves, subcontainers, and the like, which together may form a kit. One skilled in the art, without undue experimentation may determine preferred aerosols.

[0138] The pharmaceutical compositions of the invention may be prepared by any methodology well known in the pharmaceutical art. For example, a pharmaceutical composition intended to be administered by injection can be prepared by combining a compound of the invention with sterile, distilled water so as to form a solution. A surfactant may be added to facilitate the formation of a homogeneous solution or suspension. Surfactants are compounds that non-covalently interact with the compound of the invention so as to facilitate dissolution or homogeneous suspension of the compound in the aqueous delivery system.

[0139] In certain embodiments a pharmaceutical composition comprising a compound of Formulae I, II, III, IV, V and VI is administered to a mammal in an amount sufficient to inhibit eIF4E activity upon administration, and preferably with acceptable toxicity to the same. eIF4E activity of Formulae I, II, III, IV, V and VI compounds can be determined by one skilled in the art, for example, as described in the Examples below. Appropriate concentrations and dosages can be readily determined by one skilled in the art.

Therapeutic Use

[0140] The compounds of the invention, or their pharmaceutically acceptable salts, are administered in a therapeutically effective amount, which will vary depending upon a variety of factors including the activity of the specific compound employed; the metabolic stability and length of action of the compound; the age, body weight, general health, sex, and diet of the

patient; the mode and time of administration; the rate of excretion; the drug combination; the severity of the particular disorder or condition; and the subject undergoing therapy.

[0141] "Effective amount" or "therapeutically effective amount" refers to that amount of a compound of the invention which, when administered to a mammal, preferably a human, is sufficient to effect treatment, as defined below, of a eIF4E related condition or disease in the mammal, preferably a human. The amount of a compound of the invention which constitutes a "therapeutically effective amount" will vary depending on the compound, the condition and its severity, the manner of administration, and the age of the mammal to be treated, but can be determined routinely by one of ordinary skill in the art having regard to his own knowledge and to this disclosure.

[0142] Compounds of the invention or pharmaceutically acceptable salt thereof may also be administered simultaneously with, prior to, or after administration of one or more other therapeutic agents. Such combination therapy includes administration of a single pharmaceutical dosage formulation which contains a compound of the invention and one or more additional active agents, as well as administration of the compound of the invention and each active agent in its own separate pharmaceutical dosage formulation. For example, a compound of the invention and the other active agent can be administered to the patient together in a single oral dosage composition such as a tablet or capsule, or each agent administered in separate oral dosage formulations. Where separate dosage formulations are used, the compounds of the invention and one or more additional active agents can be administered at essentially the same time, i.e., concurrently, or at separately staggered times, i.e., sequentially; combination therapy is understood to include all these regimens.

[0143] In certain embodiments the disclosed compounds are useful for inhibiting the activity of eIF4E and/or can be useful in analyzing eIF4E signaling activity in model systems and/or for preventing, treating, or ameliorating a symptom associated with a disease, disorder, or pathological condition involving eIF4E, preferably one afflicting humans. A compound which inhibits the activity of eIF4E will be useful in preventing, treating, ameliorating, or reducing the symptoms or progression of diseases of uncontrolled cell growth, proliferation and/or survival, inappropriate cellular immune responses, or inappropriate cellular inflammatory responses or diseases which are accompanied with uncontrolled cell growth, proliferation and/or survival, inappropriate cellular immune responses, or inappropriate cellular inflammatory responses, particularly in which the uncontrolled cell growth, proliferation and/or survival, inappropriate cellular immune responses, or inappropriate cellular inflammatory responses is mediated by

eIF4E, such as, for example, haematological tumors, solid tumors, and/or metastases thereof, including leukemias and myelodysplastic syndrome, malignant lymphomas, for example, B-cell lymphoma, T-cell lymphoma, hairy cell lymphoma, Hodgkin's lymphoma, non-Hodgins lymphoma and Burkitt's lymphoma, head and neck tumors including brain tumors and brain metastases, tumors of the thorax including non-small cell and small cell lung tumors, gastrointestinal tumors, endocrine tumors, mammary and other gynecological tumors, urological tumors including renal, bladder and prostate tumors, skin tumors, and sarcomas, and/or metastases thereof.

[0144] Furthermore, the inventive compounds and their pharmaceutical compositions are candidate therapeutics for the prophylaxis and/or therapy of cytokine related diseases, such as inflammatory diseases, allergies, or other conditions associated with proinflammatory cytokines. Exemplary inflammatory diseases include without limitation, chronic or acute inflammation, inflammation of the joints such as chronic inflammatory arthritis, rheumatoid arthritis, psoriatic arthritis, osteoarthritis, juvenile rheumatoid arthritis, Reiter's syndrome, rheumatoid traumatic arthritis, rubella arthritis, acute synovitis and gouty arthritis; inflammatory skin diseases such as sunburn, psoriasis, erythrodermic psoriasis, pustular psoriasis, eczema, dermatitis, acute or chronic graft formation, atopic dermatitis, contact dermatitis, urticaria and scleroderma; inflammation of the gastrointestinal tract such as inflammatory bowel disease, Crohn's disease and related conditions, ulcerative colitis, colitis, and diverticulitis; nephritis, urethritis, salpingitis, oophoritis, endomyometritis, spondylitis, systemic lupus erythematosus and related disorders, multiple sclerosis, asthma, meningitis, myelitis, encephalomyelitis, encephalitis, phlebitis, thrombophlebitis, respiratory diseases such as asthma, bronchitis, chronic obstructive pulmonary disease (COPD), inflammatory lung disease and adult respiratory distress syndrome, and allergic rhinitis; endocarditis, osteomyelitis, rheumatic fever, rheumatic pericarditis, rheumatic endocarditis, rheumatic myocarditis, rheumatic mitral valve disease, rheumatic aortic valve disease, prostatitis, prostatocystitis, spondoarthropathies ankylosing spondylitis, synovitis, tenosynovotis, myositis, pharyngitis, polymyalgia rheumatica, shoulder tendonitis or bursitis, gout, pseudo gout, vasculitides, inflammatory diseases of the thyroid selected from granulomatous thyroiditis, lymphocytic thyroiditis, invasive fibrous thyroiditis, acute thyroiditis; Hashimoto's thyroiditis, Kawasaki's disease, Raynaud's phenomenon, Sjögren's syndrome, neuroinflammatory disease, sepsis, conjunctivitis, keratitis, iridocyclitis, optic neuritis, otitis, lymphoadenitis, nasopaharingitis, sinusitis, pharyngitis, tonsillitis, laryngitis, epiglottitis, bronchitis, pneumonitis, stomatitis, gingivitis. oesophagitis, gastritis, peritonitis, hepatitis,

cholelithiasis, cholecystitis, glomerulonephritis, Goodpasture's disease, crescentic glomerulonephritis, pancreatitis, endomyometritis, myometritis, metritis, cervicitis, endocervicitis, exocervicitis, parametritis, tuberculosis, vaginitis, vulvitis, silicosis, sarcoidosis, pneumoconiosis, pyresis, inflammatory polyarthropathies, psoriatric arthropathies, intestinal fibrosis, bronchiectasis and enteropathic arthropathies.

[0145] Yet further, the inventive compounds and their pharmaceutical compositions are candidate therapeutics for the prophylaxis and/or therapy of fibrotic diseases, such as various forms of fibrosis, fibromas or any disease giving rise to fibrosis whether as a main or a secondary symptom. Exemplary fibrotic diseases include without limitation, viral hepatitis, hepatic fibrosis, schistosomiasis, steatohepatitis (alcoholic or non-alcoholic), cirrhosis, idiopathic pulmonary fibrosis (IPF), systemic sclerosis (scleroderma), nephrogenic systemic fibrosis (NSF), diabetes, untreated hypertension, heart attack, hypertension, atherosclerosis, restenosis, macular degeneration, retinal and vitreal retinopathy, keloids, hypertrophic scars, Crohn's disease and Alzheimer's disease.

[0146] Although inflammation is the unifying pathogenic process of these diseases, current therapies only treat the symptoms of the disease and not the underlying cause of inflammation. The compositions of the present invention are useful for the treatment and/or prophylaxis of inflammatory diseases and related complications and disorders.

[0147] Accordingly, certain embodiments are directed to a method for treating a eIF4E dependent condition in a mammal in need thereof, the method comprising administering an effective amount of a pharmaceutical composition as described above (*i.e.*, a pharmaceutical composition comprising one or more compounds of Formulae I, II, III, IV, V and VI) to a mammal.

[0148] As described above deregulation of protein synthesis is a common event in human cancers. A key regulator of translational control is eIF4E whose activity is a key determinant of tumorigenicity. Inhibitors of eIF4E are suitable candidate therapeutics for treating cell proliferative disorders such as cancer. A wide variety of cancers, including solid tumors, lymphomas and leukemias, are amenable to the compositions and methods disclosed herein. Types of cancer that may be treated include, but are not limited to: adenocarcinoma of the breast, prostate, and colon; all forms of bronchogenic carcinoma of the lung; myeloid; melanoma; hepatoma; neuroblastoma; papilloma; apudoma; choristoma; branchioma; malignant carcinoid syndrome; carcinoid heart disease; and carcinoma (*e.g.*, Walker, basal cell, basosquamous, Brown-Pearce, ductal, Ehrlich tumor, Krebs 2, Merkel cell, mucinous, non-small cell lung, oat

cell, papillary, scirrhous, bronchiolar, bronchogenic, squamous cell, and transitional cell). Additional types of cancers that may be treated include: histiocytic disorders; leukemia; histiocytosis malignant; Hodgkin's disease; immunoproliferative small; non-Hodgkin's lymphoma; T-cell lymphoma, B-cell lymphoma, hairy cell lymphoma, Burkitt's lymphoma, plasmacytoma; reticuloendotheliosis; melanoma; chondroblastoma; chondroma; chondrosarcoma; fibroma; fibrosarcoma; giant cell tumors; histiocytoma; lipoma; liposarcoma; mesothelioma; myxoma; myxosarcoma; osteoma; osteosarcoma; chordoma; craniopharyngioma; dysgerminoma; hamartoma; mesenchymoma; mesonephroma; myosarcoma; ameloblastoma; cementoma; odontoma; teratoma; thymoma; trophoblastic tumor.

[0149] Other cancers that can be treated using the inventive compounds include without limitation adenoma; cholangioma; cholesteatoma; cyclindroma; cystadenocarcinoma; cystadenoma; granulosa cell tumor; gynandroblastoma; hepatoma; hidradenoma; islet cell tumor; Leydig cell tumor; papilloma; sertoli cell tumor; theca cell tumor; leimyoma; leiomyosarcoma; myoblastoma; myomma; myosarcoma; rhabdomyoma; rhabdomyosarcoma; ependymoma; ganglioneuroma; glioma; medulloblastoma; meningioma; neurilemmoma; neuroblastoma; neuroepithelioma; neurofibroma; neuroma; paraganglioma; paraganglioma nonchromaffin.

[0150] In one embodiment the inventive compounds are candidate therapeutic agents for the treatment of cancers such as angiokeratoma; angiolymphoid hyperplasia with eosinophilia; angioma sclerosing; angiomatosis; glomangioma; hemangioendothelioma; hemangioma; hemangiopericytoma; hemangiosarcoma; lymphangioma; lymphangiomyoma; lymphangiosarcoma; pinealoma; carcinosarcoma; chondrosarcoma; cystosarcoma phyllodes; fibrosarcoma; hemangiosarcoma; leiomyosarcoma; leukosarcoma; liposarcoma; lymphangiosarcoma; myosarcoma; myxosarcoma; ovarian carcinoma; rhabdomyosarcoma; sarcoma; neoplasms; nerofibromatosis; and cervical dysplasia.

[0151] In a particular embodiment, the present disclosure provides methods for treating solid tumor, colon cancer, rectal cancer, colorectal cancer, bladder cancer, gastric cancer, esophageal cancer, head and neck cancer, myelodysplastic syndrome, brain cancer, CNS cancer, malignant glioma, glioblastoma, hepatocellular cancers, hepatocellular carcinoma, thyroid cancer, lung cancer, non-small cell lung cancer, a hematological cancer, acute and chronic leukemia, B-cell lymphoma, Waldenström's macroglobulinemia, T-cell lymphoma, hairy cell lymphoma, diffuse large B cell lymphoma, Hodgkin's lymphoma, non-Hodgkin's lymphoma, Burkitt lymphoma, pancreatic cancer, melanoma, myeloma, multiple myeloma, pancreatic carcinoma, renal cell carcinoma, renal cancer, cervical cancer, urothelial cancer, prostate cancer, castration-resistant

prostate cancer, ovarian cancer, breast cancer, triple-negative breast cancer, hormone receptor positive breast cancer or HER2+ breast cancer. According to such a method, a therapeutically effective amount of at least one compound according to Formulae I, II, III, IV, V and VI or a stereoisomer, tautomer or pharmaceutically acceptable salt thereof can be administered to a subject who has been diagnosed with a cell proliferative disease, such as a cancer. Alternatively, a pharmaceutical composition comprising at least one compound according to Formulae I, II, III, IV, V and VI or a stereoisomer, tautomer or pharmaceutically acceptable salt thereof can be administered to a subject who has been diagnosed with cancer.

[0152] In certain embodiments the compounds in accordance with the invention are administered to a subject with cancer in conjunction with other conventional cancer therapies such as radiation treatment or surgery. Radiation therapy is well-known in the art and includes X-ray therapies, such as gamma-irradiation, and radiopharmaceutical therapies.

[0153] In certain embodiments the inventive eIF4E inhibitor compounds are used with at least one anti-cancer agent. Anti-cancer agents include chemotherapeutic drugs. A chemotherapeutic agent includes, but is not limited to, an inhibitor of chromatin function, a topoisomerase inhibitor, a microtubule inhibiting drug, a DNA damaging agent, an antimetabolite (such as folate antagonists, pyrimidine analogs, purine analogs, and sugar-modified analogs), a DNA synthesis inhibitor, a DNA interactive agent (such as an intercalating agent), and a DNA repair inhibitor.

[0154] Illustrative chemotherapeutic agents include, without limitation, the following groups: anti-metabolites/anti-cancer agents, such as pyrimidine analogs (5-fluorouracil, floxuridine, capecitabine, gemcitabine and cytarabine) and purine analogs, folate antagonists and related inhibitors (mercaptopurine, thioguanine, pentostatin and 2- chlorodeoxyadenosine (cladribine)); antiproliferative/antimitotic agents including natural products such as vinca alkaloids (vinblastine, vincristine, and vinorelbine), microtubule disruptors such as taxane (paclitaxel, docetaxel), vincristin, vinblastin, nocodazole, epothilones and navelbine, epidipodophyllotoxins (etoposide, teniposide), DNA damaging agents (actinomycin, amsacrine, anthracyclines, bleomycin, busulfan, camptothecin, carboplatin, chlorambucil, cisplatin, cyclophosphamide, Cytoxan, dactinomycin, daunorubicin, doxorubicin, epirubicin, hexamethylmelamineoxaliplatin, iphosphamide, melphalan, merchlorehtamine, mitomycin, mitoxantrone, nitrosourea, plicamycin, procarbazine, taxol, taxotere, temozolamide, teniposide, triethylenethiophosphoramide and etoposide (VP 16)); antibiotics such as dactinomycin (actinomycin D), daunorubicin, doxorubicin (adriamycin), idarubicin, anthracyclines, mitoxantrone, bleomycins, plicamycin

(mithramycin) and mitomycin; enzymes (L-asparaginase which systemically metabolizes L-asparagine and deprives cells which do not have the capacity to synthesize their own asparagine); antiplatelet agents; antiproliferative/antimitotic alkylating agents such as nitrogen mustards (mechlorethamine, cyclophosphamide and analogs, melphalan, chlorambucil), ethylenimines and methylmelamines (hexamethylmelamine and thiotepa), alkyl sulfonates -busulfan, nitrosoureas (carmustine (BCNU) and analogs, streptozocin), trazenes— dacarbazinine (DTIC); antiproliferative/antimitotic antimetabolites such as folic acid analogs (methotrexate); platinum coordination complexes (cisplatin, carboplatin), procarbazine, hydroxyurea, mitotane, aminoglutethimide; hormones, hormone analogs (estrogen, tamoxifen, goserelin, bicalutamide, nilutamide) and aromatase inhibitors (letrozole, anastrozole); anticoagulants (heparin, synthetic heparin salts and other inhibitors of thrombin); fibrinolytic agents (such as tissue plasminogen activator, streptokinase and urokinase), aspirin, dipyridamole, ticlopidine, clopidogrel, abciximab; antimigratory agents; antisecretory agents (breveldin); immunosuppressives (cyclosporine, tacrolimus (FK-506), sirolimus (rapamycin), azathioprine, mycophenolate mofetil); anti-angiogenic compounds (TNP470, genistein) and growth factor inhibitors (vascular endothelial growth factor (VEGF) inhibitors, fibroblast growth factor (FGF) inhibitors); angiotensin receptor blocker; nitric oxide donors; anti-sense oligonucleotides; antibodies (trastuzumab, rituximab); chimeric antigen receptors; cell cycle inhibitors and differentiation inducers (tretinoin); mTOR inhibitors, topoisomerase inhibitors (doxorubicin (adriamycin), amsacrine, camptothecin, daunorubicin, dactinomycin, eniposide, epirubicin, etoposide, idarubicin, irinotecan (CPT-11) and mitoxantrone, topotecan, irinotecan), corticosteroids (cortisone, dexamethasone, hydrocortisone, methylpednisolone, prednisone, and prenisolone); growth factor signal transduction kinase inhibitors; mitochondrial dysfunction inducers, toxins such as Cholera toxin, ricin, Pseudomonas exotoxin, Bordetella pertussis adenylate cyclase toxin, or diphtheria toxin, and caspase activators; and chromatin disruptors.

[0155] In certain embodiments, an additional therapeutic agent that may be used in combination with an eIF4E inhibitor is an inhibitor of an immunosuppression component, which may be an inhibitor of an immune checkpoint molecule or gene, a metabolic enzyme, an immunosuppressive cytokine, T_{reg} cells, or any combination thereof. As used herein, the term "immunosuppression component" refers to one or more cells, proteins, molecules, compounds or complexes providing inhibitory signals to assist in controlling or suppressing an immune response. For example, immunosuppression components include those molecules that partially or totally block immune stimulation; decrease, prevent or delay immune activation; or increase,

activate, or up regulate immune suppression. "Controlling or suppressing an immune response," as used herein, means reducing any one or more of antigen presentation, T cell activation, T cell proliferation, T cell effector function, cytokine secretion or production, and target cell lysis. Such modulation, control or suppression can promote or permit the persistence of a hyperproliferative disease or disorder (*e.g.*, cancer, chronic infections).

[0156] Immune checkpoint molecules include immune checkpoint ligands such as, PD-L1, PD-L2, CD80, CD86, B7-H3, B7-H4, HVEM, adenosine, GAL9, VISTA, CEACAM-1, CEACAM-3, CEACAM-5, PVRL2, and immune checkpoint receptors such as, PD-1, CTLA-4, BTLA, KIR, LAG3, TIM3, A2aR, CD244/2B4, CD160, TIGIT, LAIR-1, and PVRIG/CD112R). Metabolic enzymes include arginase and indoleamine 2,3-dioxygenase (IDO)), and immunosuppressive cytokines include IL-10, IL-4, IL-1RA, and IL-35. In certain embodiments, an inhibitor of immunosuppression component is a small molecule, an antisense moleucle, a ribozyme, an RNAi molecule (e.g., siRNA), an antibody or antigen binding fragment thereof, or fusion polypeptide (e.g., Fc fusion protein).

[0157] An antibody specific for PD-1 may be pidilizumab, nivolumab, pembrolizumab, MEDI0680 (formerly AMP-514), AMP-224, or BMS-936558.

[0158] An antibody specific for PD-L1 may be MDX-1105 (BMS-936559), durvalumab (formerly MEDI4736), atezolizumab (formerly MPDL3280A), or avelumab (formerly MSB0010718C). A compound specific for PD-L1 may be BMS-1001 or BMS-1166.

[0159] A CTLA4 inhibitor may be a CTLA4 specific antibody, such as tremelimumab or ipilimumab, or a CTLA4-Ig fusion protein (*e.g.,* abatacept, belatacept).

[0160] A LAG3 inhibitor may be LAG525, IMP321, IMP701, 9H12, or BMS-986016.

[0161] An IDO inhibitor may be levo-1-methyl tryptophan, epacadostat (INCB024360; Liu *et al.*, *Blood 115*:3520-30, 2010), ebselen (Terentis *et al., Biochem. 49*:591-600, 2010), indoximod, NLG919 (Mautino *et al.*, American Association for Cancer Research 104th Annual Meeting 2013; Apr 6-10, 2013), 1-methyl-tryptophan (1-MT)-tira-pazamine, or any combination thereof.

[0162] In certain embodiments an eIF4E inhibitor in accordance with the present invention is used simultaneously, in the same formulation or in separate formulations, or sequentially with an additional agent(s) as part of a combination therapy regimen.

[0163] eIF4E inhibitors according to Formulae I, II, III, IV, V and VI including their corresponding salts and pharmaceutically acceptable compositions of Formulae I, II, III, IV, V and VI compounds are also effective as therapeutic agents for treating or preventing cytokine mediated disorders, such as inflammation in a patient, preferably in a human. In one

embodiment, a compound or composition in accordance with the invention is particularly useful for treating or preventing a disease selected from chronic or acute inflammation, chronic inflammatory arthritis, rheumatoid arthritis, psoriasis, COPD, inflammatory bowel disease, septic shock, Crohn's disease, ulcerative colitis, multiple sclerosis and asthma.

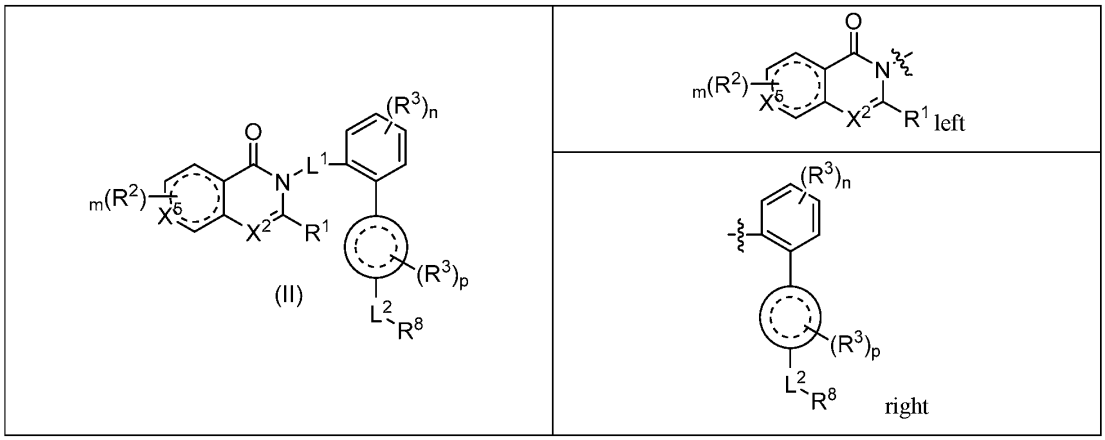
[0164] The inventive compounds their corresponding salts and pharmaceutically acceptable compositions are candidate therapeutics for treating brain related disorders which include without limitation autism, Fragile X-syndrome, Parkinson's disease and Alzheimer's disease. Treatment is effected by administering to a subject in need of treatment a compound of Formulae I, II, III, IV, V and VI, its pharmaceutically acceptable salt form, or a pharmaceutically acceptable composition of a compound of Formulae I, II, III, IV, V and VI or its salt.

[0165] The invention also supports the use of the inventive compounds or a pharmaceutically acceptable formulation of the inventive compound as an inhibitor of eIF4E activity. Such inhibition is achieved by contacting a cell expressing eIF4E with a compound or a pharmaceutically acceptable formulation, to lower or inhibit eIF4E activity, to provide therapeutic efficacy for a eIF4E dependent condition in a mammal in need thereof.

[0166] Therapeutically effective dosages of a compound according to Formulae I, II, III, IV, V and VI or a composition containing a compound of Formulae I, II, III, IV, V and VI will generally range from about 1 to 2000 mg/day, from about 10 to about 1000 mg/day, from about 10 to about 500 mg/day, from about 10 to about 250 mg/day, from about 10 to about 100 mg/day, or from about 10 to about 50 mg/day. The therapeutically effective dosages may be administered in one or multiple doses. It will be appreciated, however, that specific doses of the compounds of the invention for any particular patient will depend on a variety of factors such as age, sex, body weight, general health condition, diet, individual response of the patient to be treated, time of administration, severity of the disease to be treated, the activity of particular compound applied, dosage form, mode of application and concomitant medication. The therapeutically effective amount for a given situation will readily be determined by routine experimentation and is within the skills and judgment of the ordinary clinician or physician. In any case the compound or composition will be administered at dosages and in a manner which allows a therapeutically effective amount to be delivered based upon patient's unique condition.

General Methods for Synthesizing Compounds

[0167] Compounds described in this disclosure have a left-hand side and a right-hand side, illustrated below for Formula (II):



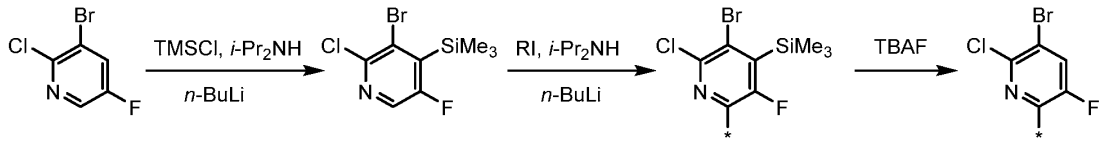
[0168] In general, the compounds described in this disclosure can be synthesized by constructing the left-hand side and the right-hand and coupling the two sides together, as described in the general methods below. Many of the reactions carried out on the left-hand side prior to coupling, such as cyanation, can be postponed until the coupling is completed. Similarly, some of the reactions listed as post-coupling protocols can be performed prior to the coupling reaction to give the same result.

Example 1. General Methods for Synthesizing 7-Aza-Thienylpyridine and Derivative Compounds

[0169] The 7-aza-thienylpyridine compounds in Table 1 can be synthesized using methods described in Example 1. For some compounds, some of the reactions described in Example 2 and/or Example 3, below, can be used to prepare the compounds.

Example 1A. Methods of synthesizing the left-hand side

Example 1A.1



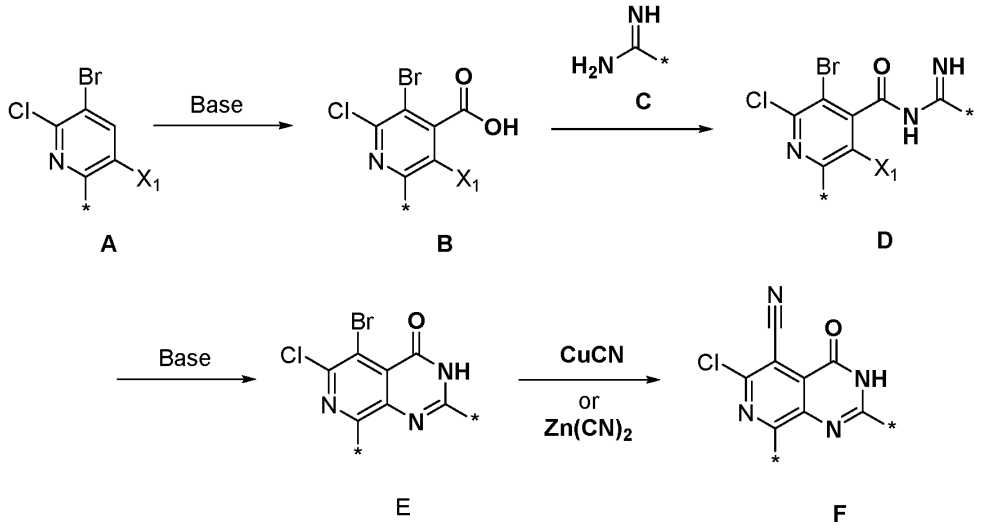
[0170] To dry N-isopropylpropan-2-amine (1.2 equiv.) in THF (0.3 M) at 0 °C is added n-butyllithium (2.5 M in hexane) (1.2 equiv.) slowly and the mixture is stirred for 10 min. The LDA solution in THF is used directly. To a solution of 3-bromo-2-chloro-5-fluoro-pyridine (**A**, 1 equiv.) in THF (0.3 M) at -78 °C is added the LDA solution and the resulting dark mixture is stirred for 45 min. Chloro(trimethyl)silane (1.7 equiv.) is added and the mixture is allowed to warm to rt within ca. 15 h. The reaction mixture is quenched with water, the layers separated,

and the aqueous layer extracted with ethylacetate. The organic layers are combined, evaporated with silica gel and the free-flowing silica gel is loaded on a column and (3-bromo-2-chloro-5-fluoro-6-methyl-4-pyridyl)-trimethyl-silane (**B**) is purified by silica gel chromatography.

[0171] To a solution of (3-bromo-2-chloro-5-fluoro-4-pyridyl)-trimethyl-silane (**B**, 1 equiv.) in THF (0.25 M) at -78 °C is added LDA solution (1.2 equiv.) prepared as above and the resulting dark mixture is stirred for 45 min. Iodomethane (10 equiv.) is added and the mixture is allowed to warm to rt within ca. 15 h. The reaction mixture is quenched with water, the layers separated, and the aqueous layer further extracted with ethylacetate. The organic layers are combined, evaporated with silica gel and the free-flowing silica gel loaded on a column and (3-bromo-2-chloro-5-fluoro-6-methyl-4-pyridyl)-trimethyl-silane (**C**) is purified via silica gel chromatography.

[0172] (3-bromo-2-chloro-5-fluoro-6-methyl-4-pyridyl)-trimethyl-silane (**C**, 1 equiv.) is dissolved in THF (0.67 M), cooled to 0 °C, and tetrabutylammonium fluoride (in THF) (1.2 equiv.) is added and the mixture stirred at 0 °C. After 10 min the reaction is quenched with NH4Cl(aq) and diluted with EtOAc. The organic phase is washed with water twice, dried, filtered, concentrated, and loaded on a column and 3-bromo-2-chloro-5-fluoro-6-methylpyridine (**D**) is purified via silica gel chromatography.

Example 1A.2



[0173] To a solution of 3-bromo-2-chloro-5-fluoro-6-methylpyridine (**A**, 1 equiv.) in tetrahydrofuran (0.40 M) at -96°C (internal temperature), lithium diisopropylamide solution (1.2 equiv.; 2 M in tetrahydrofuran) is added over a period of 60 min, maintaining internal temperature between -96 to -84 °C and the reaction mixture is maintained at -96 to -90 °C for 2

h. Carbon dioxide gas is purged into the reaction mixture for 35 minutes, maintaining internal temperature at -95 to -78 °C. Progress of the reaction is monitored by TLC and the reaction mixture is warmed to -50 to - 45 °C, quenched with saturated aqueous ammonium chloride solution, and stirred for 10 min. The solution is acidified to pH 2.0-1.5 with 6 N hydrochloric acid, diluted with ethyl acetate and the organic layer washed with water. The aqueous layer is extracted with ethyl acetate and the combined organic layers are concentrated under reduced pressure, stirred in dichloromethane and the solid precipitated is filtered, washed with dichloromethane, and dried under vacuum to afford 3-bromo-2-chloro-5-fluoro-6-methylisonicotinic acid (**B**).

[0174] To a solution of 3-bromo-2-chloro-5-fluoro-6-methylisonicotinic acid (**B**, 1 equiv.) in N,N-dimethylformamide (0.32 M), acetamidine hydrochloride (**C**, 1.4 equiv.) is added and reaction mixture is cooled at 0 °C. N,N-di-isopropylethylamine (5 equiv.) and HATU (1.1 equiv.) are added and reaction mixture is stirred at room temperature for 1 h. The reaction mixture is diluted with water, extracted with ethyl acetate and the combined organic layers are dried over anhydrous sodium sulphate, filtered and concentrated to afford 3-bromo-2-chloro-5-fluoro-N-(1-iminoethyl)-6-methylisonicotinamide (**D**).

[0175] To a stirred solution of 3-bromo-2-chloro-5-fluoro-N-(1-iminoethyl)-6-methylisonicotinamide (**D**, 1 equiv.) in tetrahydrofuran (2 M), sodium hydride (60 %) (1 equiv.) is added at 0 °C and stirred for 1 h at 0 °C. The reaction mass is slowly warmed to room temperature and stirred for 16 h. The reaction mass is cooled to 0 °C, acidified with 2 N hydrochloric acid (pH ~ 2), and the resulting solid filtered, washed with 10 % methanol in diethyl ether and dried to afford 5-bromo-6-chloro-2,8-dimethylpyrido[3,4-d]pyrimidin-4(3H)-one (**E**).

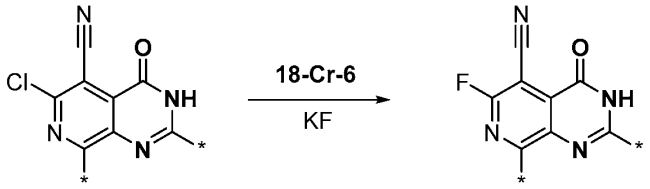
[0176] To a stirred solution of 5-bromo-6-chloro-2,8-dimethylpyrido[3,4-d]pyrimidin-4(3H)-one (**E**, 1 equiv.) in N,N-dimethylformamide (0.056 M), copper(I) cyanide (1.2 equiv.) is added at room temperature. The reaction is heated to 100 °C and stirred for 16 h. The reaction is quenched with 1 N hydrochloric acid, and the solid is filtered, washed with diethyl ether, and purified by via chromatography to afford 6-chloro-2,8-dimethyl-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidine-5-carbonitrile (**F**).

[0177] 5-bromo-6-chloro-2,8-dimethylpyrido[3,4-d]pyrimidin-4(3H)-one (**E**, 1 equiv.), copper(I) cyanide (1.2 equiv.), and NMP (0.072 M) are combined in a sealable vessel with a stir bar. The resulting mixture is sealed, stirred, and heated at 90 °C for 20 h. Upon cooling to room temperature, the reaction mixture is diluted with 1 % TFA in acetonitrile, filtered, and purified

via chromatography to afford 6-chloro-2,8-dimethyl-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidine-5-carbonitrile (**F**).

[0178] To a solution of 5-bromo-6-chloro-2,8-dimethylpyrido[3,4-d]pyrimidin-4(3H)-one (**E**, 1 equiv.) in *N,N*-dimethylacetoamide (0.07 M) is added dicyanozinc (1.4 equiv.) and tetrakis(triphenylphosphine)palladium (2.0 equiv.) at room temperature. The mixture is degassed with argon for 5 min, and stirred for 5 h at 130 °C. Upon cooling to room temperature, the mixture is diluted with dimethyl sulfoxide and acetonitrile and purified by chromatography to afford 6-chloro-2,8-dimethyl-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidine-5-carbonitrile (**F**).

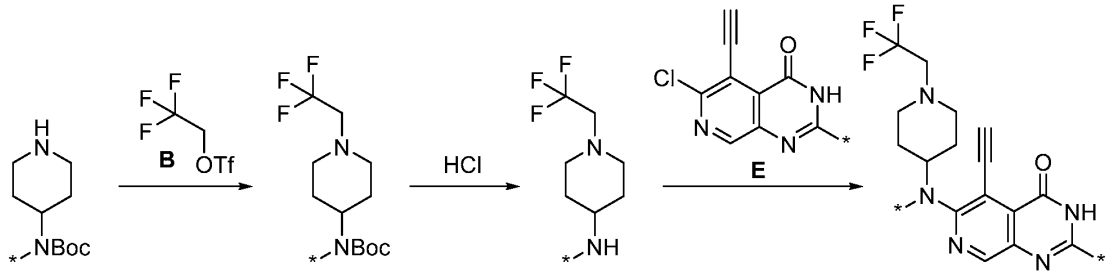
Example 1A.3



A **B**

[0179] A solution of 6-chloro-2-methyl-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidine-5-carbonitrile (**A**, 1 equiv.) in dimethyl sulfoxide (0.23 M) is purged with argon gas for 10 minutes. 18-Crown-6 ether (1.5 equiv.) and potassium fluoride (5 equiv.) are added to the reaction mixture and purging is continued for 5 minutes and stirred in a preheated oil bath at 160 °C for 2 h. The reaction mixture is cooled, poured on to ice cold water, extracted with ethyl acetate, and the ethyl acetate layer washed with brine solution, dried over anhydrous sodium sulphate, concentrated, and triturated with diethyl ether to get 6-fluoro-2-methyl-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidine-5-carbonitrile (**B**).

Example 1A.4



A **C** **D** **F**

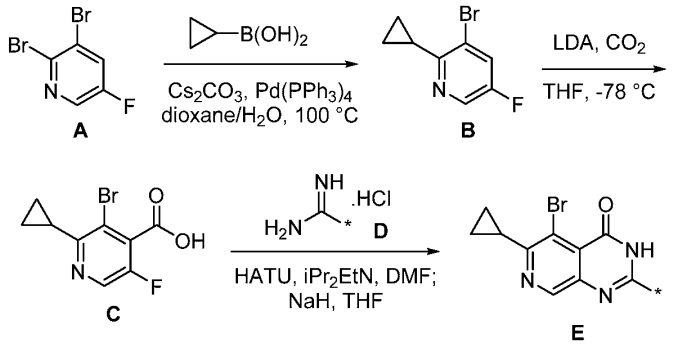
[0180] To a solution of *tert*-butyl methyl(piperidin-4-yl)carbamate (**A**, 1 equiv.) and *N,N*-diisopropylethylamine (10 equiv.) in acetonitrile (0.35 M), 2,2,2-trifluoroethyl trifluoromethanesulfonate (**2**, 1.25 equiv.) is added dropwise and the mixture stirred at room

temperature for 16 h. The reaction mixture is diluted with water, extracted with dichloromethane, and the organic layer dried over anhydrous sodium sulphate, filtered, concentrated, and purified by flash column chromatography to afford *tert*-butyl methyl(1-(2,2,2-trifluoroethyl)piperidin-4-yl)carbamate (**C**).

[0181] A solution of *tert*-butyl methyl(1-(2,2,2-trifluoroethyl)piperidin-4-yl)carbamate (**C**, 1 equiv.) in hydrochloride (4 M solution in 1,4-dioxane, 0.34 M) is stirred at room temperature for 4 h. The reaction mixture is concentrated to afford *N*-methyl-1-(2,2,2-trifluoroethyl)piperidin-4-amine hydrochloride (**D**).

[0182] A solution of 6-chloro-2-methyl-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidine-5-carbonitrile (**E**, 1 equiv.) and *N*-methyl-1-(2,2,2-trifluoroethyl)piperidin-4-amine hydrochloride (**D**, 3 equiv.) in *N,N*-dimethylacetamide (0.24 M), potassium fluoride (8 equiv.) and 18-crown-6 (1 equiv.) are added and the reaction mixture heated at 130 °C for 16 h. The reaction mixture is cooled, diluted with water, extracted with ethyl acetate, and the organic layer washed with water, dried over anhydrous sodium sulphate, filtered, concentrated, and purified by flash column chromatography to afford 2-methyl-6-(methyl(1-(2,2,2-trifluoroethyl)piperidin-4-yl)amino)-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidine-5-carbonitrile (**F**).

Example 1A.5

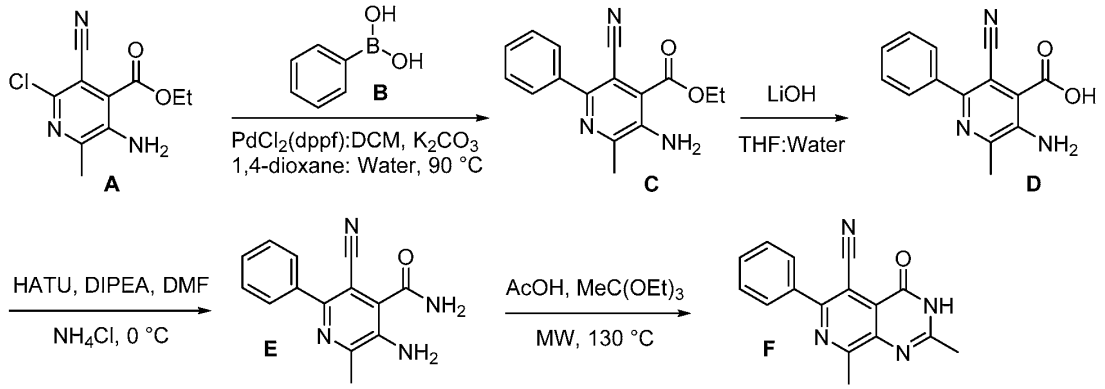


[0183] 1,4-Dioxane (24 mL) and water (8 mL) is added to a mixture of 2,3-dibromo-5-fluoropyridine (**A**, 3000 mg, 11.8 mmol), cyclopropylboronic acid (1112 mg, 12.9 mmol), and cesium carbonate (8436 mg, 25.9 mmol). The mixture is bobbled with argon bubbling for 5 min. Tetrakis(triphenylphosphine)palladium (680 mg, 0.590 mmol) is added to the mixture, and the mixture is vacuumed and backfilled with argon three times. The resulting clear yellow reaction mixture is stirred for 72 h at 110 °C. The mixture is diluted with ethyl acetate, and washed with brine, dried over anhydrous magnesium sulfate, and concentrated *in vacuo* after filtration. Purification by silica gel column chromatography (0 to 5 % ethyl acetate in hexane) gave 3-bromo-2-cyclopropyl-5-fluoropyridine (**B**).

[0184] n-Butyllithium (2.5 M in hexane, 2.1 mL, 5.30 mmol) is added to a stirred solution of diisopropylamine (0.81 mL, 5.80 mmol) in THF (5 mL) at 0 °C under argon. The resulting light yellow solution is stirred for 10 min at 0 °C and then added slowly to a stirred solution of 3-bromo-2-cyclopropyl-5-fluoropyridine (**B**, 1000 mg, 4.60 mmol) in tetrahydrofuran (20 mL) at -78 °C under argon. The resulting yellow reaction mixture is stirred at -78 °C under argon for 30 min and then carbon dioxide gas is bubbled in for 2 min. The mixture is stirred at -78 °C for 10 min and then warmed to room temperature over 5 min. The reaction is diluted with 0.1 N sodium hydroxide, and extracted with diethyl ether. Water layer is acidified by 3 M hydrogen chloride, and extracted with ethyl acetate twice, dried over anhydrous magnesium sulfate, and concentrated *in vacuo* after filtration to afford 3-bromo-2-cyclopropyl-5-fluoroisonicotinic acid (**C**).

[0185] To a *N,N*-dimethylformamide (14 mL) solution of 3-bromo-2-cyclopropyl-5-fluoroisonicotinic acid (**C**, 730.mg, 2.81 mmol) is added 1-[bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxide hexafluorophosphate (1387 mg, 3.60 mmol) and *N,N*-diisopropylethylamine (2.0 mL, 11.2 mmol) at 0 °C. The mixture is stirred for 5 min at room temperature, and acetamidine hydrochloride (**D**, 345 mg, 3.60 mmol) is added to the mixture. After stirring the mixture for 17 h at room temperature, ice-cold water is added to the mixture, and extracted with ethyl acetate twice. The combined extracts are washed with aqueous solution of ammonium chloride, aqueous solution of sodium bicarbonate, and brine, dried over anhydrous magnesium sulfate, and concentrated *in vacuo* after filtration. The residue is dissolved tetrahydrofuran (18 mL), and sodium hydride (60 % in mineral oil, 225 mg, 5.60 mmol) is added to the mixture at 0 °C. After stirring the mixture for 18 h, ice-cold water is added to the mixture, and extracted with ethyl acetate three times, dried over anhydrous magnesium sulfate, and concentrated *in vacuo* after filtration. The residue is triturated with dichloromethane, and filtered to afford 5-bromo-6-cyclopropyl-2-methylpyrido[3,4-d]pyrimidin-4(3H)-one (**E**).

Example 1A.6



[0186] To a solution of ethyl 3-amino-6-chloro-5-cyano-2-methylisonicotinate (**A**, 0.90 g, 3.75 mmol) in 1,4-dioxane and water (4:1, 10.0 mL), phenylboronic acid (**B**, 0.68 g, 5.62 mmol) and potassium carbonate (1.53 g 11.25 mmol) are added. The reaction mixture is purged with argon for 5 min. Then, [1,1-bis(diphenylphospino)ferrocene] dichloropaladium(II) (complex with dichloromethane, 0.031 g, 0.037 mmol) is added and the reaction mixture is heated at 90 °C for 5 h. After this time, the reaction mixture is cooled, diluted with water, and extracted with ethyl acetate. The organic layer is dried over anhydrous sodium sulfate, filtered, and concentrated to obtain the crude product. This is purified by silica gel (100-200 mesh) column chromatography using 30-40 % ethyl acetate in hexane to afford ethyl 3-amino-5-cyano-2-methyl-6-phenylisonicotinate (**C**).

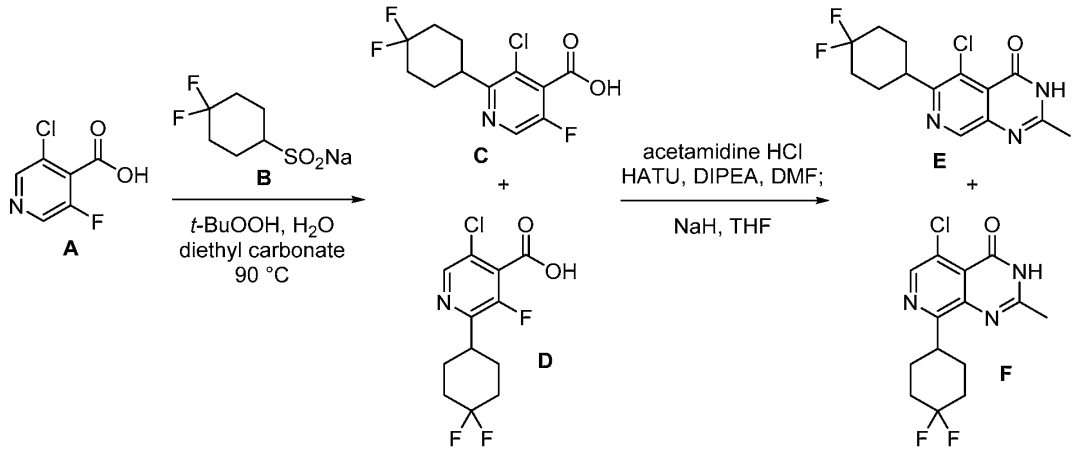
[0187] To a solution of ethyl 3-amino-5-cyano-2-methyl-6-phenylisonicotinate (**C**, 0.6 g, 2.13 mmol) in tetrahydrofuran and water (4:1, 6 mL) at room temperature, lithium hydroxide (0.44 g, 10.67 mmol) is added. This reaction mixture is stirred at room temperature for 2 h. After this time, the reaction mixture is diluted with water, acidified with 1 N hydrochloric acid, and extracted with ethyl acetate. The organic layer is dried over anhydrous sodium sulfate, filtered, and concentrated to obtain the crude product. This is washed with diethyl ether to afford 3-amino-5-cyano-2-methyl-6-phenylisonicotinic acid (**D**).

[0188] To a solution of 3-amino-5-cyano-2-methyl-6-phenylisonicotinic acid (**D**, 0.5 g, 1.97 mmol) in *N*,*N*-dimethylformamide (5.0 mL), ammonium chloride (0.31 g, 5.92 mmol) and 1-[bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxid hexafluorophosphate (0.840 g, 2.21 mmol) are added. This reaction mixture is cooled to 0 °C, *N*,*N*-di-isopropylethylamine (2.7 mL, 14.70 mmol) is added, and the reaction mixture is stirred at 0 °C for 10 min. Then, the reaction mixture is diluted with water and extracted with ethyl acetate. The organic layer is dried over anhydrous sodium sulfate, filtered, and concentrated to obtain the

crude product. This is purified by silica gel (100-200 mesh) column chromatography using 30-40 % ethyl acetate in hexanes to afford 3-amino-5-cyano-2-methyl-6-phenylisonicotinamide (**E**).

[0189] A solution of 3-amino-5-cyano-2-methyl-6-phenylisonicotinamide (**E**, 0.4 g, 1.19 mmol), in triethylorthoacetate and acetic acid (4:1, 4 mL) is heated at 130 °C for 2 h under microwave. After this time, the reaction mixture is cooled, diluted with hexanes, and filtered to afford 2,8-dimethyl-4-oxo-6-phenyl-3,4-dihydropyrido[3,4-d]pyrimidine-5-carbonitrile (**F**).

Example 1A.7

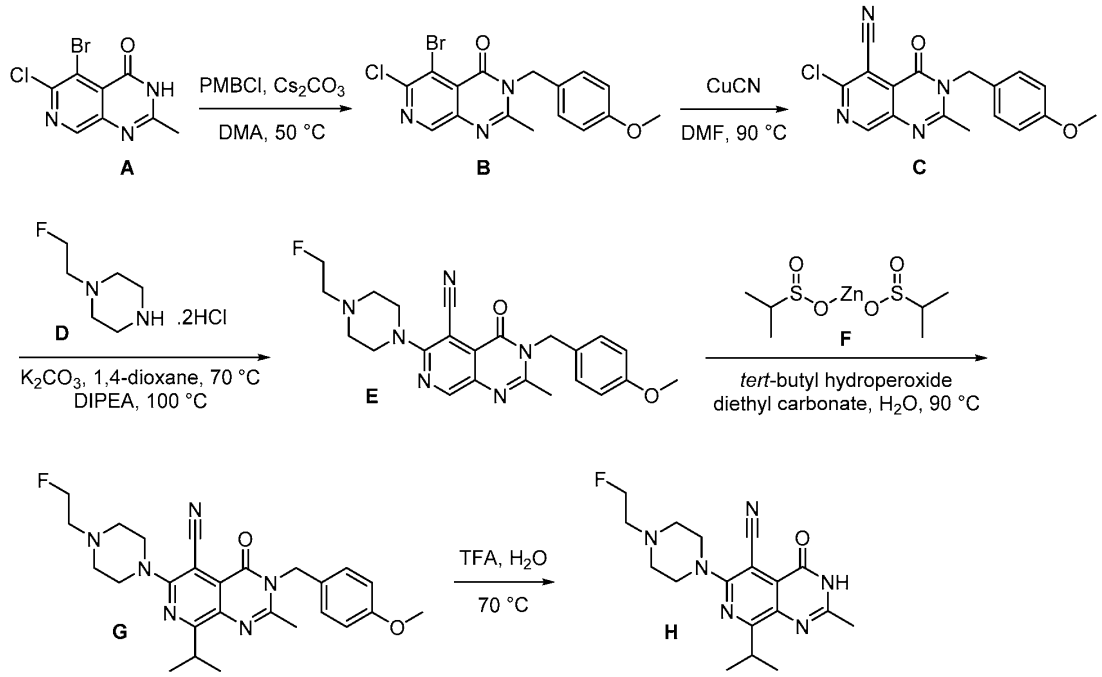


[0190] To a stirred mixture of 3-chloro-5-fluoroisonicotinic acid (**A**, 1 equiv.) in diethyl carbonate (0.29 M) and water (0.44 M) under argon is added sodium 4,4-difluorocyclohexane-1-sulfinate (**B**, 3 equiv.) and the mixture is cooled to 0 °C. *tert*-Butyl hydroperoxide (70 wt. % in water) (10 equiv.) is added and the mixture is stirred for 5 min then heated at 90 °C under argon with an oil bath for 3 h. Volatiles are removed on a rotary evaporator. The residue is taken up in a mixture of water, acetonitrile and TFA, filtered, and purified via preparatory HPLC to afford a mixture of 3-chloro-2-(4,4-difluorocyclohexyl)-5-fluoroisonicotinic acid (**C**) and 5-chloro-2-(4,4-difluorocyclohexyl)-3-fluoroisonicotinic acid (**D**).

[0191] HATU (1.1 equiv.) is added to a stirred solution of 3-chloro-2-(4,4-difluorocyclohexyl)-5-fluoroisonicotinic acid (**C**) and 5-chloro-2-(4,4-difluorocyclohexyl)-3-fluoroisonicotinic acid (**D** 1 equiv.) in DMF (0.46 M) at room temperature under argon. After 2 min *N,N*-diisopropylethylamine (1.1 equiv.) is added. After stirring at room temperature for 35 min a solution of acetamidine hydrochloride (2 equiv.) and *N,N*-diisopropylethylamine (2.2 equiv.) in DMF (5.6 M) (this is heated with a heat gun and sonicated to get all of the acetamidine dissolved) is added. The resulting solution is stirred vigorously at room temperature under argon for 1.5 h. The reaction mixture is diluted with ethyl acetate and washed three times with brine. The organics are dried over magnesium sulfate, filtered, concentrated on a rotary evaporator, and

dried under high vacuum to afford a viscous amber oil. The oil is dissolved in THF (0.046 M) with stirring under argon. Sodium hydride (2.2 equiv.) is added and the reaction mixture is stirred vigorously at room temperature under argon for 21 h. A solution of ammonium chloride (5 equiv.) in water (0.14 M) is added with vigorous stirring. The resulting mixture is partitioned between ethyl acetate and brine. The organics are dried over magnesium sulfate, filtered, and concentrated on a rotary evaporator. The residue is taken up in NMP, acetonitrile, and TFA, filtered, and purified via preparatory HPLC to afford 5-chloro-6-(4,4-difluorocyclohexyl)-2-methylpyrido[3,4-d]pyrimidin-4(3H)-one (**E**) and 5-chloro-8-(4,4-difluorocyclohexyl)-2-methylpyrido[3,4-d]pyrimidin-4(3H)-one (**F**)

Example 1A.8



[0192] 4-Methoxybenzyl chloride (1.27 mL, 9.38 mmol) is added to a stirred mixture of 5-bromo-6-chloro-2-methylpyrido[3,4-d]pyrimidin-4(3H)-one (**A**, 1.98 g, 7.21 mmol) and cesium carbonate (3.29 g, 10.1 mmol) in DMA (14 mL) at room temperature under argon. The resulting mixture is stirred vigorously and heated at 50 °C under argon for 2 h. The reaction mixture is diluted with ethyl acetate (1.5 L), washed once with water, and twice with brine. The organics are dried over magnesium sulfate, filtered, concentrated on a rotary evaporator with silica gel, and purified via silica gel chromatography (0-40 % ethyl acetate in dichloromethane) to afford 5-bromo-6-chloro-3-(4-methoxybenzyl)-2-methylpyrido[3,4-d]pyrimidin-4(3H)-one (**B**).

[0193] 5-Bromo-6-chloro-3-(4-methoxybenzyl)-2-methylpyrido[3,4-d]pyrimidin-4(3H)-one (**B**, 1.24 g, 3.14 mmol) is dissolved in DMF (20 mL) with stirring at 90 °C under argon. Copper(I) cyanide (338 mg, 3.77 mmol) is added and the resulting clear red solution is stirred and heated at 90 °C under argon for 1 h 40 min. While still hot the reaction mixture is diluted with ethyl acetate and filtered through Celite into ethyl acetate (600 mL). The filter cake is washed with ethyl acetate. The filtrate is shaken with water to give an emulsion which is filtered. The filtrate is partitioned between ethyl acetate and brine. The organics are washed twice with brine, dried over magnesium sulfate, filtered, concentrated on a rotary evaporator with silica gel, and purified via silica gel chromatography (0-100 % ethyl acetate in dichloromethane) to afford 6-chloro-3-(4-methoxybenzyl)-2-methyl-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidine-5-carbonitrile (**C**).

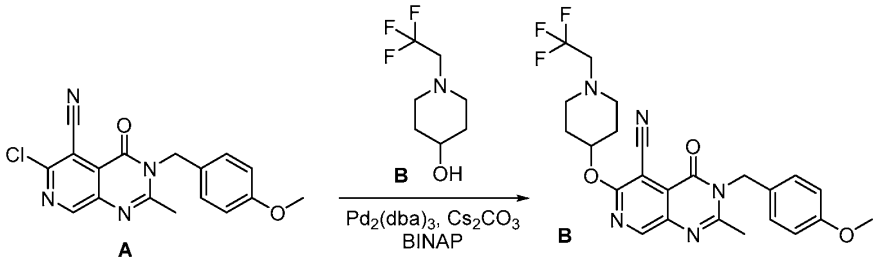
[0194] 6-Chloro-3-(4-methoxybenzyl)-2-methyl-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidine-5-carbonitrile (**C**, 100 mg, 0.293 mmol), 1-(2-fluoroethyl)piperazine bis HCl salt (**D**, 120 mg, 0.587 mmol), potassium carbonate (183 mg, 1.32 mmol), and NMP (1.5 mL) are combined in a sealable vessel with a stir bar. The resulting mixture is sealed, stirred vigorously, and heated at 70 °C with an oil bath for 40 min. *N,N*-diisopropylethylamine (0.26 mL, 1.47 mmol) is added and the resulting mixture is sealed, stirred vigorously, and heated at 100 °C with an oil bath for 1 h. After cooling to room temperature, the reaction mixture is diluted with methanol and acetic acid (0.34 mL, 5.87 mmol). The resulting mixture is filtered and purified via preparatory HPLC (10-45 % acetonitrile in water with 0.1 % TFA). Fractions containing the desired product are combined and concentrated on a rotary evaporator down to ~20 mL and then lyophilized to dryness to afford a yellow oil. The oil is dissolved in acetonitrile and loaded onto a 2-gram Strata X-C ion exchange column from Phenomenex. The column is washed sequentially with water, acetonitrile, methanol, and then 5 % ammonium hydroxide in methanol. Eluent containing the desired product is concentrated on a rotary evaporator and dried under high vacuum to afford 6-(4-(2-fluoroethyl)piperazin-1-yl)-3-(4-methoxybenzyl)-2-methyl-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidine-5-carbonitrile (**E**).

[0195] To a stirred mixture of 6-(4-(2-fluoroethyl)piperazin-1-yl)-3-(4-methoxybenzyl)-2-methyl-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidine-5-carbonitrile (**E**, 28.2 mg, 0.065 mmol) in diethyl carbonate (0.4 mL) and water (0.2 mL) under argon is added bis((isopropylsulfinyl)oxy)zinc (**F**, 54.2 mg, 0.194 mmol) followed by *tert*-butyl hydroperoxide (70 wt. % in water) (0.092 mL, 0.666 mmol). The mixture is stirred and heated at 90 °C under argon with an oil bath for 10 min. The reaction mixture is diluted with NMP, acetic acid, and methanol, filtered, and purified via preparatory HPLC (15-65 % acetonitrile in water with 0.1 %

TFA). Fractions containing the desired product are loaded onto a Strata X-C ion exchange column from Phenomenex. The column is washed sequentially with water, acetonitrile, methanol, and then 5 % ammonium hydroxide in methanol. Eluent containing the desired product is concentrated on a rotary evaporator and dried under high vacuum to afford 6-(4-(2-fluoroethyl)piperazin-1-yl)-8-isopropyl-3-(4-methoxybenzyl)-2-methyl-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidine-5-carbonitrile (**G**).

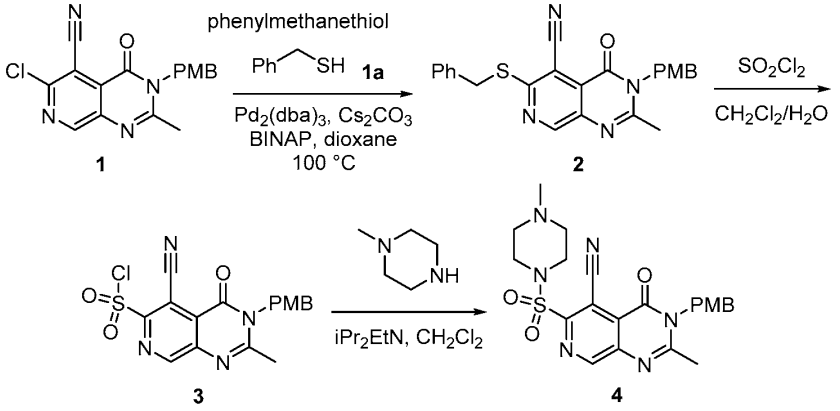
[0196] 6-(4-(2-Fluoroethyl)piperazin-1-yl)-8-isopropyl-3-(4-methoxybenzyl)-2-methyl-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidine-5-carbonitrile (**G**, 23.8mg, 0.050 mmol), TFA (2 mL), and water (0.1 mL) are combined in a sealable vessel with a stir bar, sealed, stirred, and heated at 70 °C for 1 h. Volatiles are removed on a rotary evaporator. The residue is taken up in NMP and methanol, filtered, and purified via preparatory HPLC (10-40 % acetonitrile in water with 0.1 % TFA). Fractions containing the desired product are loaded onto a Strata X-C ion exchange column from Phenomenex. The column is washed sequentially with water, acetonitrile, methanol, and then 5 % ammonium hydroxide in methanol. Eluent containing the desired product is concentrated on a rotary evaporator and dried under high vacuum to afford 6-(4-(2-fluoroethyl)piperazin-1-yl)-8-isopropyl-2-methyl-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidine-5-carbonitrile (**H**).

Example 1A.9



[0197] To a 1,4-dioxane (5.6 mL) solution of 6-chloro-3-(4-methoxybenzyl)-2-methyl-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidine-5-carbonitrile (**A**, 192 mg, 0.560 mmol) is added 1-(2,2,2-trifluoroethyl)piperidin-4-ol (**B**, 206 mg, 1.13 mmol), cesium carbonate (367 mg, 1.13 mmol), 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl (105 mg, 0.169 mmol), and tris(dibenzylideneacetone)dipalladium (103 mg, 0.113 mmol) at room temperature. The mixture is bubbled with argon for 5 min, and stirred for 2 h at 100 °C. The mixture is diluted with ethyl acetate and filtered through a pad of Celite. The filtrate is concentrated *in vacuo*. Purification by silica gel column chromatography (0-80 % ethyl acetate in hexane) gave crude 3-(4-methoxybenzyl)-2-methyl-4-oxo-6-((1-(2,2,2-trifluoroethyl)piperidin-4-yl)oxy)-3,4-dihydropyrido[3,4-d]pyrimidine-5-carbonitrile (**C**).

Example 1A.10



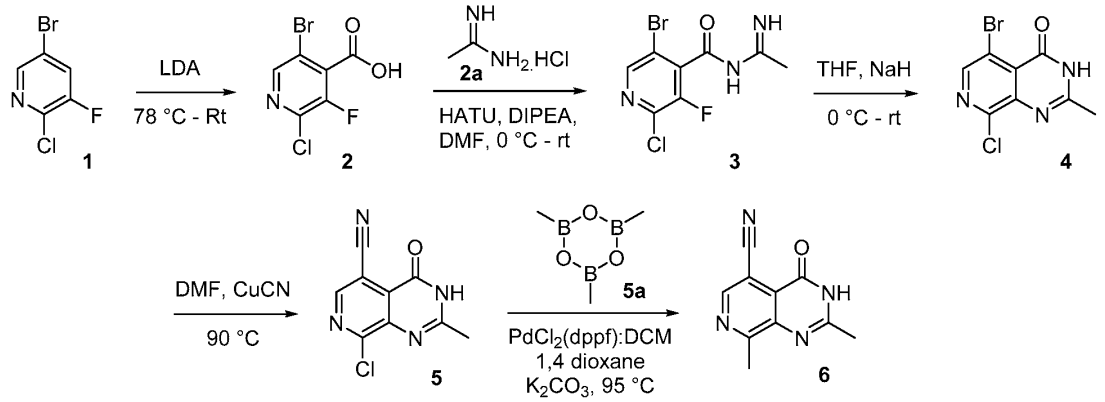
[0198] To a 1,4-dioxane (3.9 mL) solution of 6-chloro-3-(4-methoxybenzyl)-2-methyl-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidine-5-carbonitrile (**1**, 134 mg, 0.390 mmol) is added phenylmethanethiol (**1a**, 0.09 mL, 0.790 mmol), cesium carbonate (256 mg, 0.790 mmol), 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl (73 mg, 0.118 mmol), and tris(dibenzylideneacetone)dipalladium (72 mg, 0.0790 mmol) at room temperature. The mixture is bubbled with argon for 5 min, and stirred for 2 h at 100 °C. The mixture is diluted with ethyl acetate, and washed with 5 % breech in water, dried over anhydrous magnesium sulfate, and concentrated *in vacuo* after filtration. Purification by preparative HPLC (C_{18} column, 15-85 % acetonitrile in water + 0.1 % trifluoroacetic acid) gave 6-(benzylthio)-3-(4-methoxybenzyl)-2-methyl-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidine-5-carbonitrile (**2**).

[0199] To a dichloromethane (2 mL) and water (0.4 mL) solution of 6-(benzylthio)-3-(4-methoxybenzyl)-2-methyl-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidine-5-carbonitrile (**2**, 74 mg, 0.173 mmol) is added sulfuryl chloride (0.1 mL, 1.21 mmol) at 0 °C. The mixture is stirred for 1 h at room temperature. Organic layer is separated and dried over anhydrous magnesium sulfate, and concentrated *in vacuo* after filtration to give crude 5-cyano-3-(4-methoxybenzyl)-2-methyl-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidine-6-sulfonyl chloride (**3**).

[0200] To a dichloromethane (1.7 mL) solution of 5-cyano-3-(4-methoxybenzyl)-2-methyl-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidine-6-sulfonyl chloride (**3**, 70 mg, 0.173 mmol) is added 1-methylpiperazine (0.06 mL, 0.520 mmol) and diisopropylethylamine (0.09 mL, 0.520 mmol) at 0 °C. After stirring the mixture for 1 h at room temperature, the mixture is diluted with aqueous sodium bicarbonate. Organic materials are extracted with ethyl acetate twice, dried over anhydrous magnesium sulfate, and concentrated *in vacuo* after filtration. Purification by preparative HPLC (C_{18} column, 15-60 % acetonitrile in water + 0.1 % trifluoroacetic acid) gave

3-(4-methoxybenzyl)-2-methyl-6-((4-methylpiperazin-1-yl)sulfonyl)-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidine-5-carbonitrile (**4**).

Example 1A.11



[0201] A solution of 5-bromo-2-chloro-3-fluoropyridine (**1**, 30.0 g, 143.6 mmol) in tetrahydrofuran (300 mL) is cooled to -78 °C and lithiumdisopropylamide (2 M in THF, 78.9 mL, 157.9 mmol) is added dropwise. This reaction mixture is stirred at -78 °C for 1 h. Then, the reaction mixture is purged with carbon dioxide gas for 15 min allowed to warm at room temperature. The reaction mixture is quenched with ammonium chloride solution and diluted with water. The aqueous layer is washed with ethyl acetate, acidified with 6 N hydrochloric acid solution, and extracted with 15 % methanol in dichloromethane. The organic layer is dried over anhydrous sodium sulfate, filtered, and concentrated to afford 5-bromo-2-chloro-3-fluoroisonicotinic acid (**2**).

[0202] To solution of 5-bromo-2-chloro-3-fluoroisonicotinic acid (**2**, 18.0 g, 71.1 mmol) in *N,N*-dimethylformamide (30 mL) at 0 °C, acetamidine hydrochloride (**2a**, 13.4 g, 142.3 mmol) is added. Then *N,N*-diisopropylethylamine (110 mL, 711.0 mmol) and 1-[bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxid hexafluorophosphate (40.5 g, 106.6 mmol) are added and the reaction mixture is stirred at room temperature for 2 h. After this time, reaction mixture is diluted with water and extracted with ethyl acetate. The organic layer is dried over anhydrous sodium sulfate, filtered, and concentrated to afford crude 5-bromo-2-chloro-3-fluoro-*N*-(1-iminoethyl)isonicotinamide (**3**).

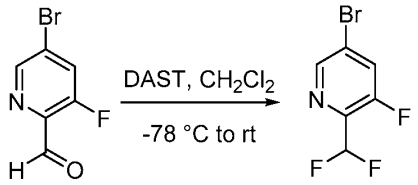
[0203] A solution of crude 5-bromo-2-chloro-3-fluoro-*N*-(1-iminoethyl)isonicotinamide (**3**, 18.0 g) in tetrahydrofuran (200 mL) is cooled to 0 °C, then 60 % sodium hydride in mineral oil (7.30 g NaH, 184.3 mmol) is added portionwise and the reaction mixture is stirred at room temperature for 12 h. After this time, the reaction mixture is poured into ice-cold water. The aqueous layer is washed with 5 % methanol in dichloromethane, acidified with 6 N hydrochloric acid solution,

and extracted with 10 % methanol in dichloromethane. The organic layer from this extraction is dried over anhydrous sodium sulfate, filtered, and concentrated to obtain the crude product which is washed with diethyl ether to afford 5-bromo-8-chloro-2-methylpyrido[3,4-d]pyrimidin-4(3*H*)-one (**4**).

[0204] To a solution of 5-bromo-8-chloro-2-methylpyrido[3,4-d]pyrimidin-4(3*H*)-one (**4**, 8.0 g, 29.3 mmol) in *N*,*N*-dimethylformamide (80.0 mL), copper(I) cyanide (4.1 g, 46.8 mmol) is added. The reaction mixture is heated at 90 °C for 3 h. After this time, the reaction mixture is cooled, diluted with water, acidified with 6 N hydrochloric acid solution, and extracted with ethyl acetate. The organic layer is concentrated to obtain the crude product which is purified by silica gel (100-200 mesh) column chromatography using 40-50 % ethyl acetate in hexanes as eluent to afford 8-chloro-2-methyl-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidine-5-carbonitrile (**5**).

[0205] To a solution of 8-chloro-2-methyl-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidine-5-carbonitrile (**5**, 1.0 g, 4.55 mmol) in 1,4-dioxane (15.0 mL) at room temperature, 2,4,6-trimethyl-1,3,5,2,4,6-trioxatriborinane (**5a**, 1.0 mL, 7.5 mmol), potassium carbonate (2.0 g, 15.0 mmol), and water (2 mL) are added. This reaction mixture is degassed with nitrogen for 10 min. Then, [1,1-bis(diphenylphospino)ferrocene] dichloropaladium(II),complex with dichloromethane (0.183 g, 0.225 mmol) is added and reaction mixture is heated at 95 °C for 12 h. After this time, the reaction mixture is cooled and concentrated under reduced pressure to obtain the crude product which is purified by silica gel (100-200 mesh) column chromatography using 10 % methanol in dichloromethane as eluent to afford 2,8-dimethyl-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidine-5-carbonitrile (**6**).

Example 1A.12

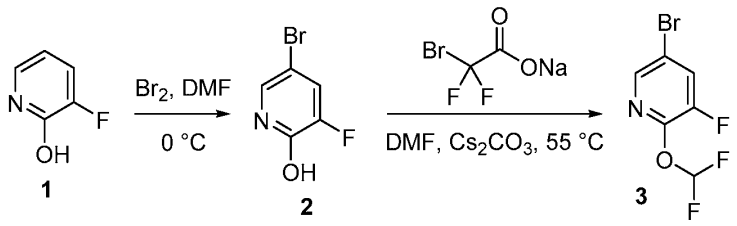


1 **2**

Diethylaminosulfur trifluoride (1.44 mL, 10.4 mmol) is added to a stirred solution of 5-bromo-3-fluoropicolinaldehyde (**1**, 0.97 g, 4.75 mmol) in DCM (20 mL) at -78 °C under argon. The cold bath is removed, and the reaction mixture is allowed to warm to room temperature under argon for 1.5 h. The reaction mixture is poured into a stirred mixture of saturated aqueous sodium bicarbonate and ice. The resulting mixture is stirred vigorously at room temperature for 1 h to fully quench the reaction mixture. The phases are separated, and the aqueous phase extracted

with dichloromethane. The combined organics are dried over sodium sulfate, filtered, concentrated on a rotary evaporator, and purified via silica gel chromatography (0-10 % ethyl acetate in hexanes) Fractions containing the desired product are combined and concentrated on a rotary evaporator at room temperature. The residue is diluted with dry THF (5 mL) and concentrated on a rotary evaporator. The residue is dried under high vacuum for 2 min to afford 5-bromo-2-(difluoromethyl)-3-fluoropyridine (**2**).

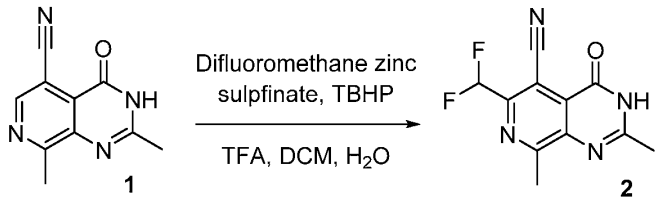
Example 1A.13



[0206] A solution of 3-fluoropyridin-2-ol (**1**, 20.0 g, 176.9 mmol) in *N,N*-dimethylformamide (220.0 mL) is cooled at 0 °C, bromine (10.30 mL, 194.6 mmol) is added drop wise and reaction mixture is stirred at 0 °C for 2 h. After completion reaction mixture is diluted with water and extracted with ethyl acetate. The organic layer is washed with sodium bicarbonate and brine, dried over anhydrous sodium sulphate, filtered and concentrated to get crude compound. Crude compound is purified by column chromatography using silica gel (100-200 mesh) and 2-3 % methanol in dichloromethane to afford 5-bromo-3-fluoropyridin-2-ol (**2**).

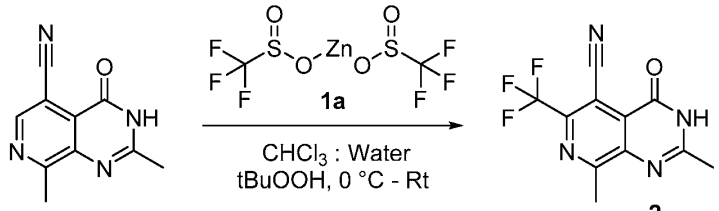
[0207] To a solution of 5-bromo-3-fluoropyridin-2-ol (**2**, 11.0 g, 57.29 mmol) in *N,N*-dimethylformamide (110 mL), cesium carbonate (24.59 g 74.47 mmol) and sodium 2-bromo-2,2-difluoroacetate (17.04 g, 85.93 mmol) are added and reaction mixture is heated at 55 °C. After completion, reaction mixture is diluted with water and extracted with diethyl ether. The organic layer is dried over anhydrous sodium sulphate, filtered and concentrated to get crude compound. Crude compound obtained is concentrated under reduced pressure to obtain crude product which is purified by column chromatography using silica gel (100-200 mesh) and 1-2 % ethyl acetate in hexane to afford 5-bromo-2-(difluoromethoxy)-3-fluoropyridine (**3**).

Example 1A.14



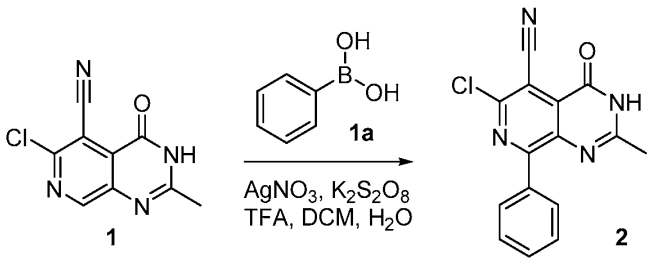
[0208] To a solution of 2,8-dimethyl-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidine-5-carbonitrile (**1**, 0.16 g, 0.8 mmol) and zinc difluoromethanesulpfinate (0.472 g, 1.6 mmol) in a mixture of dichloromethane and water (4:1, 2 mL), trifluoroaceticacid (0.06 mL, 0.8 mmol) and *tert*-butyl hydroperoxide (0.23 mL, 2.4 mmol) are added. This mixture is stirred at room temperature for 16 h. After this time, the reaction mixture is concentrated under reduced pressure, diluted with water, and extracted with dichloromethane. The combined organic layer is washed with water and then brine, dried over anhydrous sodium sulfate, filtered, and concentrated. The crude product is purified by silica gel (100-200 mesh) flash chromatography using 40 % ethyl acetate in hexanes as eluent. The desired fractions are concentrated under reduced pressure to afford 6-(difluoromethyl)-2,8-dimethyl-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidine-5-carbonitrile (**2**).

Example 1A.15



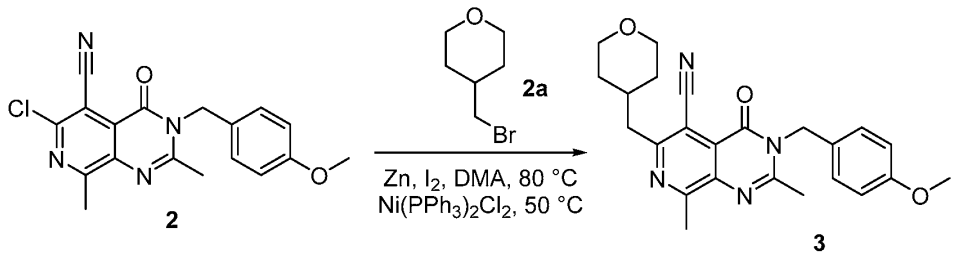
[0209] A solution of 2,8-dimethyl-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidine-5-carbonitrile (**1**, 0.200 g, 0.99 mmol) and bis(((trifluoromethyl)sulfinyl)oxy)zinc (**1a**, 0.662 g 1.99 mmol) is stirred in chloroform (2.0 mL) and water (2.0 mL), *tert*-butyl hydrogen peroxide(70 %) (0.38 mL, 2.99 mmol) is added at 0 °C. The reaction mixture is stirred at room temperature for 15 h. After this time, the reaction mixture is diluted water and extracted with ethyl acetate. The organic layer is dried over anhydrous sodium sulfate, filtered, and concentrated to obtain the crude product. The crude is purified by silica gel (100-200 mesh) column chromatography using 70-80 % ethyl acetate in hexanes as eluent. The desired fractions are concentrated under reduced pressure to afford 2,8-dimethyl-4-oxo-6-(trifluoromethyl)-3,4-dihydropyrido[3,4-d]pyrimidine-5-carbonitrile (**2**).

Example 1A.16



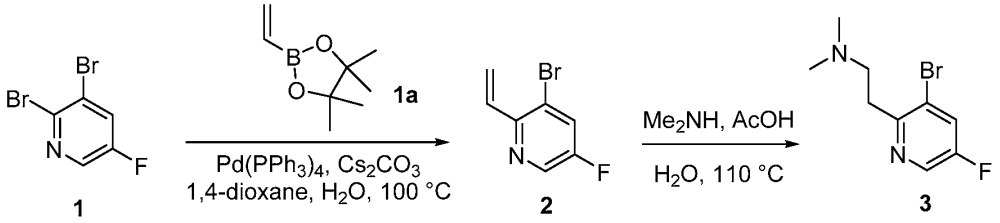
[0210] To a solution of 6-chloro-2-methyl-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidine-5-carbonitrile (**1**, 1.0 g, 4.54 mmol), in dichloromethane : water (1:1) (20.0 mL) is added 2,2,2-trifluoroacetic acid (10.4 mL, 13.63 mmol). Reaction mixture is stirred at room temperature for 15 min before the addition of phenylboronic acid (**1a**, 1.65 g, 13.63 mmol) and stirred for 40 min. Silver nitrate (0.154 g, 0.90 mmol) and Potassium persulfate (2.45 g, 9.09 mmol).is added and reaction mixture is stirred for 24 h at room temperature. After completion, reaction mixture is diluted with water and extracted with dichloromethane. The organic layer is dried over anhydrous sodium sulphate, filtered and concentrated to get crude compound. The crude is washed with 30 % diethyl ether in pentene to afford 6-chloro-2-methyl-4-oxo-8-phenyl-3,4-dihydropyrido[3,4-d]pyrimidine-5-carbonitrile (**2**).

Example 1A.17



[0211] Zinc powder (<10 micron) (37.7 mg, 0.58 mmol) is weighed out in a dry 1 dram vial and placed under argon. DMA (0.4 mL) is added followed by iodine (3.6 mg, 0.014 mmol). The resulting mixture is stirred vigorously at room temperature under argon until the red color of iodine faded (5 min). 4-(bromomethyl)tetrahydro-2H-pyran (**2a**, 0.072 mL, 0.56 mmol) is added and the resulting mixture is sealed, stirred vigorously, and heated at 80 °C for 23 h. After cooling to room temperature the reaction mixture is placed under argon and 6-chloro-3-(4-methoxybenzyl)-2,8-dimethyl-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidine-5-carbonitrile (**2**, 49.9 mg, 0.14 mmol) and bis(triphenylphosphine)nickel(II) dichloride (9.2 mg, 0.014 mmol) are added. The resulting mixture is stirred vigorously at room temperature under argon for 2.5 h and then at 50 °C for 2 h. The reaction mixture is diluted with NMP and methanol, filtered, and purified via preparatory HPLC (15-70 % acetonitrile in water with 0.1 % TFA). Fractions containing the desired product are combined and lyophilized to dryness to afford 3-(4-methoxybenzyl)-2,8-dimethyl-4-oxo-6-((tetrahydro-2H-pyran-4-yl)methyl)-3,4-dihydropyrido[3,4-d]pyrimidine-5-carbonitrile (**3**).

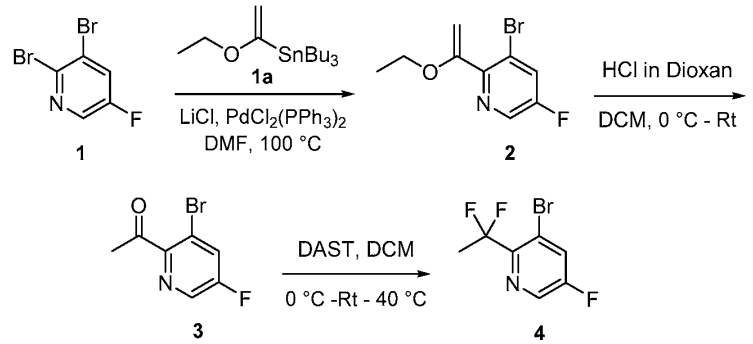
Example 1A.18



[0212] 2,3-Dibromo-5-fluoropyridine (**1**, 3.15 g, 12.4 mmol), 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (1a, 1.93 mL, 13.6 mmol), cesium carbonate (8.86 g, 27.2 mmol), 1,4-dioxane (24 mL) and water (6 mL) are combined in a 100 mL round bottom flask with a stirbar. The atmosphere in the flask is removed under vacuum and replaced with argon twice. Tetrakis(triphenylphosphine)palladium(0) (0.71 g, 0.62 mmol) is added and the atmosphere in the flask is removed under vacuum and replaced with argon twice. The resulting clear yellow reaction mixture is stirred vigorously and heated at 100 °C under argon for 12 h. After cooling to room temperature the reaction mixture is partitioned between brine and ethyl acetate. The organics are dried over magnesium sulfate, filtered, concentrated on a rotary evaporator, and purified via silica gel chromatography (2-15 % ethyl acetate in hexanes) to afford 3-bromo-5-fluoro-2-vinylpyridine (**2**).

[0213] Dimethylamine (40 wt. % in water) (34.1 mL, 108 mmol) is added to a stirred solution of 3-bromo-5-fluoro-2-vinylpyridine (**2**, 2.18 g, 10.8 mmol) in acetic acid (14.2 mL, 248 mmol). The resulting mixture is sealed, stirred vigorously, and heated at 110 °C for 68 h. After cooling to room temperature the reaction mixture is poured onto a stirred mixture of sodium hydroxide (9.93 g, 248 mmol) and sodium bicarbonate (4.53 g, 54.0 mmol) in ice water. The resulting mixture is extracted three times with dichloromethane. The combined organics are dried over magnesium sulfate, filtered, concentrated on a rotary evaporator, and purified via silica gel chromatography (0-20 % methanol in dichloromethane). Fractions containing the desired product are combined and concentrated on a rotary evaporator. The residue is concentrated down from THF twice and dried under high vacuum to afford 2-(3-bromo-5-fluoropyridin-2-yl)-*N*,*N*-dimethylethan-1-amine (**3**).

Example 1A.19

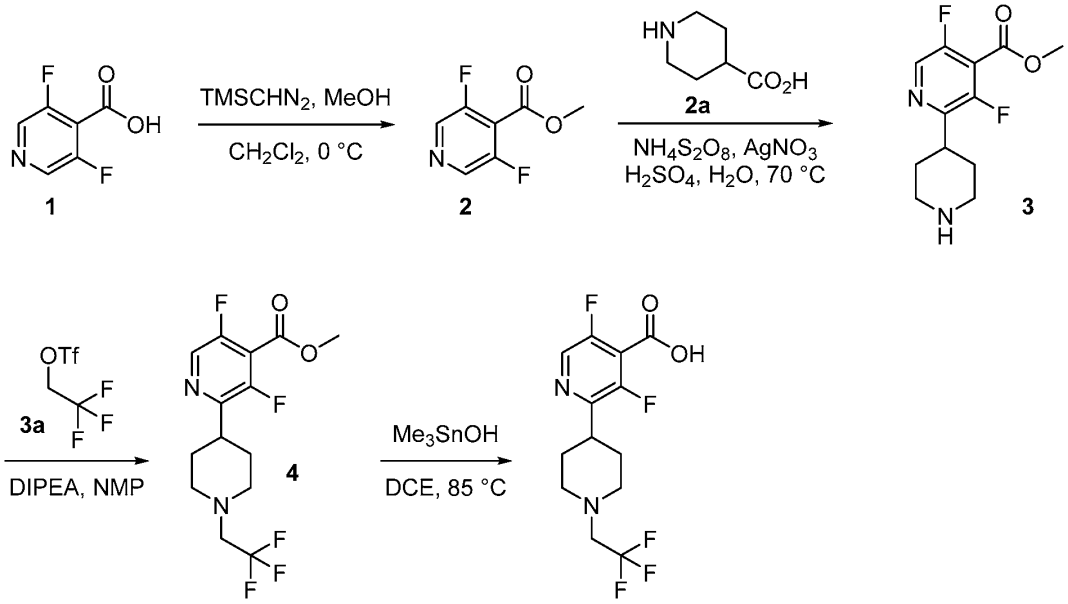


[0214] A solution of 2,3-dibromo-5-fluoropyridine (**1**, 10.0 g, 39.2 mmol), tributyl(1-ethoxyvinyl)stannane (**1a**, 15.5 mL, 43.1 mmol) and lithium chloride (4.9 g, 117.6 mmol) in *N,N*-dimethylformamide (100 mL) is degassed under nitrogen for 10 minutes. Then, bis(triphenylphosphine)palladium(II) dichloride (1.3 g, 1.9 mmol) is added and the mixture is heated at 100 °C for 4 h. The reaction mixture is cooled, diluted with water and extracted with diethyl ether. The combined organic layer is washed with water, dried over anhydrous sodium sulphate, filtered and concentrated. The crude product is purified by column chromatography using silica gel (100-200 mesh) and 0-2 % ethyl acetate in hexane to afford 3-bromo-2-(1-ethoxyvinyl)-5-fluoropyridine (2).

[0215] A solution of 3-bromo-2-(1-ethoxyvinyl)-5-fluoropyridine (**2**, 5.7 g, 23.1 mmol) in dichloromethane (60 mL) is cooled to 0 °C, hydrochloric acid in 1,4-dioxane (4 m, 10 mL) is added and the mixture is stirred at room temperature for 3 h. The reaction mixture is poured into ice cold water, neutralized with sodium bicarbonate and extracted with dichloromethane. The organic layer is dried over anhydrous sodium sulphate, filtered and concentrated. The crude product is purified by column chromatography using silica gel (100-200 mesh) and 0-5 % ethyl acetate in hexane to afford 1-(3-bromo-5-fluoropyridin-2-yl)ethan-1-one (**3**).

[0216] A solution of 1-(3-bromo-5-fluoropyridin-2-yl)ethan-1-one (**3**, 3.8 g, 17.4 mmol) in dichloromethane (40 mL) is cooled to 0 °C, diethylaminosulfur trifluoride (23.3 mL, 174.0 mmol) is added; the mixture is stirred at room temperature for 48 h and then heated at 40 °C for 72 h. The reaction mixture is cooled, poured into crushed ice (very slowly, in portions), neutralized with sodium bicarbonate and extracted with dichloromethane. The organic layer is dried over anhydrous sodium sulphate, filtered and concentrated. The crude is purified by column chromatography using silica gel (100-200 mesh) and 0-1 % ethyl acetate in hexane to afford 3-bromo-2-(1,1-difluoroethyl)-5-fluoropyridine (**4**).

Example 1A.20



[0217] (Trimethylsilyl)diazomethane (2 M in diethyl ether) (19.5 mL, 39.1 mmol) is added slowly to a stirred mixture (not all dissolved) of 3,5-difluoroisonicotinic acid (1, 5.18 g, 32.6 mmol) in wet Methanol (200 mL) at 0 °C. The resulting cloudy mixture is stirred vigorously at 0 °C under air. Bubbling is observed during the addition and continued for 45 min. Dichloromethane (100 mL) is added followed by more (trimethylsilyl)diazomethane (2 M in diethyl ether) (19.5 mL, 39.1 mmol). The resulting clear solution is stirred vigorously at 0 °C under air for 30 min. More (trimethylsilyl)diazomethane (2 M in diethyl ether) (19.5 mL, 39.1 mmol) is added and then more (trimethylsilyl)diazomethane (2 M in diethyl ether) (19.5 mL, 39.1 mmol) is added again until LCMS indicated complete conversion of the starting material. Volatiles are removed on a rotary evaporator. The residue is taken up in dichloromethane and purified via silica gel chromatography (0-50 % ethyl acetate in hexanes) (dried under high vacuum for only a few seconds) to afford methyl 3,5-difluoroisonicotinate (2).

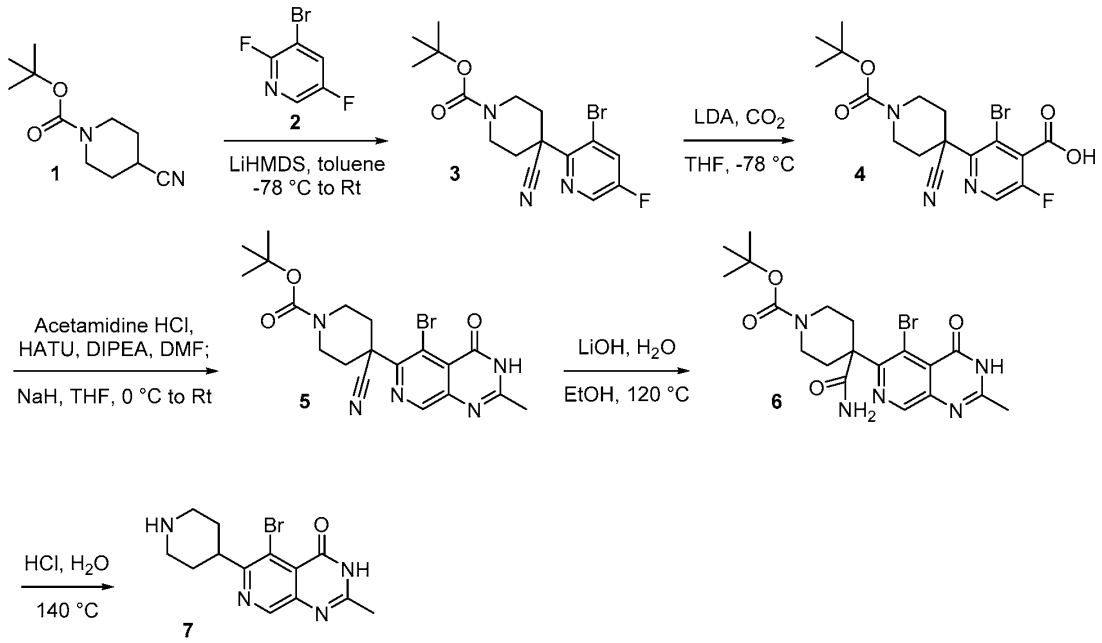
[0218] A solution of piperidine-4-carboxylic acid (2a 1.20 g, 9.27 mmol), ammonium persulfate (2.33 g, 10.2 mmol), and silver nitrate (590 mg, 3.47 mmol) in water (8 mL) is added to a stirred mixture of methyl 3,5-difluoroisonicotinate (2, 802 mg, 4.63 mmol) in 3 % sulfuric acid in water (8 mL) at 70 °C. The resulting brown mixture is heated at 70 °C with vigorous stirring for 10 min (bubbling is observed) and then cooled to room temperature. The reaction mixture is heated at 70 °C and more piperidine-4-carboxylic acid (1.20 g, 9.27 mmol), ammonium persulfate (2.33 g, 10.2 mmol), and silver nitrate (590 mg, 3.47 mmol) in water (8 mL) is added. The reaction mixture is heated at 70 °C for 10 min and then cooled to room temperature. Repeat this a total of

four times. The reaction mixture is basified with potassium carbonate. All volatiles are removed on a rotary evaporator. The residue is slurried with 20 % methanol in dichloromethane and filtered through Celite. The filter cake is washed thoroughly with 20 % methanol in dichloromethane. The filtrate is concentrated on a rotary evaporator with silica gel and purified via silica gel chromatography (0-20 % methanol in dichloromethane) to afford methyl 3,5-difluoro-2-(piperidin-4-yl)isonicotinate (3).

[0219] 2,2,2-Trifluoroethyl trifluoromethanesulfonate (3a, 1.05 mL, 7.32 mmol) is added to a stirred solution of methyl 3,5-difluoro-2-(piperidin-4-yl)isonicotinate (3, 625 mg, 2.44 mmol) and N,N-diisopropylethylamine (3.40 mL, 19.5 mmol) in NMP (10 mL) at room temperature under argon. The resulting mixture is stirred at room temperature under argon for 3 h. The reaction mixture is diluted with ethyl acetate, washed three times with brine, dried over magnesium sulfate, filtered, concentrated on a rotary evaporator, and purified via silica gel chromatography (0-50 % ethyl acetate in hexanes) to afford methyl 3,5-difluoro-2-(1-(2,2,2-trifluoroethyl)piperidin-4-yl)isonicotinate (4).

[0220] Methyl 3,5-difluoro-2-(1-(2,2,2-trifluoroethyl)piperidin-4-yl)isonicotinate (4, 505 mg, 1.49 mmol), trimethyltin hydroxide (1.08 g, 5.97 mmol), and DCE (10 mL) are combined in a 100 mL round bottom flask with a stirbar. The resulting mixture is stirred vigorously and heated at 80 °C under a reflux condenser under argon for 1 h and then at 85 °C for 3 h. Volatiles are removed on a rotary evaporator. The residue is taken up in 20 % methanol in dichloro-methane and purified via silica gel chromatography (0-20 % methanol in dichloromethane) to afford 3,5-difluoro-2-(1-(2,2,2-trifluoroethyl)piperidin-4-yl)isonicotinic acid (5).

Example 1A.21



[0221] Lithium bis(trimethylsilyl)amide (1M in toluene) (2.23 mL, 2.23 mmol) is added slowly to a stirred solution of *tert*-butyl 4-cyanopiperidine-1-carboxylate (1, 469 mg, 2.23 mmol) and 3-bromo-2,5-difluoropyridine (2, 433 mg, 2.23 mmol) in toluene (5 mL) at -78 °C under argon. The cold bath is removed and the resulting orange solution is allowed to warm to room temperature with stirring under argon and allowed to stir at room temperature for 2 h. 0.2 M HCl in water (22.3 mL, 4.46 mmol) is added with vigorous stirring. The resulting mixture is extracted with ethyl acetate. The organics are washed with brine, dried over magnesium sulfate, filtered, concentrated on a rotary evaporator, and purified via silica gel chromatography (0-50 % ethyl acetate in hexanes) to afford *tert*-butyl 4-(3-bromo-5-fluoropyridin-2-yl)-4-cyanopiperidine-1-carboxylate (3).

[0222] *n*-Butyllithium (2.5 M in hexane) (0.48 mL, 1.20 mmol) is added to a stirred solution of diisopropylamine (0.18 mL, 1.30 mmol) in THF (4 mL) at 0 °C under argon. The resulting light yellow solution is stirred for 10 min at 0 °C and then added slowly to a stirred solution of *tert*-butyl 4-(3-bromo-5-fluoropyridin-2-yl)-4-cyanopiperidine-1-carboxylate (3, 401 mg, 1.04 mmol) in THF (7 mL) at -78 °C under argon. The resulting orange reaction mixture is stirred at -78 °C under argon for 30 min and then carbon dioxide gas is bubbled in for ~1 min. (orange color fades) After 10 min 0.1 N sodium hydroxide in water (1 mL) is added to quench the reaction mixture. The resulting mixture is partitioned between 0.1 N sodium hydroxide in water (20 mL) and diethyl ether. The organics are extracted twice more with 0.1 N sodium hydroxide in water

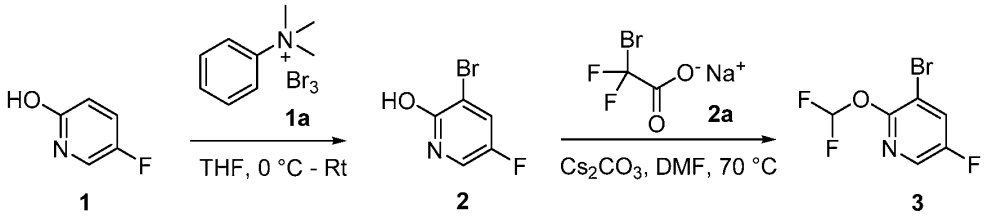
(5 mL). The organics are discarded. The water layer is acidified with 1 N HCl in water and then extracted four times with ethyl acetate. The organics are washed with brine, dried over magnesium sulfate, filtered, concentrated on a rotary evaporator, and dried under high vacuum to afford 3-bromo-2-(1-(*tert*-butoxycarbonyl)-4-cyanopiperidin-4-yl)-5-fluoroisonicotinic acid (4).

[0223] HATU (366 mg, 0.964 mmol) is added to a stirred solution of 3-bromo-2-(1-(*tert*-butoxycarbonyl)-4-cyanopiperidin-4-yl)-5-fluoroisonicotinic acid (4, 393 mg, 0.918 mmol) in DMF (6 mL) at room temperature under argon. After 2 min N,N-diisopropylethylamine (0.19 mL, 1.10 mmol) is added. The resulting orange mixture is stirred at room temperature under argon for 20 min. A solution of acetamidine hydrochloride (174 mg, 1.84 mmol) and N,N-diisopropylethylamine (0.80 mL, 4.59 mmol) in DMF (3 mL) (this is heated with a heat gun and sonicated to get all of the acetamidine dissolved) is added. The resulting orange mixture is stirred vigorously at room temperature under argon for 2 h. The reaction mixture is diluted with ethyl acetate, washed four times with brine, dried over magnesium sulfate, filtered, and concentrated on a rotary evaporator. Dry THF (10 mL) is added and volatiles are removed on a rotary evaporator again. The residue is dried under high vacuum for 10 min. The residue is dissolved with stirring in THF (15 mL) and cooled to 0 °C under argon. Sodium hydride (44.1 mg, 1.84 mmol) is added. The cold bath is removed and the resulting cloudy orange mixture is stirred vigorously at room temperature under argon for 2.5 h. A solution of ammonium chloride (147 mg, 2.75 mmol) in water (2 mL) is added and then the resulting mixture is partitioned between ethyl acetate and brine. The organics are dried over magnesium sulfate, filtered, concentrated on a rotary evaporator, and purified via silica gel chromatography (20-100 % ethyl acetate in hexanes) to afford *tert*-butyl 4-(5-bromo-2-methyl-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidin-6-yl)-4-cyanopiperidine-1-carboxylate (5).

[0224] *tert*-Butyl 4-(5-bromo-2-methyl-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidin-6-yl)-4-cyanopiperidine-1-carboxylate (5, 313 mg, 0.698 mmol), ethanol (17 mL), and lithium hydroxide (1 M in water) (6.98 mL, 6.98 mmol) are combined in a sealable vessel with a stirbar. The resulting mixture is sealed, stirred vigorously, and heated at 120 °C with an oil bath for 44 h. After cooling to room temperature the reaction mixture is diluted with methanol and concentrated on a rotary evaporator. The residue is taken up in NMP, methanol, and acetic acid (0.60 mL, 10.5 mmol), filtered, and purified via preparatory HPLC (15-60 % acetonitrile in water with 0.1 % TFA). Fractions containing the desired product are combined and lyophilized to dryness to afford *tert*-butyl 4-(5-bromo-2-methyl-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidin-6-yl)-4-carbamoylpiperidine-1-carboxylate (6).

[0225] A stirred mixture of *tert*-butyl 4-(5-bromo-2-methyl-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidin-6-yl)-4-carbamoylpiperidine-1-carboxylate TFA salt (6, 186 mg, 0.321 mmol) in 6 M HCl in water (7 mL) is heated at 140 °C with an oil bath for 2 min and then sealed, stirred vigorously, and heated at 140 °C with an oil bath for 2 h. More 6 M HCl in water (3 mL) is added and heating at 140 °C with an oil bath continued for another 21 h. After cooling to room temperature the reaction mixture is diluted with methanol, filtered, and purified via preparatory HPLC (5-18 % acetonitrile in water with 0.1 % TFA). Fractions containing the desired product are loaded onto a Strata X-C ion exchange column from Phenomenex. The column is washed sequentially with water, acetonitrile, methanol, and then 5 % ammonium hydroxide in methanol. Eluent containing the desired product is concentrated on a rotary evaporator and dried under high vacuum to afford 5-bromo-2-methyl-6-(piperidin-4-yl)pyrido[3,4-d]pyrimidin-4(3H)-one (7).

Example 1A.22



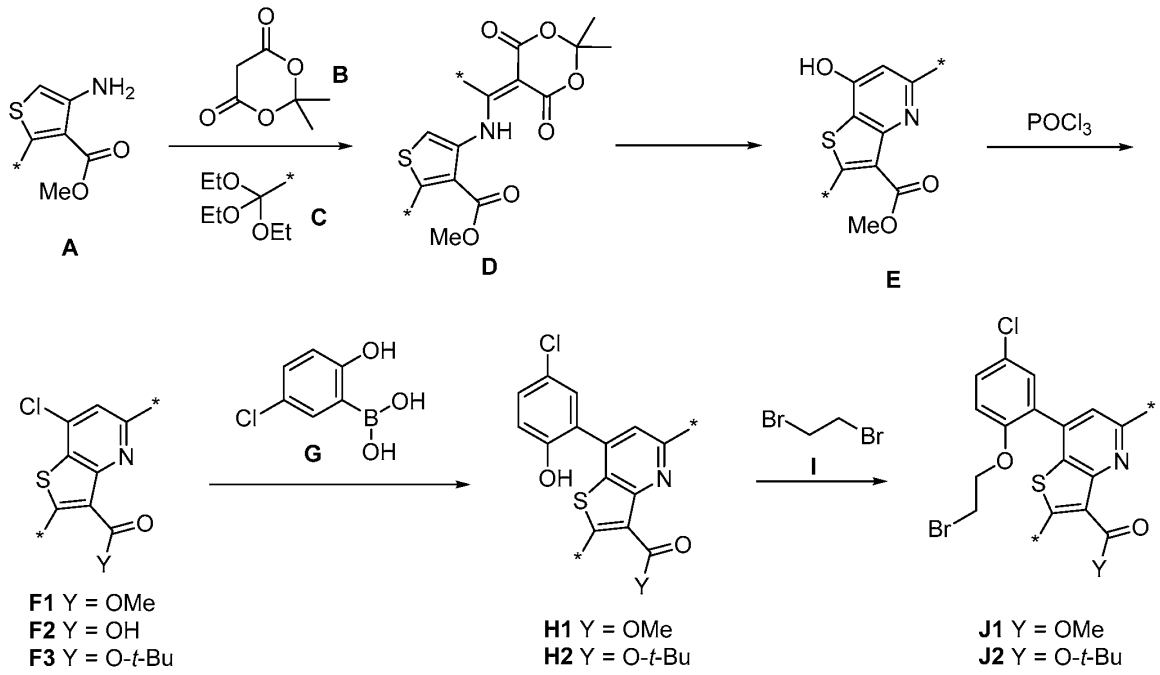
[0226] To a solution of 5-fluoropyridin-2-ol (1, 9.00 g, 0.079 mol) in tetrahydrofuran (290 mL) at 0 °C, Trimethylphenylammonium tribromide (29.9 g, 0.079 mol) is added slowly and reaction mixture is stirred at room temperature for 16 h. After 16 h, the reaction mixture is partitioned between ethyl acetate and water. Aqueous layer is separated and re-extracted with ethyl acetate. The combined organic layer is washed with 5 % sodium metabisulphite solution, saturated brine solution, dried over anhydrous sodium sulphate, filtered and concentrated to get crude product. The crude product is purified by column chromatography using silica gel (100-200 mesh) and 0-30 % ethyl acetate in hexanes afford 3-bromo-5-fluoropyridin-2-ol (2) as off white solid. Yield: 4.90 g, 27 %; MS (ESI) m/z 189.99 $[M-1]^-$.

[0227] To a solution of 3-bromo-5-fluoropyridin-2-ol (2, 4.10 g, 0.021 mol) in *N,N*-dimethylformamide (40 mL), cesium carbonate (3.48 g, 0.031 mol) and sodium 2-bromo-2,2-difluoroacetate (2a, 5.05 g, 0.025 mmol) are added and the reaction mixture is heated at 70 °C for 4 h. After completion, reaction mixture cooled down and partitioned between diethyl ether and water. Aqueous layer is separated and re-extracted with diethyl ether. The combined organic layer is washed with water, saturated brine solution, dried over anhydrous sodium sulphate, filtered and concentrated to get crude product. The crude product is purified by column

chromatography using silica gel (100-200 mesh) and hexane as eluent to afford 3-bromo-2-(difluoromethoxy)-5-fluoropyridine (3)

Example 1B. Methods of synthesizing the right-hand side

Example 1B.1



[0228] A solution of 2,2-dimethyl-1,3-dioxane-4,6-dione (**B**, 1.1 equiv.) and 1,1,1-triethoxyethane (**C**, 0.7 M) is stirred and heated at 90 °C for 2 h. methyl 4-aminothiophene-3-carboxylate (**A**, 1 equiv.) is added portionwise at 90 °C under argon atmosphere and heating at 90 °C continued for 6 h. The reaction mixture is cooled to room temperature, water added, and the mixture extracted with ethyl acetate. The organic layer is dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. The crude product is triturated with diethyl ether to afford methyl 4-((1-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)ethyl)amino)thiophene-3-carboxylate (**D**).

[0229] A solution of methyl 4-((1-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)ethyl)amino)thiophene-3-carboxylate (**D**, 1 equiv.) in Dowtherm A (0.5 M), is heated at 235 °C for 4 h. After completion, the reaction mass is cooled to room temperature, the precipitated solid isolated by filtration and dried *in vacuo*. The solid obtained is washed with diethyl ether to afford methyl 7-hydroxy-5-methylthieno[3,2-b]pyridine-3-carboxylate (**E**).

[0230] To a solution of methyl 7-hydroxy-5-methylthieno[3,2-b]pyridine-3-carboxylate (**E**, 1 equiv.) in 1,2-dichloroethane (0.22 M) are added phosphoryl trichloride (3 equiv.) and a catalytic

amount of *N,N*-dimethylformamide at room temperature and the reaction mixture heated at 90 °C for 6 h. The reaction mixture is concentrated under reduced pressure, diluted with ice cold water, and the solution basified with 10 % aqueous sodium hydroxide solution to pH ~7-8 followed by extracted with ethyl acetate. The organic layer is dried over anhydrous sodium sulfate, filtered, concentrated, and purified by column chromatography to afford methyl 7-chloro-5-methylthieno[3,2-b]pyridine-3-carboxylate (**F1**).

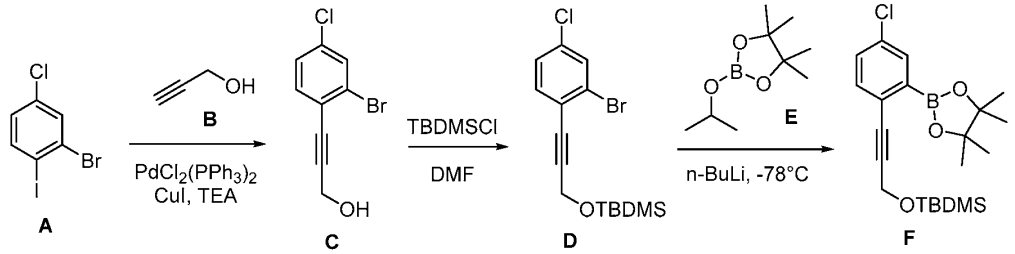
[0231] To a solution of methyl 7-chloro-5-methylthieno[3,2-b]pyridine-3-carboxylate (**F1**, 1 equiv.) in mixture of methanol (1.7 M), water (1.7 M) and tetrahydrofuran (0.64 M) is added lithium hydroxide monohydrate (2 equiv.) at room temperature and the resulting mixture is stirred for 2 h. The solid is filtered, the filtrate is concentrated and combined with the solid. The combined solids are acidified with saturated citric acid solution (up to pH=1) and filtered. The resulting solid is washed with methanol followed by diethyl ether and dried under high vacuum to afford 7-chloro-5-methylthieno[3,2-b]pyridine-3-carboxylic acid (**F2**).

[0232] To a solution of 7-chloro-5-methylthieno[3,2-b]pyridine-3-carboxylic acid (**F2**, 1 equiv.) in tert-butyl alcohol (0.4 M) is added 4-dimethylaminopyridine (1 equiv.) and Boc-anhydride (3 equiv.) at room temperature. The mixture is stirred for 48 h at 90 °C and the reaction mixture is concentrated under reduced pressure. The crude product is purified by column chromatography over silica gel to afford *tert*-butyl 7-chloro-5-methylthieno[3,2-b]pyridine-3-carboxylate (**F3**).

[0233] To a solution of *tert*-butyl 7-chloro-5-methylthieno[3,2-b]pyridine-3-carboxylate (**F3**, 1 equiv.) and (5-chloro-2-hydroxyphenyl)boronic acid (**G**, 1.2 equiv.), in 1,4-dioxane (0.5 M) and water (1.2 M) is added potassium carbonate solution (2 equiv.) at room temperature and the reaction mixture degassed with argon for 20 minutes. [1,1'-bis(diphenylphosphino)ferrocene] palladium(II) dichloride (0.05 equiv.) is added and mixture heated at 90 °C for 2 h. The reaction mixture is cooled to room temperature and filtered and the solid, washed with water followed by methanol, and dried under vacuum to afford *tert*-butyl 7-(5-chloro-2-hydroxyphenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (**H**).

[0234] To a solution of *tert*-butyl 7-(5-chloro-2-hydroxyphenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (**H**, 1 equiv.) in acetone (0.28 M) are added potassium carbonate (3.5 equiv.) and 1,2-dibromoethane (**I**, 5.0 equiv.) at room temperature and the reaction mixture heated at 40 °C for 12 h. An additional 5.0 equiv. of 1,2-dibromoethane is then added at room temperature and the mixture heated to 45 °C. The reaction mixture is filtered through a sintered funnel, washed with acetone, and the filtrate concentrated and purified by column chromatography to afford *tert*-butyl 7-(2-(2-bromoethoxy)-5-chlorophenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (**J**).

Example 1B.2

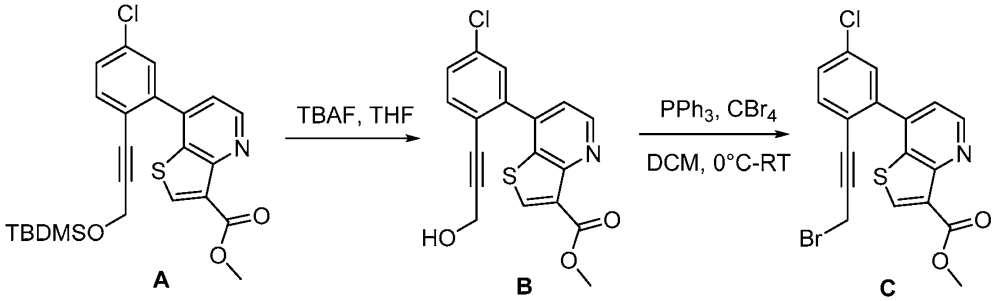


[0235] A solution of 2-bromo-4-chloro-1-iodobenzene (**A**, 1 equiv.) and prop-2-yn-1-ol (**B**, 1.3 equiv.) in triethylamine (0.3 M) is degassed with argon for 10 min. Copper(I) iodide (0.15 equiv.) and bis(triphenylphosphine)palladium chloride (0.08 equiv.) are added and the reaction mixture stirred at room temperature for 16 h. The reaction mass is concentrated under reduced pressure and the crude compound purified by Combi-flash to afford 3-(2-bromo-4-chlorophenyl)prop-2-yn-1-ol (**C**).

[0236] To a solution of 3-(2-bromo-4-chlorophenyl)prop-2-yn-1-ol (**C**, 1 equiv.) in tetrahydrofuran (0.8 M) are added imidazole (3 equiv.), 4-dimethylaminopyridine (0.045 equiv.) and *tert*-butyldimethylchlorosilane (1.2 equiv.) at room temperature and the reaction mixture stirred for 24 h. The reaction mass is diluted with water, extracted with ethyl acetate and the organic layer separated, dried over anhydrous sodium sulphate, and purified by Combi-flash to afford ((3-(2-bromo-4-chlorophenyl)prop-2-yn-1-yl)oxy)(*tert*-butyl)dimethylsilane (**D**).

[0237] To a solution of ((3-(2-bromo-4-chlorophenyl)prop-2-yn-1-yl)oxy)(*tert*-butyl)dimethylsilane (**D**, 1 equiv.) in tetrahydrofuran (0.14 M) is added dropwise *n*-butyllithium (1.23 M in *hexane*s, 1.3 equiv.) at -78 °C and the mixture stirred at -78 °C for 1 h. 2-Isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**E**, 1.2 equiv.) is added dropwise at -78 °C and stirring continued for 1 h. The reaction is quenched with chilled water, extracted with ethyl acetate, and the organic layer separated, dried over anhydrous sodium sulphate, concentrated, and purified by Combi-flash to afford *tert*-butyl((3-(4-chloro-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)prop-2-yn-1-yl)oxy)dimethylsilane (**F**).

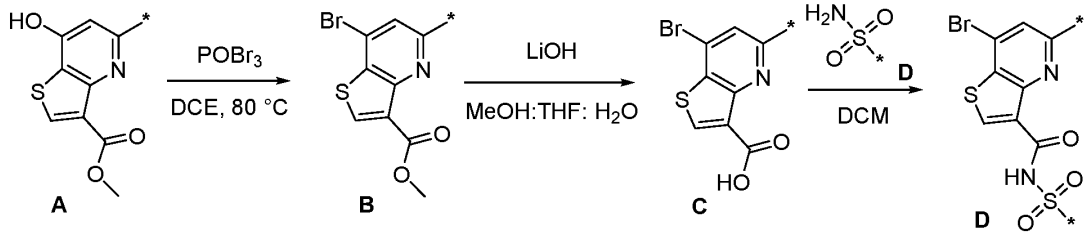
Example 1B.3



[0238] To a solution of methyl 7-(2-(3-((*tert*-butyldimethylsilyl)oxy)prop-1-yn-1-yl)-5-chlorophenyl)thieno[3,2-*b*]pyridine-3-carboxylate (**A**, 1 equiv.) in tetrahydrofuran (0.21 M) is added tetra-*n*-butylammonium fluoride (1.2 equiv.) at room temperature and the mixture stirred for 2 h. The reaction mass is diluted with ethyl acetate, washed with cold water and the organic layer separated, dried over anhydrous sodium sulphate, concentrated, and triturated with diethyl ether to afford methyl 7-(5-chloro-2-(3-hydroxyprop-1-yn-1-yl)phenyl)thieno[3,2-*b*]pyridine-3-carboxylate (**B**).

[0239] To a solution of methyl 7-(5-chloro-2-(3-hydroxyprop-1-yn-1-yl)phenyl)thieno[3,2-*b*]pyridine-3-carboxylate (**B**, 1 equiv.) in dichloromethane (10.0 mL) is added triphenylphosphine (1.5 equiv.) at room temperature and the reaction mixture cooled to 0 °C. Carbontetrabromide (1.5 equiv.) is added and the reaction mixture stirred for 3 h at room temperature. The reaction mass is concentrated and purified by Combi-flash to afford methyl 7-(2-(3-bromoprop-1-yn-1-yl)-5-chlorophenyl)thieno[3,2-*b*]pyridine-3-carboxylate (**C**).

Example 1B.4

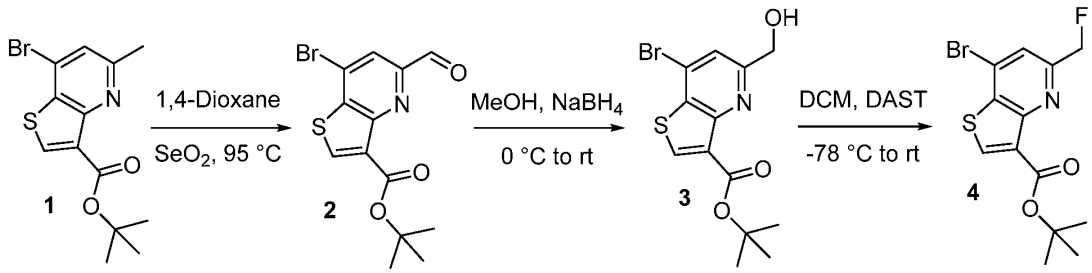


[0240] A solution of methyl 7-hydroxy-5-methylthieno[3,2-b]pyridine-3-carboxylate (**A**, 1 equiv.) and phosphorous oxybromide (10 equiv.) in 1,2 dichloroethane (0.45 M) is heated at 80 °C for 16 h. The reaction mixture is cooled to room temperature, quenched with aqueous solution of sodium bicarbonate, extracted with dichloromethane, and the combined organic layer washed with brine, dried over anhydrous sodium sulphate, filtered, concentrated, and purified by column chromatography to afford methyl 7-bromo-5-methylthieno[3,2-b]pyridine-3-carboxylate (**B**).

[0241] A solution of methyl 7-bromo-5-methylthieno[3,2-b]pyridine-3-carboxylate (**B**, 1 equiv.) and lithium hydroxide (3 equiv.) in methanol:tetrahydrofuran:water solvent mixture (1:2:1, 0.25 M) is stirred at room temperature for 16 h. The reaction is diluted with water, cooled to 0 °C and acidified with 1 N hydrochloric acid to pH ~5. The precipitate is filtered, washed with pentane and dried to afford 7-bromo-5-methylthieno[3,2-b]pyridine-3-carboxylic acid (**C**)

[0242] To a solution of 7-bromo-5-methylthieno[3,2-b]pyridine-3-carboxylic acid (**C**, 1 equiv.) and methanesulfonamide (**D**, 1.5 equiv.) in dichloromethane (0.16 M), *N*-ethyl-N′-(3-dimethylaminopropyl)carbodiimide hydrochloride (2 equiv.) and *N,N*-dimethylpyridin-4-amine (2.5 equiv.) are added at room temperature and the mixture stirred for 16 h. The reaction is diluted with water, cooled to 0 °C, acidified with 1 N hydrochloric acid to pH ~2 and extracted with dichloromethane. The combined organic layer is dried over anhydrous sodium sulphate, concentrated, and purified by column chromatography to afford 7-bromo-5-methyl-*N*-(methylsulfonyl)thieno[3,2-b]pyridine-3-carboxamide (**E**).

Example 1B.5



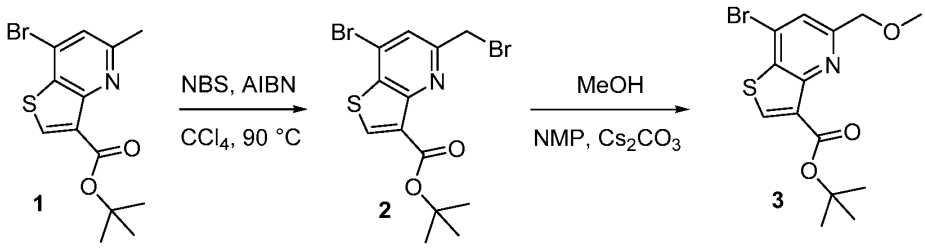
[0243] To a solution of *tert*-butyl 7-bromo-5-methylthieno[3,2-b]pyridine-3-carboxylate (**1**, 1.50 g, 4.5 mmol) in 1,4-dioxane is added selenium dioxide (0.55 g, 5.02 mmol) and reaction mixture is heated at 95 °C for 8 h. After completion, the reaction mixture is filtered over Celite bed and washed with ethyl acetate. The filtrate obtained is concentrated under reduced pressure to get crude product. The crude product obtained is purified by column chromatography using silica gel (100-200 mesh) and 10 % ethyl acetate in hexanes to afford *tert*-butyl 7-bromo-5-formylthieno[3,2-b]pyridine-3-carboxylate (**2**).

[0244] To a solution of *tert*-butyl 7-bromo-5-formylthieno[3,2-b]pyridine-3-carboxylate (**2**, 0.55 g, 1.62 mmol) in methanol (6 mL) at 0 °C is added sodium borohydride (0.12 g, 3.25 mmol) and reaction mixture is stirred at same temperature for 1 hour. After completion, the reaction mixture is quenched with ice water and concentrated under reduced pressure. The crude material is dissolved in ethyl acetate, washed with water, brine solution, dried over anhydrous sodium sulphate, filtered and concentrated to get crude compound. The crude compound obtained is

purified by column chromatography using silica gel (100-200 mesh) and 20 % ethyl acetate in hexanes to afford *tert*-butyl 7-bromo-5-(hydroxymethyl)thieno[3,2-b]pyridine-3-carboxylate (**3**).

[0245] To a solution of *tert*-butyl 7-bromo-5-(hydroxymethyl)thieno[3,2-b]pyridine-3-carboxylate (**3**, 0.325 g, 0.94 mmol) in dichloromethane (5 mL) at -78 °C, DAST (0.18 mL, 1.41 mmol) is added and reaction mixture is stirred at -78 °C for 1 hour. After completion, reaction mixture is quenched with ice cold water and extracted with dichloromethane. The organic layer is washed saturated solution of sodium bicarbonate, dried over anhydrous sodium sulphate, filtered and concentrated to get crude compound. The crude compound obtained is purified by column chromatography using silica gel (100-200 mesh) and 10 % ethyl acetate in hexane to get *tert*-butyl 7-bromo-5-(fluoromethyl)thieno[3,2-b]pyridine-3-carboxylate (**4**).

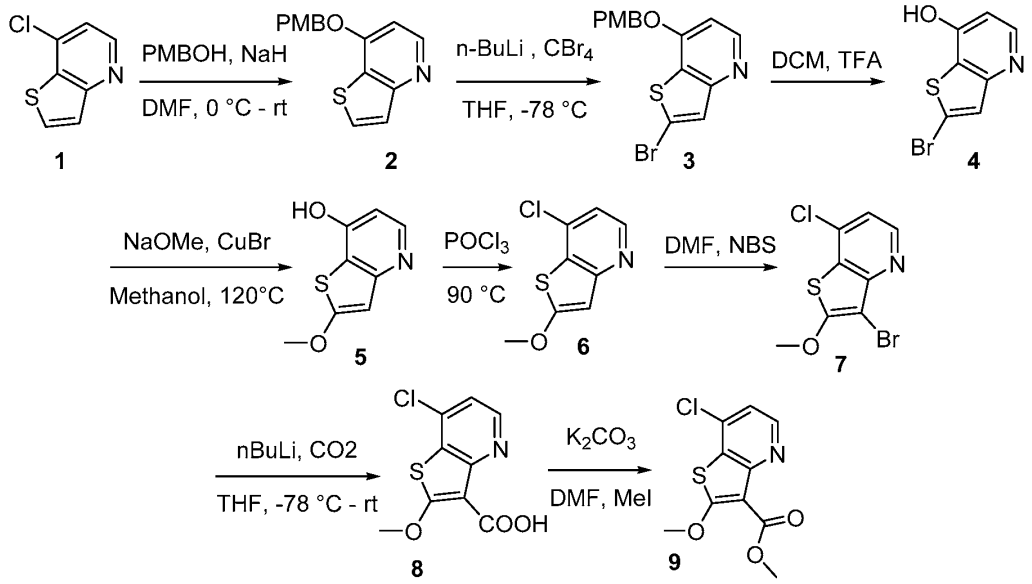
Example 1B.6



[0246] A solution of *tert*-butyl 7-bromo-5-methylthieno[3,2-b]pyridine-3-carboxylate (**1**, 500.0 mg, 1.523 mmol), Azobisisobutyronitrile (24.98 mg, 0.152 mmol) and *N*-Bromosuccinimide (271.13 mg, 1.523 mmol) in carbon tetrachloride (10 mL) is stirred at 90 °C for 5 h. After completion, reaction mixture is concentrated under reduced pressure and is diluted with dichloromethane and silica gel is added. The solvent is evaporated. The crude silica mixture is purified by Isco column chromatography using 0-10 % methanol in dichloromethane as eluent. The desired fractions are concentrated under reduced pressure to afford *tert*-butyl 7-bromo-5-(bromomethyl)thieno[3,2-b]pyridine-3-carboxylate (**2**)

[0247] To a stirred solution of *tert*-butyl 7-bromo-5-(bromomethyl)thieno[3,2-b]pyridine-3-carboxylate (**2**, 0.200 g, 0.491 mmol) in methanol (0.2 mL) and *N*-methylpyrrolidone (2.0 mL) is added cesium carbonate (0.480 g, 1.474 mmol) at RT and reaction mixture is stirred at room temperature for 8 h. After completion, the reaction mixture is diluted with dichloromethane and then silica gel is added. The solvent is then evaporated and the free flow silica gel is then loaded on the column and purified via silica gel chromatography eluting with methanol in dichloromethane to afford *tert*-butyl 7-bromo-5-(methoxymethyl)thieno[3,2-b]pyridine-3-carboxylate (**3**).

Example 1B.7



[0248] To a stirred solution of 4-methoxybenzyl alcohol (8.1 g, 59.1 mmol) in *N*,*N*-dimethylformamide (100 mL) at 0 °C, sodium hydride (3.1 g, 65.0 mmol) is added. This reaction mixture is stirred at 0 °C for 30 min. Then, 7-chlorothieno[3,2-b]pyridine (**1**, 10 g, 59.1 mmol) is added at 0 °C and reaction mixture is stirred for 16 h at room temperature. After this time, the mixture is poured into ice. The resulting precipitate is collected by filtration and dried under reduced pressure to afford 7-((4-methoxybenzyl)oxy)thieno[3,2-b]pyridine (**2**).

[0249] To a stirred solution of 7-((4-methoxybenzyl)oxy)thieno[3,2-b]pyridine (**2**, 8.0 g, 29.5 mmol) in dry tetrahydrofuran (250 mL), *n*-butyllithium (2.3 M in hexanes, 38.0 mL, 64.9 mmol) is added dropwise at -78 °C. This reaction mixture is stirred at the same temperature for 45 min. Then, carbon tetrabromide (9.7 g, 29.5 mmol) is added at -78 °C and the mixture is stirred at same temperature for 1 h. After this time, the reaction is quenched with saturated aqueous ammonium chloride solution and extracted with ethyl acetate. The organic layer is washed with water, dried over anhydrous sodium sulfate, filtered, and concentrated. The crude product is purified by silica gel (100-200 mesh) column chromatography using 15 % ethyl acetate in hexanes as eluent. The desired fractions are concentrated under reduced pressure to afford 2-bromo-7-((4-methoxybenzyl)oxy)thieno[3,2-b]pyridine (**3**).

[0250] A solution of 2-bromo-7-((4-methoxybenzyl)oxy)thieno[3,2-b]pyridine (**3**, 6.5 g, 18.62 mmol) in a mixture of trifluoroacetic acid and dichloromethane (1:1, 40 mL) is stirred at room temperature for 8 h. After this time, the reaction mixture is concentrated under reduced pressure.

The crude product is recrystallized with ether and pentanes to afford 2-bromothieno[3,2-b]pyridin-7-ol (**4**).

[0251] To a solution of 2-bromothieno[3,2-b]pyridin-7-ol (**4**, 3.5 g, 15.28 mmol) in methanol (30 mL), 30 % sodium methoxide in methanol (14.0 g, in methanol, 76.4 mmol) and copper(I) bromide (0.200 g, 1.5 mmol) are added. This reaction mixture is stirred at 120 °C for 30 h. After this time, the reaction mixture is concentrated under reduced pressure, acidified with 2 N hydrochloric acid to pH~6, and extracted with 10 % methanol in dichloromethane. The organic layer is dried over anhydrous sodium sulfate, filtered, and concentrated to afford 2-methoxythieno[3,2-b]pyridin-7-ol (**5**).

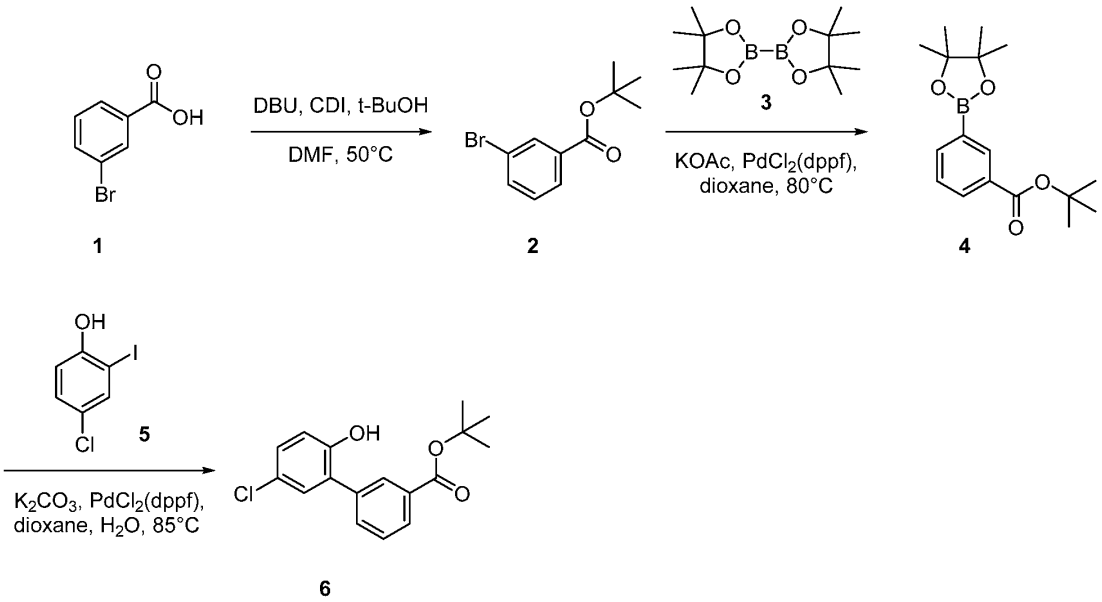
[0252] A mixture of 2-methoxythieno[3,2-b]pyridin-7-ol (**5**, 1.7 g, 9.39 mmol) and phosphoryl chloride (10 mL) is heated and stirred at 90° C for 6 h. After this time, the reaction mixture is quenched with ice, treated with aqueous 50 % sodium hydroxide solution, and extracted with ethyl acetate. The organic layer is washed with water and then saturated brine, dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The crude product is purified by Combiflash using 30 % ethyl acetate in hexanes as eluent. The desired fractions are concentrated under reduced pressure to afford 7-chloro-2-methoxythieno[3,2-b]pyridine (**6**).

[0253] To a solution of 3-bromo-7-chloro-2-methoxythieno[3,2-b]pyridine (**6**, 0.8 g, 4.0 2 mmol) in *N*,*N*-dimethylformamide (10 mL) at room temperature, *N*-bromosuccinimide (1.4 g, 8.04 mmol) is added. This reaction mixture is stirred for 30 min. Then, the reaction mixture is poured into ice and extracted with ethyl acetate. The organic layer is washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated to dryness under reduced pressure. The crude product is purified by Combiflash (12 g, RediSep column) using 10 % ethyl acetate in hexanes as eluent. The desired fractions are concentrated under reduced pressure to afford 3-bromo-7-chloro-2-methoxythieno[3,2-b]pyridine (7).

[0254] To a stirred solution of 3-bromo-7-chloro-2-methoxythieno[3,2-b]pyridine (**7**, 0.7 g, 2.52 mmol) in dry tetrahydrofuran (10 mL), *n*-butyllithium (2.3 M in hexanes, 1.97 mL, 4.54 mmol) is added dropwise at -78 °C. This reaction mixture is stirred at the same temperature for 45 min. Dry carbon dioxide gas is bubbled through the reaction mixture, which is slowly warmed up to room temperature and stirred for 16 h. The reaction mixture is quenched with 10 % aqueous citric acid solution and extracted with 10 % methanol in dichloromethane. The organic layer is dried over anhydrous sodium sulfate, filtered, and concentrated to afford 7-chloro-2-methoxythieno[3,2-b]pyridine-3-carboxylic acid (**8**).

[0255] To a solution of 7-chloro-2-methoxythieno[3,2-b]pyridine-3-carboxylic acid (**8**, 0.5 g, 2.05 mmol) in *N*,*N*-dimethylformamide (5.0 mL) at room temperature, potassium carbonate (0.85 g, 6.17 mmol) and methyl iodide (0.32 g, 2.26 mmol) are added. This reaction mixture is stirred for 16 h. After this time, the reaction mixture is poured into ice and extracted with ethyl acetate. The organic layer is washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated to dryness under reduced pressure. The crude product is purified by Combiflash (12 g, RediSep column) using 2 % methanol in dichloromethane as eluent. The desired fractions are concentrated under reduced pressure to afford methyl 7-chloro-2-methoxythieno[3,2-b]pyridine-3-carboxylate (**9**).

Example 1B.8



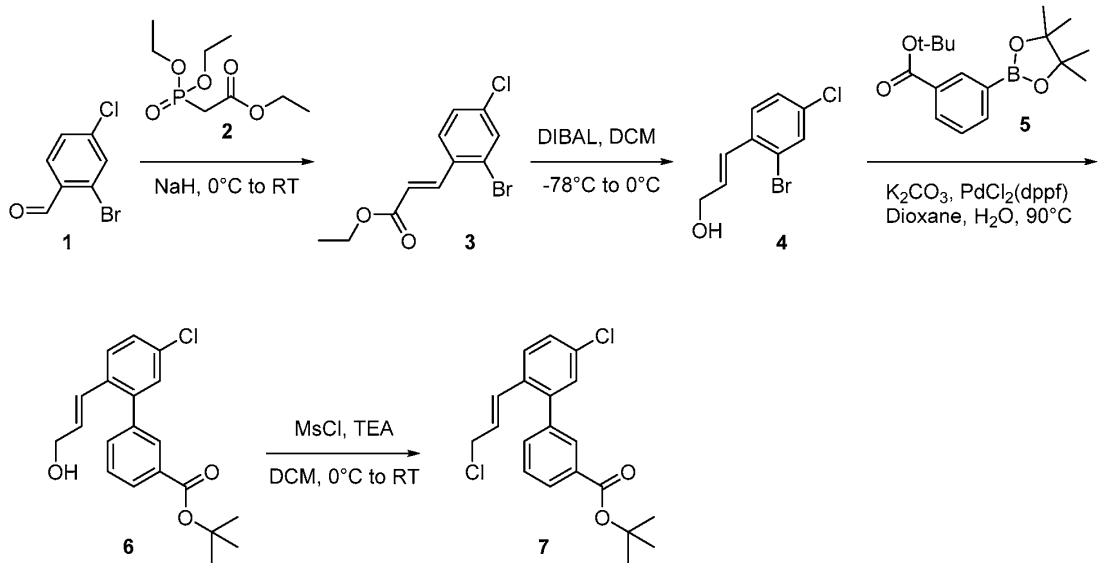
[0256] To a stirred solution of 3-bromobenzoic acid (1, 100.0 g, 497.5 mmol) in *N*,*N*-dimethylformamide (800 mL), carbodiimidazole (112.9 gm, 696.5 mmol) is added at room temperature and the reaction mixture is heated and stirred at 50 °C for 1 h. 1,8-Diazabicyclo[5.4.0]undec-7-ene (105.8 gm, 696.5 mmol) and *tert*-butanol (184.37 gm, 2487.5 mmol) are added at 50 °C and the reaction mixture is continued to stir at 50 °C for 16 h. After completion, the reaction mass is quenched with water and extracted with ethyl acetate. The organic layer is separated, dried over anhydrous sodium sulphate and concentrated under reduced pressure. The crude product obtained is purified by column chromatography using 100-200 silica gel and 2 % ethyl acetate in hexanes as eluent. The desired fractions are concentrated under reduced pressure to afford *tert*-butyl 3-bromobenzoate (2).

[0257] A stirred solution of *tert*-butyl 3-bromobenzoate (2, 113.0 g, 439.4 mmol), 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (3, 167.43 gm, 659.1 mmol) and potassium acetate (107.65 gm, 1098.5 mmol) in dioxane (600 mL) is degassed with argon for 30 min. Then [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II) is added and the reaction mixture is heated and stirred at 85 °C for 16 h. After completion, the reaction mass is quenched with water and extracted with ethyl acetate. The organic layer is separated, dried over anhydrous sodium sulphate and concentrated under reduced pressure to obtain the crude mass. This crude compound is purified by column chromatography using 100-200 silica gel and 3 % ethyl acetate in hexanes as eluent. The desired fractions are concentrated under reduced pressure to afford *tert*-butyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (4).

[0258] A stirred solution of 4-chloro-2-iodophenol (5, 60.0 g, 235.8 mmol), *tert*-butyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (4, 100.37 g, 330.1 mmol) and potassium carbonate (97.76 g, 707.4 mmol) in a mixture of dioxane and water (4:1, 1.0 Lit) is degassed with argon for 30 min. Palladium(II)bis(triphenylphosphine) dichloride is added at room temperature and stirred the reaction mixture at 100 °C for 6 h. After completion, the reaction mass is quenched with water and extracted with ethyl acetate. The organic layer is separated, dried over anhydrous sodium sulphate and concentrated under reduced pressure. The crude compound obtained is purified by column chromatography using 100-200 silica gel and 4 % ethyl acetate in hexanes as eluent. The desired fractions are concentrated under reduced pressure to afford *tert*-butyl 5'-chloro-2'-hydroxy-[1,1'-biphenyl]-3-carboxylate (6).

[0259] To a stirred solution of *tert*-butyl 5'-chloro-2'-hydroxy-[1,1'-biphenyl]-3-carboxylate (6, 55.0 g, 180.5 mmol) in 1 N aqueous solution of sodium hydroxide (1.1 Lit), tetrabutylammoniumbromide (8.72 g, 27.07 mmol) and potassium iodide (4.49 g, 27.07 mmol) are added at room temperature and the reaction mass is heated to 90 °C. 1,2-Dibromoethane (7, 57.82 mL, 667.89 mmol) is added slowly at 90 °C and the reaction mixture is stirred at 90 °C for 16 h. After completion, the reaction mass is extracted with dichloromethane. The organic layer is dried over sodium sulfate, filtered and concentrated under reduced pressure to obtain the crude mass. The crude compound is purified by column chromatography using 100-200 silica gel and 2 % ethyl acetate in hexanes to afford *tert*-butyl 2'-(2-bromoethoxy)-5'-chloro-[1,1'-biphenyl]-3-carboxylate (8).

Example 1B.9



[0260] To a stirred solution of ethyl 2-(diethoxyphosphoryl)acetate (2, 23.01 g, 102.7 mmol) in tetrahydrofuran (100 mL) at 0 °C, sodium hydride (60 %) (5.47 g, 136.9 mmol) is added and the reaction mixture is stirred at 0 °C for 1 h. 2-bromo-4-chlorobenzaldehyde (1, 15.0 g, 68.4 mmol) in tetrahydrofuran (3 mL) is added slowly and the reaction mixture is stirred at 0 °C for 2 h. After completion, the reaction mass is quenched with water and extracted with ethyl acetate. The organic layer is separated, dried over anhydrous sodium sulphate and concentrated under reduced pressure to get the crude mass. The crude material is purified by Combi-flash using 3 % ethyl acetate in hexanes as eluent. The desired fractions are concentrated under reduced pressure to afford ethyl (*E*)-3-(2-bromo-4-chlorophenyl)acrylate (3).

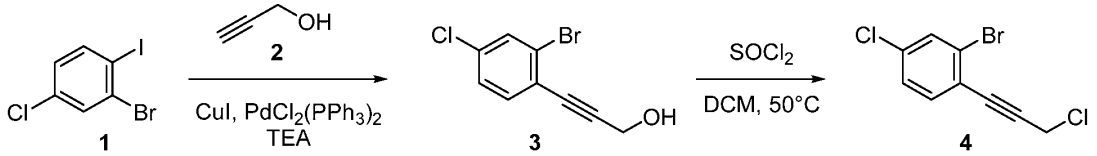
[0261] To a stirred solution of ethyl (*E*)-3-(2-bromo-4-chlorophenyl)acrylate (3, 2.0 g, 17.3 mmol) in dichloromethane (15.0 mL), diisobutylaluminium hydride (1 M in toluene) (31.1 mL,31.1 mmol) is added and stirred at -78 °C for 1 h. The reaction mixture is slowly allowed to room temperature and stirred for 1 h. After completion, the reaction mass is quenched with aqueous ammonium chloride solution and extracted with dichloromethane. The organic layer is separated, dried over anhydrous sodium sulphate and concentrated under reduced pressure to get the crude mass which is purified by Combi-flash using 13 % ethyl acetate in hexanes as eluent. The desired fractions are concentrated under reduced pressure to afford (*E*)-3-(2-bromo-4-chlorophenyl)prop-2-en-1-ol (4).

[0262] A stirred solution of (*E*)-3-(2-bromo-4-chlorophenyl)prop-2-en-1-ol (4, 1.5 g, 6.07 mmol), *tert*-butyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (5, 2.03 g, 6.68 mmol), and

potassium carbonate (2.51 g, 18.2 mmol) in a mixture of dioxane and water (4:1) (24.0 mL) is degassed with argon for 30 min. [1,1'-Bis(diphenylphosphino)ferrocene]palladium(II) dichloride (0.222 g, 0.3 mmol) is added and the reaction mixture is heated at 90 °C for 12 h. After completion, the reaction mass is quenched with water and extracted with ethyl acetate. The organic layer is separated, dried over anhydrous sodium sulphate and concentrated under reduced pressure to get the crude mass. The crude compound is purified by Combi-flash using 15 % ethyl acetate in hexanes as eluent. The desired fractions are concentrated under reduced pressure to afford *tert*-butyl (*E*)-5'-chloro-2'-(3-hydroxyprop-1-en-1-yl)-[1,1'-biphenyl]-3-carboxylate (6).

[0263] To a stirred solution of *tert*-butyl (*E*)-5'-chloro-2'-(3-hydroxyprop-1-en-1-yl)-[1,1'-biphenyl]-3-carboxylate (6, 1.5 g, 4.34 mmol) and triethylamine (1.82 mL, 13.04 mmol) in dichloromethane at 0 °C, methanesulfonyl chloride (0.67 mL, 8.69 mmol) is added and the reaction mixture is slowly allowed to room temperature and stirred for 16 h. After completion, the reaction mass is quenched with water and extracted with dichloromethane. The organic layer is separated, dried over anhydrous sodium sulphate and concentrated under reduced pressure to get the crude material. The crude compound is purified by Combi-flash using 10 % ethyl acetate in hexanes as eluent to afford *tert*-butyl (*E*)-5'-chloro-2'-(3-chloroprop-1-en-1-yl)-[1,1'-biphenyl]-3-carboxylate (7).

Example 1B.10



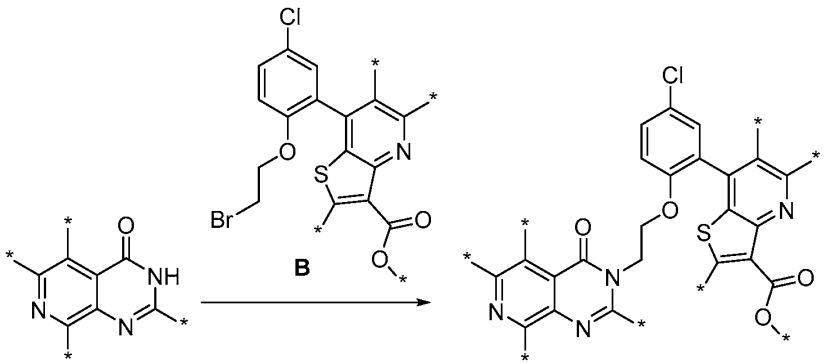
[0264] A stirred solution of 2-bromo-4-chloro-1-iodobenzene (1, 1.0 g, 3.15 mmol), prop-2-yn-1-ol (2, 0.2 mL, 3.47 mmol) & copper(I) iodide (0.024 g, 0.126 mmol) in triethyl amine (30 mL) is degassed with argon for 20 min. Dichlorobis(triphenylphosphine)palladium(II) (0.110 g, 0.15 mmol) is added and the reaction mixture is stirred at room temperature for 16 h. After completion, the reaction mass is quenched with water and extracted with ethyl acetate. The organic layer is separated, dried over anhydrous sodium sulphate and concentrated under reduced pressure to obtain the crude material. This crude compound is purified by Combi-flash using 10 % ethyl acetate in hexanes as eluent. The desired fractions are concentrated under reduced pressure to afford 3-(2-bromo-4-chlorophenyl)prop-2-yn-1-ol (3) as yellow solid. Yield: 0.725 g, 93 %, MS no ionization.

[0265] To a stirred solution of 3-(2-bromo-4-chlorophenyl)prop-2-yn-1-ol (3, 0.72 g, 2.93 mmol) in dichloromethane (10 mL), thionyl chloride (0.85 mL, 11.75 mmol) is added at 0 °C

and the reaction mixture is heated and stirred at 50 °C for 16 h. After completion, the reaction mass concentrated under reduced pressure to obtain the crude which is purified by Combi-flash using 3 % ethyl acetate in hexanes as eluent. The desired fractions are concentrated under reduced pressure to afford 2-bromo-4-chloro-1-(3-chloroprop-1-yn-1-yl) benzene (4)

Example 1C. General Coupling methods

Example 1C1

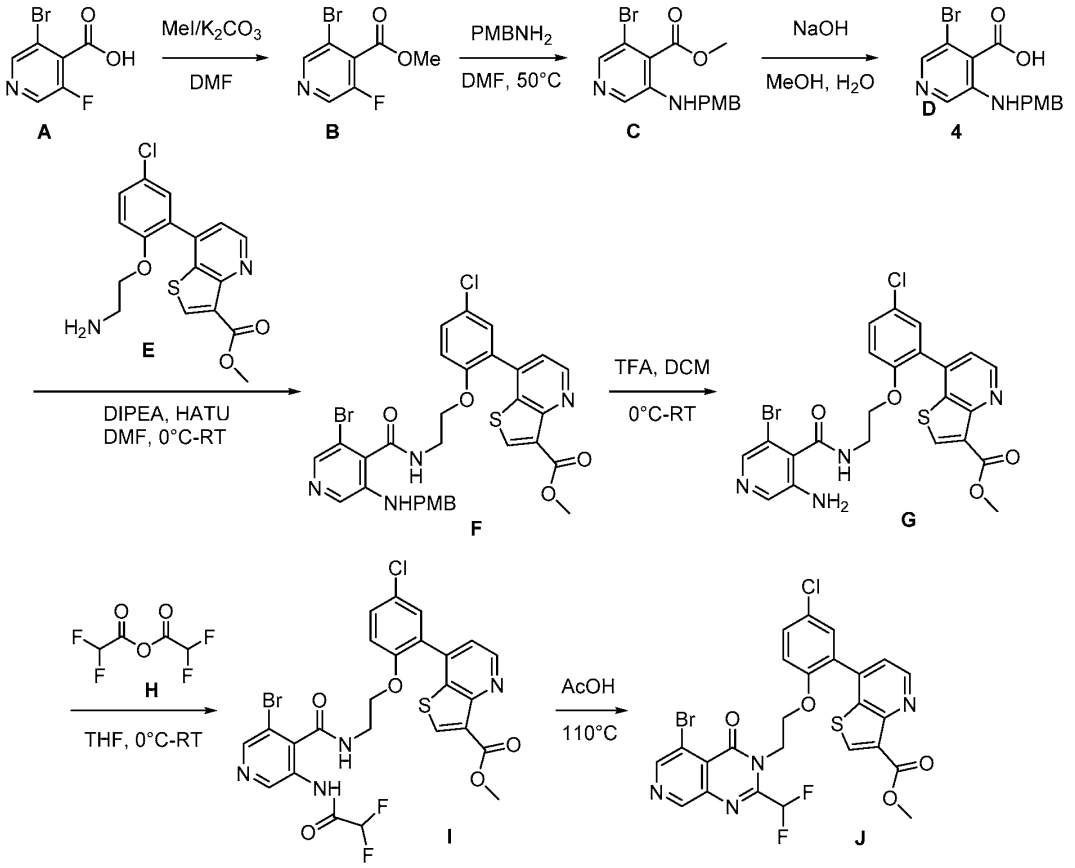


[0266] To a solution of 6-chloro-2-methyl-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidine-5-carbonitrile (**A**, 1 equiv.) in *N,N*-dimethylformamide (0.2 M solution) is added potassium carbonate (3 equiv.) and *tert*-butyl 7-(2-(2-bromoethoxy)-5-chlorophenyl)thieno[3,2-b]pyridine-3-carboxylate (**B**, 1 equiv.) and the reaction mixture is heated at 60 °C for 16 h. The reaction mixture is then cooled, diluted with water, and extracted 2x with ethyl acetate. The combined organic layer is washed with water, dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. Purification by silica gel column chromatography affords *tert*-butyl 7-(5-chloro-2-(2-(6-chloro-5-cyano-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)thieno[3,2-b]pyridine-3-carboxylate (**C**).

Example 1C2

[0267] To a solution of 6-chloro-2-methyl-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidine-5-carbonitrile (**A**, 1 equiv.) in *N,N*-dimethylformamide (0.14 M) is added *tert*-butyl 7-(2-(2-bromoethoxy)-5-chlorophenyl)thieno[3,2-b]pyridine-3-carboxylate (**B**, 1.3 equiv.), potassium iodide (0.2 equiv.), and ground potassium carbonate (3 equiv.) at room temperature. The mixture is stirred for 16 h at 50 °C, diluted with water, and extracted 2x with ethyl acetate with ethyl acetate. The combined organic layer is washed with water, dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. Purification by silica gel column chromatography gives *tert*-butyl 7-(5-chloro-2-(2-(6-chloro-5-cyano-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)thieno[3,2-b]pyridine-3-carboxylate (**C**).

Example 1C.3. Alternative coupling method



[0268] To a solution of 3-bromo-5-fluoroisonicotinic acid (**A**, 5.0 g, 21.92 mmol) in dimethylformamide (15 mL), potassium carbonate (6.07 g, 43.84 mmol) and iodomethane (2.05 mL, 32.88 mmol) are added at room temperature and stirred the reaction mixture for 2 h at room temperature. After completion, the reaction mass is diluted with ethyl acetate and washed with cold water. The organic layer is separated, dried over anhydrous sodium sulphate, filtered and concentrated to give crude. The crude is purified by flash chromatography eluting the compound with ethyl acetate in hexanes (1-10 %). The desired fractions are concentrated under reduced pressure to afford methyl 3-bromo-5-fluoroisonicotinate (**B**).

[0269] To a solution of methyl 3-bromo-5-fluoroisonicotinate (**B**, 4.0 g, 17.17 mmol) in dimethylformamide (15 mL), potassium carbonate (7.0 g, 51.51 mmol) is added followed by drop wise addition of 4-methoxy benzyl amine (3.52 mL, 25.0 mmol at room temperature The reaction mixture is stirred for 16 h at 50 °C. After completion, the reaction mass is diluted with ethyl acetate and washed with cold water. The organic layer is separated and dried over anhydrous sodium sulphate, filtered and concentrated to give crude. The crude is purified by

flash column chromatography eluting the compound with ethyl acetate in hexanes (10-20 %). The desired fractions are concentrated under reduced pressure to afford methyl 3-bromo-5-((4-methoxybenzyl)amino)isonicotinate (**C**).

[0270] To a solution of methyl 3-bromo-5-((4-methoxybenzyl)amino)isonicotinate (**C**, 2.8 g, 8.0 mmol) in methanol (5.0 mL) and water (5.0 mL) is added sodium hydroxide (0.64 g, 26.0 mmol) and stirred the reaction mixture for 6 h at room temperature. After completion, the reaction mass is concentrated to evaporate methanol. The aqueous layer is cooled to 0 °C and acidified with 2 N hydrochloric acid (pH~ 4). The precipitated solid is filtered and dried to afford 3-bromo-5-((4-methoxybenzyl)amino)isonicotinic acid (**D**).

[0271] To a solution of 3-bromo-5-((4-methoxybenzyl)amino)isonicotinic acid (**D**, 0.9 g, 26.0 mmol) in dimethylformamide (15 mL), methyl 7-(2-(2-aminoethoxy)-5-chlorophenyl)thieno[3,2-*b*]pyridine-3-carboxylate (**E**, 1.16 g, 32.0 mmol) and 1-[bis(dimethylamino)methylene]-1*H*-1,2,3-triazolo[4,5-*b*]pyridinium 3-oxide hexafluorophosphate (1.48 g, 39.0 mmol) are added at 0 °C. Diisopropylethylamine is added drop wise at 0 °C and stirred the reaction mixture at room temperature for 3 h. After completion, the reaction mass is diluted with ethyl acetate and washed with cold water. The organic layer is separated, dried over anhydrous sodium sulphate, filtered and concentrated under reduced pressure to give crude. The crude is purified by flash column chromatography eluting the compound with methanol in dichloromethane (2-5 %). The desired fractions are concentrated under reduced pressure to afford methyl 7-(2-(2-(3-bromo-5-((4-methoxybenzyl)amino)isonicotinamido)ethoxy)-5-chlorophenyl)thieno[3,2-*b*]pyridine-3-carboxylate (**F**).

[0272] To a solution of methyl 7-(2-(2-(3-bromo-5-((4-methoxybenzyl)amino)isonicotinamido)ethoxy)-5-chlorophenyl)thieno[3,2-*b*]pyridine-3-carboxylate (**F**, 1.8 g, 26.0 mmol) in dichloromethane (10 mL) is added triflouroacetic acid (10 mL) at 0 °C and is stirred the reaction mixture at room temperature for 2 h. After completion, the reaction mass is concentrated to give crude. The crude is triturated with diethyl ether to afford methyl 7-(2-(2-(3-amino-5-bromoisonicotinamido)ethoxy)-5-chlorophenyl)thieno[3,2-*b*]pyridine-3-carboxylate (**G**).

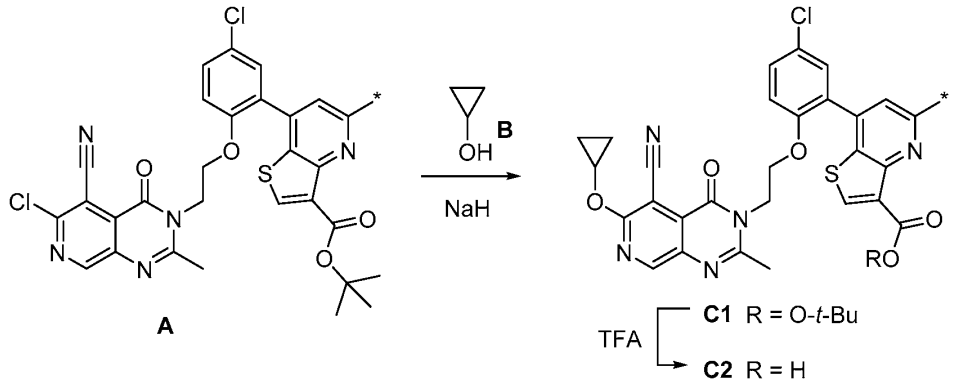
[0273] To a solution of methyl 7-(2-(2-(3-amino-5-bromoisonicotinamido)ethoxy)-5-chlorophenyl)thieno[3,2-*b*]pyridine-3-carboxylate (**G**, 1.2 g, 2.1 mmol) in tetrahydofuran (10 mL), 2,2-difluoroacetic anhydride (**H**, 0.26 mL, 2.1 mmol) is added at 0 °C and stirred the reaction mixture at room temperature for 1 h. After completion, the reaction mass is concentrated to give crude. The crude is purified by washing and triturating with diethyl ether to afford methyl

7-(2-(2-(3-bromo-5-(2,2-difluoroacetamido)isonicotinamido)ethoxy)-5-chlorophenyl)thieno[3,2-*b*]pyridine-3-carboxylate (**I**).

[0274] A solution of methyl 7-(2-(2-(3-bromo-5-(2,2-difluoroacetamido)isonicotinamido)ethoxy)-5-chlorophenyl)thieno[3,2-*b*]pyridine-3-carboxylate (**I**, 1.0 g, 1.56 mmol) in acetic acid (10 mL) is heated and stirred at 110 °C for 24 h. After completion, acetic acid is removed under reduced pressure to give crude. The crude is purified by flash column chromatography eluting the compound with ethyl acetate in hexanes (50-70 %). The desired fractions are concentrated under reduced pressure to afford methyl 7-(2-(2-(5-bromo-2-(difluoromethyl)-4-oxopyrido[3,4-*d*]pyrimidin-3(4*H*)-yl)ethoxy)-5-chlorophenyl)thieno[3,2-*b*]pyridine-3-carboxylate (**J**).

Example 1D. Post Coupling modification methods

Example 1D.1

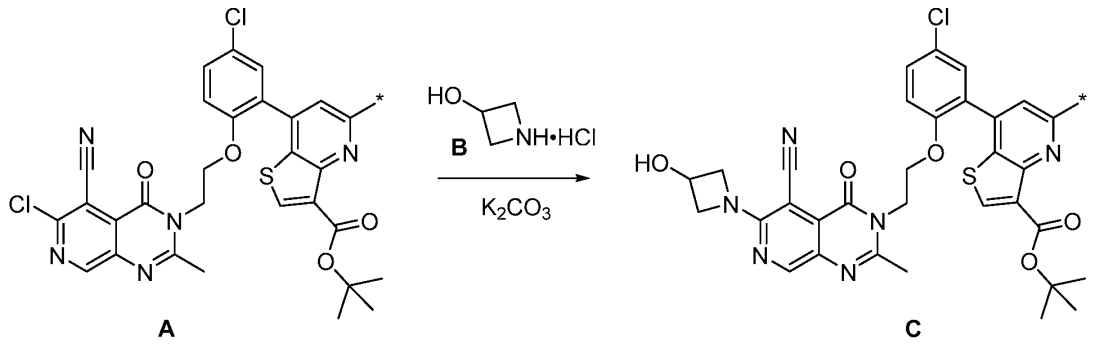


[0275] To a solution of cyclopropanol (**B**, 2.5 equiv.) in tetrahydrofuran (0.6 M), sodium hydride (3 equiv.) is added and the reaction mixture stirred at 0 °C for 10 min. *tert*-butyl 7-(5-chloro-2-(2-(6-chloro-5-cyano-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (**A**, 1 equiv.) is added to the reaction mixture at room temperature and heated at 120 °C for 6 h. The reaction mixture is cooled to room temperature, diluted with water, extracted with ethyl acetate, and the ethyl acetate layer dried over sodium sulfate, concentrated, and purified over a plug of silica gel to afford *tert*-butyl 7-(5-chloro-2-(2-(5-cyano-6-cyclopropoxy-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (**C1**).

[0276] To a solution of *tert*-butyl 7-(5-chloro-2-(2-(5-cyano-6-cyclopropoxy-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (**C1**, 1 equiv.) in dichloromethane (0.1 M), triflouroacetic acid (0.1 M) is added at 0 °C. The reaction is slowly brought to room temperature and stirred for 16 h. The reaction is

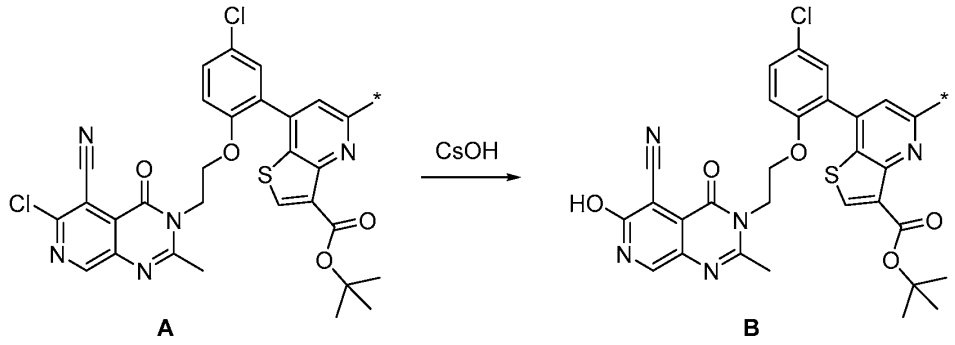
concentrated under reduced pressure, washed with diethyl ether, and purified by preparative HPLC to afford 7-(5-chloro-2-(2-(5-cyano-6-cyclopropoxy-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylic acid (**C2**)

Example 1D.2



[0277] To a solution of *tert*-butyl 7-(5-chloro-2-(2-(6-chloro-5-cyano-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (**A**, 1 equiv.), and azetidin-3-ol hydrochloride (**B**, 2 equiv.) in DMF (0.16 M), potassium carbonate (5 equiv.) is added at room temperature followed by heating at 100 °C with stirring for 16 h. The reaction mixture is diluted with water, extracted with ethyl acetate, and the organic layers washed with water and brine solution, dried over sodium sulfate, concentrated, and purified by flash chromatography to afford *tert*-butyl 7-(5-chloro-2-(2-(5-cyano-6-(3-hydroxyazetidin-1-yl)-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (**C**).

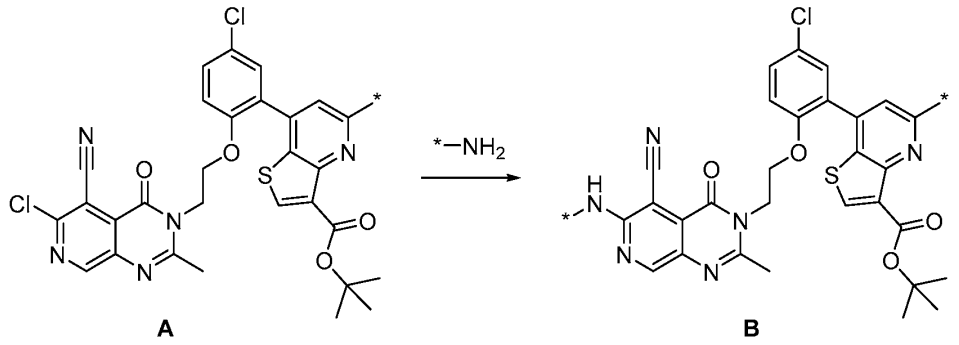
Example 1D.3



[0278] A solution of *tert*-butyl 7-(5-chloro-2-(2-(6-chloro-5-cyano-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (**A**, 1 equiv.), and cesium hydroxide (3 equiv.) in 1,4-dioxane (0.12 M) is degassed under nitrogen for 5 minutes. Tris(dibenzylideneacetone)dipalladium(0) (0.05 equiv.) and 5-(di-*tert*-

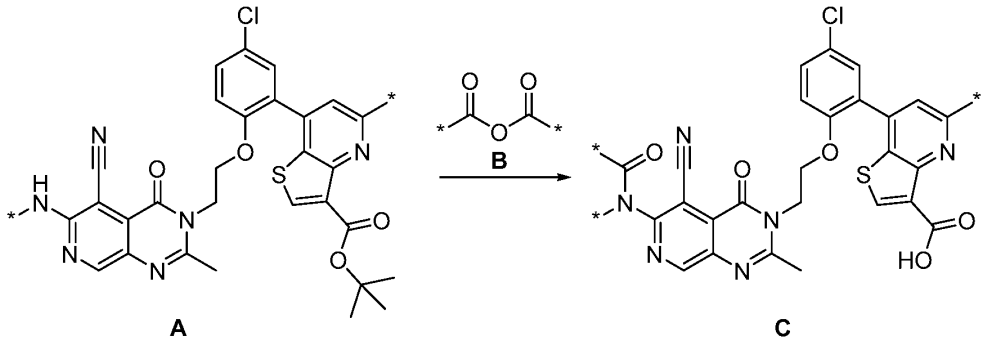
butylphosphino)-1′, 3′, 5′-triphenyl-1′H-[1,4′]bipyrazole (0.03 equiv.) are added and the mixture heated at 90 °C for 16 h. The reaction mixture is cooled, diluted with water, extracted with ethyl acetate, and the combined organic layer, dried over anhydrous sodium sulphate, filtered and concentrated to afford *tert*-butyl 7-(5-chloro-2-(2-(5-cyano-6-hydroxy-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (**B**).

Example 1D.4



[0279] A solution *tert*-butyl 7-(5-chloro-2-(2-(6-chloro-5-cyano-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (**A**, 1 equiv.) in methanolic ammonia (20 %, 0.05 M) is heated in a sealed tube at 120 °C for 16 h. The reaction mixture is concentrated to afford *tert*-butyl 7-(2-(2-(6-amino-5-cyano-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)-5-chlorophenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (**B**).

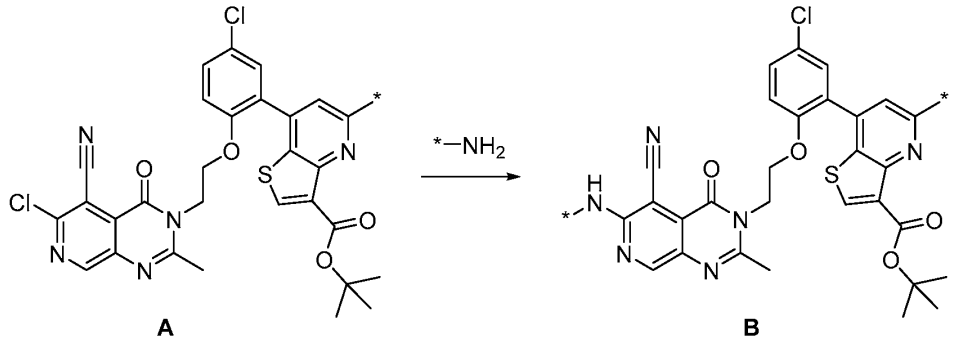
Example 1D.5



[0280] To a solution *tert*-butyl 7-(5-chloro-2-(2-(5-cyano-2-methyl-6-(methylamino)-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (**A**, 1 equiv.) in acetic anhydride (**B**, 0.06 M), acetic acid (0.24 M) is added at room temperature and the mixture is heated at 120 °C for 27 h. The reaction mixture is quenched on

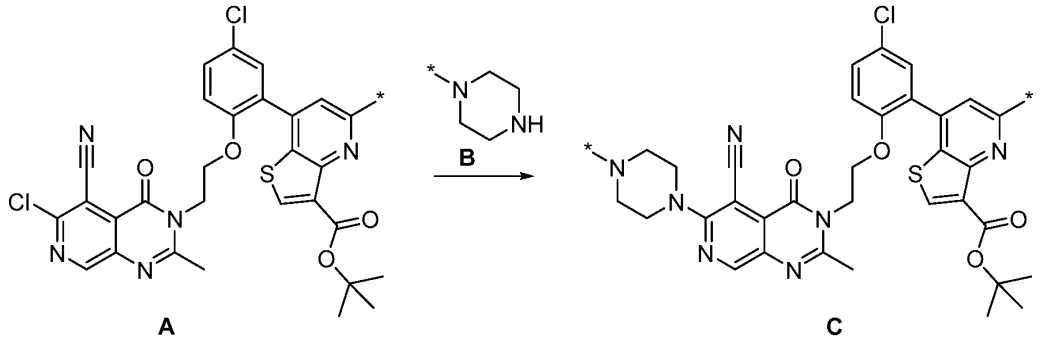
ice, extracted with ethyl acetate, and the organic layer dried over anhydrous sodium sulfate, filtered, concentrated, and purified by preparative HPLC to afford 7-(5-chloro-2-(2-(5-cyano-2-methyl-6-(*N*-methylacetamido)-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylic acid (**C**).

Example 1D.6



[0281] A solution *tert*-butyl 7-(5-chloro-2-(2-(6-chloro-5-cyano-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (**A**, 1 equiv.) in methanolic ammonia (20 %, 0.05 M) is heated in a sealed tube at 120 °C for 16 h. The reaction mixture is concentrated to afford *tert*-butyl 7-(2-(2-(6-amino-5-cyano-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)-5-chlorophenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (**B**).

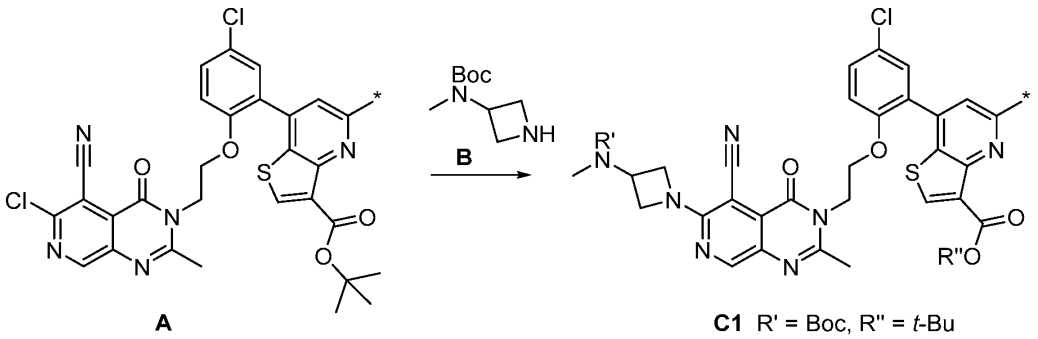
Example 1D.7



[0282] To a solution of *tert*-butyl 7-(5-chloro-2-(2-(6-chloro-5-cyano-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)-5-ethylthieno[3,2-b]pyridine-3-carboxylate (**A**, 1 equiv.) in *N,N*-dimethylformamide (0.05 M), 1-methylpiperazine (**B**, 3 equiv.), potassium fluoride (5 equiv.) and 18 crown-6 (1 equiv.) are added and the mixture heated at 90 °C for 3 h. The reaction mixture is cooled, diluted with water, extracted with ethyl acetate, and the combined organic layer dried over anhydrous sodium sulphate, filtered, and concentrated to afford *tert*-butyl 7-(5-

chloro-2-(2-(5-cyano-2-methyl-6-(4-methylpiperazin-1-yl)-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)-5-ethylthieno[3,2-b]pyridine-3-carboxylate (**C**).

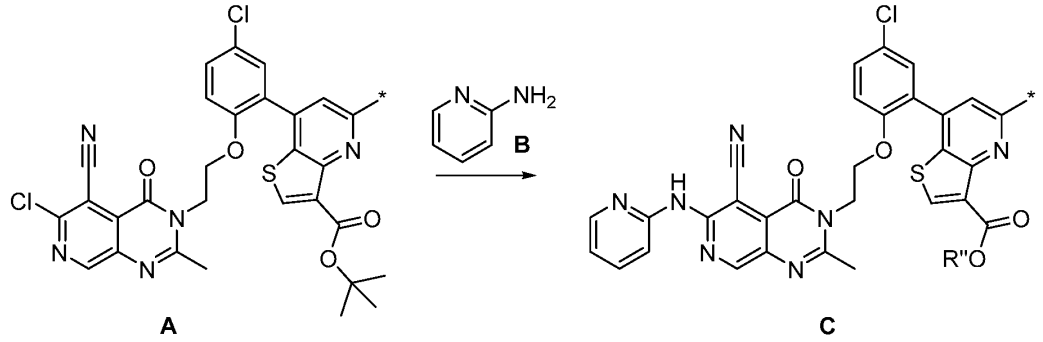
Example 1D.8



[0283] To a solution 7-(5-chloro-2-(2-(6-chloro-5-cyano-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylic acid (**A**, 1 equiv.) and tert-butyl azetidin-3-yl(methyl)carbamate hydrochloride (**B**, 2 equiv.) in 1,4-dioxane (0.088 M) is added caesium carbonate (0.172 g, 0.530 mmol) and the reaction mixture heated at 90 °C for 3 h. The reaction mixture is diluted with water, extracted with ethyl acetate, and the organic layer dried over anhydrous sodium sulphate, filtered, concentrated, and purified by column chromatography to afford 7-(2-(2-(6-(3-((tert-butoxycarbonyl)(methyl)amino)azetidin-1-yl)-5-cyano-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)-5-chlorophenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylic acid (**C1**).

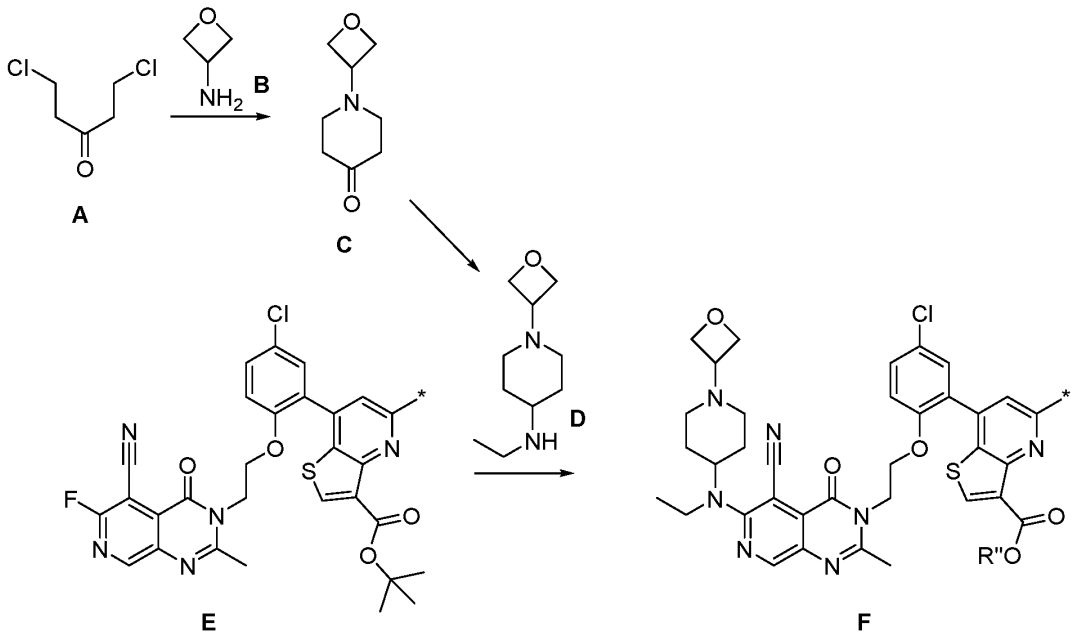
[0284] To a solution of 7-(2-(2-(6-(3-((tert-butoxycarbonyl)(methyl)amino)azetidin-1-yl)-5-cyano-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)-5-chlorophenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylic acid (**C1**, 1 equiv.) in dichloromethane (0.045 M), 2,2,2-trifluoroacetic acid (0.14 M) is added at 0 °C and the reaction mixture stirred for 16 h at room temperature. The reaction mixture is concentrated and purified by preparative HPLC to afford 7-(5-chloro-2-(2-(5-cyano-2-methyl-6-(3-(methylamino)azetidin-1-yl)-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylic acid (**C2**)

Example 1D.9



[0285] *tert*-Butyl 7-(2-(2-(6-bromo-5-cyano-2-methyl-4-oxo-7-(trifluoromethyl)quinazolin-3(4H)-yl)ethoxy)-5-chlorophenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (**A**, 1 equiv.), 3-aminopyridine (**B**, 1.1 equiv.), xantphos (0.2 equiv.), cesium carbonate (3 equiv.), and tris(dibenzylideneacetone)dipalladium(0) (0.2 equiv.) are suspended in 1,4-dioxane (0.047 M) in a screw capped vial equipped with a stir bar. The reaction mixture is sparged with argon for 3 min, then sealed and heated at 100 °C in a heating block for 75 min. The reaction mixture is cooled to room temperature and taken up in a 1:1 *N,N* dimethylformamide:methanol solution and filtered through a syringe filter. Preparatory HPLC affords *tert*-butyl 7-(5-chloro-2-(2-(5-cyano-2-methyl-4-oxo-6-(pyridin-3-ylamino)-7-(trifluoromethyl)quinazolin-3(4H)-yl)ethoxy)phenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (**C**).

Example 1D.10

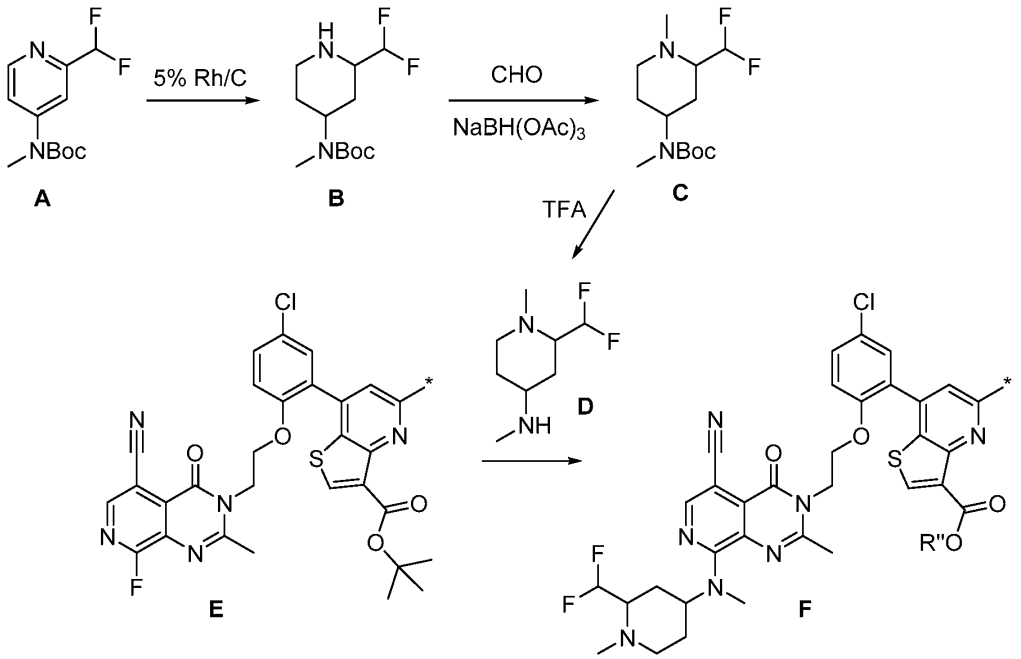


[0286] To a stirred solution of oxetan-3-amine (**B**, 1 equiv.), sodium carbonate (3.5 equiv.) in methanol (0.68 M) and 1,5-dichloropentan-3-one (**A**, 1 equiv.) are added at room temperature and the reaction mixture is heated at 75 °C for 3 h. The reaction mixture is cooled to room temperature, diluted with water, extracted with ethyl acetate, and the ethyl acetate layer is dried over sodium sulfate, concentrated, and purified over a plug of silica gel to afford 1-(oxetan-3-yl)piperidin-4-one (**C**).

[0287] To a solution of 1-(oxetan-3-yl)piperidin-4-one (**C**, 0.8 g, 5.16 mmol) in dichloromethane (0.5 M) are added ethylamine (2 M in tetrahydrofuran, 1.3 equiv.) and acetic acid (10 M) at room temperature. The reaction mixture is stirred for 60 min and sodium triacetoxyborohydride (1.3 equiv.) is added at 0 °C and stirred for 16 h at room temperature. The reaction is quenched with 10 % aqueous sodium hydroxide solution, extracted with methanol in dichloromethane (5 %), and the organic layer washed with sodium chloride solution, dried over anhydrous sodium sulfate, filtered and concentrated to afford *N*-ethyl-1-(oxetan-3-yl)piperidin-4-amine (**D**).

[0288] To a solution of *tert*-butyl 7-(5-chloro-2-(3-(5-cyano-6-fluoro-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)prop-1-yn-1-yl)phenyl)thieno[3,2-b]pyridine-3-carboxylate (**E**, 1 equiv.) in acetonitrile (0.1 M), are added *N*-ethyl-1-(oxetan-3-yl)piperidin-4-amine (**D**, 2 equiv.) and *N*,*N*-diisopropylethylamine (3 equiv.) at room temperature and the reaction mixture is stirred for 30 h at 100 °C. The reaction is cool to room temperature, quenched with water, extracted with ethyl acetate, and the organic layer washed with sodium chloride solution, dried over anhydrous sodium sulfate, filtered, concentrated and purified by Combi flash to afford *tert*-butyl 7-(5-chloro-2-(3-(5-cyano-6-(ethyl(1-(oxetan-3-yl)piperidin-4-yl)amino)-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)prop-1-yn-1-yl)phenyl)thieno[3,2-b]pyridine-3-carboxylate (**F**).

Example 1D.11



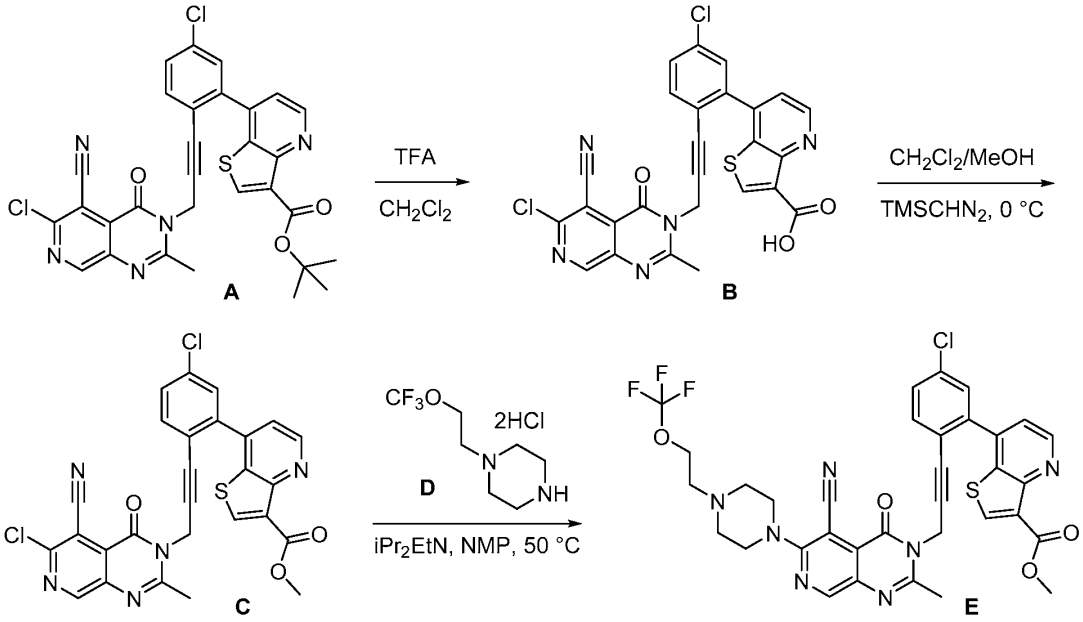
[0289] To a solution of *tert*-butyl (2-(difluoromethyl)pyridin-4-yl)(methyl)carbamate (**A**, 1 equiv.) and acetic acid (10 equiv.) in methanol (0.029 M), 5% rhodium on carbon (0.5 equiv.) is added at room temperature and the mixture heated at 80 °C under 80 psi for 15 hr. The reaction mixture is filtered and concentrated to afford *tert*-butyl (2-(difluoromethyl)piperidin-4-yl)(methyl)carbamate (**B**).

[0290] To a solution of *tert*-butyl (2-(difluoromethyl)piperidin-4-yl)(methyl)carbamate (**B**, 1 equiv.) in THF (0.19 M) are added formaldehyde (37 % solution in water, 10 equiv.), acetic acid (9 equiv.) and molecular sieves (~3x by weight). The mixture is stirred for 30 min at room temperature, sodium triacetoxyboranuide (361 mg, 1.7 mmol) is added and the mixture stirred for 30 min. The reaction mixture is diluted with methanol and the residue passed through a strata ion exchange column, eluting with water three times, then acetonitrile three times, then methanol three times. *tert*-Butyl (2-(difluoromethyl)-1-methylpiperidin-4-yl)(methyl)carbamate (**C**) is eluted by washing the column with a solution of dichloromethane, methanol, and ammonium hydroxide (50:40:10).

[0291] *tert*-Butyl (2-(difluoromethyl)-1-methylpiperidin-4-yl)(methyl)carbamate (**C**, 1 equiv.) in trifluoroacetic acid (0.006 M) is stirred at room temperature for 30 min and the reaction mixture is concentrated to afford 2-(difluoromethyl)-N,1-dimethylpiperidin-4-amine (**D**).

[0292] A mixture of 7-(5-chloro-2-(2-(5-cyano-8-fluoro-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)thieno[3,2-b]pyridine-3-carboxylic acid (**E**, 1 equiv.), 2-(difluoromethyl)-N,1-dimethylpiperidin-4-amine (**D**, 5 equiv.) and NMP (0.037 M) in DIPEA (7 equiv.) is stirred at room temperature for 30 min. The reaction mixture is filtered and purified by HPLC to afford 7-(5-chloro-2-(2-(5-cyano-8-((2-(difluoromethyl)-1-methylpiperidin-4-yl)(methyl)amino)-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)thieno[3,2-b]pyridine-3-carboxylic acid (**F**).

Example 1D.12



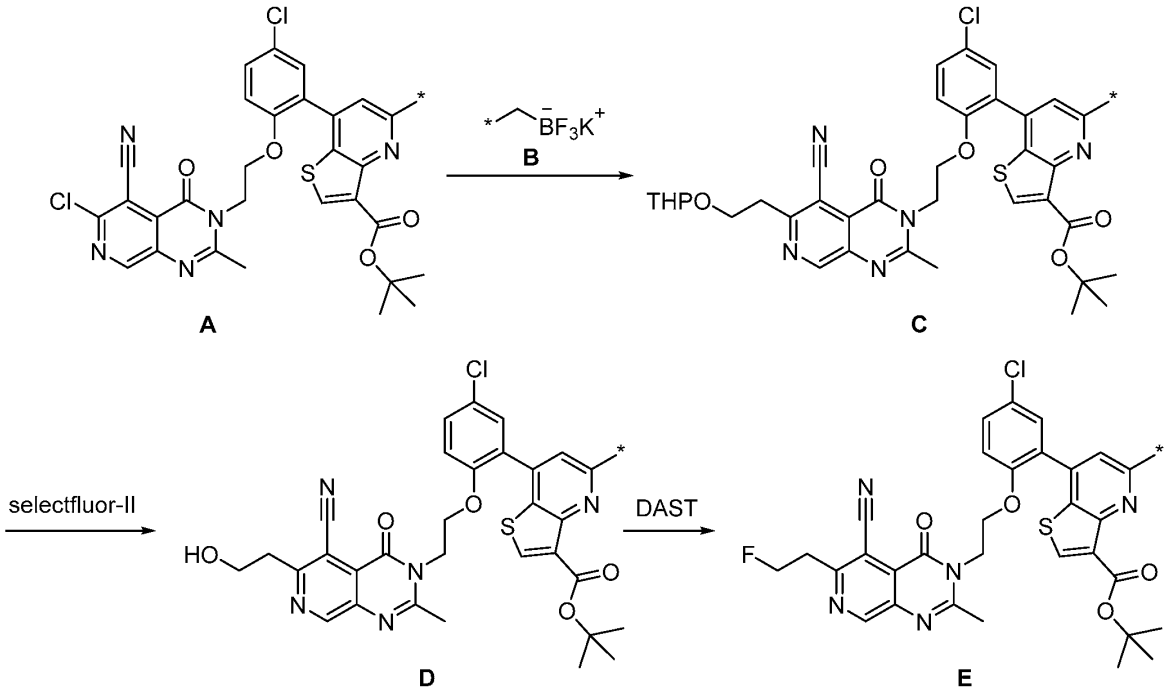
[0293] To a dichloromethane (40 mL) solution of *tert*-butyl 7-(5-chloro-2-(3-(6-chloro-5-cyano-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)prop-1-yn-1-yl)phenyl)thieno[3,2-b]pyridine-3-carboxylate (**A**, 1 equiv.) is added trifluoroacetic acid (0.25 M) at 0 °C and stirred for 17 h at room temperature. The mixture is concentrated *in vacuo*, aqueous sodium bicarbonate solution added, and washed with diethyl ether. The water layer is acidified with 3 N hydrogen chloride solution and stirred for 15 min. Filtration affords 7-(5-chloro-2-(3-(6-chloro-5-cyano-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)prop-1-yn-1-yl)phenyl)thieno[3,2-b]pyridine-3-carboxylic acid (**B**).

[0294] To a 7-(5-chloro-2-(3-(6-chloro-5-cyano-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)prop-1-yn-1-yl)phenyl)thieno[3,2-b]pyridine-3-carboxylic acid (**B**, 1160 mg, 2.12 mmol) solution in dichloromethane (0.11 M) and methanol (0.42 M) is added trimethylsilyldiazomethane (4 equiv.) at 0 °C. Upon stirring for 10 min at 0 °C, the reaction is

quenched with acetic acid (3.5 M), concentrated and purified by silica gel column chromatography to afford methyl 7-(5-chloro-2-(3-(6-chloro-5-cyano-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)prop-1-yn-1-yl)phenyl)thieno[3,2-b]pyridine-3-carboxylate (**C**).

[0295] To a methyl 7-(5-chloro-2-(3-(6-chloro-5-cyano-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)prop-1-yn-1-yl)phenyl)thieno[3,2-b]pyridine-3-carboxylate (**C**, 433 mg, 0.770 mmol) in *N*-methyl-2-pyrrolidone (0.21 M) is added 1-(2-(trifluoromethoxy)ethyl)piperazine dihydrochloride (**D**, 1.5 equiv.) at room temperature and the mixture stirred for 2 h at 50 °C followed by 17 h at room temperature. The mixture is diluted with methanol, filtered, and the filtrate purified by preparative HPLC to give methyl 7-(5-chloro-2-(3-(5-cyano-2-methyl-4-oxo-6-(4-(2-(trifluoromethoxy)ethyl)piperazin-1-yl)pyrido[3,4-d]pyrimidin-3(4H)-yl)prop-1-yn-1-yl)phenyl)thieno[3,2-b]pyridine-3-carboxylate (**E**).

Example 1D.13



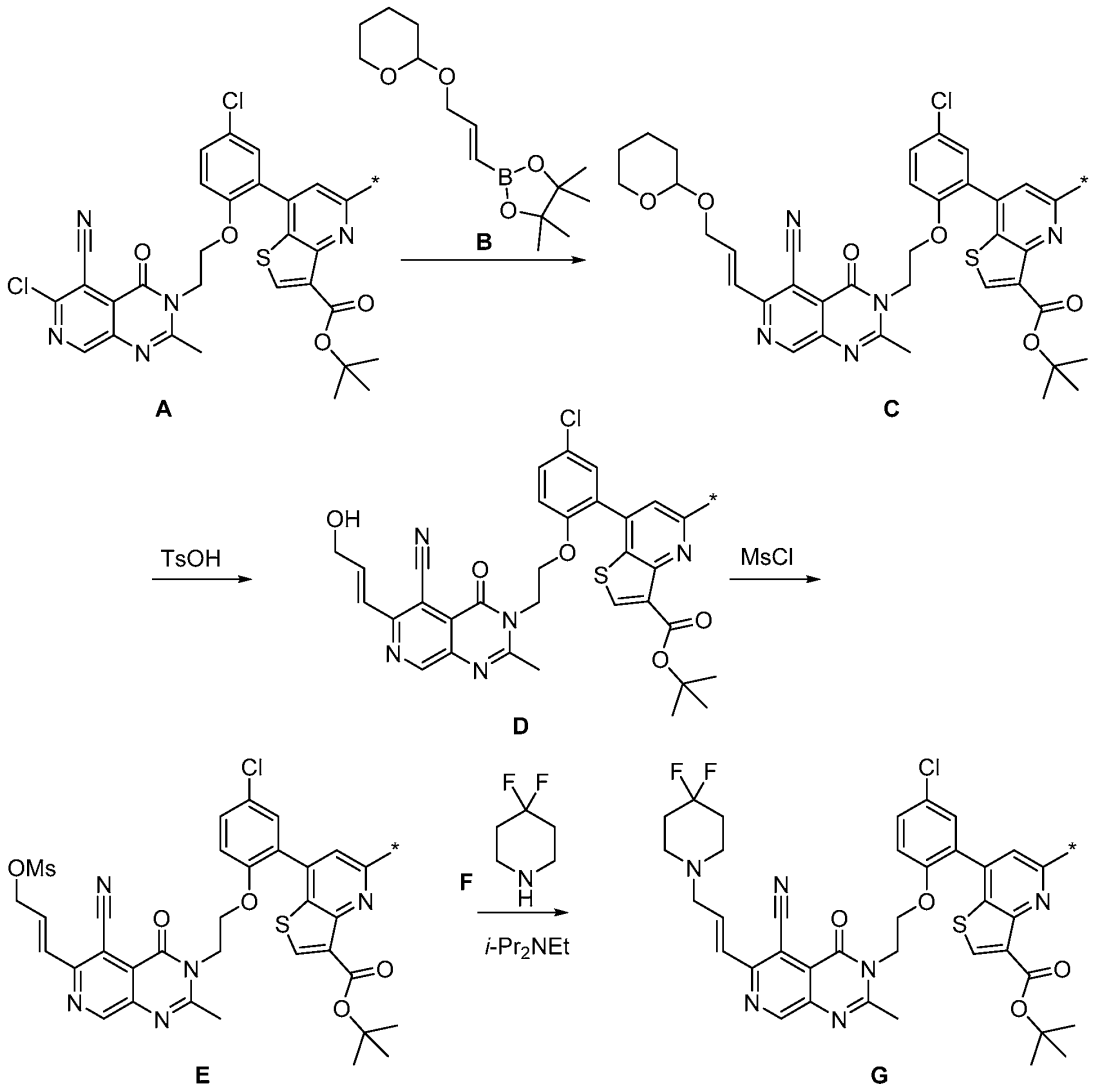
[0296] To a solution of *tert*-butyl 7-(5-chloro-2-(2-(6-chloro-5-cyano-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (**A**, 1 equiv.) and potassium trifluoro(2-((tetrahydro-2H-pyran-2-yl)oxy)ethyl)borate (**B**, 1.4 equiv.) in a mixture of toluene and water (2:1, 0.7 M) is added cesium carbonate (2 equiv.) and the reaction mixture degassed with argon for 15 min. [1,1'-Bis(diphenylphosphino)ferrocene]palladium(II) dichloride (0.1 equiv.) is added and heated at 100 °C for 16 h. The reaction mass is filtered through Celite, washed with ethyl acetate, and the filtrate dried over anhydrous sodium sulfate,

concentrated, and purified by Combiflash to afford *tert*-butyl 7-(5-chloro-2-(2-(5-cyano-2-methyl-4-oxo-6-(2-((tetrahydro-2H-pyran-2-yl)oxy)ethyl)pyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (**C**).

[0297] To a stirred solution of *tert*-butyl 7-(5-chloro-2-(2-(5-cyano-2-methyl-4-oxo-6-(2-((tetrahydro-2H-pyran-2-yl)oxy)ethyl)pyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (**C**, 1 equiv.) in a mixture of acetonitrile and water (3:1, 0.018 M), selectfluor-II (2 equiv.) is added at 0 °C and the mixture stirred at room temperature for 48 h. The reaction mixture is partitioned between water and ethyl acetate and the organic layer dried over sodium sulfate and concentrated to afford *tert*-butyl 7-(5-chloro-2-(2-(5-cyano-6-(2-hydroxyethyl)-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (**D**).

[0298] To a solution of *tert*-butyl 7-(5-chloro-2-(2-(5-cyano-6-(2-hydroxyethyl)-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (**D**, 1 equiv.) in dichloromethane (0.4 M), diethylaminosulfur trifluoride (1.5 equiv.) is added at 0 °C and the mixture stirred at room temperature for 3 h. The reaction mass is quenched with 10 % aqueous sodium hydroxide solution at 0 °C, extracted with dichloromethane, and the organic layer dried over anhydrous sodium sulfate and concentrated to afford *tert*-butyl 7-(5-chloro-2-(2-(5-cyano-6-(2-fluoroethyl)-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (**E**).

Example 1D.14



[0299] *tert*-Butyl 7-(5-chloro-2-(2-(6-chloro-5-cyano-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)thieno[3,2-b]pyridine-3-carboxylate (**A**, 1 equiv.), $PdCl_2(PPh_3)_2$ (0.18 equiv.), and (*E*)-4,4,5,5-tetramethyl-2-(3-((tetrahydro-2H-pyran-2-yl)oxy)prop-1-en-1-yl)-1,3,2-dioxaborolane (**B**, 1.6 equiv.) are suspended in 1,4-dioxane (0.054 M) in an oven dried microwave vial equipped with a stir bar. Aqueous potassium carbonate (2.0 M, 4 equiv.) is added, and the sealed vial is sparged with argon for 5 min and heated at 100 °C in a microwave reactor for 4 h. The reaction mixture is diluted with saturated aqueous sodium bicarbonate and ethyl acetate and the aqueous phase extracted with ethyl acetate three times. The combined organic material is washed with brine, dried over magnesium sulfate, filtered, and purified via silica gel chromatography to afford *tert*-butyl (E)-7-(5-chloro-2-(2-(5-cyano-2-methyl-4-oxo-6-

(3-((tetrahydro-2H-pyran-2-yl)oxy)prop-1-en-1-yl)pyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)thieno[3,2-b]pyridine-3-carboxylate (**C**).

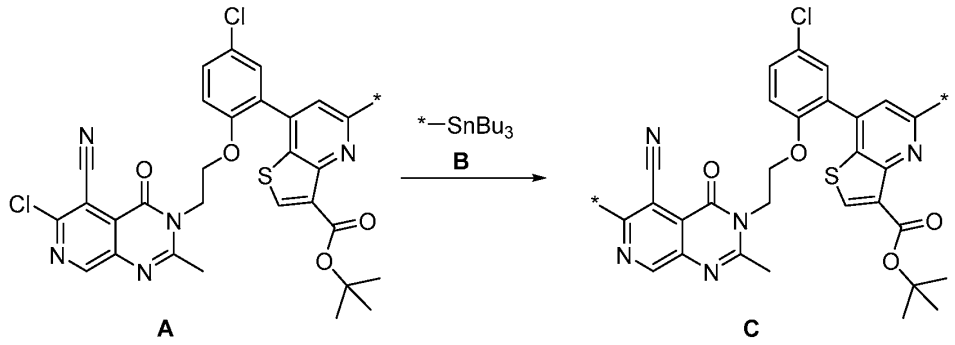
[0300] *tert*-Butyl (E)-7-(5-chloro-2-(2-(5-cyano-2-methyl-4-oxo-6-(3-((tetrahydro-2H-pyran-2-yl)oxy)prop-1-en-1-yl)pyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)thieno[3,2-b]pyridine-3-carboxylate (**C**, 1 equiv.) is suspended in methanol (0.05 M) and tetrahydrofuran (0.05 M) and water (0.05 M) in a screw capped vial equipped with a stir bar and the reaction mixture stirred at room temperature while *p*-toluenesulfonic acid (0.35 equiv.) is added in 1 portion. After 30 min the temperature is raised to 55 °C and stirred an additional 1 h. Water (0.1 M) is added and, after 1 h, the temperature raised to 80 °C and heated at this temperature for 8 h. The reaction mixture is cooled to room temperature and volatile solvent is then removed *in vacuo*. The reaction mixture is diluted with saturated aqueous sodium bicarbonate and ethyl acetate, the layers separated, and the aqueous phase extracted with ethyl acetate three times. The combined organic material is washed with brine, dried over magnesium sulfate, and the solids filtered and concentrated to afford *tert*-butyl (E)-7-(5-chloro-2-(2-(5-cyano-6-(3-hydroxyprop-1-en-1-yl)-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)thieno[3,2-b]pyridine-3-carboxylate (**D**).

[0301] *tert*-Butyl (E)-7-(5-chloro-2-(2-(5-cyano-6-(3-hydroxyprop-1-en-1-yl)-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)thieno[3,2-b]pyridine-3-carboxylate (**D**, 1 equiv.) is dissolved in dichloromethane (0.086 M) in an oven-dried screw capped vial equipped with a stir bar. The reaction mixture is stirred at 0 °C while *N,N*-diisopropylethylamine (6 equiv.) is added slowly. Methanesulfonyl chloride (2.6 equiv.) is then added dropwise at which time the ice bath is removed. After 30 min the reaction mixture is diluted with dichloromethane, washed with saturated aqueous sodium bicarbonate and brine, dried over magnesium sulfate, filtered and the solvent removed *in vacuo*, affording *tert*-butyl (E)-7-(5-chloro-2-(2-(5-cyano-2-methyl-6-(3-((methylsulfonyl)oxy)prop-1-en-1-yl)-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)thieno[3,2-b]pyridine-3-carboxylate (**E**).

[0302] *tert*-Butyl (E)-7-(5-chloro-2-(2-(5-cyano-2-methyl-6-(3-((methylsulfonyl)oxy)prop-1-en-1-yl)-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)thieno[3,2-b]pyridine-3-carboxylate (**E**, 54.5 mg, 0.07 mmol) is dissolved in 1,2-dichloroethane (0.05 M) in a screw capped vial equipped with a stir bar and the reaction mixture stirred at 10 °C while 4,4-difluoropiperidine (**F**, 3.3 equiv.) is added dropwise. *N,N*-Diisopropylethylamine (6.6 equiv.) is added dropwise and after 5 min the reaction mixture is warmed to room temperature. After 15 min the temperature is raised to 45 °C and stirring continued for 3 h. The reaction mixture is cooled to room

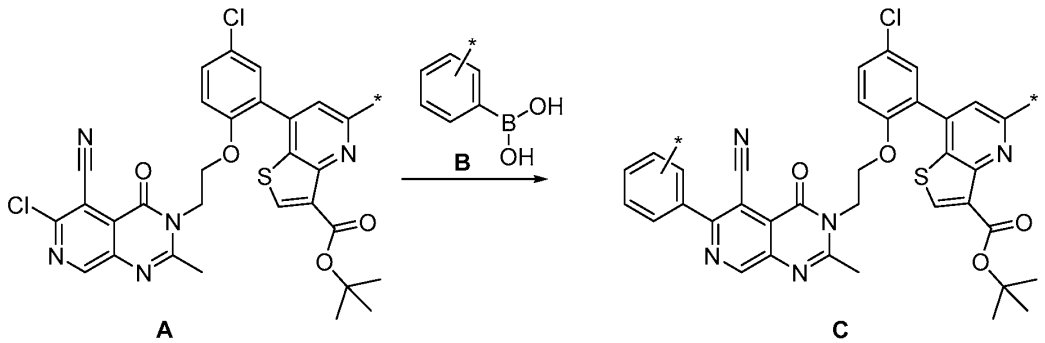
temperature and the solvent is then removed *in vacuo*. The residue is taken up in DMF and filtered through a syringe filter. Preparatory HPLC afforded the desired product, which is isolated by passing HPLC fractions through a strata ion exchange column, then washing with a solution of dichloromethane, methanol, and ammonium hydroxide. The solvent is to afford *tert*-butyl (*E*)-7-(5-chloro-2-(2-(5-cyano-6-(3-(4,4-difluoropiperidin-1-yl)prop-1-en-1-yl)-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)thieno[3,2-b]pyridine-3-carboxylate (**G**).

Example 1D.15



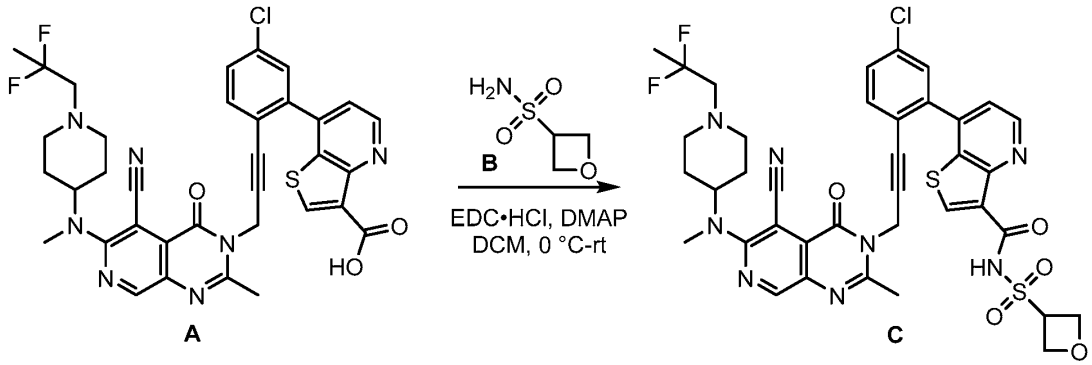
[0303] To a solution of *tert*-butyl 7-(5-chloro-2-(2-(6-chloro-5-cyano-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (**A**, 1 equiv.), tributyl(methoxymethyl)stannane (**B**, 1.5 equiv.) in 1-methyl-2-pyrrolidinone (0.1 M) is degassed using argon for 10 min and tetrakis(triphenylphosphine)palladium (0) (0.055 g, 0.048 mmol) is added at room temperature and heated at 130 ° C for 10 h. The reaction mixture is cooled to room temperature, diluted with water and, extracted with ethyl acetate, and the ethyl acetate layer dried over sodium sulfate, concentrated, and purified by preparative HPLC to afford *tert*-butyl 7-(5-chloro-2-(2-(5-cyano-6-(methoxymethyl)-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (**C**).

Example 1D.16



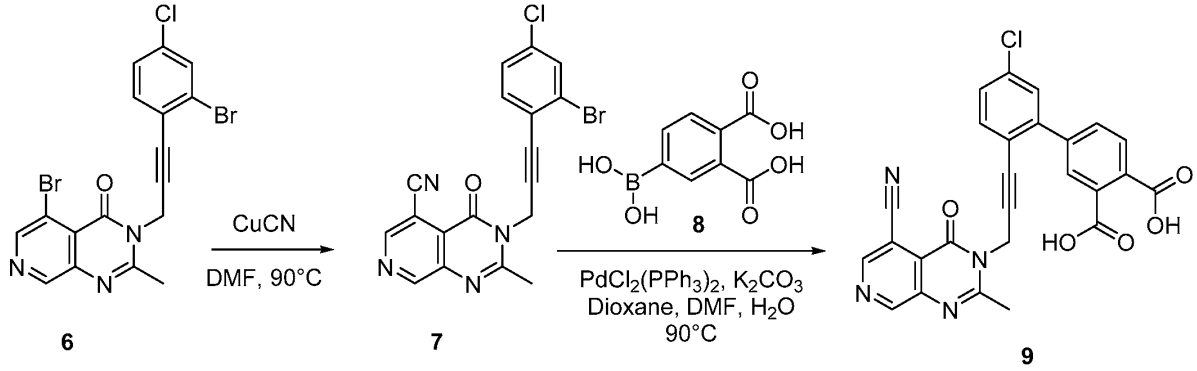
[0304] To a solution of *tert*-butyl 7-(5-chloro-2-(2-(6-chloro-5-cyano-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (**A**, 1 equiv.) and (2-fluorophenyl)boronic acid (**B**, 1.5 equiv.) in 1,4-dioxane is added 2 M aqueous potassium carbonate solution (3 equiv.) and reaction mixture degassed with argon gas for 10 min. [1,1'-Bis(diphenylphosphino)ferrocene] dichlopalladium(II)dichlomethane complex (0.05 equiv.) is added and degassed with argon gas for 5 min and the reaction mixture is heated at 90 °C for 3 h. The reaction mixture is diluted with water, extracted with ethyl acetate, and the organic layer dried over anhydrous sodium sulphate, filtered, concentrated, and purified by column chromatography to afford *tert*-butyl 7-(5-chloro-2-(2-(5-cyano-6-(2-fluorophenyl)-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)ethoxy)phenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (**C**).

Example 1D.17



[0305] To a solution of 7-(5-chloro-2-(3-(5-cyano-6-((1-(2,2-difluoropropyl)piperidin-4-yl)(methyl)amino)-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)prop-1-yn-1-yl)phenyl)thieno[3,2-b]pyridine-3-carboxylic acid (**A**, 1 equiv.) and oxetane-3-sulfonamide (**B**, 2.5 equiv.) in dichloromethane (0.07 M) is added 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (2 equiv.) and 4-(dimethylamino)pyridine (2.5 equiv.) at 0 °C and stirred at room temperature for 12 h. The reaction mixture is diluted with water, extracted with dichloromethane, and the organic layer dried over anhydrous sodium sulphate, filtered, concentrated, and purified by preparative HPLC to afford 7-(5-chloro-2-(3-(5-cyano-6-((1-(2,2-difluoropropyl)piperidin-4-yl)(methyl)amino)-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)prop-1-yn-1-yl)phenyl)-*N*-(oxetan-3-ylsulfonyl)thieno[3,2-b]pyridine-3-carboxamide (**C**).

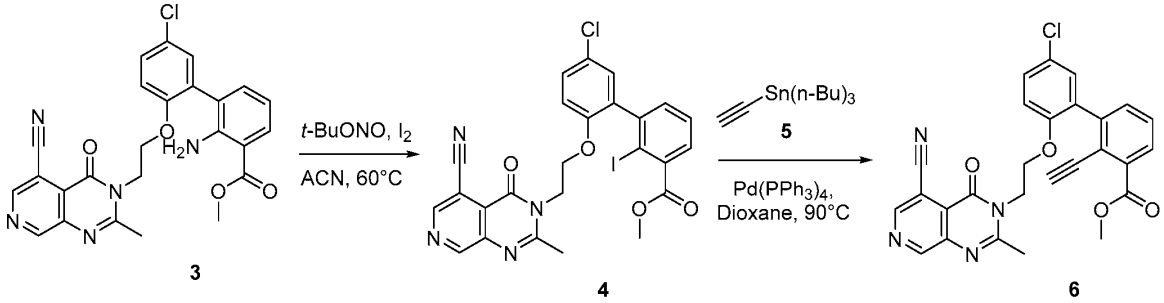
Example 1D.18



[0306] To a stirred solution of 5-bromo-3-(3-(2-bromo-4-chlorophenyl)prop-2-yn-1-yl)-2-methylpyrido[3,4-*d*]pyrimidin-4(3*H*)-one (6, 0.6 g, 1.28 mmol) in *N,N*-dimethylformamide, copper(I) cyanide (0.138 g, 1.53 mmol) is added and the reaction mixture is heated and stirred at 90 °C for16 h. After completion, the reaction mass is diluted with ethyl acetate and washed with cold water. The organic layer is separated, dried over anhydrous sodium sulphate and concentrated under reduced pressure. The crude compound is purified by Combi-flash using 50 % ethyl acetate in hexanes as eluent. The desired fractions are concentrated under reduced pressure to afford 3-(3-(2-bromo-4-chlorophenyl)prop-2-yn-1-yl)-2-methyl-4-oxo-3,4-dihydropyrido[3,4-*d*]pyrimidine-5-carbonitrile (7).

[0307] A stirred solution of 3-(3-(2-bromo-4-chlorophenyl)prop-2-yn-1-yl)-2-methyl-4-oxo-3,4-dihydropyrido[3,4-*d*]pyrimidine-5-carbonitrile (7, 0.1 g, 0.24 mmol), 4-boronophthalic acid (8, 0.075 g, 0.36 mmol) and potassium carbonate (0.099 g, 0.72 mmol) in a mixture of dioxane, *N,N*-dimethylformamide and water (1.2 mL, 0.6 mL, 0.2 mL respectively) is degassed with argon for 25 min. Dichlorobis(triphenylphosphine)palladium(II) is added and the reaction mixture is heated and stirred at 90 °C for 2 h. After completion, volatiles are removed under reduced pressure to obtain the residue. This residue is diluted with water, acidified with 1 N aqueous hydrochloric acid and extracted with ethyl acetate. The organic layer is separated, dried over anhydrous sodium sulphate and concentrated under reduced pressure to obtain the compound. This compound is purified by preparative HPLC to afford 5'-chloro-2'-(3-(5-cyano-2-methyl-4-oxopyrido[3,4-*d*]pyrimidin-3(4*H*)-yl)prop-1-yn-1-yl)-[1,1'-biphenyl]-3,4-dicarboxylic acid (**9**).

Example 1D.18

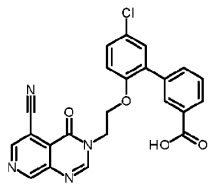
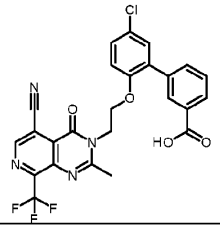
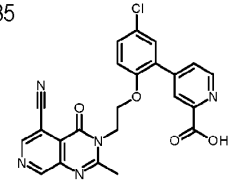
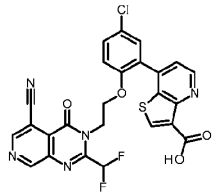
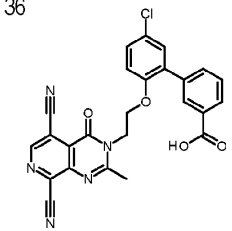
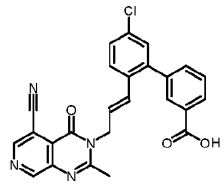


[0308] To a solution of methyl 2-amino-5'-chloro-2'-(2-(5-cyano-2-methyl-4-oxopyrido[3,4-*d*]pyrimidin-3(4*H*)-yl)ethoxy)-[1,1'-biphenyl]-3-carboxylate (3, 1.5 g, 3.06 mmol) in acetonitrile (40 mL), *tert*-butyl nitrite (0.50 g, 4.8 mmol) is added at room temperature. Suspension of copper(I) iodide (0.93 g, 3.06 mmol) in acetonitrile (10 mL) is added drop wise over a period of 10 min at room temperature. The reaction mixture is stirred at 60 °C for 4 h. After completion, the reaction mixture is diluted with water and extracted with ethyl acetate. The organic layer is washed with aqueous sodium thiosulphate, dried over anhydrous sodium sulphate, filtered and concentrated under reduced pressure to afford crude. The crude is purified by flash column chromatography using 0-40 % ethyl acetate in hexane to afford methyl 5'-chloro-2'-(2-(5-cyano-2-methyl-4-oxopyrido[3,4-*d*]pyrimidin-3(4*H*)-yl)ethoxy)-2-iodo-[1,1'-biphenyl]-3-carboxylate (4).

[0309] A solution of methyl 5'-chloro-2'-(2-(5-cyano-2-methyl-4-oxopyrido[3,4-*d*]pyrimidin-3(4*H*)-yl)ethoxy)-2-iodo-[1,1'-biphenyl]-3-carboxylate (4, 0.57 g, 0.95 mmol) in dioxane (20 mL) is degassed for 10 min using argon. Tributyl(ethynyl)stannane (5, 0.6 g, 1.86 mmol) and tetrakis(triphenylphosphine)palladium(0) (0.076 g, 0.066 mmol) are added and the reaction mixture is stirred at 90 °C for 16 h. After completion, reaction mixture is diluted with water and extracted with ethyl acetate. The organic layer is dried over anhydrous sodium sulfate filtered and concentrated to dryness under reduced pressure. The crude is purified by flash column chromatography using 0-40 % ethyl acetate in hexanes to afford methyl 5'-chloro-2'-(2-(5-cyano-2-methyl-4-oxopyrido[3,4-*d*]pyrimidin-3(4*H*)-yl)ethoxy)-2-ethynyl-[1,1'-biphenyl]-3-carboxylate (6).

[0310] Compounds made using one or more of the general methods described above are shown in Table 1. Where provided, characterization data is to the right of the compounds.

Table 1. 7-Aza-Thienylpyridine and Derivative Compounds

Compound	Characterization	Compound	Characterization
34 	MS (ESI) m/z 447.30 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.98 (s, 1H), 9.23 (s, 1H), 9.07 (s, 1H), 8.20 (s, 1H), 7.88 (s, 1H), 7.84 (d, J = 7.68, 1H), 7.61 (d, J = 7.72, 1H), 7.45 - 7.39 (m, 2H), 7.33 (d, J = 2.5 Hz, 1H), 7.21 (d, J = 8.84Hz, 1H), 4.35 (s, 4H)	38 	MS (ESI) m/z 529.45 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.98 (s, 1H), 9.13 (s, 1H), 7.87-7.85 (m, 2H), 7.56 (d, J = 7.76 Hz, 1H), 7.42-7.38 (m, 2H), 7.29 (d, J = 2.64 Hz, 1H), 7.21 (d, J = 8.92 Hz, 1H), 4.37 (m, 4H), 2.24 (s, 3H)
35 	MS (ESI) m/z 462.39 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.19 (s, 1H), 9.03 (s, 1H), 8.63 (d, J = 4.8 Hz, 1H), 7.94 (d, J = 0.8 Hz, 1H), 7.59 (dd, J = 4.8 Hz, 1H), 7.48 (dd, J = 4.4 Hz, 1H), 7.409 (d, J = 2.8 Hz, 1H), 7.249 (d, J = 8.8 Hz, 1H), 4.386 (s, 4H), 2.22 (s, 3H)	39 	MS (ESI) m/z 554.13 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.22 (s, 1H), 9.19 (s, 1H), 8.79 (d, J = 4.8 Hz, 1H), 8.45 (s, 1H), 7.61 (dd, J = 2.64, 8.88, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.45 (d, J = 2.68 Hz, 1H), 7.37 (d, J = 8.96 Hz, 1H), 6.72-6.46 (t, J = 51.6 Hz, 1H), 4.41 (d, J = 4.64 Hz, 2H), 4.36 (d, J = 4.52 Hz, 2H)
36 	MS (ESI) m/z 486.38 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.16 (s, 1H), 7.87 (d, J=7.68 Hz, 1H), 7.83 (s, 1H), 7.49 (d, J = 7.68 Hz, 1H), 7.43-7.38 (m, 2H), 7.27 (d, J = 2.6 Hz, 1H), 7.20 (d, J = 8.88 Hz, 1H), 4.39-4.35 (dd, J =12.52 Hz, 4H), 2.29 (s, 3H)	44 	MS (ESI) m/z 457.42 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.06 (s, 1H), 9.18 (s, 1H), 9.04 (s, 1H), 7.9-7.83 (m, 1H), 7.76 (s, 1H), 7.72 (d, J = 8.4 Hz, 1H), 7.52-7.44 (m, 3H), 7.36 (d, J = 2.2 Hz, 1H), 6.42 -6.35 (m, 1H), 6.22 (d, J = 16.04 Hz, 1H), 4.82 (d, J = 4.8 Hz, 2H), 2.58 (s, 3H)

45	MS (ESI) m/z 510.44 [M-1]-; 1H NMR (400 MHz, DMSO-d6) δ 9.01 (s, 1H), 8.98 (s, 1H), 8.96 (d, J = 4.56 Hz, 1H), 8.17 (d, J = 7.52 Hz, 1H), 7.64 (s, 1H), 7.56 (dd, J = 8.92 Hz, 1H), 7.44 (d, J = 4.56 Hz, 1H), 7.30 (d, J = 2.56 Hz, 1H), 7.26 (d, J = 8.96 Hz, 1H), 7.19 (d, J =7.6 Hz, 1H), 4.33-4.29 (m, 2H), 4.24-4.17 (m, 1H), 4.12-4.06 (m, 1H), 1.84 (s, 3H)	50	MS (ESI) m/z 619.07 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.86 (d, J = 4.4 Hz, 1H), 8.24 (s, 1H), 8.08 (s, 1H), 7.60 (dd, J = 8.8, 2.6 Hz, 1H), 7.51 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.6 Hz, 1H), 7.36 (d, J = 8.8 Hz, 1H), 4.41 (t, J = 4.7 Hz, 2H), 4.25 (t, J = 4.7 Hz, 2H), 1.69 (s, 3H)
48	MS (ESI) m/z 475.16 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.16 (s, 1H), 9.18 (s, 1H), 9.05 (s, 1H), 7.36 (dd, J = 8.8 Hz, 1H), 7.28 (t, 2H), 7.24 – 7.18 (m, 5 H), 4.57 (t, 2H), 4.33 (t, 2H), 2.87 (t, 2H) 2.57 (t, 2H)	140	MS (ESI) m/z 518.50 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.029 (d, J = 1.24 Hz, 2H), 8.835 (d, J = 4.76 Hz, 1H), 8.379 (s, 1H), 7.596 (dd, J = 2.6, 8.96 Hz, 1H), 7.48 (d, J = 4.72 Hz, 1H), 7.439 (d, J = 2.52 Hz, 1H), 7.35 (d, J = 9.0 Hz, 1H), 4.403 (t, J = 4.68 Hz, 2H), 4.255 (t, J = 6.04 Hz, 2H), 1.787 (s, 3H)
49	MS (ESI) m/z 553.18 [M+1]+; 1H NMR (400 MHz, DMSO-d6) d 12.17 (bs, 1H), 8.84 (d, J = 4.76 Hz, 1H), 8.41 (s, 1H), 7.72 (dd, J = 10.68 Hz, 7.56 Hz, 1H),7.60 (dd, J = 8.08, 2.60 Hz, 1H), 7.48 (d, J = 4.76 Hz, 1H), 7.41 (d, J = 2.52 Hz, 1H), 7.36 (d, J = 8.08 Hz, 1H), 4.39 (t, J = 4.64 Hz, 2H). 4.23 (t, J = 4.68 Hz, 2H), 1.77 (s, 3H)	147	MS (ESI) m/z 505 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.16 (s, 1H), 9.00 (s, 1H), 8.139 (m, J = 8.04 Hz, 2H), 7.44 (m, J = 7.92 Hz, 2H), 7.28 (d, J = 2.76 Hz, 1H), 7.19 (d, J = 8.92 Hz ,1H), 4.35 (s, 4H), 2.22 (s, 3H)

149		MS (ESI) m/z 497.38 [M-1]-; 1H NMR (400 MHz, DMSO-d6) δ 9.158 (s, 1H), 9.033 (s, 1H), 8.291 (s, 1H), 8.117 (d, J = 8.2 Hz, 1H), 7.63 (d, J = 8.28 Hz, 1H), 7.6 (dd, J = 1.96, 8.12 Hz, 1H), 7.53 (d, J = 1.96 Hz, 1H), 7.49 (dd, J = 2.2, 8.4 Hz, 1H), 5.05 (s, 2H), 2.35 (s, 3H)	
150FA		MS (ESI) m/z 497 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.20 (s, 1H), 9.03 (s, 1H), 7.68-7.63 (m, 2H), 7.47-7.38 (m, 3H), 7.23 (d, J = 2.6 Hz, 1H), 7.18 (d, J = 8.88 Hz, 1H), 4.37-4.22 (m, 4H), 2.25 (s, 3H)	
150FB		MS (ESI) m/z 539 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.19 (s, 1H), 9.03 (s, 1H), 7.25 (d, J = 2.6 Hz, 1H), 7.19 (d, J = 8.8 Hz, 1H),7.63-7.67 (m, 2H), 7.50 (d, J = 6.5 Hz, 1H), 7.41 - 7.44 (m, 1H), 7.41 (dd, J =2.8 Hz, J'= 2.6 Hz, 1H), 4.36 (s, 4H), 4.41-4.48 (m, 1H), 2.24 (s, 3H), 1.19 (d, J = 6.2 Hz, 6H)	
150FC		MS (ESI) m/z 472 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.9 (s, 1H), 8.62 (d, J = 5.2 Hz, 1H), 7.91 (d, J = 5.16 Hz, 1H), 7.63-7.72 (m, 2H), 7.40-7.44 (m, 3H), 7.24 (d, J = 2.64 Hz, 1H), 7.19 (d, J=8.84, 1H), 4.33-4.37 (m, 4H), 2.28 (s, 3H)	
151		MS (ESI) m/z 696.11 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.69 (bs, 1H), δ 8.92 (d, J = 4.4 Hz, 1H), δ 8.34 (s, 1H), δ 8.09 (s, 1H), δ 7.63-7.57 (m, 2H), δ 7.45 (d, J = 2.0 Hz, 1H), δ 7.36 (d, J = 8.8 Hz, 1H), δ 4.42 (t, 4.8 Hz, 2H), δ 4.24 (t, J = 4.8, 2H), δ 3.56 (s, 3H), δ 1.65 (s, 3H)	
152		MS (ESI) m/z 579.03 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.96 (b, 1H), 8.74(d, J = 4.72 Hz, 1H), 8.62 (s, 1H), 8.13 (d, J = 9.76 Hz, 1H), 7.76 (d, J = 9.76 Hz, 1H), 7.68 (t, J = 2.04 Hz, 1H), 7.53 (d, J = 4.72 Hz, 1H), 7.3 (t, J = 53.68 Hz, 1H), 4.88 (s, 2H), 2.22(s, 3H)	

155		MS (ESI) m/z 485.13 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.89 (bs, 1H), 9.17 (s, 1H), 9.00 (s, 1H), 7.88 (m, 1H), 7.46-7.36 (m, 3H), 7.16-7.12 (m, 2H), 4.32 (bs, 4H), 3.67 (s, 1H), 1.98 (s, 3H)	184		MS (ESI) m/z 561.16 [M-1]-; 1H NMR (400 MHz, DMSO-d6) δ 9.26 (s, 1H), 9.08 (s, 1H), 8.32 (s, 1H), 7.63 (d, J = 8.4 Hz, 1H), 7.39-7.16 (m, 5H), 4.34 (d, J = 3.6 Hz, 6H), 3.25-3.18 (m, 3H), 2.89 (s, 2H), 1.42 (d, J = 15 Hz, 4H), 1.27-1.18 (m, 2H)
157		MS (ESI) m/z 511.48 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.87 (s, 1H), 9.23 (s, 1H), 7.88-7.86 (dd, J = 1.28, J = 6.8 Hz, 1H), 7.80 (d, J = 1.6 Hz, 1H), 7.53 (d, J = 7.6 Hz, 1H), 7.45-7.17 (m, 5H), 4.36 (s, 4H), 2.19 (s, 3H)	260		MS (ESI) m/z 636.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.99 (s, 1H), 8.82 (d, J = 4.9 Hz, 1H), 8.40 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.44 (d, J = 2.7 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.40 (t, J = 5.0 Hz, 2H), 4.25 (t, J = 5.0 Hz, 2H), 3.50 – 3.41 (m, 1H), 2.24 – 1.94 (m, 8H), 1.83 (s, 3H)
183		MS (ESI) m/z 690.4 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 10.15 (s, 1H), 8.79 (d, J = 4.8 Hz, 1H), 8.59 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.46 (d, J = 4.8 Hz, 1H), 7.44 (d, J = 2.6 Hz, 1H), 7.38 (d, J = 9.0 Hz, 1H), 4.89 (dt, J = 47.1, 4.7 Hz, 2H), 4.44 – 4.33 (m, 3H), 4.23 (t, J = 5.1 Hz, 2H), 3.93 (hept, J = 6.8 Hz, 1H), 3.79 – 3.52 (m, 7H), 1.87 (s, 3H), 1.25 (d, J = 6.8 Hz, 6H)	284		MS (ESI) m/z 636.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.94 (s, 1H), 8.80 (d, J = 4.8 Hz, 1H), 8.60 (s, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.49 (d, J = 4.8 Hz, 1H), 7.45 (d, J = 2.7 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.42 (t, J = 4.9 Hz, 2H), 4.25 (t, J = 4.9 Hz, 2H), 3.94 – 3.82 (m, 1H), 2.23 – 1.94 (m, 6H), 1.86 (td, J = 12.7, 12.1, 4.2 Hz, 2H), 1.80 (s, 3H)

338		MS (ESI) m/z 560.1 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) d / ppm = 8.89 (s, 1H), 8.49 (s, 1H), 7.59 (dd, J = 8.9, 2.6 Hz, 1H), 7.43-7.41 (m, 2H), 7.36 (d, J = 8.9 Hz, 1H), 4.43 (t, J = 4.8 Hz, 2H), 4.26 (t, J = 4.8 Hz, 2H), 3.19 (q, J = 7.5 Hz, 2H), 2.69 (s, 3H), 1.93 (s, 3H), 1.27 (t, J = 7.5 Hz, 3H)	365		MS (ESI) m/z 603.3 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.58 (s, 1H), 8.96 (s, 1H), 8.34 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.42 (s, 1H), 7.41 (d, J = 2.7 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.41 (t, J = 5.0 Hz, 2H), 4.28 (t, J = 5.1 Hz, 2H), 3.69 – 3.61 (m, 2H), 3.58 – 3.50 (m, 2H), 2.93 (s, 3H), 2.92 (s, 3H), 2.72 (s, 3H), 1.92 (s, 3H)
339		MS (ESI) m/z 572.1; 1H-NMR (400 MHz, d6-DMSO) d / ppm = 8.77 (s, 1H), 8.59 (s, 1H), 7.59 (dd, J = 8.9, 2.6 Hz, 1H), 7.42 (d, J = 2.6 Hz, 1H), 7.41 (s, 1H), 7.36 (d, J = 8.9 Hz, 1H), 4.42 (t, J = 5.0 Hz, 2H), 4.27 (t, J = 5.0 Hz, 2H), 3.21-3.11 (m, 1H), 2.68 (s, 3H), 1.92 (s, 3H), 1.33-1.26 (m, 1H), 1.21-1.15 (m, 1H)	372		MS (ESI) m/z 582.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.12 (s, 1H), 8.59 (s, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.52 (t, J= 53.5 Hz, 1H), 7.44 (d, J = 2.6 Hz, 1H), 7.40 (s, 1H), 7.35 (d, J = 9.0 Hz, 1H), 4.42 (t, J = 5.0 Hz, 2H), 4.27 (t, J = 5.0 Hz, 2H), 2.66 (s, 3H), 1.90 (s, 3H)
340		MS (ESI) m/z 600.2 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) d / ppm = 9.11 (s, 1H), 8.63 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.46-7.44 (m, 2H), 7.36 (d, J = 8.9 Hz, 1H), 4.44 (t, J = 4.9 Hz, 2H), 4.30 (t, J = 4.9 Hz, 2H), 2.70 (s, 3H), 2.05 (s, 3H)	384		MS (ESI) m/z 552.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.99 (s, 1H), 8.75 (d, J = 4.8 Hz, 1H), 8.62 (s, 1H), 7.80 – 7.73 (m, 1H), 7.72 – 7.65 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 4.86 (s, 2H), 2.67 – 2.61 (m, 1H), 2.09 (s, 3H), 1.29 – 1.15 (m, 4H)

385		MS (ESI) m/z 649.1 [M+1]+; ; 1H NMR (400 MHz, DMSO-d6) δ 12.91 (s, 1H), 8.84 (s, 1H), 8.56 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.43 (s, 1H), 7.40 (d, J = 2.7 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 4.41 (t, J = 5.1 Hz, 2H), 4.25 (t, J = 5.1 Hz, 2H), 3.57 (s, 3H), 2.68 (s, 3H), 2.61 (tt, J = 7.6, 4.9 Hz, 1H), 1.87 (s, 3H), 1.31 – 1.13 (m, 4H)	419	MS (ESI) m/z 546.7 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.89 (s, 1H), 8.38 (s, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.42 (s, 1H), 7.41 (d, J = 2.6 Hz, 1H), 7.35 (d, J = 8.9 Hz, 1H), 4.40 (t, J = 5.0 Hz, 2H), 4.25 (t, J = 5.0 Hz, 2H), 2.79 (s, 3H), 2.71 (s, 3H), 1.88 (s, 3H)
400		MS (ESI) m/z 644.5 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.47 (s, 1H), 7.59 (dd, J = 8.9, 2.6 Hz, 1H), 7.44 – 7.38 (m, 2H), 7.37 (d, J = 9.0 Hz, 1H), 4.42 (t, J = 5.0 Hz, 2H), 4.25 (t, J = 5.0 Hz, 2H), 3.87 – 3.78 (m, 2H), 3.26 (td, J = 11.7, 2.1 Hz, 2H), 2.96 (d, J = 7.1 Hz, 2H), 2.73 (s, 3H), 2.69 (s, 3H), 2.15 – 2.02 (m, 1H), 1.92 (s, 3H), 1.56 – 1.47 (m, 2H), 1.33 (qd, J = 12.0, 4.4 Hz, 2H)	420	MS (ESI) m/z 588.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.92 (s, 1H), 8.46 (s, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.43 (s, 1H), 7.42 (d, J = 2.5 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.39 (t, J = 5.1 Hz, 2H), 4.24 (t, J = 5.1 Hz, 2H), 2.71 (s, 3H), 1.86 (s, 3H), 1.58 (s, 9H)
418		MS (ESI) m/z 572.5 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.84 (s, 1H), 8.42 (s, 1H), 7.59 (dd, J = 8.8, 2.6 Hz, 1H), 7.42 (s, 1H), 7.41 (d, J = 2.6 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.40 (t, J = 5.0 Hz, 2H), 4.25 (t, J = 5.0 Hz, 2H), 2.70 (s, 3H), 2.65-2.56 (m, 1H), 1.86 (s, 3H), 1.27-1.14 (m, 4H)	432	MS (ESI) m/z 574.6 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.98 (s, 1H), 8.42 (s, 1H), 7.59 (dd, J = 8.9, 2.6 Hz, 1H), 7.42 (d, J = 2.6 Hz, 1H), 7.42 (s, 1H), 7.35 (d, J = 9.0 Hz, 1H), 4.39 (t, J = 4.9 Hz, 2H), 4.25 (t, J = 5.0 Hz, 2H), 3.64 (hept, J = 6.8 Hz, 1H), 2.70 (s, 3H), 1.87 (s, 3H), 1.33 (d, J = 6.7 Hz, 6H)

435		MS (ESI) m/z 587.6 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.52 – 8.47 (m, 2H), 7.56 (dd, J = 8.9, 2.7 Hz, 1H), 7.40 – 7.35 (m, 2H), 7.31 (d, J = 9.0 Hz, 1H), 4.37 – 4.29 (m, 6H), 4.16 (t, J = 5.1 Hz, 3H), 2.68 (s, 3H), 2.40 – 2.28 (m, 2H), 1.79 (s, 3H)	450		MS (ESI) m/z 638.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.86 (s, 1H), 8.64 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.69 (dd, J = 8.4, 2.2 Hz, 1H), 7.63 (d, J = 2.1 Hz, 1H), 7.46 (s, 1H), 4.81 (s, 2H), 4.35 (d, J = 14.1 Hz, 2H), 3.62 (d, J = 12.0 Hz, 2H), 3.48 – 3.23 (m, 6H), 2.92 (d, J = 3.5 Hz, 3H), 2.74 (s, 3H), 2.66 (s, 3H), 2.17 (s, 3H)
441		MS (ESI) m/z 655.5 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.65 (d, J = 2.7 Hz, 1H), 8.48 (s, 1H), 8.06 (dd, J = 9.1, 2.8 Hz, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.49 – 7.34 (m, 3H), 4.46 (t, J = 5.0 Hz, 2H), 4.30 (t, J = 5.1 Hz, 2H), 2.79 (s, 3H), 2.72 (s, 3H), 2.35 (s, 3H), 2.00 (s, 3H)	459		MS (ESI) m/z 560.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.73 (d, J = 4.8 Hz, 1H), 8.63 (s, 1H), 7.76 (d, J = 8.2 Hz, 1H), 7.72 – 7.63 (m, 2H), 7.53 (d, J = 4.8 Hz, 1H), 4.85 (s, 2H), 2.78 (d, J = 10.6 Hz, 6H), 2.15 (s, 3H)
448		MS (ESI) m/z 630.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.89 (s, 1H), 8.82 (d, J = 4.8 Hz, 1H), 8.48 (s, 1H), 7.61 (dd, J = 9.0, 2.7 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.41 – 7.37 (m, 2H), 4.43 (t, J = 5.1 Hz, 2H), 4.33 (d, J = 14.1 Hz, 2H), 4.24 (t, J = 5.1 Hz, 2H), 3.60 (d, J = 11.9 Hz, 2H), 3.33 – 3.19 (m, 2H), 2.91 (d, J = 3.1 Hz, 3H), 2.66 (s, 3H), 1.89 (s, 3H)	474		LCMS: 640.2 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ 8.50 (s, 1H), 7.99 – 7.89 (m, 2H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.48 – 7.31 (m, 5H), 4.45 (t, J = 5.0 Hz, 2H), 4.28 (t, J = 5.1 Hz, 2H), 2.79 (s, 3H), 2.71 (s, 3H), 1.97 (s, 3H)

475		LCMS: 640.2 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ 8.48 (s, 1H), 7.79 – 7.68 (m, 2H), 7.66 – 7.57 (m, 2H), 7.45 – 7.34 (m, 4H), 4.45 (t, J = 5.1 Hz, 2H), 4.29 (t, J = 5.0 Hz, 2H), 2.80 (s, 3H), 2.71 (s, 3H), 1.99 (s, 3H)	
476		LCMS: 640.2 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ 8.57 (s, 1H), 7.72 (td, J = 7.7, 1.9 Hz, 1H), 7.67 – 7.57 (m, 2H), 7.47 – 7.34 (m, 5H), 4.44 (t, J = 5.0 Hz, 2H), 4.28 (t, J = 5.0 Hz, 2H), 2.80 (s, 3H), 2.71 (s, 3H), 1.96 (s, 3H)	
477		LCMS: 636.7 [M+H]+; ; 1H NMR (400 MHz, DMSO-d6) δ 8.52 (s, 1H), 7.81 – 7.75 (m, 2H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.46 – 7.32 (m, 5H), 4.45 (t, J = 5.0 Hz, 2H), 4.28 (t, J = 5.1 Hz, 2H), 2.78 (d, J = 0.7 Hz, 3H), 2.71 (s, 3H), 2.42 (s, 3H), 1.94 (s, 3H)	
478		LCMS: 636.8 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ 8.50 (s, 1H), 7.70 – 7.63 (m, 2H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.48 – 7.33 (m, 5H), 4.45 (t, J = 5.0 Hz, 2H), 4.28 (t, J = 5.0 Hz, 2H), 2.79 (s, 3H), 2.71 (s, 3H), 2.43 (s, 3H), 1.94 (s, 3H)	
479		LCMS: 636.8 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ 8.52 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.44 (dq, J = 3.9, 2.0 Hz, 4H), 7.42 – 7.31 (m, 3H), 4.44 (t, J = 5.0 Hz, 2H), 4.28 (d, J = 4.9 Hz, 2H), 2.77 (s, 3H), 2.71 (s, 3H), 2.18 (s, 3H), 1.90 (s, 3H)	
480		LCMS: 656.4 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ 8.49 (s, 1H), 7.92 (d, J = 2.1 Hz, 1H), 7.91 (d, J = 2.1 Hz, 1H), 7.68 – 7.63 (m, 2H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.45 – 7.36 (m, 3H), 4.45 (t, J = 5.0 Hz, 2H), 4.29 (t, J = 4.9 Hz, 2H), 2.79 (s, 3H), 2.70 (s, 3H), 1.97 (s, 3H)	

481		LCMS: 656.6 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ 8.46 (s, 1H), 7.94 (td, J = 1.9, 0.6 Hz, 1H), 7.85 (dt, J = 7.1, 1.7 Hz, 1H), 7.67 – 7.57 (m, 3H), 7.45 – 7.36 (m, 3H), 4.46 (t, J = 5.1 Hz, 2H), 4.29 (t, J = 5.0 Hz, 2H), 2.79 (s, 3H), 2.72 (s, 3H), 1.99 (s, 3H)	492		MS (ESI) m/z 560.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.48 (s, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.42 – 7.35 (m, 4H), 4.43 (t, J = 5.1 Hz, 2H), 4.26 (t, J = 5.1 Hz, 2H), 2.72 (d, J = 3.2 Hz, 6H), 2.70 (s, 3H), 1.96 (s, 3H)
482		LCMS: 656.7 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ 8.54 (s, 1H), 7.70 – 7.63 (m, 2H), 7.62 – 7.52 (m, 3H), 7.46 – 7.41 (m, 2H), 7.38 (d, J = 9.0 Hz, 1H), 4.44 (t, J = 5.0 Hz, 2H), 4.28 (s, 2H), 2.79 (s, 3H), 2.71 (s, 3H), 1.94 (s, 3H)	597		MS (ESI) m/z 532.14 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.0 (d, J = 5.6 Hz, 1H), 8.38 (s, 1H), 7.59 (dd, J = 8.8, 2.5 Hz, 1H), 7.41 (d, J = 2.1 Hz, 2H), 7.35 (d, J = 9.0 Hz, 1H), 4.4 (t, J = 4.2 Hz, 2H), 4.26 (t, J = 4.8 Hz, 2H), 2.7 (s, 3H), 1.85 (s, 3H)
491		MS (ESI) m/z 574.5 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.92 (s, 1H), 8.59 (s, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.50 – 7.41 (m, 2H), 7.35 (d, J = 9.0 Hz, 1H), 4.42 (t, J = 5.0 Hz, 2H), 4.26 (t, J = 5.1 Hz, 2H), 4.12 – 4.00 (m, 1H), 2.68 (s, 3H), 1.94 (s, 3H), 1.26 (d, J = 6.8 Hz, 6H)	600		MS (ESI) m/z 609.11 [M+1; 1H NMR (400 MHz, DMSO-d6) δ 12.94 (s, 1H), 9.01 (d, J = 5.44, 1H), 8.51 (s, 1H), 7.62-7.56 (m, 1H), 7.49-7.31 (m, 3H), 4.41 (s, 2H), 4.26 (s, 2H), 3.58 (s, 3H), 2.69 (s, 3H), 1.91 (s, 3H)

601		MS (ESI) m/z 526.12 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.14 (s, 1H), 9.08 (s, 1H), 8.61 (s, 1H), 7.75 (d, J = 8.2 Hz, 1H), 7.69-7.66 (m, 2H), 7.46 (s, 1H), 4.87 (s, 2H), 2.61 (s, 3H), 2.16 (s, 3H)	
602		MS (ESI) m/z 598.13 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.78 (s, 1H), 8.40 (s, 1H), 7.85 (t, J = 72.0 Hz, 1H), 7.59 (d, J = 8.92 Hz, 1H), 7.42 (bs, 2H), 7.35 (d, J = 8.96 Hz, 1H), 4.40 (t, J = 5.12 Hz, 2H), 4.25 (t, J = 4.44 Hz, 2H), 2.71 (s, 3H), 1.82 (s, 3H)	
603		MS (ESI) m/z 642.4 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 10.85 (s, 1H), 8.82 (d, J = 4.8 Hz, 1H), 8.53 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.7 Hz, 1H), 7.39 (d, J = 9.0 Hz, 1H), 4.55 – 4.38 (m, 3H), 4.30 – 4.15 (m, 2H), 3.66 – 3.44 (m, 4H), 3.27 – 3.12 (m, 1H), 3.05 – 2.83 (m, 4H), 2.64 (s, 3H), 1.85 (s, 3H), 1.44 – 1.22 (m, 2H)	
604		MS (ESI) m/z 598.18 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 8.66 (s, 1H), 8.54 (s, 1H), 7.82 (t, J = 71.4 Hz, 1H), 7.60 (dd, J = 2.52, 8.84 Hz, 1H), 7.42 (d, J = 2.5 Hz, 1H), 7.40 (s, 1H), 7.36 (d, J = 8.8 Hz, 1H), 4.42 (t, J = 5.46 Hz, 2H), 4.29 (t, J = 5.46 Hz, 2H), 2.71 (s, 3H), 2.01 (s, 3H)	
624		MS (ESI) m/z 512.02 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.15 (s, 1H), 9.06 (s, 1H), 8.74 (d, J = 4.76 Hz, 1H), 8.61 (s, 1H), 7.76 (d, J = 8.96, 1H), 7.70-7.65 (m, 2H), 7.54 (d, J = 4.76, 1H), 4.87 (s, 2H), 2.13 (s, 3H)	
656		MS (ESI) m/z 636.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 10.83 (s, 0H), 8.78 (d, J = 4.8 Hz, 1H), 8.67 (s, 1H), 7.76 (d, J = 8.3 Hz, 1H), 7.69 (dd, J = 8.3, 2.2 Hz, 1H), 7.66 (d, J = 2.1 Hz, 1H), 7.54 (d, J = 4.8 Hz, 1H), 4.91 – 4.76 (m, 2H), 4.57 (d, J = 14.5 Hz, 1H), 3.73 – 3.12 (m, 4H), 3.08 – 2.87 (m, 4H), 2.71 (s, 3H), 2.10 (s, 3H), 1.51 (s, 1H), 1.41 – 1.29 (m, 1H)	

673		LCMS (ESI) m/z 546.0 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.80 (s, 1H), 8.44 (s, 1H), 7.56 (dd, J = 8.9, 2.7 Hz, 1H), 7.41 – 7.35 (m, 2H), 7.33 (d, J = 9.0 Hz, 1H), 4.40 (s, 2H), 4.23 (s, 2H), 2.72 (s, 3H), 2.67 (s, 3H), 1.88 (s, 3H)	721		MS (ESI) m/z 560.99 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.73 (bs, 1H), 8.85 (s, 1H), 7.68 (s, 1H), 7.47 (dd, J = 2.64, 8.88 Hz, 1H), 7.28 (d, J = 2.60 Hz, 1H), 7.24 (d, J= 8.88 Hz, 1H), 7.19 (d, J = 8.00 Hz, 1H), 6.98 (d, J = 8.16 Hz, 1H), 4.34 (t, J = 4.60 Hz, 2H), 4.24 (t, J = 4.32 Hz, 2H), 3.93 (s, 3H), 2.79 (s, 3H), 1.86 (s, 3H)
674		LCMS (ESI) m/z 531.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.85 (s, 1H), 8.82 (dd, J = 4.8, 1.0 Hz, 1H), 8.48 (d, J = 2.0 Hz, 1H), 7.64 – 7.56 (m, 1H), 7.52 – 7.40 (m, 2H), 7.36 (dd, J = 9.0, 4.8 Hz, 1H), 4.43 (t, J = 5.0 Hz, 2H), 4.25 (t, J = 4.9 Hz, 2H), 2.76 (s, 3H), 1.85 – 1.78 (m, 3H)	722		MS (ESI) m/z 544.96 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.92 (s, 1H), 8.84 (s, 1H), 7.92 (s, 1H), 7.49 (dd, J=2.48 Hz, J=8.84 Hz, 1H), 7.28-7.24 (m, 3H), 7.13 (d, J = 7.32 Hz, 1H), 4.35 (t, J=4.56 Hz, 2H), 4.21 (t, J=4.48 Hz, 2H), 2.79 (s, 3H), 2.67 (s, 3H), 1.76 (s, 3H)
707		MS (ESI) m/z 616.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.89 (s, 1H), 8.83 (d, J = 4.8 Hz, 1H), 8.70 (s, 1H), 8.43 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.41 (d, J = 2.7 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 4.40 (t, J = 4.9 Hz, 2H), 4.32 (d, J = 14.2 Hz, 2H), 4.24 (t, J = 5.0 Hz, 2H), 3.61 (d, J = 12.0 Hz, 2H), 3.45 (t, J = 13.1 Hz, 2H), 3.32 – 3.21 (m, 2H), 2.91 (d, J = 3.5 Hz, 3H), 1.84 (s, 3H)	723		MS (ESI) m/z 564.90 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.15 (bs, 1H), 8.52 (s, 1H), 7.97 (s, 1H), 7.53-7.48 (m, 2H), 7.34 (d, J=2.4Hz , 1H), 7.28 (d, J=8.8 Hz, 1H), 7.23 (d, J=7.6 Hz, 1H), 4.36 (t, J=4.44 Hz, 2H), 4.22 (t, J=4.4 Hz, 2H), 2.81 (s, 3H), 1.79 (s, 3H)

725		MS (ESI) m/z 574 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.92 (bs, 1H), 8.35 (s, 1H), 7.96 (s, 1H), 7.49 (dd, J = 8.84, 2.48 Hz, 1H), 7.27-7.21 (m, 3H), 7.12 (d, J = 7.32 Hz, 1H), 4.33 (t, J = 4.56 Hz, 2H), 4.17 (t, J = 4.44 Hz, 2H) 3.41 (s, 6H), 2.65 (s, 3H), 1.67 (s, 3H)	728		MS (ESI) m/z 595.96 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.49 (s, 1H) 7.60 (dd, J = 8.88, 2.76 1H), 7.42-7.08 (m, 4H), 4.43 (t, J = 4.68 Hz, 2H), 4.27 (t, J = 4.44 Hz, 2H), 2.79 (s, 3H), 2.70 (s, 3H), 1.91 (s, 3H)
726		MS (ESI) m/z 560.99 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.83 (s, 1H), 8.58 (s, 1H), 7.94 (s, 1H), 7.48 (dd, J= 8.88, 2.64 Hz, 1H), 7.28-7.22 (m, 3H), 7.37 (d, J=7.36 Hz, 1H), 4.34 (s, 2H), 4.20 (s, 2H), 4.09 (s, 3H), 2.67 (s, 3H), 1.80 (s, 3H)	730		MS (ESI) m/z 614.03 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.50 (bs, 1H), 8.48 (s, 1H), 7.59 (d, J = 8.72 Hz, 1H), 7.42 (d, J = 4.8 Hz, 2H), 7.37 (d, J = 8.8 Hz, 1H), 4.44 (bs, 2H), 4.29 (bs, 2H), 2.80 (s, 3H), 2.71 (s, 1H), 1.94 (s, 1H
727		MS (ESI) m/z 574.98 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.98 (s, 1H), 8.96 (s, 1H), 7.93 (s, 1H), 7.48 (dd, J = 8.88, 2.56 Hz, 1H), 7.28-7.24 (m, 3H), 7.12 (d, J = 7.36, 1H), 4.95 (s, 2H), 4.34 (t, J = 4.4 Hz, 2H), 4.20 (t, J = 4.84 Hz, 2H), 3.41 (s, 3H), 2.66 (s, 3H), 1.74 (s, 3H)	731		MS (ESI) m/z 622.99 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.89 (s, 1H), 8.83 (s, 1H), 8.63 (s, 1H), 7.61 (dd, J = 2.44, 8.84 Hz, 1H), 7.45 (s,1H), 7.39 (d, J = 9.4 Hz, 2H), 4.43 (t, J = 4.48 Hz, 2H), 4.28 (t, J = 4.6 Hz, 2H), 3.56 (s, 3H), 2.75 (s, 3H), 2.69 (s, 3H), 2.01 (s, 3H)

732		MS (ESI) m/z 616.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6 at high temperature) δ 8.96 (s, 1H), 8.75 (s, 1H), 7.56-7.52 (dd, J = 6.4 Hz, 9.2 Hz, 1H), 7.38 (d, J = 2.8 Hz, 1H), 7.36 (s, 1H), 7.27 (bs, 1H), 4.43 (t, J = 5.2 Hz, 2H), 4.28 (t, J = 4.8 Hz, 2H), 2.73 (s, 3H), 2.63 (s, 3H), 2.00 (s, 3H)	737		MS (ESI) m/z 622.05 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.51 (bs, 1H), 8.50 (s, 1H), 7.55 (bs, 2H), 7.64-7.45 (m, 4H), 7.42-7.36 (m, 3H), 4.44 (bs, 2H), 4.28 (bs, 2H), 2.78 (s, 3H), 2.69 (s, 3H), 1.94 (s, 3H)
733		MS (ESI) m/z 599.99 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.51 (s, 1H), 8.11 (s, 1H), 7.55-7.52 (dd, J = 2.4, 8.8 Hz, 1H), 7.41 (d, J = 2.4 Hz, 1H), 7.31 (d, J = 9.2 Hz, 1H), 7.19 (s, 1H), 5.74-5.69 (m, 1H), 4.38 (t, J = 4.4 Hz, 2H), 4.26 (t, J = 4.4 Hz, 2H), 2.79 (s, 3H), 2.57 (s, 3H), 1.79 (s, 3H)	742		MS (ESI) m/z 586.06 [M+1]+; 1H NMR (400 MHz, DMSO-d6): δ 13.5 (bs, 1H), 8.49 (s, 1H), 7.60-7.57 (dd, J = 2.4, 8.8 Hz, 1H), 7.39-7.35 (m, 3H), 4.42 (t, J = 4.4 Hz, 2H), 4.25 (t, J = 3.6 Hz), 2.68 (s, 3H), 2.66 (s, 3H), 1.90 (s, 3H), 1.18-1.16 (m, 4H)
734		MS (ESI) m/z 644.20 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.48 (s, 1H), 7.59 (dd, J = 8.88, 2.44 Hz, 1H), 7.41 (s, 2H), 7.36 (d, J = 8.96, 1H), 4.42 (t, J = 4.52 Hz, 2H), 4.25 (t, J = 4.4 Hz, 2H), 3.79 (t, J = 10.28 Hz, 2H), 3.26 (t, J = 11.36 Hz, 2H), 2.96 (d, J = 6.92 Hz, 2H), 2.73 (s, 3H), 2.69 (s, 3H), 2.09 (bs, 1H), 1.92 (s, 3H), 1.51 (d, J = 11.16 Hz, 2H), 1.39-1.28 (m, 2H)	749		MS (ESI) m/z 668.00 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 11.6 (bs, 1H), 8.86 (s, 1H), 8.47 (s, 1H), 7.58-7.55 (m, 1H), 7.51 (d, J = 2.4 Hz, 1H), 7.39 (s, 1H), 7.34 (d, J = 8.8 Hz, 1H), 4.41 (t, J = 4.8 Hz, 2H), 4.27 (t, J = 5.20 Hz, 2H), 2.77 (s, 3H), 2.59 (s, 3H), 1.73 (s, 3H)

756		MS (ESI) m/z 541.2 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 13.42 (bs, 1H), 9.11 (bs, 1H), 8.89 (s, 1H), 7.76 (d, J = 2.16 Hz, 1H), 7.74-7.62 (m, 2H), 7.53-7.38 (m, 2H), 7.11 (t, J = 7.80 Hz, 1H), 4.46 (s, 2H), 4.23 (s, 2H), 2.62-2.57 (m, 1H), 1.89 (s, 3H), 1.29-1.08 (m, 4H)	763		MS (ESI) m/z 622.01 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.9 (bs, 1H), 9.19 (s, 1H), 8.76 (d, J= 5.24, 1H), 7.89 (s, 1H), 7.85 (s, 1H), 7.77 (s, 1H), 7.51 (dd, J= 8.84, 2.52 Hz, 1H), 7.29-7.26 (m, 3H), 7.15 (d, J= 7.32 Hz, 1H), 4.36 (t, J= 3.96 Hz, 2H), 4.25 (t, J= 4.96 Hz 2H), 2.68 (s, 3H), 2.65 (s, 3H), 1.78 (s, 3H)
757		MS (ESI) m/z 548.02 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.54 (bs, 1H), 9.02 (s, 1H), 8.44 (d, J = 4.8 Hz 1H), 7.45 (dd, J = 2.8, 8.8 Hz , 1H), 7.26-7.20 (m, 3H), 4.31 (s, 4H), 2.62-2.58 (m, 1H), 2.02 (s, 3H), 1.93 (s, 3H), 1.20 (d , J = 8.0 Hz ,2H), 1.12 (s, 2H)	770		MS (ESI) m/z 588.72 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.25 (s, 1H), 8.88 (d, J = 5.64 Hz, 2H), 8.79 (d, J = 4.76 Hz, 1H), 8.63 (s, 1H), 8.00 (d, J = 5.72 Hz, 2H), 7.77 (d, J = 8.08 Hz, 1H), 7.70 -7.68 (m, J = 8.0 Hz, 2H) 7.55 (d, J = 4.76 Hz, 1H), 4.89 (s, 2H), 2.22 (s, 3H)
762		MS (ESI) m/z 607.99 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.93 (s, 1H), 9.16 (s, 1H), 8.84 (d, J=5.80, 2H), 7.91 (d, J=5.92 Hz, 2H), 7.80 (s, 1H), 7.50 (dd, J=8.84, 2.56 Hz, 1H), 7.29-7.26 (m, 3H), 7.15 (d, J=7.32 Hz, 1H), 4.36 (t, J=5.64, 2H), 4.25 (t, J=3.80, 2H), 2.68 (s, 3H), 1.79 (s, 3H)	771		MS (ESI) m/z 585.00 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.94 (bs, 1H), 8.94 (s, 1H), 7.76 (s, 1H), 7.48 (dd, J = 2.52, 8.76 Hz, 1H), 7.26-7.24 (m, 2H), 7.06 (s, 1H), 4.32 (t, J = 4.48 Hz, 2H) 4.20 (t, J = 5.08 Hz, 2H), 2.62-2.59 (m, 1H), 2.49 (s, 3H), 2.33 (s, 3H), 1.75 (s, 3H), 1.22 (bs, 2H), 1.14 (bs, 2H)

772		MS (ESI) m/z 588.02 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.84 (s, 1H), 8.70 (d, J=5.12 Hz, 1H), 7.59 (dd, J=8.88, 2.48 Hz, 1H), 7.42-7.39 (m, 2H), 7.35 (d, J=8.96 Hz, 1H), 4.44 (t, J=4.25 Hz, 2H), 4.29 (t, J=4.28 Hz, 2H), 3.66 (s, 3H), 2.62-2.59 (m, 1H), 1.87 (s, 3H), 1.24-1.19 (m, 4H)	792		MS (ESI) m/z 565.91 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.84 (s, 1H), 8.39 (s, 1H), 7.59 (dd, J = 8.84, 2.52 Hz, 1H), 7.42 (s, 2H), 7.34 (d, J = 8.96 Hz, 1H), 4.42-4.37 (m, 2H), 4.29-4.24 (m, 2H), 2.71 (s, 3H),.1.81(s, 3H)
773		MS (ESI) m/z 590.98 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.16 (bs, 1H), 8.98 (s, 1H), 7.83 (s, 1H), 7.53-7.49 (m, 2H), 7.33-7.22 (m, 3H), 4.34 (t, J = 4.8 Hz, 2H), 4.22 (t, J = 4.4 Hz, 2H), 2.60-2.58 (m, 1H), 1.77 (s, 3H), 1.22-1.15 (m, 4H)	793		MS (ESI) m/z 585.97 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (s, 1H), 8.39 (s, 1H), 7.61 (dd, J= 8.88, 2.68 Hz, 1H), 7.45-7.43 (m, 2H), 7.37 (d, J= 8.96 Hz, 1H), 4.41 (t, J=5.08 Hz, 2H), 4.25 (t, J=5.24 Hz, 2H), 3.02 (q, J=7.56,7.52 Hz, 2H), 2.67 (bs, 1H), 1.83 (s, 3H), 1.35 (t, J= 7.52 Hz, 3H), 1.24-1.19 (m, 4H)
791		MS (ESI) m/z 574.95 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.57 (bs, 1H), 8.56 (s, 1H), 8.48 (s, 1H), 7.58 (dd, J = 8.8, 2.48 Hz, 1H), 7.41 (d, J = 2.52 Hz, 1H), 7.38 (s, 1H), 7.35 (d, J = 9.4 Hz, 1H), 4.39-4.36 (m, 2H), 4.21-4.18 (m, 2H), 3.25 (s, 6H), 2.70 (s, 3H), 1.80 (s, 3H)	794		MS (ESI) m/z 571.07 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.00 (bs, 1H), 8.94 (s, 1H), 7.80 (s, 1H), 7.50 (dd, J = 8.84, 2.4 Hz, 1H), 7.26-7.21 (m, 3H), 7.12 (d, J = 7.32 Hz, 1H), 4.34 (t, J = 4.8 Hz, 2H), 4.21 (t, J = 4.44 Hz, 2H), 2.66 (s, 3H), 2.62-2.57 (m, 1H), 1.73 (s, 3H), 1.22 -1.15 (m, 4H)

807		MS (ESI) m/z 608.7 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.97 (s, 1H), 8.41 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.45 – 7.40 (m, 2H), 7.35 (d, J = 9.0 Hz, 1H), 4.45 – 4.35 (m, 2H), 4.26 (dtt, J = 14.9, 10.4, 5.0 Hz, 2H), 3.54 (td, J = 11.5, 7.9 Hz, 1H), 2.70 (s, 3H), 2.54-2.44 (m,1H), 2.37 – 2.23 (m, 1H), 1.86 (s, 3H)	814		MS (ESI) m/z 600.3 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.06 (s, 1H), 8.82 (d, J = 4.8 Hz, 1H), 8.43 (s, 1H), 7.60 (dd, J = 9.0, 2.6 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.44 (d, J = 2.6 Hz, 1H), 7.35 (d, J = 8.9 Hz, 1H), 4.40 (t, J = 5.0 Hz, 2H), 4.27 (t, J = 5.0 Hz, 2H), 4.16 (q, J = 10.7 Hz, 2H), 1.83 (s, 3H)
809		MS (ESI) m/z 558.4 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.97 (d, J = 0.6 Hz, 1H), 8.41 (s, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.42 (d, J = 2.7 Hz, 1H), 7.42 (s, 1H), 7.35 (d, J = 9.0 Hz, 1H), 7.33 – 7.24 (m, 1H), 6.66 (dd, J = 16.7, 1.9 Hz, 1H), 5.88 (dd, J = 10.6, 1.9 Hz, 1H), 4.40 (t, J = 5.1 Hz, 2H), 4.26 (t, J = 5.0 Hz, 2H), 2.70 (s, 3H), 1.83 (s, 3H)	815		MS (ESI) m/z 644.6 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.8 Hz, 1H), 8.71 (s, 1H), 8.37 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.7 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.40 (t, J = 5.0 Hz, 2H), 4.23 (t, J = 5.0 Hz, 2H), 4.20 – 4.24 (m, 2H), 3.60-3.40 (m, 2H), 3.30 (d, J = 14.1 Hz, 2H), 2.81 (d, J = 4.7 Hz, 3H), 1.79 (s, 3H), 1.43 (s, 3H), 1.38 (s, 3H)
813		MS (ESI) m/z 546.6 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.96 (s, 1H), 8.83 (d, J = 4.9 Hz, 1H), 8.41 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.49 (d, J = 4.8 Hz, 1H), 7.44 (d, J = 2.6 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.40 (t, J = 5.0 Hz, 2H), 4.25 (t, J = 5.0 Hz, 2H), 3.11 (q, J = 7.5 Hz, 2H), 1.81 (s, 3H), 1.34 (t, J = 7.5 Hz, 3H)	816		MS (ESI) m/z 644.6 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.78 (d, J = 4.8 Hz, 1H), 8.72 (s, 1H), 8.58 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.46 (s, 1H), 7.46 (d, J = 2.2 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 4.45-4.38 (m, 2H), 4.37- 4.28 (m, 2H), 4.22 (t, J = 5.1 Hz, 2H), 3.29 – 3.08 (m, 4H), 2.96 (d, J = 3.9 Hz, 3H), 1.76 (s, 3H), 1.68 (s, 3H), 1.48 (s, 3H)

817		MS (ESI) m/z 660.8 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.81 (d, J = 4.8 Hz, 1H), 8.47 (d, J = 9.3 Hz, 2H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.6 Hz, 1H), 7.38 (d, J = 9.0 Hz, 1H), 4.91 (bs, 2H), 4.78 (bs, 2H), 4.49-4.38 (m, 2H), 4.30-4.14 (m, 2H), 3.55-2.82 (br, 4H), 1.79 (s, 3H), 1.32-0.83 (m, 4H)	820		MS (ESI) m/z 699.5 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.84 (dd, J = 4.9, 0.9 Hz, 1H), 8.71 (s, 1H), 8.42 (d, J = 1.5 Hz, 1H), 7.60 (dd, J = 9.0, 2.7 Hz, 1H), 7.50 (dd, J = 4.9, 2.6 Hz, 1H), 7.43 (d, J = 2.6 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 5.37-5.27 (m, 1H), 4.39 (t, J = 5.0 Hz, 2H), 4.22 (t, J = 5.0 Hz, 2H), 3.43-3.26 (m, 2H), 3.02-2.90 (m, 2H), 2.81-2.69 (m, 2H), 2.12-2.01 (m, 2H), 1.90-1.79 (m, 2H), 1.75 (s, 3H)
818		MS (ESI) m/z 678.6 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.81 (d, J = 4.8 Hz, 1H), 8.49 (s, 1H), 8.40 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.48 (d, J = 4.9 Hz, 1H), 7.42 (d, J = 2.7 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 6.26 (tt, J = 55.6, 4.2 Hz, 1H), 4.49-4.35 (m, 2H), 4.29 – 4.12 (m, 2H), 3.25 – 2.72 (m, 8H), 1.75 (s, 3H), 0.64-0.53 (m, 2H)	821		MS (ESI) m/z 680.3 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.04 (s, 1H), 8.85 (d, J = 4.8 Hz, 1H), 8.39 (s, 1H), 7.61 (dd, J = 8.9, 2.7 Hz, 1H), 7.50 (d, J = 4.8 Hz, 1H), 7.46 (d, J = 2.7 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 4.42 (t, J = 5.0 Hz, 2H), 4.29 (t, J = 5.0 Hz, 2H), 4.05 (br, 2H), 3.62-3.16 (br, 6H), 2.89 (s, 3H), 1.77 (s, 3H)
819		MS (ESI) m/z 617.4 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.79 (d, J = 4.8 Hz, 1H), 8.60 (s, 1H), 8.36 (s, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.44 (d, J = 2.7 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.59-4.58 (m, 2H), 4.40 (t, J = 5.1 Hz, 2H), 4.20 (t, J = 5.1 Hz, 2H), 3.84-3.76 (m, 1H), 3.66-3.54 (m, 2H), 1.91 – 1.84 (m, 2H), 1.78 (s, 3H), 1.53-1.41 (m, 2H)	822		MS (ESI) m/z 648.6 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.76 – 8.71 (m, 2H), 8.66 (s, 1H), 7.75 (dd, J = 8.0, 0.9 Hz, 1H), 7.71 – 7.64 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 4.81 (s, 2H), 4.59 (bd, J = 16.5 Hz, 4H), 4.41 (s, 4H), 3.08 (br, 1H), 2.09 (s, 3H), 0.81-0.76 (m, 4H)

823		826	
MS (ESI) m/z 706.5 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.8 Hz, 1H), 8.61 (s, 1H), 8.47 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.46 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.7 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 6.22 (t, J = 53.9 Hz, 1H), 4.56 (br, 6H), 4.38 (t, J = 5.0 Hz, 2H), 4.25 (br, 2H), 4.20 (t, J = 5.0 Hz, 2H), 1.79 (s, 3H), 1.32 (s, 6H)		MS (ESI) m/z 688.7 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.9 Hz, 1H), 8.61 (s, 1H), 8.48 (s, 1H), 7.64 – 7.58 (dd, J = 8.9, 2.6 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 4.4 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.71 – 4.42 (m, 8H), 4.38 (t, J = 5.2 Hz, 2H), 4.28 – 4.16 (m, 4H), 1.80 (s, 3H), 1.26 (s, 6H)	
824		827	
MS (ESI) m/z 678.4 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.85 (d, J = 4.9 Hz, 1H), 8.60 (s, 1H), 8.50 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.51 (d, J = 4.9 Hz, 1H), 7.45 (d, J = 2.7 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 6.26 (tt, J = 55.5, 4.2 Hz, 1H), 4.44 – 4.37 (m, 2H), 4.26-4.14 (m, 2H), 3.44 (dd, J = 7.8, 6.6, 4.1 Hz, 2H), 3.19 – 2.84 (m, 6H), 1.74 (s, 3H), 0.81 (q, J = 6.6 Hz, 1H), 0.69 – 0.63 (m, 1H)		MS (ESI) m/z 718.4 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.75 (d, J = 4.8 Hz, 1H), 8.72 (s, 1H), 8.66 (s, 1H), 7.76 (d, J = 9.0 Hz, 1H), 7.71 – 7.67 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 4.59 – 4.47 (m, 2H), 4.33 – 3.54 (br, 8H), 3.14 (s, 3H), 2.63 (br, 1H), 2.06 (s, 3H)	
825		828	
MS (ESI) m/z 686.4 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.78 (d, J = 4.8 Hz, 1H), 8.57 (s, 1H), 8.44 (s, 1H), 7.57 (dd, J = 8.9, 2.7 Hz, 1H), 7.43 (d, J = 4.8 Hz, 1H), 7.39 (d, J = 2.7 Hz, 1H), 7.32 (d, J = 9.0 Hz, 1H), 4.65 (d, J = 48.5 Hz, 2H), 4.45 (br, 4H), 4.35 (t, J = 5.2 Hz, 2H), 4.27 (br, 4H), 4.17 (t, J = 5.2 Hz, 2H), 1.76 (s, 3H), 1.29 (br, 2H), 0.97 (br, 2H)		MS (ESI) m/z 710.4 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.75 (d, J = 4.8 Hz, 1H), 8.72 (s, 1H), 8.65 (s, 1H), 7.78 – 7.74 (m, 1H), 7.71 – 7.67 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 4.53-4.45 (m, 1H), 4.49 (d, J = 47.2 Hz, 2H) 4.42 – 4.36 (m, 1H), 4.31-4.24 (m, 1H), 4.15-4.07 (m, 1H), 3.99 – 3.92 (m, 1H), 3.15 (s, 3H), 2.79 – 2.40 (m, 4H), 2.06 (s, 3H), 1.24 (d, J = 1.9 Hz, 6H)	

829		MS (ESI) m/z 682.5 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.8 Hz, 1H), 8.58 (s, 1H), 8.46 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.7 Hz, 1H), 7.35 (d, J = 9.0 Hz, 1H), 4.45 (s, 2H), 4.37 (t, J = 5.1 Hz, 2H), 4.34 (s, 2H), 4.19 (t, J = 5.1 Hz, 2H), 3.98 – 3.87 (m, 1H), 2.76 (s, 3H), 2.69-2.42 (m, 4H), 1.76 (s, 3H), 1.10 – 0.99 (m, 1H), 0.93-0.72 (m, 4H)	837		MS (ESI) m/z = 652.1 [M+1]+; 1H; -NMR (400 MHz, d6-DMSO) δ /ppm = 8.79 (d, J = 4.8 Hz, 1H), 8.48 (s, 1H), 8.46 (s, 1H), 7.57 (dd, J = 8.9, 2.7 Hz, 1H), 7.44 (d, J = 4.8 Hz, 1H), 7.38 (d, J = 2.7 Hz, 1H), 7.35 (d, J = 8.9 Hz, 1H), 4.94-4.81 (m, 2H), 4.40 (t, J = 4.6 Hz, 2H), 4.28-4.19 (m, 4H), 3.88-3.77 (m, 2H), 1.80 (s, 3H) [remaining CH2-protons presumably obscured by water-peak]
830		MS (ESI) m/z 676.6 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.75 (d, J = 4.8 Hz, 1H), 8.71 (s, 1H), 8.66 (s, 1H), 7.77 – 7.74 (m, 1H), 7.71 – 7.66 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 4.80 (s, 2H), 4.48 (s, 2H), 4.36 (s, 2H), 3.99 – 3.88 (m, 1H), 2.76 (s, 3H), 2.70 – 2.42 (m, 4H), 2.08 (s, 3H), 1.09-0.99 (m, 1H), 0.92-0.72 (m, 4H)	838		MS (ESI) m/z = 666.4 [M+1]+; ; 1H-NMR (400 MHz, d6-DMSO) δ /ppm = 8.81 (d, J = 4.8 Hz, 1H), 8.53 (s, 1H), 8.47 (s, 1H), 7.60 (dd, J = 8.8, 2.7 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.7 Hz, 1H), 7.38 (d, J = 8.8 Hz, 1H), 4.85 (bt, J = 12.4 Hz, 2H), 4.42 (t, J = 5.0 Hz, 2H), 4.24 (t, J = 5.0 Hz, 2H), 4.24-4.14 (b, 2H), 2.87-2.71 (b, 3H), 1.83 (s, 3H), remaining protons appear to be obscured by water peak
831		MS (ESI) m/z = 586.3 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ /ppm = 8.89 (s, 1H), 8.40 (s, 1H), 7.59 (dd, J = 9.0, 2.6, 1H), 7.43-7.41 (m, 2H), 7.35 (d, J = 9.0 Hz, 1H), 4.39 (t, J = 5.2 Hz, 2H), 4.39 (t, J = 5.2 Hz, 2H), 2.71 (s, 3H), 1.86 (s, 3H), 1.47 (s, 3H), 1.12-1.07 (m, 2H), 0.92-0.88 (m, 2H)	839		MS (ESI) m/z = 640.0 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ /ppm = 9.00 (s, 1H), 8.38 (s, 1H), 7.59 (dd, J = 8.9, 2.8 Hz, 1H), 7.42 (d, J = 2.8 Hz, 1H), 7.41 (s, 1H), 7.35 (d, J = 8.9 Hz, 1H), 4.40 (t, J = 4.9 Hz, 2H), 4.26 (t, J = 4.9 Hz, 2H), 2.70 (s, 3H), 1.90 (s, 3H), 1.63-1.58 (m, 2H), 1.54-1.48 (m, 2H)

840	MS (ESI) m/z = 696.3 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ /ppm = 8.78 (d, J = 4.8 Hz, 1H), 8.55 (s, 1H), 8.44 (s, 1H), 7.56 (dd, J = 8.9, 2.7 Hz, 1H), 7.42 (d, J = 4.8 Hz, 1H), 7.39 (d, J = 8.9 Hz, 1H), 4.44 (s, 4H), 4.34 (t, J = 5.0 Hz, 2H), 4.15 (t, J = 5.0 Hz, 2H), 3.89-3.51 (b), 3.12-2.76 (b), 1.73 (s, 3H)	844	MS (ESI) m/z = 712.3 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ /ppm = 9.98-9.78 (b, 1H), 8.83 (d, J = 4.9 Hz, 1H), 8.70 (s, 1H), 8.43 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.48 (d, J = 4.9 Hz, 1H), 7.41 (d, J = 2.7 Hz, 1H), 7.38 (d, J = 8.9 Hz, 1H), 4.41 (t, J = 4.8 Hz, 2H), 4.38-4.28 (m, 2H), 4.24 (t, J = 4.8 Hz, 2H), 3.32-3.21 (m, partially obscured by water peak), 2.47-2.33 (m, 2H), 2.02-1.91 (m,2 H), 1.85 (s, 3H); remaining signals obscured by water peak
842	MS (ESI) m/z = 610.3 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ /ppm = 9.98-9.88 (b, 1H), 8.84 (s, 1H), 8.75 (d, J = 4.8 Hz, 1H), 8.64 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.71-7.65 (m, 2H), 7.53 (d, J = 4.8 Hz, 1H), 4.83 (s, 2H), 4.36 (bd, J = 14 Hz, 2H), 3.36-3.24 (m, 2H), 2.91 (s, 3H), 2.13 (s, 3H); remaining signals are obscured by water peak	845	MS (ESI) m/z = 726.3 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ /ppm = 10.29-9.70 (b, 1H), 8.83 (d, J = 4.7 Hz, 1H), 8.71 (s, 1H), 8.44 (s, 1H), 7.61 (dd, J= 8.9, 2.7 Hz, 1H), 7.48 (d, J = 4.7 Hz, 1H), 7.42 (d, J = 2.7 Hz, 1H), 7.37 (d, J = 8.9 Hz, 1H), 4.41 (t, J = 4.5 Hz, 2H), 4.24 (t, J = 4.5 Hz, 2H), 4.50-3.20 (broad signals, partially obscured by water peak), 2.99 (bq, J = 11 Hz, 2H), 1.85 (s, 3H), 1.52 (s, 6H)
843	MS (ESI) m/z = 712.5 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ /ppm = 9.98-9.79 (b, 1H), 8.81 (d, J = 4.9 Hz, 1H), 8.52 (s, 1H), 8.49 (s, 1H), 7.61 (dd, J = 8.9, 2.8 Hz, 1H), 7.48 (d, J = 4.9 Hz, 1H), 7.42 (d, J = 2.8 Hz, 1H), 7.39 (d, J = 8.9 Hz, 1H), 5.21-5.08 (m, 2H), 4.43 (t, J = 5.0 Hz, 2H), 4.23 (t, J = 5.0 Hz, 2H), 3.76-3.62 (m, partially obscured by water peak), 3.38-3.14 (m, partially obscured by water peak), 2.49-2.36 (m, 2H), 2.03-1.93 (m, 2H), 1.83 (s, 3H)	846	MS (ESI) m/z 631.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 10.31 (s, 1H), 9.85 (s, 1H), 8.73 (d,J= 8.1 Hz, 1H), 7.60 (dd, J= 8.9, 2.7 Hz, 1H), 7.42 (s, 1H), 7.40 – 7.33 (m, 2H), 5.69 (d, J= 7.2 Hz, 1H), 5.60 – 5.42 (m, 1H), 4.78 (s, 1H), 4.59 – 4.46 (m, 2H), 4.41 (t, J= 5.2 Hz, 2H), 4.29 (q, J= 5.9, 5.4 Hz, 3H), 3.04 – 2.96 (m, 3H), 2.71 (s, 3H), 2.54 (d, J= 6.4 Hz, 3H), 2.11 (d, J= 22.1 Hz, 3H)

848		MS (ESI) m/z 671.9 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.55 (s, 1H), 7.56 (dd,J= 8.9, 2.7 Hz, 1H), 7.38 – 7.29 (m, 4H), 4.61 – 4.42 (m, 1H), 4.36 (t, J= 5.0 Hz, 2H), 4.20 (t, J= 5.0 Hz, 2H), 3.18 – 3.09 (m, 2H), 3.04 (s, 3H), 2.78 (d, J= 4.6 Hz, 3H), 2.67 (s, 4H), 2.17 – 1.94 (m, 3H), 1.92 (s, 3H)	854		MS (ESI) m/z 644.3 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.8 Hz, 1H), 8.61 (s, 1H), 8.40 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.7 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.39 (t, J = 5.0 Hz, 2H), 4.21 (s, 2H), 3.08 (s, 3H), 2.81 (d, J = 4.7 Hz, 3H), 2.07 (d, J = 8.4 Hz, 5H), 1.77 (s, 3H)
850		LCMS: 574.6 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ 8.46 (s, 1H), 7.56 (dd, J= 8.9, 2.7 Hz, 1H), 7.40 – 7.28 (m, 3H), 4.39 (t, J= 5.1 Hz, 2H), 4.22 (t, J= 5.0 Hz, 2H), 3.00 (q, J= 7.6 Hz, 2H), 2.70 (s, 3H), 2.66 (s, 3H), 1.90 (s, 3H), 1.28 (t, J= 7.5 Hz, 3H)	857		LCMS: 642.7 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ 9.57 (s, 1H), 8.80 (d, J = 4.8 Hz, 1H), 8.59 (s, 1H), 8.46 (s, 1H), 7.61 (dd, J = 8.9, 2.7 Hz, 1H), 7.49 – 7.34 (m, 3H), 4.43 (t, J = 5.0 Hz, 2H), 4.24 (d, J= 5.0 Hz, 2H), 3.35 (t, J = 10.8 Hz, 3H), 2.79 (d, J = 3.4 Hz, 3H), 2.23 (s, 2H), 2.08 (d, J = 8.1 Hz, 2H), 1.86 (s, 3H)
851		LCMS: 560.4 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ 8.78 (d, J = 4.8 Hz, 1H), 8.46 (s, 1H), 7.56 (dd, J = 8.9, 2.7 Hz, 1H), 7.43 (d, J = 4.8 Hz, 1H), 7.39 (d, J = 2.7 Hz, 1H), 7.33 (d, J = 9.0 Hz, 1H), 4.39 (t, J = 5.0 Hz, 2H), 4.21 (t, J = 5.0 Hz, 2H), 3.01 (q, J = 7.5 Hz, 2H), 2.71 (s, 3H), 1.80 (s, 3H), 1.28 (t, J = 7.5 Hz, 3H)	860		LCMS: 678.5 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ 8.81 – 8.73 (m, 2H), 8.66 (s, 1H), 7.76 (d, J = 9.0 Hz, 1H), 7.69 (dd, J= 6.2, 2.3 Hz, 2H), 7.54 (d, J= 4.8 Hz, 1H), 4.82 (s, 2H), 3.69 (t, J= 4.7 Hz, 4H), 3.30 (q, J= 10.2 Hz, 2H), 2.84 (t, J= 4.8 Hz, 4H), 2.07 (s, 3H)

861		LCMS: 712.7 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ 8.79 (d, J = 4.8 Hz, 1H), 8.50 (s, 1H), 8.37 (s, 1H), 7.60 (dd, J = 9.0, 2.7 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.6 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 4.69 (s, 1H), 4.43 (t, J = 5.1 Hz, 2H), 4.22 (d, J = 5.1 Hz, 2H), 3.22 (s, 1H), 3.13 (s, 3H), 3.04 (d, J = 11.2 Hz, 2H), 2.00 – 1.81 (m, 1H), 1.78 (s, 3H)
862		LCMS: 662.5 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ 9.80 (s, 1H), 8.80 (d, J = 4.8 Hz, 1H), 8.45 (d, J = 9.3 Hz, J = 8.9, 2.7 Hz, 1H), 7.48 – 7.41 (m, 2H), 7.39 (d, J = 9.0 Hz, 1H), 5.50 (s, 1H),J = 11.4 Hz, 1H), 5.02 (d, J = 12.3 Hz, 1H), 4.44 (q, J = 4.8 Hz, 2H), J = 5.1 Hz, 2H), 3.85 (d, J = 12.3 Hz, 1H), 3.26 (d, J = 1.6 Hz, 3H), 2.87 (d, J = 4.1. 12H), 7.61 (dd, 5.38 (s, 1H), 5.10 (d, 4.25 (t, Hz, 3H), 2.20 – 2.03 (m, 1H), 1.80 (s, 3H)
863		LCMS: 670.2 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ 9.64 (s, 1H), 9.51 (s, 1H), 8.82 – 8.75 (m, 1H), 8.44 – 8.38J = 8.9, 2.6 Hz, 1H), 7.49 (t, J = 5.0 Hz, 1H), 7.44 (dd, J = 9.0, 2.7 Hz, 1H),J = 9.0 Hz, 1H), 5.18 (dq, J = 11.7, 5.8 Hz, 1H), 5.05 (s, 1H), 4.44 (q, J = 5.2 Hz, 2H), J = 5.0 Hz, 2H), 4.05 – 3.78 (m, 2H), 3.17 (d, J = 9.9 Hz, 1H), 3.07 (s, 3H), 2.72 –J = 3.4 Hz, 5H)
864		LCMS: 694.5 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ 8.75 (d, J = 4.9 Hz, 1H), 8.40 (d, J = 2.3 Hz, 2H), 7.58 (dd, J = 8.9, 2.7 Hz, 1H), 7.44 (d, J = 4.8 Hz, 1H), 7.40 – 7.32 (m, 2H), 6.55 (t, J = 52.5 Hz, 2H), 4.89 (s, 1H), 4.48 – 4.32 (m, 2H), 4.21 (t, J = 5.3 Hz, 2H), 3.10 (s, 3H), 2.91 (s, 4H), 2.33 – 2.08 (m, 4H), 2.05 – 1.88 (m, 3H), 1.74 (s, 3H)
865		LCMS: 712.6 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.8 Hz, 1H), 8.60 (s, 1H), 8.45 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.7 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.38 (t, J = 5.0 Hz, 2H), 4.33 – 4.13 (m, 3H), 3.07 (s, 3H), 2.73 – 2.52 (m, 3H), 2.03 – 1.82 (m, 2H), 1.77 (d, J = 28.9 Hz, 5H), 1.25 (d, J = 16.2 Hz, 1H)
866		LCMS: 694.5 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.8 Hz, 1H), 8.63 (s, 1H), 8.42 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.7 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 6.49 (d, J = 52.7 Hz, 1H), 4.64 (d, J = 15.0 Hz, 1H), 4.39 (t, J = 5.0 Hz, 2H), 4.22 (t, J = 5.1 Hz, 2H), 3.09 (s, 3H), 2.94 (s, 3H), 1.76 (s, 3H)

868		MS (ESI) m/z 670.5 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.50 (s, 1H), 8.64 (s, 1H), 7.56 (dd, J= 8.9, 2.7 Hz, 1H), 7.38 – 7.30 (m, 3H), 4.90 (s, 2H), 4.36 (t, J= 5.1 Hz, 2H), 4.22 (t, J= 5.1 Hz, 2H), 3.56 (d, J= 12.1 Hz, 2H), 3.30 (t, J= 10.9 Hz, 2H), 2.80 (s, 2H), 2.67 (s, 3H), 2.02 (d, J= 2.5 Hz, 4H), 1.93 (s, 3H)	872		LCMS (ESI) m/z 650.8 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.47 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.49 – 7.45 (m, 2H), 7.38 (d, J = 9.0 Hz, 1H), 7.30 (dd, J = 8.2, 6.9 Hz, 1H), 7.21 – 7.16 (m, 2H), 4.45 (t, J = 5.0 Hz, 2H), 4.26 (t, J = 5.0 Hz, 2H), 2.77 (s, 3H), 2.72 (s, 3H), 2.00 (s, 6H), 1.84 (s, 3H)
869		LCMS: 1.54 Min, 617.5 [M+H]+; 1H NM:R (400 MHz, DMSO-d6) δ 9.07 (s, 1H), 8.80 (s, 1H), 8.72 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.44 – 7.33 (m, 3H), 5.62 (p, J = 6.2 Hz, 1H), 4.58 – 4.45 (m, 2H), 4.41 (t, J = 5.1 Hz, 2H), 4.25 (dt, J = 20.4, 5.8 Hz, 4H), 2.71 (s, 3H), 2.54 (s, 3H), 2.11 (s, 3H)	873		LCMS (ESI) m/z 637.0 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.48 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.49 – 7.43 (m, 2H), 7.38 (d, J = 9.0 Hz, 1H), 7.30 (dd, J = 8.2, 6.9 Hz, 1H), 7.19 (d, J = 8.0 Hz, 2H), 4.45 (t, J = 5.0 Hz, 2H), 4.26 (t, J = 4.9 Hz, 2H), 2.77 (s, 3H), 2.72 (s, 3H), 2.00 (s, 6H)
871		LCMS (ESI) m/z 654.8 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.50 (s, 1H), 7.57 (dd, J = 8.9, 2.7 Hz, 1H), 7.51 – 7.39 (m, 3H), 7.34 (d, J = 9.0 Hz, 1H), 7.26 – 7.14 (m, 2H), 4.43 (td, J = 8.9, 7.7, 3.7 Hz, 1H), 4.37 (dd, J = 10.3, 4.5 Hz, 1H), 4.23 (t, J = 5.1 Hz, 2H), 2.75 (s, 3H), 2.68 (s, 3H), 2.12 (s, 3H), 1.83 (s, 3H)	874		LCMS (ESI) m/z 656.0 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.36 (s, 1H), 8.54 (s, 1H), 8.30 (dd, J = 9.3, 5.7 Hz, 1H), 7.66 – 7.57 (m, 2H), 7.48 – 7.33 (m, 3H), 6.96 (ddd, J = 8.2, 5.8, 2.3 Hz, 1H), 4.43 (t, J = 5.0 Hz, 2H), 4.24 (t, J = 5.0 Hz, 2H), 2.72 (d, J = 4.6 Hz, 6H), 1.87 (s, 3H)

875		LCMS (ESI) m/z 644.1 [M+1]+; 1H NMR (400 MHz, Chloroform-d) δ 8.48 (s, 1H), 7.61 (dd, J = 8.9, 2.7 Hz, 1H), 7.43 (s, 1H), 7.42 – 7.37 (m, 2H), 4.42 (d, J = 5.3 Hz, 2H), 4.33 (s, 1H), 4.30 (s, 1H), 4.25 (d, J = 5.0 Hz, 2H), 3.61 (d, J = 12.2 Hz, 2H), 3.44 (d, J = 13.6 Hz, 4H), 3.24 (d, J = 11.0 Hz, 1H), 2.92 (d, J = 4.4 Hz, 3H), 2.73 (s, 3H), 2.66 (s, 4H), 1.98 (s, 3H)	883		LCMS (ESI) m/z 617.1 [M+1]+; ; 1H NMR (400 MHz, DMSO-d6) δ 8.53 (s, 1H), 8.47 (d, J = 0.8 Hz, 1H), 7.55 (dd, J = 8.9, 2.7 Hz, 1H), 7.41 – 7.34 (m, 2H), 7.39 – 7.28 (m, 2H), 7.44 – 4.40 (m, 2H), 4.34 (t, J = 5.1 Hz, 2H), 4.16 (t, J = 5.1 Hz, 2H), 3.86 (dd, J = 11.5, 4.8 Hz, 2H), 3.73 (ddd, J = 11.1, 8.1, 3.4 Hz, 1H), 3.54 (d, J = 11.6 Hz, 1H), 2.67 (s, 3H), 2.05 – 1.94 (m, 1H), 1.90 (s, 2H), 1.76 (s, 3H)
878		LCMS (ESI) m/z 630.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (s, 1H), 8.44 (s, 1H), 7.57 (dd, J = 8.9, 2.7 Hz, 1H), 7.41 – 7.31 (m, 2H), 4.39 (d, J = 10.4 Hz, 1H), 4.39 (s, 1H), 4.20 (s, 1H), 3.79 (t, J = 4.9 Hz, 2H), 3.28 (s, 2H), 2.68 (s, 2H), 2.62 (s, 2H), 1.94 (s, 2H)	884		LCMS (ESI) m/z 614.9 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.61 (s, 1H), 8.45 (s, 1H), 7.56 (dd, J = 8.9, 2.7 Hz, 1H), 7.39 – 7.29 (m, 3H), 4.36 (t, J = 5.1 Hz, 2H), 4.24 (s, 2H), 4.22 – 4.14 (m, 4H), 2.71 (t, J = 7.7 Hz, 2H), 2.68 (s, 3H), 1.86 (s, 3H)
882		LCMS (ESI) m/z 634.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.91 (s, 1H), 8.80 (d, J = 4.8 Hz, 1H), 8.35 (s, 1H), 7.56 (dd, J = 8.9, 2.7 Hz, 1H), 7.47 – 7.38 (m, 2H), 7.32 (d, J = 9.0 Hz, 1H), 6.27 (s, 1H), 4.37 (t, J = 5.0 Hz, 2H), 4.21 (t, J = 4.9 Hz, 2H), 2.87 – 2.75 (m, 4H), 2.22 (dq, J = 14.1, 6.8 Hz, 2H), 1.75 (s, 3H).	885		LCMS (ESI) m/z 662.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.79 (d, J = 4.8 Hz, 1H), 8.46 (s, 1H), 7.57 (dd, J = 9.0, 2.6 Hz, 1H), 7.44 (d, J = 4.8 Hz, 1H), 7.39 – 7.32 (m, 2H), 4.98 – 4.74 (m, 2H), 4.40 (t, J = 5.1 Hz, 2H), 4.29 (s, 2H), 4.21 (t, J = 5.1 Hz, 2H), 3.64 (s, 2H), 3.56 (s, 2H), 3.47 (s, 2H), 3.31 (s, 2H), 2.66 (s, 3H), 1.86 (s, 3H)

886		LCMS (ESI) m/z 698.3 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.9 Hz, 1H), 8.54 (s, 1H), 7.60 (dd, J = 8.8, 2.8 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.41 (d, J = 2.7 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 4.41 (s, 2H), 4.21 (s, 2H), 3.65 (s, 5H), 3.29 (q, J = 10.2 Hz, 2H), 2.82 (s, 4H), 2.64 (s, 3H), 1.80 (s, 3H)	890		LCMS (ESI) m/z 469.5 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.87 (s, 1H), 8.76 (d, J = 4.8 Hz, 1H), 8.61 (s, 1H), 7.76 (d, J = 8.2 Hz, 1H), 7.76 – 7.65 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 6.51 (t, J = 54 Hz, 1H), 5.43 (s, 1H), 4.84 (s, 2H), 2.28 (s, 2H), 2.18 (s, 1H), 2.12 (s, 3H)
888		LCMS (ESI) m/z 613.4 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.92 (s, 1H), 8.98 (s, 1H), 8.83 (d, J = 4.8 Hz, 1H), 8.36 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.46 (dd, J = 13.2, 3.7 Hz, 2H), 7.36 (d, J = 9.0 Hz, 1H), 6.51 (s, 1H), 4.40 (d, J = 5.3 Hz, 2H), 4.27 (d, J = 5.0 Hz, 2H), 4.14 (d, J = 17.9 Hz, 1H), 3.91 (s, 1H), 3.69 (d, J = 11.9 Hz, 1H), 3.35 (s, 1H), 2.95 (d, J = 4.5 Hz, 6H), 1.81 (s, 3H)	891		LCMS (ESI) m/z 528.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.80 (d, J = 4.8 Hz, 1H), 8.69 (s, 1H), 7.76 (d, J = 9.1 Hz, 1H), 7.72 – 7.64 (m, 2H), 7.56 (d, J = 4.8 Hz, 1H), 4.78 (s, 2H), 1.92 (s, 3H)
889		1H NMR (400 MHz, DMSO-d6) δ 8.91 (s, 1H), 8.80 (d, J = 4.8 Hz, 1H), 8.37 (s, 1H), 7.56 (d, J = 8.8 Hz, 1H), 7.43 (d, J = 15.4 Hz, 2H), 7.32 (d, J = 9.0 Hz, 1H), 6.40 (s, 1H), 4.37 (s, 2H), 4.21 (s, 2H), 3.35 (d, J = 9.9 Hz, 1H), 2.91 (s, 3H), 2.66 (s, 1H), 1.75 (s, 3H)	892		LCMS (ESI) m/z 654.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 10.05 (s, 1H), 8.73 – 8.67 (m, 2H), 8.63 (s, 1H), 7.72 (dd, J = 8.1, 0.8 Hz, 1H), 7.73 – 7.61 (m, 2H), 7.51 (d, J = 4.8 Hz, 1H), 4.78 (s, 2H), 4.74 – 4.67 (m, 1H), 4.64 – 4.55 (m, 3H), 4.49 (s, 2H), 4.40 (t, J = 6.9 Hz, 4H), 3.59 (d, J = 4.6 Hz, 1H), 3.52 (s, 1H), 2.07 (s, 3H), 1.21 (s, 1H)

893		LCMS (ESI) m/z 672.2 [M+1]+; ; 1H NMR (400 MHz, DMSO-d6) δ 8.75 – 8.67 (m, 2H), 8.63 (s, 1H), 7.72 (dd, J = 8.1, 0.8 Hz, 1H), 7.69 – 7.61 (m, 2H), 7.51 (d, J = 4.8 Hz, 1H), 6.34 (t, J = 52 Hz, 1 H), 4.78 (s, 2H), 4.50 (s, 5H), 4.45 (s, 3H), 3.81 (s, 1H), 2.94 (s, 2H), 2.35 (s, 6H), 2.07 (s, 3H)	897		MS (ESI) m/z 562.07 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.59 (bs, 1H), 8.72 (s, 1H), 8.42 (s, 1H), 7.58 (dd, J = 2.56, 8.72 Hz, 1H), 7.40 (bs, 2H), 7.34 (d, J = 8.92 Hz, 1H), 4.39 (t, J = 4.00 Hz, 2H), 4.39 (t, J = 4.52 Hz, 2H), 4.11 (s, 3H), 2.70 (s, 3H), 1.85 (s, 3H)
894		LCMS (ESI) m/z 720.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 10.05 (s, 1H), 8.75 – 8.71 (m, 2H), 8.66 (s, 1H), 7.78 – 7.73 (m, 1H), 7.72 – 7.64 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 4.81 (s, 2H), 4.65 (s, 2H), 4.52 (s, 2H), 4.44 (d, J = 3.7 Hz, 4H), 4.37 – 4.29 (m, 2H), 3.61 (s, 2H), 2.10 (s, 3H)	898		MS (ESI) m/z 586.06 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.5 (bs, 1H), 8.49 (s, 1H), 7.60-7.57 (dd, J= 4.0, 8.8 Hz, 1H), 7.39 (m, 3H), 4.44 (t, J = 6.0 Hz, 2H), 4.25 (t, J = 3.6 Hz, 2H), 2.68 (s, 6H), 1.90 (s, 3H), 1.18-1.16 (m, 4H)
895		MS (ESI) m/z 650.4 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.78 (s, 1H), 8.85 (s, 1H), 8.75 (d, J = 4.8 Hz, 1H), 8.65 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.69 (dd, J = 8.4, 2.2 Hz, 1H), 7.66 (d, J = 2.1 Hz, 1H), 7.53 (d, J = 4.8 Hz, 1H), 4.84 (s, 2H), 4.38 (d, J = 14.1 Hz, 2H), 3.75 (d, J = 12.0 Hz, 2H), 3.60 – 3.48 (m, 2H), 3.33 – 3.23 (m, 2H), 3.17 – 3.11 (m, 2H), 2.14 (s, 3H), 1.18 – 1.08 (m, 1H), 0.72 – 0.66 (m, 2H), 0.45 – 0.37 (m, 2H)	900		MS (ESI) m/z 572.02 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.39 (bs, 1H), 8.91 (s, 1H), 8.35 (s, 1H), 8.07 (s, 1H), 7.60-7.57 (dd, J = 7.48, 2.56 Hz, 1H), 7.41 (d, J = 2.52 Hz, 1H), 7.33 (d, J = 8.92 Hz, 1H), 4.41-4.35 (m, 2H), 4.30-4.20 (m, 2H), 3.01 (s, 3H), 2.67-2.60 (m, 1H), 1.81 (s, 3H), 1.28-1.12 (m, 4H)

910		MS (ESI) m/z 648.05 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.41 (bs, 1H), 8.64 (s, 1H), 8.08 (d, J = 3.32 Hz, 2H), 7.58 (dd, J = 2.48, 8.84 Hz, 1H), 7.53 (d, J = 2.48 Hz, 3H), 7.42-7.35 (d, J = 2.48 Hz, 1H), 7.35-7.38 (m, 2H), 4.43 (t, J = 5.80 Hz, 2H), 4.28 (t, J = 4.52 Hz, 2H), 2.66-2.55 (m, 1H), 2.55 (s, 3H), 1.95 (s, 3H), 1.23 (d, J = 4.28 Hz, 4H)	913		MS (ESI) m/z 596.04 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.55 (bs, 1H), 9.00 (s, 1H), 8.42 (s, 1H), 7.58 (d, J = 8.68 Hz, 1H), 7.41 (s, 2H), 7.35 (d, J = 8.88 Hz, 1H), 4.40 (t, J = 4.88 Hz, 2H), 4.27 (t, J = 5.4 Hz, 2H), 2.70 (s, 3H), 2.16 (t, J = 19.28 Hz, 3H), 1.89 (s, 3H)
911		MS (ESI) m/z 637.07 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.72 (d, J = 5.2 Hz, 1H), 8.47 (s, 1H), 7.83 (s, 1H), 7.79 (d, J = 4.48 Hz, 1H), 7.60 (dd, J = 2.52, 8.84 Hz, 1H), 7.42-7.34 (m, 3H), 4.45 (t, J = 6.12 Hz, 2H), 4.30 (t, J = 5.72 Hz, 2H), 2.80 (s, 3H), 2.71 (s, 3H), 2.65 (s, 3H), 2.01 (s, 3H)	914		MS (ESI) m/z 582.03 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.06 (s, 1H), 8.40 (s, 1H), 7.59 (dd, J= 8.8, 2.5 Hz, 1H), 7.43-7.16 (m, 4H), 4.40 (t, J = 6.0 Hz, 2H), 4.28 (t, J = 2.6 Hz, 2H), 2.70 (s, 2H), 1.84 (s, 3H)
912		MS (ESI) m/z 586.20 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.90 (s, 1H), 8.54 (s, 1H), 7.58 (dd, J = 8.92, 2.44 Hz, 1H), 7.42 (d, J = 2.52 Hz, 1H), 7.40 (s, 1H), 7.35 (d, J = 8.92 Hz, 1H), 4.95 (t, J = 8.68, 1H), 4.41 (t, J = 5.8 Hz, 2H), 4.24 (t, J = 5.84, 2H), 2.68 (s, 3H), 2.37-2.32 (m, 3H), 2.13-2.08 (m, 2H), 1.91 (s, 3H), 1.91 (bs, 2H)	915		MS (ESI) m/z 617.10 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.53 (bs, 1H), 9.02 (s, 1H), 8.36 (s, 1H), 7.59 (dd, J = 8.88 Hz, 2.52 Hz, 1H), 7.41-7.39 (m, 2H), 7.34 (d, J = 8.96 Hz, 1H), 5.72 (d, J = 47.16 Hz, 2H), 4.40 (t, J = 7.44 Hz, 2H), 4.27 (t, J = 4.48 Hz, 2H), 2.69 (s, 3H), 1.88 (s, 3H)

916		MS (ESI) m/z 585.97 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (s, 1H), 8.39 (s, 1H), 7.61 (dd, J = 8.88Hz, J = 2.68 Hz, 1H), 7.45-7.43 (m, 2H), 7.37 (d, J = 8.96 Hz, 1H), 4.42-4.39 (m, 2H), 4.26 - 4.23 (m, 2H), 3.02 (q, J = 7.56 Hz, J = 7.52 Hz, 2H), 2.67 (s, 1H), 1.83 (s, 3H), 1.35 (t, J = 7.52 Hz, 3H), 1.24-1.19 (m, 4H)	923		MS (ESI) m/z 560.11 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.95 (s, 1H), 8.35 (s, 1H), 7.59-7.56 (dd, J = 2.4, 8.4 Hz, 1H), 7.41-7.33 (m, 3H), 4.40 (t, J = 4.8 Hz, 2H), 4.26 (t, J = 4.8 Hz, 2H), 3.12 (m, 2H), 2.68 (s, 3H), 1.88 (s, 3H), 1.35 (t, J = 7.2 Hz, 3H)
917		MS (ESI) m/z 590.02 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.01 (s, 1H), 8.86 (s, 1H), 8.43 (s, 1H), 7.60 (dd, J = 2.48, 8.88 Hz, 1H), 7.51 (s, 1H), 7.43 (d, J = 2.52 Hz, 1H), 7.35 (d, J = 8.96, 1H), 5.69 (d, J = 46.8 Hz, 2H), 4.40 (t, J = 3.96 Hz, 2H), 4.23 (t, J = 4.40 Hz, 2H), 2.61-2.57 (m, 1H), 1.77 (s, 3H), 1.23-1.15 (m, 4H)	924		MS (ESI) m/z 690 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.4 (s, 1H), 8.50 (s, 1H), 7.94 (d, J = 7.8 Hz, 1H), 7.89 (t, J = 7.2 Hz, 1H), 7.81 (t, J = 8.4 Hz, 1H), 7.61 (dd, J = 2.4, 8.8 Hz, 1H), 7.43 (s, 2H), 7.38 (d, J = 8.82 Hz, 1H), 4.44 (bs, 2H), 4.27 (bs, 2H), 2.80 (s, 3H), 2.71 (s, 3H), 1.92 (s, 3H)
922		MS (ESI) m/z 540.10 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.96 (s, 1H), 8.87 (s, 1H), 7.74 (s, 1H) 7.67 (d, J = 2.3 Hz, 1H), 7.62 (dd, J = 8.84, 2.40 Hz, 1H), 7.35 (d, J =8.92 Hz, 1H), 4.44 (s, 4H), 2.68 (s, 3H), 2.58-2.57 (m, 1H), 1.20-1.14 (m, 4H)	925		MS (ESI) m/z 690.02 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.45 (s, 1H), 8.24 (s, 1H), 8.19 (d, J = 7.76 Hz, 1H), 7.94 (d, J = 7.6 Hz, 1H), 7.84 (t, J = 7.8 Hz, 1H), 7.60 (dd, J = 2.56, 8.8 Hz, 1H), 7.43 (s, 1H), 7.39 (d, J = 2.2 Hz, 2H), 4.46 (t, J = 3.6 Hz, 2H), 4.30 (t, J = 4.4 Hz, 2H), 2.80 (s, 3H), 2.71 (s, 3H), 2.00 (s, 3H)

926		MS (ESI) m/z 690.02 [M+1] +; 1H NMR (400 MHz, DMSO-d6) δ 13.44 (bs, 1H), 8.49 (s, 1H), 8.10 (d, J = 8.08 Hz, 2H), 7.95 (d, J = 8.20 Hz, 2H), 7.60 (dd, J = 8.88, 2.60 Hz, 1H), 7.43 (s, 1H), 7.42-7.37 (m, 2H), 4.45 (t, J = 4.64 Hz, 2H), 4.30 (t, J = 4.36 Hz, 2H), 2.80 (s, 3H), 2.71 (s, 3H), 1.99 (s, 3H)	929		MS (ESI) m/z 636.20 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.20 (bs, 1H), 9.04 (s, 1H), 8.37 (s, 1H), 7.61-7.56 (m, 1H), 7.44-7.38 (m, 2H), 7.34 (d, J = 8.96 Hz, 1H), 4.40-4.36 (m, 2H), 4.27-4.15 (m, 3H), 2.68 (s, 3H), 2.59-2.56 (m, 1H), 2.32-2.17 (m, 3H), 2.07-2.03 (m, 1H), 1.93-1.83 (m, 4H)
927		MS (ESI) m/z 654.03 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.50 (bs, 1H), 8.48 (s, 1H), 7.60 (dd, J = 2.4, 8.7 Hz, 1H), 7.43-7.37 (m, 5H), 7.30-7.26 (m, 1H), 4.44 (t, J = 5.2 Hz, 2H), 4.27 (t, J = 5.8 Hz, 2H), 2.77 (s, 3H), 2.71 (s, 3H), 2.13 (s, 3H), 1.93 (s, 3H)	930		MS (ESI) m/z 636.20 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.50 (bs, 1H), 8.99 (s, 1H), 8.38 (s, 1H), 7.59 (dd, J = 8.88, 2.52 Hz, 1H),7.40 (s, 2H), 7.35 (d, J = 8.96 Hz, 1H), 4.41-4.36 (m, 2H), 4.31-4.23 (m, 2H), 4.08-4.02 (m, 1H), 2.70 (s, 3H), 2.63-2.57 (m, 2H), 2.38-2.32 (m, 1H), 2.29-2.26 (m, 2H), 2.09-2.05 (m, 1H), 1.91 (s, 3H)
928		MS (ESI) m/z 622.13 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.03 (s, 1H), 8.35 (s, 1H), 7.58 (dd, J = 2.52, 8.8 Hz, 1H), 7.39 (t, J = 2.68 Hz, 2H), 7.35 (d, J = 9 Hz, 1H), 4.39 (t, J = 4.4 Hz, 2H), 4.26 (t, J = 4.28 Hz, 2H), 4.04-3.95 (m, 1H), 3.11-3.05 (m, 4H), 2.70 (s, 3H), 1.91 (s, 3H)	931		MS (ESI) m/z 650.13 [M+1] +; 1H NMR (400 MHz, DMSO-d6) δ 8.96 (s, 1H), 8.35 (s, 1H), 7.59 (dd, J = 8.88, 2.56 Hz, 1H), 7.44-7.40 (m, 2H), 7.35 (d, J = 8.96 Hz, 1H), 4.40 (t, J = 4.68 Hz, 2H), 4.25 (t, J = 4.68, 2H), 3.60-3.50 (bs, 1H), 2.70 (s, 3H), 2.40-2.21 (m, 2H), 2.20-2.09 (m, 1H), 2.00.1.80 (m, 6H), 1.68-1.63 (m, 2H)

940		MS (ESI) m/z 534.16 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.08 (bs, 1H), 8.82 (s, 1H), 7.61-7.56 (m, 2H), 7.36-7.26 (m, 3H), 6.73 (d, J = 7.88 Hz, 1H), 4.46-4.30 (m, 4H), 2.60-2.59 (m, merged, 1H), 2.57 (s, 3H), 1.28-1.10 (m, 4H)	943		MS (ESI) m/z 626.05 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.55 (bs, 1H), 9.03 (s, 1H), 8.41 (s, 1H), 7.99-7.95 (m, 2H), 7.59 (dd, J = 2.56, 8.88 Hz, 1H), 7.45-7.41 (m, 4H), 7.36 (d, J = 8.96 Hz, 1H), 4.42 (t, J = 4.76 Hz, 2H), 4.28 (t, J = 4.52 Hz, 2H), 2.70 (s, 3H), 1.90 (s, 3H)
941		MS (ESI) m/z 626.17 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.56 (bs, 1H), 9.09 (s, 1H), 8.48 (s, 1H), 7.74-7.71 (m, 1H), 7.65-7.58 (m, 2H), 7.45-7.34 (m, 4H), 7.35 (d, J = 8.8 Hz, 1H), 4.41 (t, J = 4.60 Hz, 2H), 4.28 (t, J = 4.60 Hz, 2H), 2.70 (s, 3H), 1.90 (s, 3H)	944		MS (ESI) m/z 622.08 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.03 (s, 1H), 8.43 (s, 1H), 7.60 (dd, J = 8.92 Hz, 2.64 Hz, 1H), 7.47-7.35 (m, 7H), 4.42 (t, J = 5.64 Hz, 2H), 4.27 (t, J = 4.4 Hz, 2H), 2.73 (s, 3H), 2.19 (s, 3H), 1.86 (s, 3H)
942		MS (ESI) m/z 626.19 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.55 (bs, 1H), 9.04 (s, 1H), 8.38 (s, 1H), 7.74 (t, J = 6.92 Hz, 2H), 7.67-7.58 (m, 2H), 7.45-7.41 (m, 3H), 7.36 (d, J = 8.76 Hz, 1H), 4.42 (t, J = 4.68 Hz, 2H), 4.28 (t, J = 4.08, Hz, 2H), 2.66 (s, 3H), 1.98 (s, 3H)	945		MS (ESI) m/z 622.05 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.02 (s, 1H), 8.41 (s, 1H), 7.90 (s, 1H), 7.68 (s, 1H), 7.58 (dd, J = 8.2, 2.12 Hz, 1H), 7.48-7.35 (m, 5H), 4.42 (t, J = 4.48, 2H), 4.27 (t, J = 5.68, 2H), 2.71 (s, 3H), 2.43 (s, 3H), 1.88 (s, 3H)

946		MS (ESI) m/z 622.08 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.5 (s, 1H), 9.027 (s, 1H), 8.40 (s, 1H), 7.80 (d, J = 8.0 Hz, 2H), 7.58 (dd, J = 2.56 Hz, J = 2.52 Hz, 1H), 7.34- 7.42 (m, 5H), 4.40-4.42 (bs, 2H), 4.26 - 4.28 (bs, 2H), 2.70 (s, 3H), 2.42 (s, 3H), 1.87 (s, 3H)	949		MS (ESI) m/z 642.01 [M+1] +; 1H NMR (400 MHz, DMSO-d6) δ 9.04 (s, 1H), 8.40 (s, 1H), 7.94 (d, J = 8.5 Hz, 2H), 7.67 (d, J = 8.5 Hz, 2H), 7.59 (dd, J = 8.9, 2.6 Hz, 1H), 7.45-7.40 (m, 2H), 7.36 (d, J = 8.9 Hz, 1H), 4.42 (t, J = 8.3 Hz, 2H), 4.28 (t, J = 4.4 Hz, 2H), 2.70 (s, 3H), 1.90 (s, 3H)
947		MS (ESI) m/z 642.01 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.54 (bs, 1H), 9.07 (s, 1H), 8.43 (s, 1H), 7.70-7.68 (m, 2H), 7.66-7.54 (m, 3H), 7.43-7.42 (m, 2H), 7.35 (d, J = 9.0 Hz, 1H), 4.41 (t, J = 6.16 Hz, 2H), 4.27 (t, J = 4.48 Hz, 2H), 2.71 (s, 3H), 1.88 (s, 3H)	950		MS (ESI) m/z 676 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.03 (s, 1H), 8.41 (s, 1H), 7.97 (d, J = 7.6 Hz, 1H), 7.91 (t, J = 7.6 Hz, 1H), 7.83 (t, J = 8.0 Hz, 2H), 7.61 (dd, J = 2.8, 8.8 Hz, 1H), 7.44 (s, 1H), 7.36 (d, J = 9.2 Hz) 1H), 4.42 (bs, 1H), 4.27 (bs, 1H), 2.72 (s, 3H), 1.87 (s, 3H)
948		MS (ESI) m/z 642.06 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.50 (bs, 1H), 9.03 (s, 1H), 8.37 (s, 1H), 7.97 (t, J = 2.0 Hz 1H), 7.90-7.84 (m, 1H), 7.67-7.58 (m, 3H), 7.42-7.40 (m, 2H), 7.41 (d, J = 2.6 Hz, 1H), 4.42 (t, J = 5.48 Hz, 2H), 4.28 (t, J = 4.40 Hz, 2H), 2.71 (s, 3H), 1.91 (s, 3H)	951		MS (ESI) m/z 676.10 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.06 (s, 1H), 8.37 (s, 1H), 8.27 (s, 1H), 8.22 (d, J = 7.6 Hz ,1H), 7.96 (d, J = 7.4 Hz, 1H), 7.84 (t, J = 7.8 Hz, 1H), 7.60 (dd, J = 2.52, 8.8 Hz, 1H), 7.43 (s, 1H), 7.41 (d, J = 2.5 Hz ,1H), 7.37 (d, J = 8.9 Hz, 1H), 4.43 (t, J = 5.4 Hz, 2H), 4.29 (t, J = 4.96 Hz, 2H), 2.75 (s, 3H), 1.92 (s, 1H)

952		MS (ESI) m/z 676.01 [M+1] +; 1H NMR (400 MHz, DMSO-d6) δ 13.49 (bs, 1H), 9.07 (s, 1H), 8.41 (s, 1H), 8.13 (d, J = 8.16 Hz, 2H), 7.98 (d, J = 8.28 Hz, 2H), 7.60 (dd, J = 8.92, 2.60 Hz 1H), 7.43-7.40 (m, 2H), 7.36 (d, J = 8.96 Hz 1H), 4.42 (t, J = 6.48 Hz 2H), 4.29 (t, J = 4.48 Hz 2H), 2.71 (s, 3H), 1.92 (s, 3H)	970		MS (ESI) m/z 521.01 [M+1] +; 1H NMR (400 MHz, DMSO-d6) δ 12.47 (bs, 1H), 8.96 (s, 1H), 7.70 (s, 1H), 7.29 (d, J = 8.8 Hz, 1H), 7.17 (s, 1H), 7.10 (d, J = 8.8 Hz, 1H), 6.83 (s, 1H), 4.53 (t, J = 6.4 Hz, 2H), 4.39 (t, J = 4.8 Hz, 2H), 3.99 (s, 2H), 2.65 (s, 3H), 2.57 (bs, 1H), 1.20 (d, J = 7.6 Hz, 2H), 0.93 (d, J = 6.4 Hz, 2H)
953		MS (ESI) m/z 655.99 [M+1]+; ; 1H NMR (400 MHz, DMSO-d6) δ, 9.03(s, 1H), 8.33 (s, 1H), 7.62-7.58 (m, 2H), 7.52 (dd, J = 2.16, 8.24 Hz, 1H), 7.47-7.42 (m, 3H), 7.37 (d, J = 8.92 Hz, 1H), 4.43 (t, J = 4.96 Hz, 2H), 4.29 (t, J = 3.88 Hz, 2H), 2.72 (s, 3H), 2.15 (s, 3H), 1.85 (s, 3H)	971		MS (ESI) m/z 643.13 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.38 (bs, 1H), 8.63 (s, 1H), 8.46 (s, 1H), 7.59 (dd, J = 2.5, 8.9 Hz, 1H), 7.42 (d, J = 2.4 Hz, 1H), 7.36 (s, 1H), 7.34 (s, 1H), 4.76-4.69 (m, 2H), 4.38 (t, J = 4.3 Hz, 2H), 4.21 (t, J = 6.2 Hz, 2H), 3.43 (s, 3H), 2.69 (s, 3H), 1.81 (s, 3H)
954		MS (ESI) m/z 675.95 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.06 (s, 1H), 8.36 (s, 1H), 7.90 (s, 1H), 7.74-7.68 (m, 2H), 7.59 (d, J = 6.6 Hz, 1H), 7.42 (s, 2H), 7.35 (d, J = 8.8 Hz, 1H), 4.42 (s, 2H), 4.28 (s, 2H), 2.72 (s, 3H), 1.89 (s, 3H)	972		MS (ESI) m/z 629.09 [M+1]+; ; 1H NMR (400 MHz, DMSO-d6) δ 8.65 (s, 1H), 8.43 (s, 1H), 7.77 (t, J = 6.0 Hz, 1H), 7.57 (d, J = 9.0 Hz, 1H), 7.41 (s, 1H), 7.35 (t, J = 5.3 Hz, 2H), 4.37-4.30 (m, 4H), 4.20 (bs, 2H), 2.68 (s, 3H), 1.78 (s, 3H)

973		MS (ESI) m/z 625.11 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.59 (s, 1H), 8.44 (s, 1H), 7.59 (dd, J = 2.56, 6.28 Hz, 1H), 7.40 (bs, 2H), 7.35 (d, J = 8.96 Hz, 1H), 6.38 (tt, J = 4.08, 59.88 Hz, 1H), 4.38 (t, J = 6.20 Hz, 2H), 4.21 (t, J = 4.48 Hz, 2H), 4.16-4.12 (m, 2H), 3.39 (s, 3H), 2.71 (s, 3H), 1.84 (s, 3H)	976		MS (ESI) m/z 591.19 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.75 (s, 1H), 8.23 (bs, 1H), 7.57 (d, J = 8.4 Hz, 1H), 7.38 (s, 1H), 7.33 (m, 2H), 4.37 (t, J = 5.2 Hz, 2H), 4.22 (t, J = 4.0 Hz, 2H), 3.84 (s, 3H), 3.26 (s, 3H), 2.66 (s, 3H), 1.63 (s, 3H)
974		MS (ESI) m/z 611.18 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.60 (s, 1H), 8.47 (s, 1H), 7.60-7.55 (m, 2H), 7.40 (s, 2H), 7.34 (d, J = 8.96 Hz 1H), 6.21 (tt, J = 5.28, 57.68 Hz, 1H), 4.36 (t, J = 4.60 Hz, 2H), 4.20 (t, J = 4.60 Hz, 2H), 3.93-3.86 (m, 2H), 2.70 (s, 3H), 1.80 (s, 3H)	977		MS (ESI) m/z 615.03 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.92 (s, 1H), 8.44 (s, 1H), 7.59 (dd, J1 = 2.5 Hz, J2 = 8.8 Hz, 1H), 7.41-7.40 (m, 2H), 7.35 (d, J = 9.0 Hz, 1H), 4.40 (t, J = 8.8 Hz, 2H), 4.25 (t, J = 9.1 Hz, 2H), 4.08, (t, J = 13.6 Hz, 2H), 2.70 (s, 3H), 2.60-2.58 (m, 2H), 2.20 (t, J = 14.3 Hz, 2H), 1.87 (s, 3H)
975		MS (ESI) m/z 560.11 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.14 (s, 1H), 8.61 (s, 1H), 7.62-7.59 (dd, J = 2.4, 8.4 Hz, 1H), 7.46 (s, 1H), 7.42 (d, J = 2.4 Hz, 1H), 7.37 (d, J = 9.2 Hz, 1H), 4.88 (t, J = 9.6 Hz, 2H), 4.40 (t, J = 4.4 Hz, 2H), 4.23 (t, J = 4.8 Hz, 2H), 4.17 (t, J = 9.6 Hz, 2H), 3.52 (s, 1H), 2.66 (s, 3H), 1.86 (s, 3H)	978		MS (ESI) m/z 604.24 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.54 (s, 1H), 8.48 (s, 1H), 7.59 (dd, J = 8.8 Hz, 2.48 Hz, 1H), 7.42-7.39 (m, 2H), 7.35 (d, J = 8.96 Hz, 1H), 4.37 (d, J = 4.48 Hz, 2H), 4.19 (d, J = 4.8 Hz, 2H), 3.05 (s, 3H), 2.70 (s, 3H), 2.53 (s, 6H), 1.78 (s, 3H)

979		MS (ESI) m/z 590.16 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.69 (bs, 1H), 8.57 (s, 1H), 8.46 (s, 1H), 7.59 (dd, J = 8.88 Hz, 2.44 Hz, 1H), 7.43-7.41 (m, 2H), 7.34 (d, J = 8.96 Hz, 1H), 4.36 (t, J = 4.28 Hz, 2H), 4.18 (t, J = 4.6 Hz, 2H), 2.70 (s, 9H), 1.71 (s, 3H)	982		MS (ESI) m/z 649.06 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.60 (s, 1H), 8.69 (s, 1H), 8.47 (s, 1H), 7.60 (dd, J = 2.56 Hz, J = 8.88 Hz, 1H), 7.42-7.35 (m, 4H), 7.29 (d, J = 7.25 Hz, 1H), 7.12 (t, J = 7.52 Hz, 1H), 6.96 (t J = 7.24 Hz, 1H), 4.41 (t, J = 5.04 Hz, 2H), 4.34 (t, J = 8.04 Hz, 2H), 4.24 (t, J = 4.76 Hz, 2H), 3.22 (t, J = 7.88 Hz, 2H), 2.71 (s, 3H), 1.83 (s, 3H)
980		MS (ESI) m/z 716.23 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 8.76 (d, J = 3.60 Hz, 1H), 8.68 (s, 1H), 8.59 (s, 1H), 7.74 (d, J = 8.40 Hz, 1H), 7.67-7.64 (m, 2H), 7.43 (d, J = 3.60 Hz, 1H), 4.80 (s, 2H), 4.25 (bs, 1H), 3.83 (s, 3H), 3.10 (s, 3H), 3.02 (d, J = 9.6 Hz, 2H), 2.78-2.71 (m, 2H), 2.39-2.34 (m, 2H), 2.03 (s, 3H), 1.93-1.91 (m, 2H), 1.76-1.05 (m, 5H)	983		MS (ESI) m/z 647.10 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.99 (s, 1H), 8.43 (s, 1H), 7.92 (d, J = 3.36 Hz, 1H), 7.74 (d, J = 8.12 Hz 1H), 7.69 (s, J = 7.60 Hz 1H), 7.61 (dd, J = 8.88, 2.48 Hz 1H), 7.45 (s, 1H), 7.43 (d, J = 2.48 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 7.29-7.20 (m, 2H), 6.84 (d, J = 3.28 Hz, 1H), 4.44 (d, J = 4.48 Hz, 2H), 4.29 (d, J = 4.48 Hz, 2H), 2.70 (s, 3H), 1.87 (s, 3H)
981		MS (ESI) m/z 554.13 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.22 (s, 1H), 9.19 (s, 1H), 8.79 (d, J = 4.8 Hz, 1H), 8.45 (s, 1H), 7.61 (dd, J = 2.64, 8.88, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.45 (d, J = 2.68 Hz, 1H), 7.37 (d, J = 8.96 Hz, 1H), 6.72-6.46 (t, J = 51.6 Hz, 1H), 4.41 (d, J = 4.64 Hz, 2H), 4.36 (d, J = 4.52 Hz, 2H)	984		MS (ESI) m/z 598.05 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.91 (s, 1H), 8.58 (s, 1H), 8.44 (s, 1H), 7.96 (s, 1H), 7.59 (d, J = 8.76 Hz, 1H), 7.42 (s, 2H), 7.35 (d, J = 8.88 Hz, 1H), 6.70 (s, 1H), 4.41 (t, J = 4.12 Hz, 2H), 4.27 (t, J = 4.00 Hz, 2H), 2.71 (s, 3H), 1.83 (s, 3H)

985		MS (ESI) m/z 561.13 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.52 (bs, 1H), 8.59 (s, 1H), 8.47 (s, 1H), 7.58 (dd, J = 8.8, 2.12 Hz, 1H), 7.41 (s, 1H), 7.381H), 7.33 (d, J = 8.96 Hz, 1H), 7.28-7.20 (m, 1H), 4.36 (t, J = 5.68 Hz, 2H), 4.18 (t, J = 6.16 Hz, 2H), 2.97 (d, J = 4.24 Hz, 3H), 2.69 (s, 3H), 1.75 (s, 3H)	988		MS (ESI) m/z 590.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.01 (s, 1H), 8.40 (s, 1H), 7.60 (dd, J = 8.8 Hz, 2.4 Hz, 1H), 7.43-7.42 (m, 2H), 7.35 (d, J = 8.9 Hz, 1H), 4.95-4.90 (m, 1H), 4.39 (s, 2H), 4.23-4.20 (m, 2H), 3.22 (s, 3H), 2.70 (s, 3H), 1.84 (s, 3H), 1.50 (s, 3H)
986		MS (ESI) m/z 637.13 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.59 (bs, 1H), 8.76 (s, 1H), 8.52 (s, 1H), 7.58 (dd, J = 8.84, 2.48 Hz, 1H), 7.43-7.32 (m, 5H), 7.18 (d, J = 8.00 Hz, 2H), 7.12 (t, J = 7.20 Hz, 1H), 4.35 (t, J = 5.48 Hz, 2H), 4.18 (t, J = 3.64 Hz, 2H), 3.53 (s, 3H), 2.72 (s, 3H), 1.78 (s, 3H)	989		MS (ESI) m/z 626.13 [M+1]+; 1H NMR (400 MHz, DMSO-d6 with D2O) δ 9.14 (s, 1H), 7.79 (s, 1H), 7.50 (dd, J = 8.64 Hz, 1.96 Hz, 1H), 7.31 (d, J = 2.56 Hz, 1H), 7.25 (d, J = 8.68 Hz, 1H), 7.04 (s, 1H), 6.63 (s, 1H), 6.41 (s, 1H), 4.33 (s, 2H), 4.25 (s, 2H), 2.66 (s, 3H), 1.82 (s, 3H)
987		MS (ESI) m/z 651.29 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.45 (bs, 1H), 8.69 (s, 1H), 8.62 (s, 1H), 8.13 (t, J = 3.36 Hz, 2H), 7.58 (dd, J = 2.52, 8.84 Hz, 1H), 7.53 -7.51 (m, 3H), 7.42 (d, J = 2.52 Hz, 1H), 7.39-7.36 (m, 2H), 4.41 (t, J = 4.60 Hz, 2H), 4.25 (t, J = 4.4 Hz, 2H), 3.31 (s, 6H), 2.56 (s, 3 H) 1.88 (s, 3H)	993		MS (ESI) m/z 665.02 [M+1]+; ; 1H NMR (400 MHz, DMSO-d6) δ 13.53 (bs, 1H), 9.56 (s, 1H), 9.11 (s, 1H), 8.72 (s, 1H), 8.32 (bs, 1H), 8.28 (d, J = 8.56 Hz, 1H), 8.06 (d, J = 8.48 Hz,1H), 7.59 (dd, J = 8.92Hz, 2.36 Hz, 1H), 7.41 (d, J = 2.28 Hz, 1H), 7.37-7.35 (m, 2H), 4.42 (t, J = 6.24 Hz, 2H), 4.30 (t, J=4.56 Hz, 2H), 2.70 (s, 3H), 1.90 (s, 3H)

994		999	
MS (ESI) m/z 640.13 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.88 (s, 1H), 8.39 (s, 1H), 7.59 (dd, J = 8.88, 2.62 Hz, 1H), 7.41 (t, J = 2.8 Hz, 2H), 7.36 (d, J = 8.8 Hz, 1H), 4.40 (t, J 5.2 Hz, 2H), 4.27 (t, J = 5.2 Hz, 2H), 2.94 (d, 4.4 Hz, 1H), 2.70 (s, 3H), 2.66 - 2.60 (m, 1H), 1.91 (s, 3H), 1.68 (t, 7.2 Hz, 2H)		MS (ESI) m/z 674.0 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.50 (bs, 1H), 8.50 (s, 1H), 7.72-7.68 (m, 2H), 7.59 (dd, J = 2.56, 8.92 Hz, 1H), 7.53-7.45 (m, 1H), 7.43-7.41 (m, 2H), 7.34 (d, J = 9.2 Hz, 1H), 4.45 (t, J = 4.96 Hz, 2H), 4.29 (bs, 2H), 2.78 (s, 3H), 2.70 (s, 3H), 1.98 (s, 3H)	
997		1004	
MS (ESI) m/z 673.99 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.50 (s, 1H), 8.50 (s, 1H), 7.86 (dd, J = 2.56, 6.08 Hz, 1H), 7.70 (dd, J = 4.60, 8.60 Hz, 1H), 7.58 (dd, J = 2.52, 8.92 Hz, 1H), 7.49 (t, J = 9.28 Hz, 2H), 7.42-7.36 (m, 2H), 4.44 (t, J = 4.40 Hz, 2H), 4.29 (t, J = 4.40 Hz, 2H), 2.79 (s, 3H), 2.70 (s, 3H), 2.00 (s, 3H)		MS (ESI) m/z 548.02 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.62 (bs, 2H), 8.51 (s, 1H), 8.30 (bs, 1H), 7.59 (dd, J = 8.88, 2.52 Hz, 1H), 7.42 (s, 2H), 7.34 (d, J = 9.00 Hz 1H), 4.35 (t, J = 5.48 Hz, 2H), 4.15 (t, J=3.64 Hz, 2H), 2.71 (s, 3H), 1.65 (s, 3H)	
998		1008	
MS (ESI) m/z 658.03 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.50 (s, 1H), 8.52 (s, 1H), 7.64-7.61 (m, 1H), 7.60 (dd, J = 2.4, 8.92 Hz, 1H), 7.50-7.47 (m, 2H), 7.42 (bs, 1H), 7.40 (d, J = 2.56 Hz, 1H), 7.37 (d, J = 9.00 Hz, 1H), 4.44 (t, J = 4.72 Hz, 2H), 4.29 (t, J = 4.52 Hz, 2H) 2.79 (s, 3H), 2.70 (s, 3H), 2.06 (s, 3H)		MS (ESI) m/z 663.13 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.68 (s, 1H), 8.10-8.08 (m, 2H), 7.60 (dd, J = 2.4, 6.8 Hz, 2H), 7.51-7.50 (m, 3H), 7.41-7.36 (m, 3H), 4.42 (t, J = 4.8 Hz, 6H), 4.24 (t, J = 4.4 Hz, 2H), 2.57 (s, 3H), 2.42-2.32 (m, 2H), 1.97 (s, 3H)	

1010		MS (ESI) m/z 617.14 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.59 (s, 1H), 8.55 (s, 1H), 8.47 (s, 1H), 7.58 (d, J = 8.72 Hz, 1H), 7.40-7.38 (m, 2H), 7.34 (d, J = 8.76 Hz, 1H), 4.55 (t, J = 6.76 Hz, 2H), 4.36 (m, 3H), 4.18-4.13 (m, 4H), 3.28 (s, 3H), 2.70 (s, 3H), 1.80 (s, 3H)	1016		MS (ESI) m/z 622.14 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.73 (bs, 1H), 9.02 (s, 1H), 8.39 (s, 1H) 7.94-7.87 (m, 2H), 7.61-7.58 (m, 4H), 7.46-7.43 (m, 2H), 7.36 (d, J = 8.96 Hz, 1H), 4.42 (t, J = 5.6 Hz, 2H), 4.27 (t, J= 4.32 Hz, 2H), 3.02 (q, J = 7.52 Hz, 2H), 1.83 (s, 3H) 1.35 (t, J = 7.56 Hz, 3H)
1011		MS (ESI) m/z 603.09 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.55 (s, 1H), 8.48 (s, 1H), 7.59 (dd, J = 2.4, 8.8 Hz 1H), 7.41 (d, J = 2.4 Hz, 1H), 7.39 (s, 1H), 7.35 (d, J = 9.2 Hz 1H), 5.79 (d, J = 5.2 Hz, 1H), 4.58 (m, 3H), 4.36 (bs, 2H), 4.19 (bs, 2H), 4.07 (d, J = 6.8 Hz, 2H), 2.70 (s, 3H), 1.78 (s, 3H)	1037		MS (ESI) m/z 688.18 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.86 (bs, 1H), 8.87 (s, 1H), 8.11 (s, 1H), 7.54 (d, J = 8.72 Hz, 1H), 7.36 (s, 1H), 7.30 (d, J = 8.88 Hz, 1H), 7.23 (s, 1H), 4.48 (t, J = 4.4 Hz, 1H), 4.35 (t, J = 4.08, 2H), 4.22 (t, J = 3.24, 2H), 2.66 (s, 3H), 1.80 (s, 3H), 0.86 (d, J = 5.56 Hz, 2H), 0.81 (s, 2H)
1015		MS (ESI) m/z 636.14 [M+1]+1H; NMR (400 MHz, DMSO-d6) δ 13.67 (bs, 1H), 8.50 (s, 1H), 7.87 (m, 2H), 7.61-7.55 (m, 4H), 7.46 (s, 1H), 7.42 (d, J = 2.5 Hz, 1H), 7.37 (s, 1H), 4.45 (t, J = 5.3 Hz, 2H), 4.27 (t, J = 4.6 Hz, 2H), 3.04-2.98 (m, 2H), 2.78 (s, 3H), 1.35 (s, 3H), 1.08 (t, J = 7.5 Hz, 3H)	1038		MS (ESI) m/z 624.06 [M+1] +; 1H NMR (400 MHz, DMSO-d6) δ 13.57 (bs, 1H), 8.62 (s, 1H), 8.44 (s, 1H), 7.60 (dd, J = 8.8 Hz, 2.4 Hz 1H), 7.54-7.46 (m, 2H), 7.45-7.40 (m, 2H), 7.36 (d, J = 8.8 Hz, 1H), 7.35-7.28 m, 3H), 4.41 (t, J = 4.4 Hz, 2H), 4.26 (t, J = 5.2 Hz, 2H), 2.71 (s, 3H), 1.82 (s, 3H)

1039		MS (ESI) m/z 639.08 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.62 (bs, 1H), 8.71 (s, 1H), 8.59 (d, J = 4 Hz, 1H), 8.43 (s, 1H), 7.89 (t, J = 7.08 Hz, 1H), 7.60-7.57 (m, 2H), 7.40 (s, 2H), 7.39-7.34 (m, 2H), 5.68 (s, 2H), 4.40 (t, J = 5.36 Hz, 2H), 4.24 (t, J = 4.36 Hz,2H), 2.70 (s, 3H), 1.85 (s, 3H)	1043		MS (ESI) m/z 667.13 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.56 (s, 1H), 8.47 (s, 1H), 7.57 (dd, J = 2.52, 8.8 Hz, 1H), 7.40 (t, J = 2.4 Hz, 2H), 7.34 (d, J = 8.84 Hz, 1H), 6.35-6.06 (m, 1H), 4.59 (t, J = 6.24 Hz, 2H), 4.36 (t, J = 4.8 Hz, 2H), 4.18 (d, J = 6.8 Hz, 4H), 3.84-3.75 (m, 2H), 2.70 (s, 3H), 1.80 (s, 3H)
1041		MS (ESI) m/z 653.12 [M+1]+; 1H NMR (400 MHz, DMSO-d6)) δ 8.58 (s, 1H), 8.46 (s, 1H), 7.58 (dd, J = 2.4, 8.8 Hz, 1H), 7.40 (t, J = 2.4 Hz, 2H), 7.35 (d, J = 8.8 Hz, 1H), 7.03-6.65 (m, 1H), 5.12 (t, J = 3.6 Hz, 1H), 4.72 (m, 2H), 4.38 (t, J = 5.2 Hz, 2H), 4.32 (m, 2H), 4.21 (t, J = 4.4 Hz, 2H), 3.40 (s, 1H), 2.71 (s, 3H), 1.83 (s, 3H)	1044		MS (ESI) m/z 685.20 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.58 (bs, 1H), 8.57 (s, 1H), 8.47 (s, 1H), 7.58 (dd, J = 2.48, 8.88 Hz, 1H), 7.40 (d, J = 2.56 Hz, 1H), 7.39 (s, 1H), 7.34 (d, J = 9.00 Hz, 1H), 4.65-4.58 (m, 3H), 4.37 (t, J = 6.08 Hz, 2H), 4.25-4.19 (m, 6H), 2.70 (s, 3H), 1.81 (s, 3H)
1042		MS (ESI) m/z 671.16 [M+1] +; ; 1H NMR (400 MHz, DMSO-d6) δ 8.60 (s, 1H), 8.47 (s, 1H), 7.60 (dd, J = 2.8, 8.8 Hz, 1H), 7.41-7.40 (m, 2H), 7.36 (d, J = 8.8 Hz, 1H), 5.36-5.33 (m, 1H), 4.79-4.75 (m, 2H), 4.43 (t, J = 3.2 Hz, 2H), 4.40 (t, J = 7.6 Hz, 2H), 4.21 (d, J = 4.4 Hz, 2H), 2.17 (s, 3H), 1.85 (s, 3H)	1045		MS (ESI) m/z 659.25 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.59 (bs, 1H), 8.55 (s, 1H), 8.47 (s, 1H), 7.59 (dd, J = 2.48, 8.84 Hz, 1H), 7.41 (d, J = 2.52 Hz, 1H), 7.39 (s, 1H), 7.34 (d, J = 8.96 Hz, 1H), 4.68-4.65 (m, 1H), 4.61-4.57 (m, 2H), 4.34 (t, J = 4.68 Hz, 2H), 4.16 (t, J = 3.72 Hz, 2H), 4.06-4.03 (m, 2H), 2.67 (s, 3H), 1.82 (s, 3H), 1.15 (s, 9H)

1051		MS (ESI) m/z 641.11 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.52 (s, 1H), 9.06 (s, 1H), 8.67 (d, J = 2.76 Hz, 1H), 8.36 (s, 1H), 8.06 (dd, J = 2.64, 9.0 Hz, 1H), 7.60 (dd, J = 2.52, 8.8 Hz , 1H), 7.43 (s, 2H), 7.36 (d, J = 8.96 Hz, 1H), 4.43 (t, J = 5.0 Hz, 2H), 4.29 (t, J = 5.5 Hz, 2H), 2.72 (s, 3H), 2.36 (s, 3H), 1.91 (s, 3H)	1056		MS (ESI) m/z 617.15 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.55 (s, 1H), 8.50 (s, 1H), 7.59 (dd, J = 8.8 Hz, 2.44 Hz, 1H), 7.42-7.40 (m, 2H), 7.35 (d, J = 9 Hz, 1H), 4.38 (bs, 1H), 4.36 (m, 2H), 4.21-4.18 (m, 2H), 3.93-3.87 (m, 3H), 3.78-3.73 (m,1H), 3.56 (d, J = 11.68 Hz, 1H), 2.70 (s, 3H), 2.04-2.02 (m, 1H), 1.94-1.92 (m, 1H), 1.79 (s, 3H)
1052		MS (ESI) m/z, 640.13 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.51 (bs, 1H), 9.03 (s, 1H), 8.37 (s, 1H), 7.60 (dd, J= 2.40, 8.84 Hz, 1H), 7.43 (bs, 4H), 7.34 (d, J = 8.92 Hz, 1H), 7.32-7.28 (m, 1H), 4.42 (t, J = 4.72 Hz, 2H), 4.27 (t, J = 4.76 Hz, 2H), 2.72 (s, 3H), 2.14 (s, 3H), 1.86 (s, 3H)	1057		MS (ESI) m/z 617.18 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.59 (bs, 1H), 8.56 (s, 1H), 8.47 (s, 1H), 7.58 (d, J = 8.64 Hz, 1H), 7.40 (d, J = 8.84 Hz, 2H), 7.34 (d, J = 8.88 Hz, 1H), 5.70 (bs, 1H) 4.36 (t, J = 6.56 Hz, 2H), 4.20 (m, 6H), 2.70 (s, 3H), 1.77 (s, 3H), 1.47 (s, 3H)
1053		MS (ESI) m/z 603.17 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.94 (s, 1H), 8.38 (s, 1H), 7.59 (d, J=8.72 Hz, 1H), 7.42 (s, J = 2.76, 2H), 7.36 (d, J = 8.96 Hz, 1H), 4.41 (s, 2H), 4.26 (s, 2H), 3.34 (s, 3H), 2.71 (s, 3H), 2.00 (bs, 3H), 1.84 (s, 3H)	1062		MS (ESI) m/z 574.12 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.7 (bs, 1H), 8.92 (s, 1H), 8.35 (s, 1H), 7.60 (d, J = 8.4 Hz, 1H), 7.44-7.43 (m, 2H), 7.36 (d, J = 8.8 Hz, 1H), 4.40 (t, J = 4.4 Hz, 2H), 4.25 (t, J = 4.0 Hz, 2H), 3.12-3.07(m, 2H), 3.03-2.97 (m, 2H), 1.83 (s, 3H), 1.36 (t, J = 7.2 Hz, 6H)

1063		MS (ESI) m/z 573.12 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.86 (s, 1H), 8.30 (s, 1H), 7.55 (dd, J = 8.88 Hz, 2.32 Hz, 1H), 7.35-7.30 (m, 3H), 4.36 (t, J = 6.6 Hz, 2H), 4.22 (t, J = 5.12 Hz, 2H), 3.02 (t, J = 7.36 Hz, 2H), 2.71 (s, 3H), 1.90 (s, 3H), 1.80-1.74 (m, 2H),0.93 (t, J=14.6Hz, 3H)	1066		MS (ESI) m/z 576.18 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.58 (s, 1H), 8.98 (s, 1H), 8.35 (s, 1H), 7.58 (s, 1H), 7.41-7.35 (m, 3H), 4.74 (s, 2H), 4.39 (s, 2H), 4.26 (s, 2H), 3.38 (s, 3H) 2.69 (s, 3H), 1.85 (s, 3H)
1064		MS (ESI) m/z 578.19 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.98 (s, 1H), 8.40 (s, 1H), 7.59 (dd, J = 8.88 Hz, 2.62 Hz, 1H), 7.41 (s, 2H), 7.35 (d, J = 8.89 Hz, 1H), 4.94 (dt, J = 48 Hz, 6.0 Hz, 2H), 4.40 (t, J = 5.2 Hz, 2H), 4.26 (t, J = 4.8 Hz, 2H), 3.49 (dt, J = 25 Hz, 6.0 Hz, 2H), 2.70 (s, 3H), 1.89 (s, 3H)	1067		MS (ESI) m/z 576.14 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.69 (s, 1H), 8.42 (s, 1H), 7.57 (dd, J = 2.52, 8.8 Hz, 1H), 7.41 (s, 2H), 7.35 (d, J = 8.92 Hz, 1H), 4.59-4.54 (m, 2H), 4.39 (t, J = 4.4 Hz, 2H), 4.23 (t, J = 4.3 Hz, 2H), 2.71 (s, 3H), 1.84 (s, 3H)
1065		MS (ESI) m/z 578.14 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.50 (bs, 1H), 9.03 (s, 1H), 8.39 (s, 1H), 7.59 (dd, J = 8.8, 2.2 Hz 1H), 7.45-7.38 (m, 2H), 7.35 (d, J = 8.92 Hz, 1H), 6.24-6.15 (dq, J = 47.20, 6.80 Hz, 1H), 4.47-4.35 (m, 2H), 4.35-4.29 (m, 2H), 2.69 (s, 3H), 1.87 (s, 3H), 1.78 (dd, J = 24.4, 6.32 Hz, 3H)	1068		MS (ESI) m/z 602.16 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.70 (bs, 1H), 8.69 (s, 1H), 8.37 (s, 1H), 7.59 (dd, J = 8.88, 2.64 Hz, 1H), 7.40 (d, J = 2.60 Hz, 1H), 7.38 (s, 1H), 7.34 (d, J = 8.96 Hz, 1H), 4.41-4.31 (m, 4H), 4.23 (t, J = 4.60 Hz, 2H), 2.70 (s, 3H), 1.83 (s, 3H), 1.40-1.40 (m, 1H), 0.65-0.58 (m, 2H), 0.46-0.39 (m, 2H)

1068		MS (ESI) m/z 561.20 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.59 (bs, 1H), 8.55 (s, 1H), 7.58 (d, J = 8.0 Hz, 1H), 7.40-7.34 (m, 3H), 7.03 (s, 2H), 4.38 (t, J = 5.9 Hz, 2H), 4.17 (t, J = 4.0 Hz, 2H), 2.69 (s, 3H), 2.56 (s, 3H), 1.72 (s, 3H)	1072		MS (ESI) m/z 547.10 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.49 (s, 1H), 8.47 (s, 1H) 7.59 (dd, J = 8.92, 2.44 Hz, 1H), 7.45-7.39 (m, 2H), 7.33 (d, J = 8.92 Hz 1H), 7.21 (bs, 2H), 4.36 (t, J = 6.0 Hz, 2H), 4.17 (t, J = 6.04 Hz, 2H), 2.70 (s, 3H), 1.68 (s, 3H)
1070		MS (ESI) m/z 575.20 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.56 (s, 1H), 7.60 (dd, J = 2.0, 8.8 Hz, 1H), 7.44 (t, J = 3.6 Hz, 2H), 7.36 (d, J = 9.2 Hz, 1H), 7.03 (bs, 2H), 4.40 (bs, 2H), 4.17 (bs, 2H), 3.03 (m, 2H), 2.55 (s, 3H), 1.69 (s, 3H), 2.96 (t, J = 7.6 Hz, 3H)	1076		MS (ESI) m/z 600.18 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.71 (s, 1H), 8.81 (s, 1H), 8.35 (s, 1H), 7.60 (dd, J = 2.4, 8.8 Hz, 1H), 7.43 (s, 1H), 7.36 (d, J = 9.2 Hz, 1H), 4.41 (t, J = 4.8 Hz, 2H), 4.24 (t, J = 4.4 Hz, 2H), 2.96 (t, J = 7.2 Hz, 2H), 2.66 (m, 1H), 1.85-1.75 (m, 5H), 1.23-1.18 (m, 2H), 1.10-1.06 (m, 2H), 1.00 (t, J = 7.2 Hz, 3H)
1071		MS (ESI) m/z 561.21 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.80 (bs, 1H), 8.47 (s, 1H), 8.44 (s, 1H) 7.59 (d, J = 9.20 Hz, 1H), 7.44 (s, 2H), 7.33 (d, J = 9.0 Hz, 1H), 7.21 (bs, 2H), 4.35 (t, J = 5.48 Hz, 2H), 4.16 (t, J = 6.28 Hz, 2H), 3.01 (q, J = 7.52 Hz, 2H), 1.64 (s, 3H), 1.34 (t, J = 7.48 Hz, 3H)	1086		MS (ESI) m/z 644.20 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.70 (bs, 1H), 9.90 (bs, 1H), 8.66 (s, 1H), 8.38 (s, 1H) 7.60 (dd, J = 8.88, 2.36 Hz, 1H), 7.46 (s, 1H), 7.41 (d, J = 2.36 Hz 1H), 7.37 (d, J = 8.96 Hz, 1H), 4.40 (t, J = 4.88 Hz, 2H), 4.31 (d, J = 13.92 Hz, 2H), 4.22 (t, J = 5.84 Hz, 2H), 3.61 (d, J = 11.36 Hz, 2H), 3.44 (t, J = 11.92 Hz, 2H), 3.30-3.28 (m, 2H), 3.02 (q, J = 7.44 Hz, 2H), 2.91 (s, 3H), 1.84 (s, 3H), 1.37 (t, J = 7.52 Hz, 3H)

1089		1097	
MS (ESI) m/z 586.27 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.75 (s, 1H), 7.68 (s, 1H), 7.52 (d, J = 7.0 Hz, 1H), 7.34-7.28 (m, 3H), 7.09 (s, 1H), 4.34 (S, 2H), 4.20 (s , 2H), 3.65 (s, 4H), 2.58 (s, 4H), 2.49 (s, 3H), 2.24 (s, 3H), 1.8 (s, 3H)		MS (ESI) m/z 651.21 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.64 (s, 1H), 8.42 (s, 1H), 7.59 (dd, J = 8.8, 2.56 Hz, 1H), 7.41 (s, 2H), 7.36 (d, J = 8.95 Hz, 1H), 4.39 (t, J = 6.9 Hz, 2H), 4.22 (t, J = 4.56 Hz, 2H), 3.87-3.75 (m, 4H), 2.71 (s, 3H), 2.21-2.15 (m, 4H) 1.87 (s, 3H)	
1091		1099	
MS (ESI) m/z 644.27 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 14.39 (bs, 1H), 8.62 (s, 1H), 7.59 (dd, J = 2.48, 8.88 Hz ,1H), 7.40-7.38 (m, 2H), 7.35 (d, J = 8.92 Hz, 1H), 4.63-4.59 (m, 2H), 4.47 (bs, 2H), 4.39 (t, J = 4.64 Hz, 2H), 4.23 (t, J = 4.64 Hz, 3H), 2.82 (bs, 6H), 2.70 (s, 3H), 2.54 (s, 3H), 1.94 (s, 3H)		MS (ESI) m/z 325.5 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 7.39 – 7.28 (m, 5H), 7.19 (d, J = 7.9 Hz, 1H), 4.99 (s, 2H), 3.50 (t, J = 12.4 Hz, 4H), 3.29 – 3.17 (m, 1H), 2.04 (t, J = 10.8 Hz, 2H), 1.77 (d, J = 12.4 Hz, 2H), 1.70 (d, J = 12.8 Hz, 2H), 1.15 (dq, J = 12.9, 3.2 Hz, 2H), 0.99 (q, J = 13.3 Hz, 2H)	
1092		1100	
MS (ESI) m/z 670.20 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.58 (s, 1H), 7.55 (d, J = 8.8 Hz, 1H), 7.33-7.30 (m, 3H), 4.88 (s, 2H), 4.35 (s, 2H), 4.22 (s, 2H), 3.53 (d, J = 12 Hz, 2H), 3.31 (d, J = 11.6 Hz, 2H), 2.79 (s, 3H), 2.66 (s, 3H), 2.46 (s, 3H), 2.05 (s, 7H)		MS (ESI) m/z 714.6 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.76 (d, J = 4.7 Hz, 1H), 8.71 (s, 1H), 8.66 (s, 1H), 7.78-7.74 (m, 1H), 7.69 (dd, J = 6.4, 2.2 Hz, 2H), 7.55 (d, J = 4.8 Hz, 1H), 4.92 (br, 4H), 4.82 (s, 2H), 4.33 (br, 2H), 3.13 (s, 3H), 2.07 (s, 3H), 2.03 – 1.61 (m, 8H)	

1101		MS (ESI) m/z 670.4 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.8 Hz, 1H), 8.77 (s, 1H), 8.36 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.44 (d, J = 2.7 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.40 (br, 2H), 4.23 (br, 2H), 3.81-3.03 (br, 6H), 1.79 (s, 3H), 1.62 (br, 3H), 1.31 (br, 4H), 0.96 – 0.75 (m, 4H)	1104		MS (ESI) m/z 722.5 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (s, 1H), 8.74 (d, J = 4.7 Hz, 1H), 8.62 (s, 1H), 7.74 (d, J = 8.4 Hz, 1H), 7.71 – 7.61 (m, 2H), 7.43 (d, J = 4.7 Hz, 1H), 4.82 (s, 2H), 4.54 (bs, 2H), 3.86 (s, 3H), 3.68-3.23 (br, 2H), 2.15 (s, 3H). Some aliphatic protons were not seen
1102		MS (ESI) m/z 664.4 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.90 (s, 1H), 8.75 (d, J = 4.8 Hz, 1H), 8.63 (s, 1H), 7.78 – 7.73 (m, 1H), 7.69 (dd, J = 6.6, 2.2 Hz, 2H), 7.55 (d, J = 4.8 Hz, 1H), 4.85 (d, J = 7.1 Hz, 2H), 3.83-2.97 (br, 6H), 2.12 (s, 3H), 1.63 (br 3H), 1.34 (br, 3H), 1.23 – 0.78 (m, 5H)	1105		MS (ESI) m/z 829.4 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.84 (d, J = 4.9 Hz, 1H), 8.82 (s, 1H), 8.75 (s, 1H), 7.78 (d, J = 9.1 Hz, 1H), 7.71 (dd, J = 6.6, 2.2 Hz, 2H), 7.64 (d, J = 4.9 Hz, 1H), 7.26 – 6.94 (m, 1H), 6.59 (tt, J = 54.1, 4.3 Hz, 2H), 4.84 (s, 2H), 4.56 (br, 1H), 4.48 (td, J = 14.7, 4.3 Hz, 2H), 3.12 (s, 3H), 2.34-1.97 (br, 8H), 1.95 (s, 3H), 1.76 (t, J = 19.4 Hz, 3H)
1103		MS (ESI) m/z 738.3 [M+1]+; 1; H NMR (400 MHz, DMSO-d6) δ 8.77 (d, J = 4.8 Hz, 1H), 8.72 (s, 1H), 8.66 (s, 1H), 7.78 – 7.73 (m, 1H), 7.71-7.67 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 6.79 – 6.41 (m, 1H), 4.82 (s, 2H), 4.36 (br, 1H), 3.11 (s, 3H), 2.07 (s, 3H), 2.05-1.82 (br, 2H). Protons on piperidine were not seen	1106		MS (ESI) m/z 710.4 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 10.06 (s, 1H), 8.76 (d, J = 4.8 Hz, 1H), 8.73 (s, 1H), 8.66 (s, 1H), 7.76 (d, J = 9.0 Hz, 1H), 7.71 – 7.66 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 5.00 – 4.86 (m, 1H), 4.83 (s, 2H), 4.81-4.68 (m, 1H), 3.78-3.29 (m, 2H), 3.19 (s, 3H), 2.87 (s, 3H), 2.44-2.11 (m, 5H), 2.08 (s, 3H), 2.06-1.77 (m, 5H)

1107	MS (ESI) m/z 752.3 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.77 (d, J = 4.8 Hz, 1H), 8.73 (s, 1H), 8.66 (s, 1H), 7.78 – 7.74 (m, 1H), 7.71 – 7.67 (m, 2H), 7.55 (d, J = 4.9 Hz, 1H), 4.82 (s, 2H), 4.38 (br, 1H), 3.11 (s, 3H), 2.08 (s, 3H), 2.07-1.92 (br, 2H), 1.84 (t, J = 20.0 Hz, 3H). Piperidine protons were not seen	1110	MS (ESI) m/z 854.4 [M+1]+; ; 1H NMR (400 MHz, DMSO-d6) δ 9.29 (dd, J = 2.4, 0.8 Hz, 1H), 8.92 (dd, J = 4.8, 1.6 Hz, 1H), 8.83 (d, J = 4.9 Hz, 1H), 8.69 (s, 1H), 8.54 (ddd, J = 8.2, 2.4, 1.6 Hz, 1H), 8.47 (s, 1H), 7.77 – 7.67 (m, 3H), 7.66 (dd, J = 2.2, 0.5 Hz, 1H), 7.62 (dd, J = 4.8, 0.4 Hz, 1H), 4.84 (br, 4H), 4.80 (s, 2H), 4.39 – 4.27 (m, 1H), 3.28 (br, 1H), 3.09 (s, 3H), 2.14 – 2.05 (m, 2H), 2.02-1.94 (m, 2H), 1.91 (s, 3H), 1.74 (q, J = 12.2 Hz, 2H), 1.42 (q, J = 11.9 Hz, 2H)
1108	MS (ESI) m/z 791.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.47 (s, 1H), 8.82 – 8.78 (m, 2H), 8.76 (s, 1H), 7.77 (dd, J = 8.3, 0.6 Hz, 1H), 7.73 – 7.66 (m, 2H), 7.62 (d, J = 4.9 Hz, 1H), 4.83 (s, 2H), 4.78 (br, 4H), 4.36 – 4.22 (m, 2H), 3.54 (s, 3H), 3.09 (s, 3H), 2.12 – 2.02 (m, 2H), 1.98 (s, 3H), 1.80-1.67 (m, 3H), 1.46-1.32 (m, 3H)	1111	MS (ESI) m/z 854.4 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.98 – 8.93 (m, 2H), 8.84 (d, J = 4.9 Hz, 1H), 8.70 (s, 1H), 8.48 (s, 1H), 8.11 – 8.06 (m, 2H), 7.76 (dd, J = 8.4, 0.5 Hz, 1H), 7.70 (dd, J = 8.4, 2.2 Hz, 1H), 7.64 (dd, J = 4.9, 0.4 Hz, 1H), 4.84 (br, 4H), 4.81 (s, 2H), 4.38 – 4.25 (m, 1H), 3.28 (br, 1H), 3.08 (s, 3H), 2.15 – 2.06 (m, 2H), 2.01-1.94 (m, 2H), 1.92 (s, 3H), 1.73 (q, J = 12.1 Hz, 2H), 1.41 (q, J = 11.8 Hz, 2H)
1109	MS (ESI) m/z 854.4 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.01 (s, 1H), 8.89 (d, J = 4.8 Hz, 1H), 8.72 (ddd, J = 4.6, 1.7, 0.9 Hz, 1H), 8.66 (s, 1H), 8.59 (s, 1H), 8.27 (dt, J = 8.0, 1.1 Hz, 1H), 8.25 – 8.18 (m, 1H), 7.79 – 7.72 (m, 2H), 7.72 – 7.68 (m, 2H), 7.66 (d, J = 4.9 Hz, 1H), 4.82 (s, 2H), 4.76 (br, 4H), 4.34 – 4.23 (m, 1H), 3.24 (br, 1H), 3.07 (s, 3H), 2.13 – 2.01 (m, 2H), 1.97 (br, 2H), 1.94 (s, 3H), 1.71 (q, J = 12.1 Hz, 2H), 1.38 (q, J = 12.0 Hz, 2H)	1112	MS (ESI) m/z 688.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.76 (d, J = 4.8 Hz, 1H), 8.74 (s, 1H), 8.65 (s, 1H), 7.77 – 7.74 (m, 1H), 7.71 – 7.67 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 6.52 (t, J = 53.4 Hz, 1H), 4.83 (s, 2H), 4.50 (bs, 1H), 3.11 (s, 3H), 2.25 – 1.98 (m, 7H)

1113	MS (ESI) m/z 702.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.77 (d, J = 4.7 Hz, 1H), 8.69 (s, 1H), 8.59 (s, 1H), 7.74 (dd, J = 8.1, 0.8 Hz, 1H), 7.68 – 7.64 (m, 2H), 7.44 (d, J = 4.7 Hz, 1H), 6.15 (tt, J = 55.8, 4.4 Hz, 1H), 4.81 (s, 2H), 4.26 (ddt, J = 11.6, 7.7, 4.0 Hz, 1H), 3.84 (s, 3H), 3.10 (s, 3H), 3.03 (d, J = 11.2 Hz, 2H), 2.76 (td, J = 15.7, 4.3 Hz, 2H), 2.33 (t, J = 11.5 Hz, 2H), 2.03 (s, 3H), 1.92 (qd, J = 12.1, 3.9 Hz, 2H), 1.79 (d, J = 11.7 Hz, 2H); 19F NMR (377 MHz, DMSO-d6) δ -118.73 (dt, J = 55.8, 15.7 Hz, 2F)	1117	MS (ESI) m/z 683.3 [M+1]+; 1H NMR (400 MHz, Chloroform-d) δ 9.12 (s, 1H), 8.78 (d, J = 4.8 Hz, 1H), 8.45 (s, 1H), 7.48 (dd, J = 8.9, 2.6 Hz, 1H), 7.32 – 7.27 (m, 2H), 7.03 (d, J = 8.9 Hz, 1H), 4.41 (t, J = 4.9 Hz, 2H), 4.29 (t, J = 4.9 Hz, 2H), 3.64 – 3.48 (m, 6H), 3.13 – 3.01 (m, 2H), 2.46 – 2.32 (m, 2H), 1.89 (s, 3H)
1115	MS (ESI) m/z 683.3 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.94 (s, 1H), 8.79 (d, J = 4.8 Hz, 1H), 8.59 (s, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.45 (d, J = 2.7 Hz, 1H), 7.35 (d, J = 9.0 Hz, 1H), 4.42 (t, J = 4.9 Hz, 2H), 4.25 (t, J = 5.0 Hz, 2H), 3.82 – 3.70 (m, 1H), 3.20 – 3.09 (m, 2H), 2.78 – 2.67 (m, 2H), 1.92 – 1.79 (m, 7H)	1118	MS (ESI) m/z 694.3 [M+1]+; 1H NMR (400 MHz, Chloroform-d) δ 8.75 (s, 1H), 8.71 (d, J = 4.8 Hz, 1H), 8.49 (s, 1H), 7.59 (d, J = 8.4 Hz, 1H), 7.52 (dd, J = 8.4, 2.1 Hz, 1H), 7.40 (d, J = 2.1 Hz, 1H), 7.38 (d, J = 4.9 Hz, 1H), 5.36 (d, J = 7.0 Hz, 2H), 4.77 – 4.64 (m, 3H), 4.34 (d, J = 7.0 Hz, 2H), 3.37 (d, J = 11.5 Hz, 2H), 3.28 (t, J = 12.1 Hz, 2H), 3.19 (s, 3H), 2.84 – 2.70 (m, 2H), 2.44 (s, 3H), 2.34 (d, J = 13.5 Hz, 2H), 1.85 (s, 3H)
1116	MS (ESI) m/z 677.1 [M+1]+; 1H NMR (400 MHz, Chloroform-d) δ 9.16 (s, 1H), 8.78 (d, J = 4.9 Hz, 1H), 8.56 (s, 1H), 7.59 (d, J = 8.4 Hz, 1H), 7.51 (dd, J = 8.4, 2.1 Hz, 1H), 7.46 – 7.41 (m, 2H), 4.81 (s, 2H), 3.66 – 3.38 (m, 5H), 3.01 (t, J = 11.8 Hz, 2H), 2.50 – 2.31 (m, 5H), 2.13 (d, J = 14.0 Hz, 2H)	1119	MS (ESI) m/z 756.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.77 (d, J = 4.8 Hz, 1H), 8.72 (s, 1H), 8.66 (s, 1H), 7.76 (d, J = 9.0 Hz, 1H), 7.71 – 7.66 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 4.35 – 4.24 (m, 1H), 3.38 – 3.22 (m, 2H), 3.12 – 3.00 (m, 5H), 2.63 – 2.52 (m, 2H), 2.06 (s, 3H), 2.00 – 1.86 (m, 2H), 1.85 – 1.75 (m, 2H)

1120		MS (ESI) m/z 623.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.80 – 8.58 (m, 3H), 7.78 – 7.63 (m, 3H), 7.53 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 4.27 (t, J = 11.8 Hz, 1H), 3.09 (s, 3H), 2.04 (s, 3H), 1.89 – 1.75 (m, 4H), 1.71 – 1.56 (m, 3H), 1.38 (q, J = 12.8, 12.2 Hz, 2H), 1.16 (q, J = 13.1 Hz, 1H)	1123		LCMS (ESI) m/z 627.3 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.01 (s, 1H), 8.83 (d, J = 4.8 Hz, 1H), 8.38 (s, 1H), 7.67 – 7.58 (m, 2H), 7.48 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.7 Hz, 1H), 7.37 (d, J = 9.1 Hz, 1H), 7.04 (d, J = 15.0 Hz, 1H), 4.42 (t, J = 5.0 Hz, 2H), 4.28 (t, J = 5.0 Hz, 2H), 2.98 (s, 6H), 1.86 (s, 3H), 1.53 (s, 2H), 1.35 (s, 2H)
1121		LCMS (ESI) m/z 677.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.01 (s, 1H), 8.83 (d, J = 4.8 Hz, 1H), 8.36 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.44 (s, 1H), 7.42 – 7.33 (m, 2H), 7.19 (dt, J = 14.8, 7.3 Hz, 1H), 4.41 (t, J = 4.9 Hz, 2H), 4.33 – 4.09 (m, 4H), 2.08 (d, J = 4.4 Hz, 3H), 1.80 (s, 3H)	1124		LCMS (ESI) m/z 677.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.92 (s, 1H), 8.84 (dd, J = 4.8, 1.4 Hz, 1H), 8.38 (d, J = 2.2 Hz, 1H), 7.60 (ddd, J = 9.0, 2.7, 0.8 Hz, 1H), 7.50 (s, 1H), 7.51 – 7.41 (m, 1H), 7.35 (d, J = 9.0 Hz, 1H), 7.11 (d, J = 15.4 Hz, 1H), 6.93 (d, J = 15.4 Hz, 1H), 6.06 (tt, J = 56.0, 4.2 Hz, 1H), 4.40 (t, J = 4.9 Hz, 2H), 4.24 (t, J = 4.9 Hz, 2H), 3.19 (tq, J = 15.5, 4.2 Hz, 2H), 2.61 (s, 3H), 1.73 (d, J = 1.3 Hz, 3H), 1.16 – 1.13 (m, 2H), 1.12 – 1.01 (m, 2H)
1122		LCMS (ESI) m/z 631.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.00 (s, 1H), 8.83 (d, J = 4.8 Hz, 1H), 8.37 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.44 (d, J = 2.7 Hz, 1H), 7.36 (d, J = 9.0 Hz, 2H), 7.05 (dt, J = 14.5, 6.8 Hz, 1H), 5.46 (d, J = 57.5 Hz, 1H), 4.56 (s, 2H), 4.46 – 4.32 (m, 4H), 4.26 (t, J = 5.0 Hz, 4H), 1.79 (s, 3H)	1125		LCMS (ESI) m/z 728.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.78 – 8.71 (m, 2H), 8.64 (s, 1H), 7.75 (dd, J = 7.9, 1.0 Hz, 1H), 7.71 – 7.64 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 2.09 (s, 3H), 0.70 (s, 2H), 0.65 (s, 2H)

1126		1129	
LCMS (ESI) m/z 734.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.79 (d, J = 4.8 Hz, 1H), 8.58 (s, 1H), 8.38 (s, 1H), 7.57 (dd, J = 8.9, 2.7 Hz, 1H), 7.47 – 7.37 (m, 2H), 7.33 (d, J = 9.0 Hz, 1H), 4.49 (bs, 1H), 4.36 (t, J = 4.9 Hz, 2H), 4.18 (t, J = 4.9 Hz, 2H), 2.99 (s, 3 H), 1.73 (s, 3H), 1.51 (ddd, J = 13.2, 8.1, 4.9 Hz, 1H), 0.71 – 0.60 (m, 4H)		LCMS (ESI) m/z 730.3 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.81 – 8.71 (m, 2H), 8.65 (s, 1H), 7.76 (dd, J = 7.9, 1.0 Hz, 1H), 7.72 – 7.66 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 4.83 (s, 2H), 3.11 (s, 3H), 2.40 – 2.18 (m, 2H), 2.11 (s, 4H), 1.03 (d, J = 6.9 Hz, 6H)	
1127		1130	
LCMS (ESI) m/z 714.4 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.79 (d, J = 4.8 Hz, 1H), 8.54 (s, 1H), 8.34 (s, 1H), 7.57 (dd, J = 8.9, 2.7 Hz, 1H), 7.44 (d, J = 4.8 Hz, 1H), 7.39 – 7.29 (m, 2H), 4.51 (s, 1H), 4.46 – 4.30 (m, 4H), 4.19 (t, J = 5.1 Hz, 2H), 3.50 (d, J = 11.8 Hz, 2H), 3.26 – 3.11 (m, 2H), 3.08 (s, 3H), 2.75 – 2.66 (m, 1H), 2.25 (d, J = 12.7 Hz, 2H), 2.03 (d, J = 12.8 Hz, 2H), 1.79 (s, 3H), 1.07 (d, J = 6.9 Hz, 6H)		LCMS (ESI) m/z 469.5 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.76 – 8.69 (m, 4H), 8.62 (s, 2H), 7.76 – 7.61 (m, 7H), 7.52 (d, J = 4.8 Hz, 2H), 4.79 (s, 5H), 4.51 (s, 1H), 3.71 (s, 1H), 3.34 (s, 1H), 2.07 (s, 8H), 2.01 (s, 1H), 1.22 (s, 14H)	
1128		1131	
LCMS (ESI) m/z 712.4 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.79 (d, J = 4.8 Hz, 1H), 8.53 (s, 1H), 8.33 (s, 1H), 7.57 (dd, J = 8.9, 2.7 Hz, 1H), 7.44 (d, J = 4.9 Hz, 1H), 7.38 – 7.30 (m, 2H), 4.58 – 4.43 (m, 3H), 4.36 (t, J = 5.1 Hz, 2H), 4.19 (t, J = 5.0 Hz, 2H), 3.52 (d, J = 11.8 Hz, 3H), 3.18 (t, J = 12.7 Hz, 2H), 3.07 (s, 3H), 2.24 (d, J = 12.7 Hz, 2H), 2.17 – 1.95 (m, 3H), 1.80 (s, 3H), 1.06 (dd, J = 23.8, 2.3 Hz, 4H)		LCMS (ESI) m/z 744.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.76 (d, J = 4.8 Hz, 1H), 8.68 (d, J = 14.8 Hz, 2H), 7.76 (d, J = 9.0 Hz, 1H), 7.73 – 7.66 (m, 2H), 7.55 (d, J = 4.7 Hz, 1H), 4.82 (s, 2H), 4.21 (d, J = 6.9 Hz, 1H), 3.75 (s, 1H), 3.07 (s, 3H), 3.00 (s, 2H), 2.05 (s, 3H), 1.77 (s, 4H), 0.85 (s, 4H)	

1132		LCMS (ESI) m/z 718.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.73 (d, J = 4.8 Hz, 1H), 8.70 (s, 1H), 8.61 (s, 1H), 7.72 (d, J = 8.9 Hz, 1H), 7.68 – 7.63 (m, 2H), 7.51 (d, J = 4.8 Hz, 1H), 4.79 (s, 2H), 4.50 (s, 1H), 3.71 (t, J = 13.7 Hz, 7H), 3.08 (s, 3H), 2.22 (s, 2H), 2.06 (s, 3H), 2.03 – 1.91 (m, 2H)	1135		LCMS (ESI) m/z 744.0 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.75 (d, J = 1.8 Hz, 2H), 8.65 (s, 1H), 7.76 (d, J = 8.2 Hz, 1H), 7.69 (d, J = 8.9 Hz, 2H), 7.55 (d, J = 4.8 Hz, 1H), 6.72 (t, J = 75.2 Hz, 1H), 4.83 (s, 2H), 4.78 (s, 1H), 4.56 (s, 1H), 3.94 (d, J = 8.4 Hz, 1H), 3.57 (d, J = 11.9 Hz, 2H), 3.12 (s, 3H), 3.06 (d, J = 10.5 Hz, 2H), 2.77 – 2.64 (m, 2H), 2.54 (s, 1H), 2.11 (s, 7H). 19F NMR (377 MHz, DMSO-d6) δ -73.82, -82.25 (d, J = 75.1 Hz)
1133		LCMS (ESI) m/z 732.4 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.79 – 8.71 (m, 2H), 8.65 (s, 1H), 7.79 – 7.72 (m, 1H), 7.72 – 7.65 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 3.76 (s, 2H), 3.11 (s, 3H), 2.08 (s, 3H)	1136		LCMS: 1.77 Min, 700.2. [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 10.73 (s, 1H), 8.78 – 8.72 (m, 2H), 8.64 (s, 1H), 7.81 – 7.73 (m, 1H), 7.72 – 7.67 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 6.40 (t, J = 53.2 Hz, 1H), 4.82 (s, 2H), 4.12 (s, 4H), 3.92 (t, J = 16.0 Hz, 2H), 3.64 (d, J = 31.4 Hz, 4H), 2.06 (s, 3H)
1134		LCMS (ESI) m/z 720.0 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.76 – 8.68 (m, 2H), 8.62 (s, 1H), 7.76 – 7.69 (m, 1H), 7.69 – 7.62 (m, 2H), 7.52 (d, J = 4.8 Hz, 1H), 4.86 – 4.58 (m, 2H), 4.79 (s, 3H), 4.42 (s, 1H), 2.05 (s, 3H), 1.92 (bs, 3H)	1137		LCMS: 1.71 Min, 714.5 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 10.61 (s, 1H), 8.81 – 8.72 (m, 2H), 8.64 (s, 1H), 7.79 – 7.72 (m, 1H), 7.71 – 7.64 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 4.32 – 3.89 (m, 6H), 3.64 (m, 4H), 2.07 (d, J = 1.6 Hz, 6H), 2.00 (s, 3H), 1.74 (t, J = 19.6 Hz, 3H)

1139		MS (ESI) m/z 708.4 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.8 Hz, 1H), 8.61 (s, 1H), 8.41 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.7 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.39 (t, J = 5.0 Hz, 2H), 4.21 (t, J = 5.0 Hz, 2H), 3.75 – 3.30 (m, 10H), 3.09 (s, 3H), 1.75 (s, 6H)	1142		MS (ESI) m/z 698.4 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.78 – 8.73 (m, 2H), 8.65 (s, 1H), 7.76 (dd, J = 8.1, 0.8 Hz, 1H), 7.72 – 7.66 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 4.83 (s, 2H), 4.57 (d, J = 12.1 Hz, 1H), 3.67 (d, J = 12.6 Hz, 2H), 3.48 (dd, J = 22.6, 5.0 Hz, 2H), 3.33 (d, J = 11.5 Hz, 1H), 3.12 (s, 3H), 2.40 – 2.26 (m, 2H), 2.15 – 1.98 (m, 5H), 1.50 (d, J = 21.4 Hz, 6H)
1140		MS (ESI) m/z 706.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.77 (d, J = 4.8 Hz, 1H), 8.69 (d, J = 22.6 Hz, 2H), 7.76 (d, J = 9.0 Hz, 1H), 7.71 – 7.66 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 4.31 (s, 1H), 3.34 (s, 1H), 3.10 (s, 5H), 2.61 (s, 2H), 2.06 (s, 3H), 1.96 (q, J = 11.8 Hz, 2H), 1.82 (d, J = 12.1 Hz, 2H)	1143		MS (ESI) m/z 842.3 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 1H NMR (400 MHz, DMSO-d6) δ 13.21 (bs, 1H), 9.97 (s, 1H), 8.97 – 8.93 (m, 2H), 8.85 (d, J = 4.9 Hz, 1H), 8.69 (s, 1H), 8.50 (s, 1H), 8.10 – 8.05 (m, 2H), 7.77 (dd, J = 8.4, 0.5 Hz, 1H), 7.70 (dd, J = 8.4, 2.2 Hz, 1H), 7.66 (dd, J = 2.2, 0.5 Hz, 1H), 7.64 (dd, J = 4.9, 0.4 Hz, 1H), 4.82 (s, 2H), 4.57 (s, 1H), 3.96 – 3.26 (m, 4H), 3.11 (s, 3H), 2.26 (s, 2H), 2.04 (dd, J = 20.6, 10.2 Hz, 2H), 1.92 (s, 3H), 1.78 (t, J = 19.5 Hz, 3H)
1141		MS (ESI) m/z 702.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.76 (d, J = 4.8 Hz, 1H), 8.74 (s, 1H), 8.65 (s, 1H), 7.78 – 7.74 (m, 1H), 7.71 – 7.67 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 4.83 (s, 2H), 3.11 (s, 3H), 2.09 (s, 3H), 1.78 (t, J = 19.5 Hz, 3H)	1144		MS (ESI) m/z 842.4 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.12 (s, 1H), 9.28 (d, J = 2.3 Hz, 1H), 8.92 (d, J = 4.6 Hz, 1H), 8.84 (d, J = 4.9 Hz, 1H), 8.67 (s, 1H), 8.56 – 8.51 (m, 1H), 8.48 (s, 1H), 7.73 (ddd, J = 16.1, 10.9, 8.4 Hz, 3H), 7.66 (d, J = 2.2 Hz, 1H), 7.63 (d, J = 4.9 Hz, 1H), 4.81 (s, 2H), 3.11 (s, 3H), 1.90 (s, 3H)

1145		MS (ESI) m/z 630.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.89 (s, 1H), 8.69 (s, 1H), 8.41 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.42 (s, 1H), 7.40 (d, J = 2.7 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 4.40 (t, J = 5.1 Hz, 2H), 4.31 (d, J = 14.2 Hz, 2H), 4.24 (t, J = 5.1 Hz, 2H), 3.61 (d, J = 12.0 Hz, 2H), 3.45 (t, J = 13.1 Hz, 2H), 3.24 (q, J = 10.2 Hz, 2H), 2.91 (d, J = 3.4 Hz, 3H), 2.72 (s, 3H), 1.90 (s, 3H)	1149		MS (ESI) m/z 631.26 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 13.60 (bs, 1H), 8.56 (s, 1H), 7.58 (dd, J = 8.8, 2.4 Hz, 1H), 7.40 – 7.35 (m, 3H), 5.02 (bs, 1H), 4.39 (s, 2H), 4.19 (s, 2H), 3.90-3.82 (m, 2H), 3.74 (t, J = 8.0 Hz, 1H), 3.54 (d, J = 11.6 Hz 1H), 2.70 (s, 3H), 2.59 (s, 3H), 2.05 – 1.85 (m, 2H), 1.84 (s, 3H)
1146		MS (ESI) m/z 842.4 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 1H NMR (400 MHz, DMSO-d6) δ 13.03 (s, 1H), 8.90 (d, J = 4.9 Hz, 1H), 8.72 (ddd, J = 4.6, 1.7, 0.9 Hz, 1H), 8.65 (s, 1H), 8.60 (s, 1H), 8.30 – 8.25 (m, 1H), 8.21 (td, J = 7.7, 1.7 Hz, 1H), 7.80 – 7.72 (m, 2H), 7.72 – 7.68 (m, 2H), 7.66 (d, J = 4.8 Hz, 1H), 4.83 (s, 2H), 3.09 (s, 3H), 1.94 (s, 3H), 1.77 (t, J = 18.9 Hz, 2H)	1152		MS (ESI) m/z 616.24 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 13.56 (bs, 1H), 9.01 (s, 1H), 8.39 (s, 1H), 7.59 (dd, J = 2.8, 9.2 Hz, 1H), 7.41 (d, J = 2.4 Hz, 1H), 7.39 (s 1H), 7.34 (d, J = 8.8 Hz, 1H), 4.38 (s, 2H) 4.24 (s, 2H), 4.0-3.9 (m, 1H), 3.67-3.61 (m, 1H), 3.19 (s, 3H), 2.69 (bs, 5H), 2.35-2.31 (m, 2H), 1.86 (s, 3H)
1148		MS (ESI) m/z 676.21. [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.22 (bs, 1H), 8.83 (d, J = 4.6 Hz, 1H), 8.49 (s, 1H), 7.94 (d, J = 7.8 Hz, 1H), 7.87 (t, J = 7.4 Hz, 1H), 7.77 (m, 2H), 7.60 (dd, J = 2.4, 8.8 Hz, 1H), 7.47 (d, J = 4.7 Hz, 1H), 7.44 (d, J = 2.4 Hz, 1H), 7.37 (d, J = 8.9 Hz, 1H), 4.44 (s, 2H), 4.27 (s, 2H), 2.77 (s, 3H), 1.85 (s, 3H)	1157		MS (ESI) m/z 789.51 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.66 (s, 1H), 8.87 (d, J = 4.8 Hz, 1H), 8.60 (m, 1H), 8.58 (s, 1H), 7.60 (dd, J = 8.8, 2.4 Hz, 1H), 7.54 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.4 Hz, 1H), 7.38 (d, J = 9.2 Hz, 1H), 4.39 (t, J = 6.0 Hz, 2H), 4.35-4.25 (m, 1H), 4.19 (t, J = 6.0 Hz, 2H), 3.58 (s, 3H), 3.40-3.20 (m, 2H), 3.07 (s, 5H), 2.65-2.55 (m, 2H), 1.99-1.90 (m, 2H), 1.85-1.79 (m, 2H), 1.74 (s, 3H)

1160		MS (ESI) m/z 692.45 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 13.05 (bs, 1H), 8.83 (s, 1H), 8.75 (d, J = 4.6 Hz, 1H), 8.64 (s, 1H), 7.75 (d, J = 8.2 Hz, 1H), 7.69 (s, 1H), 7.66 (s, 1H), 7.52 (d, J = 4.5 Hz, 1H), 4.83 (s, 2H), 4.31 (bs, 1H), 3.43 (bs, 7H), 2.85 (s, 4H), 2.11 (s, 3H)	1163		MS (ESI) m/z 686.0 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 13.03 (s, 1H), 8.83 (s, 1H), 8.75 (d, J = 4.8 Hz, 1H), 8.64 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.70-7.66 (m, 1H), 7.53 (d, J = 4.8 Hz, 1H), 4.72 (s, 2H), 3.80 (bs, 4H), 3.39 (bs, 4H), 3.05-3.02 (m, 5H), 2.16 (s, 3H)
1161		MS (ESI) m/z 708.3 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.84 (s, 1H), 8.76 (d, J = 4.8 Hz, 1H), 8.65 (s, 1H), 7.76 (dd, J = 8.3, 0.5 Hz, 1H), 7.71 – 7.65 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 4.84 (s, 2H), 4.53 (s, 2H), 4.06 – 2.83 (m, 8H), 2.13 (s, 3H)	1164		MS (ESI) m/z 694.52 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.8 Hz, 1H), 8.68 (s, 1H), 8.45 (s, 1H), 7.60 (dd, J = 8.8 Hz, 2.4 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.8 Hz, 1H), 7.36 (d, J = 8.8 Hz, 1H), 4.72-4.54 (m, 2H), 4.39 (bs, 2H), 4.22 (bs, 2H), 3.25-2.78 (m, 10H), 1.81 (s, 3H), 1.45 (bs, 3H)
1162		MS (ESI) m/z 636.25 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.18 (bs, 1H), 8.84 (s, 1H), 8.75 (d, J = 4.8 Hz, 1H), 8.65 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.70-7.65 (m, 2H), 7.53 (d, J = 4.8 Hz, 1H), 4.84 (s, 2H), 4.38 (m, 2H), 3.79 (m, 2H,), 3.49 (m, 4H), 3.03 (m, 1H), 2.14 (s, 3H), 0.93 (m, 4H)	1165		MS (ESI) m/z, 714.50 [M+1] +; 1H-NMR (400 MHz, DMSO-d6) δ 9.80 (bs, 1H), 8.76 (s, 1H), 8.75 (s, 1H), 8.65 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.70-7.67 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 4.83 (s, 2H), 4.56 (bs, 1H), 3.56 (bs, 4H), 3.11 (bs, 1H), 3.06 (s, 3H), 3.05 (bs, 4H), 2.13 (bs, 4H), 2.11 (s, 3H)

1166		1169	
MS (ESI) m/z 714.58 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 8.76-8.74 (m, 2H), 8.65 (s, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.70-7.67 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 4.58-4.38 (m, 2H), 3.11 (s, 3H), 2.90-2.88 (m, 2H), 2.50-2.32 (m, 4H), 2.20-2.15 (m, 5H), 2.12-2.10 (m, 2H)		MS (ESI) m/z 696.24 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 8.76-8.75 (m, 2H), 8.64 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.69-7.67 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 4.54 (s, 1H), 3.74-3.72 (m, 4H), 3.31-3.29 (m, 2H), 3.12 (s, 3H), 2.28-2.22 (m, 2H), 2.13-2.10 (m, 5H), 1.25 (d, J = 19.6 Hz, 2H), 0.96 (d, J = 8.0 Hz, 2H)	
1167		1170	
MS (ESI) m/z 668.42 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.08 (bs, 1H), 10.22 (bs, 1H), 8.85 (s, 1H), 8.76 (d, J = 4.8 Hz, 1H), 8.65 (s, 1H), 7.76 (d, J = 8.4 Hz, 1H), 7.69-7.66 (m, 2H), 7.53 (d, J = 4.8 Hz, 1H), 4.83 (s, 2H), 4.39 (d, J = 11.6 Hz, 2H), 3.76 (bs, 6H), 3.43 (bs, 2H), 2.14 (s, 3H), 1.29 (d, J = 18.8 Hz, 2H), 0.99 (d, J = 7.6 Hz, 2H)		MS (ESI) m/z 736.43 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 8.76-.8.74 (m, 2H), 8.64 (s, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.70-7.67 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 4.56-4.52 (m, 3H), 3.67-3.55 (m, 4H), 3.25-3.19 (m, 2H), 3.11 (s, 3H), 2.23-2.20 (m, 2H), 2.17-2.10 (m, 5H)	
1168		1171	
MS (ESI) m/z 722.51 [M+1] +; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.8 Hz, 1H), 8.61 (s, 1H), 8.41 (s, 1H), 7.60 (dd, J = 8.8 Hz, 2.4 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.8 Hz, 1H), 7.36 (d, J = 9.2 Hz, 1H), 4.52 (bs, 1H), 4.39 (s, 2H), 4.21 (s, 2H), 3.90-3.82 (m, 1H), 3.36-3.31 (m, 6H), 3.09 (s, 3H), 2.33-2.27 (m, 1H), 2.02-2.07 (m, 4H), 1.79 (s, 3H), 0.99 (t, J = 7.2 Hz, 3H)		MS (ESI) m/z 664.42 [M+1] +; 1H NMR (400 MHz, DMSO-d6) δ 8.76 (d, J = 6.0 Hz, 2H), 8.65 (s, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.70-7.67 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 4.83 (s, 2H), 4.60-4.59 (m, 1H), 3.66 (d, J = 11.6 Hz, 2H), 3.43-3.22 (m, 2H), 3.09 (s, 3H), 2.85 (bs, 1H), 2.10 (s, 7H), 0.95-0.85 (m, 4H)	

1172 Chiral	MS (ESI) m/z 744.02 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 8.76-8.74 (m, 2H), 8.64 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.70-7.67 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 6.89-6.52 (m, 1H), 4.82 (s, 2H), 4.58-4.45 (m, 2H), 3.48-3.38 (m, 5H), 3.10 (s, 3H), 3.08-3.06 (m, 2H), 2.40.2.38 (m, 2H), 2.20-2.10 (m, 5H)	1174	MS (ESI) m/z 710.42 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 9.40 (bs, 1H), 8.76-8.74 (m, 2H), 8.64 (s, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.70-7.67 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 4.56-4.53 (m, 1H), 3.94-3.80 (m, 4H), 3.66-3.59 (m, 4H), 3.11 (s, 3H), 2.40-2.34 (m, 3H), 2.27-2.24 (m, 1H), 2.10-2.01 (m, 5H), 1.91-1.88 (m, 1H), 1.70-1.63 (m, 1H)
1173a Chiral	MS (ESI) m/z 762.47 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 8.77-8.75 (m, 2H), 8.65 (s, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.70 (d, J = 2.0 Hz, 1H), 7.68 (s, 1H), 7.56 (d, J = 4.8 Hz, 1H), 4.83 (s, 2H), 4.73 (quin, J = 7.2 Hz, 1H), 4.59 (bs, 1H), 3.62 (bs, 4H), 3.41 (bs, 1H), 3.12 (bs, 5H), 2.89 (bs, 2H), 2.11 (bs, 7H)	1175 Chiral	MS (ESI) m/z 732.40 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.77-8.74 (m, 2H), 8.65 (s, 1H), 7.76 (d, J = 8.4 Hz, 1H), 7.69 (d, J = 1.6 Hz, 1H), 7.68 (s, 1H), 7.55 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 4.48 (bs, 1H), 3.65 (m, 4H), 3.10 (s, 3H), 2.50-2.39 (m, 2H), 2.09 (s, 3H), 2.04 (bs, 4H), 1.44-1.33 (m, 2H)
1173b	MS (ESI) m/z 671.41 [M+1] +; 1H-NMR (400 MHz, DMSO-d6) δ 8.76 (d, J = 4.8 Hz, 1H), 8.68 (d, J = 1.6 Hz, 2H), 7.75 (d, J = 8.4 Hz, 1H), 7.70-7.67 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 4.82 (s, 3H), 3.38-3.28 (m, 4H), 3.11 (s, 9H), 2.02 (s, 3H), 1.97-1.91 (m, 2H), 1.89-1.83 (m, 2H)	1176	MS (ESI) m/z 720.44 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.77 (d, J = 4.4 Hz, 1H), 8.74 (s, 1H), 8.67 (s, 1H), 7.76 (d, J = 8.8 Hz, 1H), 7.69-7.67 (m, 2H), 7.56 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 4.18-4.15 (m, 1H), 3.67-3.64 (m, 2H), 3.29 (bs, 2H), 3.07 (d, J = 9.2 Hz, 2H), 2.60-2.55 (m, 2H), 2.06 (s, 3H), 1.96-1.94 (m, 2H), 1.85-1.82 (m, 2H), 1.11 (t, J = 6.8 Hz, 3H)

1177		1182	
MS (ESI) m/z 716.60 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.14 (bs, 1H), 8.77 (d, J = 4.4 Hz, 2H), 8.66 (s, 1H), 7.77-7.74 (m, 1H), 7.69-7.68 (m, 2H), 7.56 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 4.39 (bs, 1H), 3.63 (bs, 4H), 3.30 (bs, 4H), 2.34 (bs, 2H), 2.08 (s, 5H), 1.75 (t, J = 18.0 Hz, 3H), 1.13 (t, J = 6.8 Hz, 3H)		MS (ESI) m/z 730.45 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.76 (d, J = 4.8 Hz 1H), 8.71 (s, 1H), 8.65 (s, 1H), 7.76-7.74 (m, 1H), 7.69-7.67 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 6.46 (t, J = 54.4 Hz, 1H), 4.81 (s, 2H), 4.50 (d, J = 6.8 Hz, 2H), 4.44 (d, J = 6.4 Hz, 2H), 4.32-4.28 (m, 1H), 3.16 (s, 3H), 2.91-2.89 (m, 2H), 2.59-2.53 (m, 2H), 2.05 (s, 3H), 1.89-1.86 (m, 4H)	
1180		1183	
MS (ESI) m/z 713.37 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.62 (bs, 1H), 8.79 (s, 1H), 8.75 (d, J = 4.8 Hz, 1H), 8.65 (s, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.70-7.68 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 4.83 (s, 2H), 4.41-4.39 (d, J = 12.8 Hz, 2H), 3.83-3.69 (m, 4H), 3.23-3.14 (m, 4H), 2.43 (m, 2H), 2.33-2.25 (m, 3H), 2.10 (s, 3H), 1.91-1.88 (m, 2H)		MS (ESI) m/z 821.52 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 12.71 (s, 1H), 8.82 (d, J = 4.8 Hz, 1H), 8.75 (d, J = 2.4 Hz, 2H), 7.77 (d, J = 8.8 Hz, 1H), 7.71-7.68 (m, 2H), 7.62 (d, J = 4.8 Hz, 1H), 5.21 (quin, J = 7.6 Hz, 1H), 4.97-4.90 (m, 4H), 4.82 (s, 2H), 4.59 (m, 1H), 3.69-3.49 (m, 4H), 3.11 (bs, 5H), 2.32 (m, 2H), 1.98 (m, 2H), 1.93 (s, 3H), 1.76 (t, J = 19.6 Hz, 3H)	
1181	Chiral	1184	
MS (ESI) m/z 696.32 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.74 (bs, 1H), 8.78-8.72 (m, 2H), 8.64 (s, 1H), 7.75 (d, J = 8.1 Hz, 1H), 7.70-7.62 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 5.35-5.18 (m, 1H), 4.82 (s, 2H), 4.60-4.52 (m, 1H), 4.04-3.98 (m, 1H), 3.60-3.50 (m, 2H), 3.15-2.95 (m, 5H), 2.80-2.45 (m, 4H), 2.20-2.00 (m, 7H)		MS (ESI) m/z 728.48 [M+1] +; 1H-NMR (400 MHz, DMSO-d6) δ 13.11 (bs, 1H), 8.78-8.76 (m, 2H), 8.65 (s, 1H), 7.76 (d, J = 9.2 Hz, 1H), 7.70-7.68 (m, 2H), 7.56 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 4.37 (bs, 1H), 3.75- 3.59 (m, 5H), 3.05 (bs, 6H), 2.15 (bs, 4H), 2.10 (s, 3H), 1.16 (t, J = 6.4 Hz, 3H)	

1185		MS (ESI) m/z 712.32 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 13.09 (bs, 1H), 8.76-8.74 (m, 2H), 8.64 (s, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.70-7.67 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 4.82-4.75 (m, 6H), 4.55 (bs, 1H), 3.91-3.85 (m, 2H), 3.52-3.35 (m, 4H), 3.10 (s, 3H), 2.32-2.21 (m, 2H), 2.09 (bs, 5H)	1188		MS (ESI) m/z 791.62 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.47 (s, 1H), 8.81-8.78 (m, 3H), 7.77 (d, J = 8.40 Hz, 1H), 7.71-7.67 (m, 2H), 7.62 (d, J = 4.80 Hz, 1H), 4.83 (s, 2H), 4.59 (bs, 1H), 3.74-3.54 (m, 6H), 3.08 (s, 3H), 2.98-2.88 (m, 6H), 2.11-2.05 (m, 4H), 2.00 (s, 3H)
1186		MS (ESI) m/z 694.43 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.78 (d, J = 2.8 Hz, 1H), 8.76 (s, 1H), 8.65 (s, 1H), 7.76 (d, J = 9.2 Hz, 1H), 7.69 (d, J = 6.8 Hz, 2H), 7.55 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 4.75 (bs, 4H), 4.38 (bs, 2H), 3.61 (d, J = 6.8 Hz, 2H), 3.52 (bs, 2H), 3.16 (bs, 2H), 2.16-2.10 (m, 7H), 1.15 (t, J = 6.8 Hz, 3H)	1189		MS (ESI) m/z 758.56 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.76-8.74 (m, 2H), 8.64 (s, 1H), 7.76 (d, J = 8.4 Hz, 1H), 7.70-7.67 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 6.65 (t, J = 74.4 Hz, 1H), 4.82 (s, 2H), 4.57-4.47 (m, 2H), 3.53 (d, J = 11.6 Hz, 2H), 3.23-3.10 (m, 7H), 2.54-2.49 (m, 2H), 2.32-2.28 (m, 1H), 2.16-2.09 (m, 7H), 2.06-1.91 (m, 2H)
1187		MS (ESI) m/z 715.47 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.75 (d, J = 4.8 Hz, 1H), 8.73 (s, 1H), 8.63 (s, 1H), 7.75 (d, J = 8.8, 1H), 7.68-7.68 (m, 2H), 7.63 (d, J = 4.8 Hz, 1H), 6.69 (t, J = 75.2 Hz, 1H), 4.81 (s, 2H), 4.70 (t, J = 5.6 Hz, 1H), 4.04 (d, J = 13.2 Hz, 2H), 3.60 (t, J = 6.4 Hz, 2H), 3.32-3.27 (m, 2H), 3.00 (t, J = 6.8 Hz, 2H), 2.37 (bs, 1H), 2.05 (s, 3H), 1.80 (d, J = 10.4 Hz, 2H), 1.39-1.32 (m, 2H)	1190		MS (ESI) m/z 716.53 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.09 (bs, 1H), 9.32 (bs, 1H), 8.76-8.74 (m, J = 7.8 Hz, 2H), 8.64 (s, 1H) 7.75 (d, J = 8.2 Hz, 1H), 7.71-7.65 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 4.60-4.50 (m, 1H), 3.69 (d, J = 10.4 Hz, 2H), 3.30-311 (m, 4H), 3.10 (s, 3H), 2.50-2.32 (merged, 2H), 2.20-2.05 (m, 7H), 1.70 (t, J = 19.2 Hz, 3H)

1191		1196	
MS (ESI) m/z 752.52 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.15 (s, 1H), 8.77-8.741 (m, 2H), 8.66 (s, 1H), 7.75 (d, J = 9.2 Hz, 1H), 7.68 (d, J = 6.0 Hz, 2H), 7.55 (d, J = 4.8 Hz, 1H), 6.57 (t, J = 52.0 Hz, 1H), 4.81 (s, 2H), 4.29 (bs, 1H), 3.64 (d, J = 6.8 Hz, 2H), 3.03 (bs, 4H), 2.50 (s, 2H), 2.06 (s, 3H), 1.98-1.84 (m, 4H), 1.13-1.08 (m, 3H)		MS (ESI) m/z 644.27 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 14.39 (bs, 1H), 8.62 (s, 1H), 7.59 (dd, J = 2.48, 8.88 Hz, 1H), 7.40-7.38 (m, 2H), 7.35 (d, J = 8.92 Hz, 1H), 4.63-4.59 (m, 2H), 4.47 (bs, 2H), 4.39 (t, J = 4.64 Hz, 2H), 4.23 (t, J = 4.64 Hz, 3H), 2.82 (bs, 6H), 2.70 (s, 3H), 2.54 (s, 3H), 1.94 (s, 3H)	
1194	Chiral	1198	
MS (ESI) m/z 602.22 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 13.62 (bs, 1H), 9.01 (s, 1H), 8.41 (s, 1H), 7.62-7.57 (m, 2H), 7.41 (d, J = 2.4 Hz, 1H), 7.39 (s, 1H), 7.34 (d, J = 8.0 Hz, 1H), 4.38 (s, 2H), 4.24 (s, 2H), 4.19-4.15 (m, 1H), 3.56 (bs, 1H), 2.68-2.62 (m, 5H), 2.32-2.27 (m, 2H), 1.84 (s, 3H)		MS (ESI) m/z 620.15 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.63 (bs, 1H) 8.55 (s, 1H), 7.59 (dd, J = 8.88, 2.62 Hz, 1H), 7.42 (t, J = 6.0 Hz, 2H), 7.35 (d, J = 8.8 Hz, 1H), 4.40 (d, J = 4.4 Hz, 2H), 4.26 (s, 2H), 4.26 (t, J = 4.8 Hz, 2H), 2.98 - 3.04 (m, 2H), 2.55 (d, J = 4.0 Hz, 1H), 1.93 (s, 3H), 1.13-1.36 (m, 7H)	
1195		1199	
MS (ESI) m/z 720.41 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 8.76 (d, J = 4.56 Hz, 1H), 8.68 (s, 1H), 8.59 (s, 1H), 7.74 (d, J = 8.12 Hz, 1H), 7.67-7.64 (m, 2H), 7.43 (d, J = 4.64 Hz, 1H), 4.80 (s, 2H), 4.29-4.23 (m, 1H), 3.83 (s, 3H), 3.21 (q, J = 10.08 Hz, 2H), 3.10 (s, 3H), 3.04 (d, J = 11.4 Hz, 2H), 2.54 (bs, 2H), 2.03 (s, 3H), 1.98-1.89 (m, 2H), 1.78 (d, J = 10.52 Hz, 2H)		MS (ESI) m/z 629.24 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.69 (bs, 1H), 8.49 (s, 1H), 7.59 (dd, J = 8.88, 2.62 Hz, 1H), 7.36 - 7.43 (m, 3H), 4.41 (t, J = 6.0 Hz, 2H), 4.20 (t, J = 6.0 Hz, 2H), 4.26 (t, J = 4.8 Hz, 2H), 3.34 (s, 6H), 2.96 - 3.01 (m, 2H), 2.40 (d, J = 4.0 Hz, 1H), 1.81 (s, 3H), 1.31 (t, J = 12.8 Hz, 3H), 1.03 - 1.12 (m, 4H)	

1202 Chiral		MS (ESI) m/z 656.33 [M+1]+; 1H NMR (400 MHz, DMSO-d6) 14.39 (bs, 1H), 10.23 (bs, 1H), 8.68 (s, 1H), 7.59 (d, J = 8.0, 2.4 Hz, 1H), 7.45-7.38 (m, 2H), 7.39 (d, J = 8.8 Hz, 1H), 4.87 (d, J = 4.8 Hz, 2H), 4.39 (bs, 2H), 4.23 (bs, 2H), 3.91-3.82 (m, 2H), 3.60-3.49 (m, 2H), 3.00-2.88 (m, 2H), 2.75 (s, 3H), 2.70 (s, 3H), 2.53 (s, 3H), 1.86 (s, 3H)	
1203		MS (ESI) m/z 656.33 [M+1]+; 1H NMR (400 MHz, DMSO-d6) 14.39 (bs, 1H), 10.23 (bs, 1H), 8.68 (s, 1H), 7.59 (d, J = 8.0, 2.4 Hz, 1H), 7.45-7.38 (m, 2H), 7.39 (d, J = 8.8 Hz, 1H), 4.87 (d, J = 4.8 Hz, 2H), 4.39 (bs, 2H), 4.23 (bs, 2H), 3.91-3.82 (m, 2H), 3.60-3.49 (m, 2H), 3.00-2.88 (m, 2H), 2.75 (s, 3H), 2.70 (s, 3H), 2.53 (s, 3H), 1.86 (s, 3H)	
1204		MS (ESI) m/z 554.23 [M+1] +; 1H NMR (400 MHz, DMSO-d6) δ 11.14 (s, 1H), 8.99 (s, 1H), 7.37 (s, 1H), 7.31-7.28 (m, 2H), 7.21 (d, J = 2.4 Hz, 1H), 7.14 (d, J = 9.2 Hz, 1H), 6.92 (s, 1H), 6.38 (bs 1H), 4.33 (bs, 2H), 4.30 (bs, 2H), 3.80 (s, 2H), 2.60 (t, J = 3.6 Hz, 1H), 2.18 (s, 3H), 1.21 (d, J = 7.6 Hz, 2H), 1.12 (bs, 2H)	
1216		MS (ESI) m/z 641.37 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 13.75 (bs, 1H), 8.84 (s, 1H), 8.31 (s, 1H), 7.60 (dd, J = 2.52, 8.88 Hz, 1H), 7.45 (s, 1H), 7.41 (d, J = 2.48 Hz, 1H), 7.36 (d, J = 8.96 Hz, 1H), 4.39 (t, J = 4.40 Hz, 2H), 4.26 (t, J = 4.44 Hz, 2H), 3.84 (bs, 2H), 3.52 (bs, 2H), 3.31 (s, 3H), 3.01 (q, J = 7.48 Hz, 2H), 2.97 (bs, 1H), 2.91 (bs, 2H), 1.97 (s, 3H), 1.36 (t, J = 7.56 Hz, 3H)	
1217		MS (ESI) m/z 706.31[M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 13.43 (bs, 1H), 8.59 (s, 1H), 8.16 (d, J = 3.6 Hz, 2H), 7.59 (dd, J = 2.0, 7.2 Hz, 1H), 7.54 (bs, 3H), 7.41 (bs, 3H), 4.45 (bs, 4H), 4.27 (bs, 2H), 3.60 (bs, 2H), 3.48 (bs, 2H), 3.33 (bs, 2H), 2.90 (s, 3H), 2.66 (bs, 3H), 2.008 (s, 3H)	
1219		MS (ESI) m/z 656.26 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 8.56 (s, 1H), 8.41 (s, 1H), 7.58 (dd, J = 2.48, 8.92 Hz, 1H), 7.42 (m, 2H), 7.35 (d, J = 8.9 Hz, 1H), 4.39-4.37 (m, 2H), 4.20-4.19 (m, 2H), 3.36-3.33 (m, 1H), 3.13-3.07 (m, 1H), 3.01 (q, J 7.5 Hz, 2H), 2.75-2.72 (m, 2H), 2.32 (s, 3 H), 2.20-2.15 (m, 1H), 1.75 (s, 3H), 1.34 (t, J = 7.5 Hz, 3H), 0.70-0.65 (m, 2H), 0.55-0.70 (m, 2H)	

1220		1231	
MS (ESI) m/z 642.25 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 13.76 (bs, 1H), 9.42 (bs, 2H), 8.62 (s, 1H), 8.41 (s, 1H), 7.60 (dd, J = 2.4, 8.8 Hz, 1H), 7.46 (s, 1H), 7.42 (d, J = 2.4 Hz, 1H), 7.37 (d, J = 8.8 Hz, 1H), 4.44-4.40 (m, 3H), 4.22 (s, 2H), 3.51-3.38 (m, 1H), 3.41-319 (m, 2H), 3.04 (m, 3H), 1.83 (s, 3H), 1.36 (m, 4H), 0.84 (m, 1H)		MS (ESI) m/z 592.13 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.79-8.77 (m, 2H), 8.15 (s, 1H), 7.57 (dd, J = 2.60, 8.84 Hz, 1H), 7.34-7.32 (m, 3H), 4.38 (t, J = 4.60 Hz, 2H), 4.26 (t, J = 4.56 Hz, 2H), 1.77 (s, 3H), 1.63 (s, 9H)	
1227		1232	
MS (ESI) m/z 638.14 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 13.56 (bs, 1H), 9.65 (bs, 1H), 9.01 (s, 1H), 8.45 (s, 1H), 7.59 (dd, J = 2.4, 8.8 Hz, 1H), 7.42 (d, J = 2.4 Hz, 2H), 7.36-7.32 (m, 2H), 7.28-7.23 (m, 2H), 4.41 (bs, 2H), 4.26 (bs, 2H), 2.70 (s, 3H), 2.16 (s, 3H), 1.38 (s, 3H)		MS (ESI) m/z 615.03[M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.96 (s, 1H), 8.34 (s, 1H), 7.60 (dd, J = 8.8 Hz, 2.4 Hz, 1H), 7.47 (s, 1H), 7.44 (d, J = 2.4 Hz, 1H), 7.35 (d, J = 8.8 Hz, 1H), 4.40-3.79 (m, 10H), 3.05-3.00 (m, 2H), 2.95 (s, 3H). 1.83 (s, 3H), 1.38-1.34 (t, J = 7.6 Hz, 3H)	
1229	Chiral	1233	
MS (ESI) m/z 698.43 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.59 (bs, 1H), 8.76 (d, J = 4.8 Hz, 1H), 8.72 (s, 1H), 8.65 (s, 1H), 7.75 (d, J = 9.2 Hz, 1H), 7.70-7.65 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 4.90-4.79 (m, 4H), 4.40-4.29 (m, 1H), 3.65-3.35 (m, 3H), 3.09 (s, 3H), 2.85-2.80 (m, 3H), 2.18-1.65 (m, 11H)		MS (ESI) m/z 586.32 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.94 (s, 1H), 8.68 (d, J = 4.80 Hz, 1H), 8.51 (s, 1H), 7.74 (d, J = 8.40 Hz, 1H), 7.67-7.63 (m, 3H), 7.40 (d, J = 4.80 Hz, 1H), 4.88 (s, 2H), 2.18 (s, 3H), 1.59 (s, 9H)	

1234		MS (ESI) m/z 631.23 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.56 (s, 1H), 8.49 (s, 1H), 7.59 (dd, J = 8.88, 2.50 Hz, 1H), 7.41 (d, J = 2.60 Hz, 1H), 7.40 (s, 1H), 7.35 (d, J = 8.96 Hz, 1H), 4.37 (t, J = 5.00 Hz, 2H), 4.19 (t, J = 5.00 Hz, 2H), 4.11 (bs, 1H), 3.92-3.70 (m, 4H), 3.29 (s, 3H), 2.70 (s, 3H), 2.11-2.04 (m, 2H), 1.81 (s, 3H)	1257		MS (ESI) m/z 572.27 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.86 (s, 1H), 8.65 (d, J = 4.8 Hz, 1H), 7.71 (d, J = 5.2 Hz, 1H), 7.55 (dd, J = 8.8, 2.8 Hz, 1H), 7.44 (d, J = 5.2 Hz, 1H), 7.39 (d, J = 2.4 Hz, 1H), 7.31 (d, J = 9.2 Hz, 1H), 7.21 (d, J = 4.4 Hz, 1H), 4.36–4.23 (m, 6H), 3.60 (d, J = 12.0 Hz, 2H), 3.41 (t, J = 11.6 Hz, 2H), 3.29-3.16 (m, 2H), 2.90 (s, 3H), 1.81 (s, 3H)
1235		MS (ESI) m/z 631.26 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.76 (s, 1H), 8.54 (s, 1H), 8.48 (s, 1H), 7.59 (dd, J =8.8 Hz, 2.4 Hz, 1H) 7.43 (s, 2H), 7.35 (d, J =8.8 Hz, 1H), 5.07 (d, J =2.8 Hz, 1H), 4.41 (bs, 1H), 4.37-4.36 (m, 2H), 4.42 (m, 2H), 3.93-3.87 (m, 2H), 3.79-3.75 (m, 1H), 3.59 (d, J =11.2 Hz, 1H), 3.01 (q, J =7.6 Hz, 2H), 2.04-2.01 (m, 1H), 1.93 (bs, 1H), 1.75 (s, 3H), 1.35 (t, J =7.6 Hz, 3H)	1258		MS (ESI) m/z 559.20 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.69 (s, 1H), 8.65 (d, J = 3.8, 1H), 7.75 (d, J = 4.76, 1H), 7.55-7.53 (m, 1H), 7.47 (d, J = 5.0 Hz, 1H), 7.39 (s, 1H), 7.31 (d, J = 8.6 Hz, 1H), 7.21 (d, J = 3.6 Hz, 1H), 5.07 (s, 1H), 4.41 (s, 1H), 4.35 (t, J = 3.6 Hz, 2H), 4.19 (t, J = 5.6 Hz, 2H), 3.89 (t, J = 5.9 Hz, 2H), 3.77-3.73 (m, 1H), 3.58 (d, J = 11.4 Hz, 1H), 2.00-1.98 (m, 1H), 1.93 (bs, 1H), 1.74 (s, 3H)
1236		MS (ESI) m/z 631.23 [M+1]+ ; 1H NMR (400 MHz, DMSO-d6) δ 14.35 (bs, 1H), 8.53 (s, 1H), 7.58 (dd, J = 8.96, 2.36 Hz, 1H), 7.39-7.34 (m, 3H), 4.45-4.36 (m, 3H), 4.21 (t, J = 4.24 Hz, 2H), 3.92-3.86 (m, 2H), 3.78-3.68 (m, 2H), 3.56 (d, J = 12.04 Hz, 1H), 2.70 (s, 3H), 2.53 (s, 3H), 2.22-1.86 (m, 5H)	1264		MS (ESI) m/z 633.24 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.99 (s, 1H), 8.83 (d, J = 4.8 Hz, 1H), 8.37 (s, 1H), 7.61 (d, J = 9.2 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.44 (s, 1H), 7.36 (d, J = 8.8 Hz, 1H), 4.41 (t, J = 5.2 Hz, 2H), 4.27 (t, J = 4.0 Hz, 2H), 3.52 (bs, 6H), 3.77-3.25 (m, 2H), 2.92 (d, J = 3.2 Hz, 3H), 1.82 (s , 3H)

1265		1273	
MS (ESI) m/z 642.16 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 9.54 (s, 1H), 8.80 (d, J = 4.8 Hz,1H), 8.55 (s, 1H), 7.57 (dd, J = 2.4, 8.8 Hz ,1H), 7.45 (d, J = 4.8 Hz, 1H), 7.40-7.36 (m, 2H), 4.55 (s, 2H), 4.48 (d, J = 14 Hz, 4H), 4.40 (s, 2H), 4.22 (d, J = 14.4 Hz, 4H), 2.85 (d, J = 4 Hz, 3H), 2.60 (s, 3H), 1.86 (s, 3H)		MS (ESI) m/z 624.30 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.00 (bs, 1H), 8.76 (d, J = 4.80 Hz, 1H), 8.66 (s, 1H), 7.76-7.64 (m, 3H), 7.53 (d, J = 4.80 Hz, 1H), 4.82 (s, 2H), 4.38-4.35 (m, 2H), 3.63-3.60 (m, 2H), 3.48-3.25 (m, 4H), 2.91 (s, 3H), 2.73 (s, 3H), 2.14 (s, 3H)	
1266		1274	
MS (ESI) m/z 629.0 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 8.80 (d, J = 4.8 Hz, 1H), 8.55 (s, 1H), 8.49 (bs, 2H), 7.57 (dd, J = 2.4, 8.8 Hz, 1H), 7.45 (d, J = 4.8 Hz, 1H), 7.40-7.36 (m, 2H), 4.52 (s, 4H), 4.39 (d, J = 4.8 Hz, 2H), 4.22 (d, J = 5.2 Hz, 6H), 2.60 (s, 3H), 1.85 (s, 3H)		MS (ESI) m/z 680.33 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.81 (d, J = 4.72 Hz, 1H), 8.52 (s, 1H), 7.59 (dd, J = 8.88, 2.44 Hz, 1H), 7.44 (d, J = 4.68, 1H), 7.40 (d, J = 2.4 Hz, 1H), 7.36 (d J = 9.0 Hz, 1H), 6.35-6.05 (m, 1H), 4.40 (t, J = 4.48 Hz, 2H), 4.20 (t, J = 4.72 Hz, 2H), 3.64 (s, 4H), 2.87-2.878 (m, 2H), 2.71 (s, 4H), 2.63 (s, 3H), 1.78 (s, 3H)	
1268		1279	
MS (ESI) m/z 678.28 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.82 (bs, 1H), 8.74 (d, J = 4.8 Hz, 1H), 8.48 (s, 1H), 8.05 (d, J = 8.4 Hz, 2H), 7.76 (s, 1H), 7.56 (dd, J = 8.8, 2.4 Hz, 1H), 7.41 (d, J = 2.8 Hz, 1H), 7.34 (d, J = 8.9 Hz, 1H), 7.28 (d, J = 4.4 Hz, 1H), 7.10 (d, J = 8.8 Hz, 2H), 4.43-4.36 (m, 2H), 4.27-4.17 (m, 4H), 3.86 (s, 3H), 3.62-3.53 (m, 2H), 3.41-3.29 (m, 2H), 3.21-3.10 (m, 2H), 2.90 (s, 3H), 1.78 (s, 3H)		MS (ESI) m/z 622.22 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.01 (s, 1H), 8.82 (d, J = 4.8 Hz, 1H), 8.39 (s, 1H), 7.59 (dd, J = 8.8, 2.4 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.4 Hz, 1H), 7.35 (d, J = 8.8 Hz, 1H), 4.45-4.36 (m, 2H), 4.30-4.20 (m, 2H), 4.15-4.00 (m, 1H), 2.70-2.50 (m, 2H), 2.44-2.20 (m, 3H), 2.14-2.01 (m, 1H), 1.84 (s, 3H)	

1281		MS (ESI) m/z 687.47 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 10.05 (bs, 1H), 8.87 (d, J = 3.2 Hz, 1H), 8.74 (s, 1H), 8.72 (d, J = 4.8 Hz, 1H), 8.47 (s, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.69 (d, J = 2.0 Hz, 2H), 7.66 (s, 1H), 7.49 (d, J = 4.4 Hz, 1H), 6.53 (tt, J = 5.2, 51.2 Hz, 1H), 4.82 (s, 2H), 4.49 (bs, 1H), 3.64 (bs, 4H), 3.38 (bs, 2H), 3.16 (s, 3H), 2.17 (bs, 2H), 2.04 (bs, 5H)	1301		MS (ESI) m/z 628.33 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 10.82 (bs, 1H), 8.83 (d, J = 4.8 Hz, 1H), 8.67 (s, 1H), 8.46 (s, 1H), 7.60 (dd, J = 8.8, 2.4 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.8 Hz, 1H), 7.37 (d, J = 8.8 Hz, 1H), 4.48 - 4.40 (m, 3H), 4.29-4.19 (m, 2H), 3.45-3.19 (m, 3H), 3.10-2.89 (m, 5H), 1.80 (s, 3H), 1.48-1.27 (m, 2H)
1282		MS (ESI) m/z 630.28 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 14.09 (bs, 1H), 8.77 (d, J = 4.8 Hz, 1H), 8.61 (s, 1H), 7.59 (dd, J = 8.8, 2.4 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.40 (d, J = 2.4 Hz, 1H), 7.35 (d, J = 9.2 Hz, 1H), 4.39 (s, 2H), 4.21 (s, 2H), 3.64 (s, 4H), 2.55-2.35 (m, 7H), 2.23 (s, 3H), 1.83 (s, 3H)	1302		MS (ESI) m/z 648.15 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 10.15 (bs, 1H), 8.83 (d, J = 4.8 Hz, 1H), 8.70 (s, 1H), 8.43 (s, 1H), 7.57 (dd, J = 2.4, 8.8 Hz , 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.41-7.36 (m, 2H), 4.95 (s, 1H), 4.84 (s, 1H), 4.39 (d, J = 4.4 Hz, 2H), 4.30 (d, J = 7.6 Hz, 2H), 4.23 (s, 2H), 3.83-3.59 (m, 4H), 3.53-3.34 (m, 4H), 1.83 (s, 3H)
1297		MS (ESI) m/z 644.30 [M+1]+; 1 H NMR (400 MHz, DMSO-d6) δ 13.46 (bs, 1H), 8.66 (d, J = 4.8 Hz, 1H), 7.55 (dd, J = 8.8, 2.4 Hz, 1H), 7.37-7.28 (m, 3H), 4.42-4.34 (m, 2H), 4.21 (s, 2H), 3.63 (bs, 4H), 2.64 (s, 3H), 2.49-2.35 (m, 7H), 2.22 (s, 3H), 1.84 (s, 3H)	1303		MS (ESI) m/z 666.24 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.8 Hz, 1H), 8.68 (s, 1H), 8.46 (s, 1H), 7.60 (dd, J = 8.8 Hz, 2.4 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.4 Hz, 1H), 7.37-7.35 (m, 1H), 6.46 (t, J = 54.8 Hz, 1H), 4.41-4.38 (m, 2H), 4.28-4.22 (m, 2H), 3.87-3.83 (m, 4H), 3.38-3.32 (m, 2H), 3.24-3.11 (m, 4H), 1.80 (s, 3H)

1304		1307	
MS (ESI) m/z 684.26 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 11.77 (bs, 1H), 8.81 (d, J = 4.8 Hz, 1H), 8.66 (s, 1H), 8.40 (s, 1H), 7.58 (dd, J = 9.2, 6.8 Hz, 1H), 7.45-7.40 (m, 2H), 7.34 (d, J = 8.8 Hz, 1H), 4.37 (s, 2H), 4.20 (s, 2H), 3.65 (s, 4H), 3.35-3.20 (m, 2H), 2.81 (s, 4H), 1.75 (s, 3H)		MS (ESI) m/z 692.28[M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.31 (bs, 1H), 8.82 (d, J = 4.8 Hz, 1H), 8.68 (s, 1H), 8.43 (s, 1H), 7.59 (dd, J = 2.40, 8.8 Hz, 1H), 7.46 (d, J = 4.4 Hz, 1H), 7.41 (d, J = 2.0 Hz, 1H), 7.36 (d, J = 8.8 Hz, 1H), 4.39 (s, 2H), 4.22 (s, 2H), 3.76 (m, 4H), 3.19-2.93 (m, 8H), 2.32 (m, 1H), 1.80 (s, 3H)
1305		1308	
MS (ESI) m/z 666 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.8 Hz, 1H), 8.70 (s, 1H), 8.43 (s, 1H), 7.61 (dd, J = 2.4, 8.8 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.8 Hz, 1H), 7.37 (d, J = 8.8 Hz, 1H), 6.73-6.46 (m, 1H), 4.39 (s, 2H), 4.34 (s, 1H), 4.23 (s, 2H), 4.18 (s, 1H), 3.56-3.15 (m, 5H), 2.83 (s, 3H), 1.82 (s, 3H)		MS (ESI) m/z 698.28 [M+1] +; 1H NMR (400 MHz, DMSO-d6) δ 13.33 (bs, 1H), 8.82 (d, J = 4.76 Hz, 1H), 8.69 (s, 1H), 8.43 (s, 1H), 7.59 (dd, J = 2.4, 8.8 Hz, 1H), 7.46 (d, J = 4.7 Hz, 1H), 7.41 (d, J = 2.5 Hz, 1H), 7.35 (d, J = 8.9 Hz, 1H) , 4.39 (t, J = 4.8 Hz, 2H), 4.22 (t, J = 4.4 Hz, 2H), 3.38 (bs, 8H), 2.82 (s, 4H), 1.81 (s, 3H)
1306		1309	
MS (ESI) m/z 642.35 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.43 (bs, 1H), 8.83 (d, J = 4.8 Hz, 1H), 8.70 (s, 1H), 8.44 (s, 1H), 7.61 (dd, J = 8.8 Hz, J = 2.4 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.41-7.38 (m, 2H), 4.41-4.40 (m, 4H), 4.31 (t, J = 2.4 Hz, 2H), 3.47 (bs, 6H), 3.01 (bs, 1H), 1.85 (s, 3H), 1.00-0.88 (bs, 2H)		MS (ESI) m/z 694.37 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.8 Hz, 1H), 8.67 (s, 1H), 8.45 (s, 1H), 7.59 (dd, J = 2.4, 8.8 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.0 Hz, 1H), 7.36 (d, J = 9.2 Hz, 1H), 6.22 (m, 1H), 4.39 (s, 2H), 4.21 (s, 2H), 3.72 (m, 4H), 2.96 (s, 4H), 1.79 (s, 3H), 1.23 (s, 6H)

1310		1313	
	MS (ESI) m/z 692.51 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.8 Hz, 1H), 8.64 (s, 1H), 8.48 (s, 1H), 7.60 (dd, J = 8.8, 2.4 Hz, 1H), 7.49 (d, J = 4.80, 1H), 7.43 (d, J = 2.4 Hz, 1H), 7.35 (d, J = 8.8 Hz, 1H), 6.04 (t, J = 55.6 Hz, 1H), 4.38 (s, 2H), 4.20 (s, 2H), 3.55 (s, 4H), 3.01 (s, 4H), 1.75 (s, 3H), 0.90-078 (m, 4H)		MS (ESI) m/z 658.37 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.43 (bs, 1H), 8.82 (d, J = 4.8 Hz, 1H), 8.70 (s, 1H), 8.41 (s, 1H), 7.60 (dd, J = 8.8 Hz, 2.4 Hz, 1H), 7.47 (d, J = 4.4 Hz, 1H), 7.41-7.36 (m, 2H), 4.42-4.39 (m, 4H), 4.24 (s, 2H), 3.72 (d, J = 12 Hz, 2H), 3.51 (t, J = 12.4 Hz, 2H), 3.19 (d, J = 9.6 Hz, 2H), 1.86 (s, 3H), 1.39 (s, 9H)
1311		1314	
	MS (ESI) m/z 678.43 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.8 Hz, 1H), 8.66 (s, 1H), 8.45 (s, 1H) 7.60 (dd, J = 9.2 Hz, 2.8 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.4 Hz, 1H), 7.36 (d, J = 9.2 Hz, 1H), 4.39 (bs, 2H), 4.32 (d, J = 12.8 Hz, 2H), 4.22 (bs, 4H), 3.64 (bs, 1H), 3.38 (bs, 1H), 3.19 (bs, 2H), 2.93 (bs, 2H), 2.15 (bs, 1H), 1.759 (s, 3H)		MS (ESI) m/z 654.34 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.22 (bs, 1H), 8.82 (d, J = 4.7 Hz, 1H), 8.57 (s, 1H), 8.46 (s, 1H), 7.59 (dd, J = 8.8, 2.5 Hz, 1H), 7.45 (d, J = 4.7 Hz, 1H), 7.42 (d, J = 2.4 Hz, 1H), 7.34 (d, J = 9.0 Hz, 1H), 4.41 (s, 4H), 4.36 (s, 2H), 4.18 (s, 2H), 3.49 (bs, 4H), 1.90 (bs, 1H), 1.73 (s, 3H), 0.42-0.20 (m, 4H)
1312		1315	
	MS (ESI) m/z 680.29 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.22 (bs, 1H), 8.82 (d, J = 4.8 Hz 1H), 8.66 (s, 1H), 8.44 (s, 1H), 7.598 (dd, J = 2.4, 8.8 Hz, 1H), 7.47 (d, J = 4.4 Hz, 1H), 7.42 (d, J = 2.4 Hz, 1H), 7.35 (d, J = 8.8 Hz, 1H), 6.25 (m, 1H), 4.38 (s, 2H), 4.21 (s, 2H), 3.64 (m, 4H), 2.97 (m, 4H), 2.63 (s, 1H), 1.77 (s, 3H), 1.16 (s, 3H)		MS (ESI) m/z 698.12 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.4 Hz, 1H), 8.65 (s, 1H), 8.47 (s, 1H), 7.60 (dd, J = 8.8, 2.4 Hz, 1H), 7.49 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.4 Hz, 1H), 7.35 (d, J = 8.8 Hz, 1H), 4.42-4.34 (m, 2H), 4.20 (s, 2H), 3.63-3.57 (m, 5H), 2.90-2.80 (m, 4H), 1.76 (s, 3H), 1.21 (d, J = 6.8 Hz, 3H)

1316		MS (ESI) m/z 712.41 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.8 Hz, 1H), 8.65 (s, 1H), 8.47 (s, 1H), 7.59 (dd, J = 8.8, 2.4 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.4 Hz, 1H), 7.35 (d, J = 8.8 Hz, 1H), 4.41-4.35 (m, 2H), 4.23-4.16 (m, 2H), 3.61 (s, 4H), 2.93 (s, 4H), 1.75 (s, 3H), 1.32 (s, 6H)	1319		MS (ESI) m/z 670.45 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.76 Hz, 1H), 8.62 (s, 1H), 8.41 (s, 1H), 7.60 (dd, J = 8.9 Hz, 2.4 Hz, 1H), 7.47 (d, J = 4.7 Hz, 1H), 7.42 (d, J = 2.5 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.57-4.52 (m, 1H), 4.39 (d, J = 5.6 Hz, 2H), 4.17 (d, J = 5.28, 2H), 3.65 (d, J = 11.44, 2H), 3.95 (bs, 2H), 3.07 (s, 3H), 2.83 (bs, 1H), 2.07 (s, 4H), 1.76 (s, 3H), 0.94-0.85 (m, 4H)
1317		MS (ESI) m/z 676.42 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.23 (bs, 1H), 8.82 (d, J = 4.8 Hz, 1H), 8.64 (s, 1H), 8.45 (s, 1H), 7.59-7.57 (m, 1H), 7.45 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.0 Hz, 1H), 7.35 (d, J = 8.8 Hz, 1H), 4.38 (s, 2H), 4.20 (s, 2H), 3.65 (s, 4H), 2.67 (s, 4H), 2.60-2.48 (m, 2H), 1.74 (s, 3H), 1.35 (J = 21.6 Hz, 6H)	1320		MS (ESI) m/z 686.26 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.32 (s, 1H), 8.82 (d, J = 4.8, 1H), 8.61 (s, 1H), 8.40 (s, 1H), 7.59 (dd, J = 2.4, 8.8 Hz, 1H), 7.46 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.4 Hz, 1H), 7.36 (d, J = 8.8 Hz, 1H), 4.77-4.76 (m, 4H), 4.55 (bs, 1H), 4.39 (s, 3H), 4.21 (s, 2H), 3.26-3.15 (m, 2H), 3.09-2.97 (m, 5H), 2.21-2.08 (m, 4H), 1.77 (s, 3H)
1318		MS (ESI) m/z 7694.3 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.78 (d, J = 4.8 Hz, 1H), 8.51 (s, 1H), 8.31 (s, 1H), 7.59 (dd, J = 2.4, 8.8 Hz, 1H), 7.45 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.4 Hz, 1H), 7.36 (d, J = 9.2 Hz, 1H), 6.54 (t, J = 57.2 Hz, 1H), 4.49 (bs, 2H), 4.39 (bs, 2H), 4.21 (bs, 2H), 3.60 (bs, 4H), 3.08 (t, J = 12.0 Hz, 2H), 3.08 (s, 3H), 2.17 (bs, 1H), 2.03 (bs, 4H) 1.76 (s, 3H)	1321		MS (ESI) m/z 652.12 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (s, 1H), δ 8.74 (d, J = 4.8 Hz, 1H), 8.64 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.69-7.66 (m, 2H), 7.53 (d, J = 4.4 Hz, 1H), 4.83 (s, 2H), 4.76 (s, 4H), 4.37 (bs, 4H), 4.04 (bs, 1H), 3.34-2.82 (m, 4H), 2.12 (s, 3H)

1322		1325	
	MS (ESI) m/z 664.45 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.74 (d, J = 4.8 Hz, 1H), 8.70 (s, 1H), 8.64 (s, 1H), 7.76-7.73 (m, 1H), 7.69-7.66 (m, 2H), 7.52 (d, J = 4.8 Hz, 1H), 4.80 (s, 2H), 4.54 (t, J = 6.4 Hz, 2H), 4.47 (s, 4H), 4.35 (t, J = 6 Hz, 2H), 3.69 (t, J = 5.6 Hz, 1H), 3.42 (s, 4H), 2.0 (s, 3H)		MS (ESI) m/z 652.36 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.23 (bs, 1H), 9.09 (s, 1H), 9.00 (s, 1H), 8.85 (d, J = 4.4 Hz, 1H), 8.38 (s, 1H), 8.31 (d, J = 8.0 Hz, 1H), 7.65 (d, J = 8.0 Hz, 1H), 7.60 (dd, J = 8.8, 2.4 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.4 Hz, 1H), 7.36 (d, J = 8.8 Hz, 1H), 4.42 (s, 2H), 4.28 (s, 2H), 3.66 (s, 2H), 2.26 (s, 6H), 1.83 (s, 3H)
1323		1326	
	MS (ESI) m/z 630.32 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.62 (s, 1H), 8.80 (d, J = 4.8 Hz, 1H), 8.59 (s, 1H), 8.50 (s, 1H), 7.59 (dd, J = 2.4, 8.8 Hz, 1H), 7.45 (d, J = 4.8 Hz, 1H), 7.40 (d, J = 2.4 Hz, 1H), 7.36 (d, J = 9.2 Hz, 1H), 7.19 (s, 1H), 4.41 (t, J = 4.8 Hz, 2H), 4.24 (t, J = 4.8 Hz, 2H), 3.64 (s, 2H), 2.96 (m, 5H), 2.5 (m, 3H), 2.10 (m, 2H), 1.85 (s, 3H)		MS (ESI) m/z 631.39 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.23 (bs, 1H), 8.97 (s, 1H), 8.83 (d, J = 4.8 Hz, 1H), 8.36 (s, 1H), 7.60 (dd, J = 9.2, 2.0 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.44 (d, J = 2.4 Hz, 1H), 7.35 (d, J = 8.8 Hz, 1H), 4.81 (d, J = 46.4 Hz, 2H), 4.47-4.38 (m, 4H), 4.26 (s, 2H), 3.65-3.30 (m, 2H), 2.86 (s, 3H), 1.77 (s, 3H)
1324		1327	
	MS (ESI) m/z 652.29 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.17 (s, 1H), 8.85 (d, J = 4.81 Hz, 1H), 8.36 (s, 1H), 7.62-7.59 (m, 2H), 7.47 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.8 Hz, 1H), 7.36 (d, J = 8.8 Hz, 1H), 7.06 (bs, 1H), 4.44 (s, 2H), 4.33 (s, 2H), 3.29 (s, 6H), 2.60 (s, 3H), 1.92 (s, 3H)		MS (ESI) m/z 667.38 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.16 (bs, 1H), 8.94 (s, 1H), 8.83 (d, J = 4.8 Hz, 1H), 8.38 (s, 1H), 7.59 (dd, J = 9.2, 2.4 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.4 Hz, 1H), 7.34 (d, J = 8.8 Hz, 1H), 4.39 (s, 2H), 4.25 (s, 2H), 3.88 (s, 2H), 3.37 (q, J = 10.0 Hz, 2H), 2.54 (s, 3H), 1.73 (s, 3H)

1328		1332	
MS (ESI) m/z 633.40 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.40 (bs, 1H), 10.08 (bs, 1H), (9.01 (s, 1H), 8.82 (d, J = 4.8 Hz, 1H), 8.36 (s, 1H), 7.60 (dd, J = 8.9, 2.5 Hz, 1H), 7.48 (d, J = 4.7 Hz, 1H), 7.45-7.33 (m, 3H), 7.21-7.18 (m, 1H), 4.88 (d, J = 47.2 Hz, 2H), 4.41 (t, J = 4.9 Hz, 2H), 4.27-4.13 (m, 4H), 3.70-3.55 (m, merged, 2H), 2.90 (s, 3H), 1.81 (s, 3H)		MS (ESI) m/z 655.5 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.98 (s, 1H), 8.84 (d, J = 4.8 Hz, 1H), 8.23 (s, 1H), 7.61 (dd, J = 9.2, 2.8 Hz, 1H), 7.46 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.4 Hz, 1H), 7.37 (d, J = 9.2 Hz, 1H), 4.42 (bs, 2H), 4.30 (bs, 2H), 2.82 (bs, 2H), 2.72 (s, 6H), 2.61 (bs, 2H) 1.30 (s, 9H)	
1329		1333	
MS (ESI) m/z 625.37 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.92 (s, 1H), 8.83 (d, J = 4.8 Hz, 1H), 8.34 (s, 1H), 7.59 (dd, J = 8.8, 2.4 Hz, 1H), 7.48 (d, J = 4.4 Hz, 1H), 7.43 (d, J = 2.4 Hz, 1H), 7.35 (d, J = 8.8 Hz, 1H), 4.40 (bs, 2H), 4.25 (bs, 2H), 2.74 (bs, 6H), 1.75 (s, 3H), 1.36 (bs, 4H)		MS (ESI) m/z 676.51 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.33 (bs, 1H), 9.75 (bs, 1H), 8.83 (d, J = 4.8 Hz, 1H), 8.71 (s, 1H), 8.38 (s, 1H), 7.61-7.58 (dd, J = 2.8, 9.2 Hz, 1H), 7.47 (d, J = 4.4 Hz, 1H), 7.42 (d, J = 2.4 Hz, 1H), 7.37 (d, J = 9.2 Hz, 1H), 4.97-4.79 (m, 2H), 4.39 (bs, 2H), 4.22 (bs, 2H), 3.88-3.48 (m, 6H), 1.79 (s, 3H), 1.45 (s, 3H), 1.40 (s, 3H)	
1330		1334	
MS (ESI) m/z 617.43 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.38 (bs, 1H), 10.15 (bs, 1H), 9.02 (s, 1H), 8.82 (d, J = 4.8 Hz, 1H), 8.34 (s, 1H), 7.60 (dd, J = 2.4, 8.8 Hz, 1H), 7.46 (d, J = 4.4 Hz, 1H), 7.43 (d, J = 2.8 Hz, 1H), 7.35 (d, J = 9.2 Hz, 1H), 5.27 (d, J = 8.0 Hz, 1H), 4.40 (bs, 2H), 4.32-4.23 (m, 2H), 3.94 (t, J = 12.4 Hz, 1H), 3.78 (bs, 2H), 3.49 (bs, 2H), 3.24 (bs, 1H), 2.99 (s, 3H), 1.81 (s, 3H)		MS (ESI) m/z 684.26 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.38 (s, 1H), 8.82 (d, J = 4.8 Hz, 1H), 8.67 (s, 1H), 8.43 (s, 1H), 7.59 (d, J = 7.2 Hz, 1H), 7.47 (d, J = 4.4 Hz, 1H), 7.43 (s, 1H), 7.35 (d, J = 9.2 Hz, 1H), 4.38 (s, 2H), 4.21 (s, 2H), 4.08 (d, J = 11.2 Hz, 1H), 3.82-3.05 (m, 5H), 2.67 (s, 1H), 2.50 (s, 3H), 1.76 (s, 3H)	

1335		1338	
	MS (ESI) m/z 630.46[M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.85 (s, 1H), 8.85 (d, J = 8.4 Hz, 1H), 8.67 (s, 1H), 8.40 (s, 1H), 7.61 (d, J = 8.8 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.41 (m, 2H), 4.74 (bs, 1H), 4.42 (m, 2H), 4.23 (m, 4H), 3.52 (m, 2H), 3.32 (m, 2H). 2.91 (s, 3H), 1.78 (s, 3H), 1.49 (d, J = 6.8 Hz, 3H), 1.04 (d, J = 5.6 Hz, 1H)		MS (ESI) m/z 674.53 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.21 (bs, 1H), 8.83 (d, J = 4.8 Hz, 1H), 8.68 (s, 1H), 8.39 (s, 1H), 7.60 (dd, J = 8.8, 2.0 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.4 Hz, 1H), 7.36 (d, J = 8.8 Hz, 1H), 4.83-4.72 (m, 2H), 4.39 (s, 2H), 4.23 (s, 2H), 3.98-3.53 (m, 8H), 1.77 (s, 3H), 1.03 (bs, 4H)
1336		1339	
	MS (ESI) m/z 674.50 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.8 Hz, 1H), 8.67 (s, 1H), 8.45 (s, 1H), 7.60 (dd, J = 9.2, 2.8 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.4 Hz, 1H), 7.36 (d, J = 8.8 Hz, 1H), 4.62 (d, J = 49.6 Hz, 2H), 4.40-4.35 (m, 2H), 4.25-4.15 (m, 2H), 3.75-3.55 (m, 4H), 3.30-3.00 (m, 4H), 1.79 (s, 3H), 1.15-.0.80 (m, 4H)		MS (ESI) m/z 708.26 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.27 (bs, 1H), 8.82 (d, J = 8.0 Hz, 1H), 8.67 (s, 1H), 8.43 (s, 1H), 7.59 (d, J = 6.8 Hz, 1H), 7.46 (d, J = 4.4 Hz, 1H), 7.42 (s, 1H), 7.36 (d, J = 9.2 Hz, 1H), 4.39 (s, 2H), 4.22 (s, 2H), 3.59-3.30 (m, 12H), 3.10 (s, 3H), 1.79 (s, 3H)
1337		1340	
	MS (ESI) m/z 642.53 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.37 (bs, 1H), 8.82 (d, J = 4.4 Hz, 1H), 8.70 (s, 1H), 8.38 (s, 1H), 7.60 (t, J = 6.8 Hz, 1H), 7.47-7.21 (m, 3H), 4.39 (s, 2H), 4.23 (s, 2H), 4.05 (bs, 2H), 3.93 (bs, 2H), 3.52 (bs, 2H), 2.99 (s, 3H), 1.79 (s, 3H), 1.26-1.07 (m, 4H)		MS (ESI) m/z 692.45 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.8 Hz, 1H), 8.63 (s, 1H), 8.47 (s, 1H), 7.60 (dd, J = 2.4, 8.8 Hz, 1H), 7.47 (d, J = 4.8 Hz , 1H), 7.43 (d, J = 2.4 Hz, 1H), 7.36 (d, J = 8.8 Hz, 1H), 4.57 (t, J = 8.0 Hz, 2H), 4.38 (bs, 4H), 4.20 (bs, 2H), 3.94 (bs, 1H), 3.07 (bs, 4H), 2.20 (bs, 4H), 1.76 (s, 3H)

1341		1344	
MS (ESI) m/z 664.51 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.8 Hz, 1H), 8.58 (s, 1H), 8.47 (s, 1H), 8.48 (s, 1H), 7.59 (dd, J = 2.4, 8.8 Hz , 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.35 (d, J = 9.2 Hz, 1H), 4.47-4.42 (m, 2H), 4.37 (bs, 2H), 4.18 (bs, 2H), 4.13-4.10 (m, 2H), 3.95-3.74 (m, 5H), 1.74 (s, 3H)		MS (ESI) m/z 651.48 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.96 (s, 1H), 8.83 (d, J = 4.4 Hz, 1H), 8.36 (s, 1H), 7.60 (dd, J = 8.8, 2.4 Hz, 1H), 7.48 (d, J = 4.4 Hz, 1H), 7.44 (d, J = 2.4 Hz, 1H), 7.35 (d, J = 9.2 Hz, 1H), 4.80-4.60 (m, 1H), 4.40 (s, 2H), 4.25 (s, 2H), 3.55-3.30 (m, merged, 2H), 2.50-2.30 (m, 1H), 2.22-1.91 (m, 4H), 1.75 (s, 3H), 1.04-0.61 (m, 4H)
1342		1345	
MS (ESI) m/z 655.35 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.27 (bs, 1H), 8.83 (d, J = 4.8 Hz, 1H), 8.67 (s, 1H), 8.43 (s, 1H), 7.60 (dd, J = 8.8, 2.4 Hz, 1H), 7.46 (d, J = 4.0 Hz, 1H), 7.43 (d, J = 2.4 Hz, 1H), 7.35 (d, J = 9.2 Hz, 1H), 4.43-4.35 (m, 2H), 4.25-4.15 (m, 2H), 4.13- 4.00 (m, 2H), 3.16- 3.10 (m, 1H), 2.97-2.83 (m, 4H), 2.48-2.33 (m, 2H), 2.30 (s, 3H), 1.74 (s, 3H)		MS (ESI) m/z 635.42 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.40 (bs. 1H), 9.67 (bs, 1H), 8.96 (s, 1H), 8.82 (d, J = 4.7 Hz, 1H), 8.32 (s, 1H), 7.60 (dd, J = 8.92, 2.36 Hz, 1H), 7.47 (d, J = 4.7 Hz, 1H), 7.43 (d, J = 2.4 Hz, 1H), 7.36 (d, J = 8.9 Hz, 1H), 4.92-4.76 (m, 1H), 4.40 (t, J = 4.4 Hz, 2H), 4.26 (t, J = 5.0 Hz, 2H), 3.62-3.52 (m, 2H), 3.40-3.20 (m, 2H), 3.18 (t, J = 7.24 Hz, 2H), 2.88 (s, 3H), 2.31-2.17 (m, 2H), 1.82 (s, 3H)
1343		1346	
MS (ESI) m/z 683.44 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.8 Hz, 1H), 8.69 (s, 1H), 8.43 (s, 1H), 7.60 (dd, J = 8.8, 2.4 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.37 (d, J = 8.8 Hz, 1H), 4.40 (s, 2H), 4.23 (s, 2H), 3.95 (s, 2H), 3.57-3.40 (m, 4H), 3.30-3.15 (m, 4H), 1.83 (s, 3H), 1.46 (s, 6H)		MS (ESI) m/z 639.42 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.97 (s, 1H), 8.83 (d, J = 4.7 Hz, 1H), 8.37 (s, 1H), 7.59 (dd, J = 8.9, 2.4 Hz, 1H), 7.47 (d, J = 4.7 Hz, 1H), 7.44 (d, J = 2.4 Hz, 1H), 7.34 (d, J = 9.0 Hz, 1H), 4.65-4.35 (m, 4H), 4.25 (t, J = 3.8 Hz, 2H), 2.85 (bs, 3H), 1.75 (s, 3H), 1.36 (s, 3H), 1.03 (bs, 2H), 0.72 (bs, 2H)

1347		MS (ESI) m/z 624.49 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.08 (bs, 1H), 8.86 (s, 1H), 8.79 (d, J = 4.4 Hz, 1H), 8.66 (s, 1H), 7.88 (d, J = 8.4 Hz, 1H), 7.61 (d, J = 4.8 Hz, 1H), 7.52 (s, 1H), 7.42 (d, J = 4.8 Hz, 1H), 6.52-6.38 (m, 1H), 5.89 (d, J = 16.0 Hz, 1H), 4.68 (d, J = 4.0 Hz, 2H), 4.39 (d, J = 13.2 Hz, 1H), 3.11 (t, J = 12.4 Hz, 2H), 2.82-2.65 (m, 1H), 2.40-2.10 (m, 8H), 0.72-0.45 (m, 2H)	1350		MS (ESI) m/z 694.59 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.8 Hz, 1H), 8.65 (s, 1H), 8.41 (s, 1H), 7.59 (dd, J = 2.0, 8.8 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.0 Hz, 1H), 7.36 (d, J = 8.8 Hz, 1H), 6.15 (bs, 1H), 4.39 (s, 2H), 4.21-4.16 (m, 2H), 4.14 (bs, 2H), 3.01 (bs, 6H), 1.77 (s, 3H), 1.21 (s, 6H)
1348		MS (ESI) m/z 628.18 [M+1]+; ; 1H NMR (400 MHz, DMSO-d6), δ 8.81 (d, J = 4.8 Hz, 1H), δ 8.62 (s, 1H), 8.43 (s, 1H), 7.59 (dd, J = 8.8 Hz, 2.4 Hz, 1H), 7.45-7.42 (m, 2H), 7.35 (d, J = 8.8 Hz, 1H), 4.78 (bs, 1H), 4.37 (t, J = 5.1 Hz, 2H), 4.27 (t, J = 4.5 Hz, 2H), 3.45-3.43 (m, 2H), 3.32-2.8 (m, 4H), 2.75-2.56 (m, 2H), 1.93-1.90 (m, 2H), 1.74 (s, 3H)	1351		MS (ESI) m/z 658.47 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 2.36 Hz, 1H), 8.74 (s, 1H), 8.40 (s, 1H), 7.60 (dd, J = 8.9, 2.5 Hz, 1H), 7.47 (d, J = 4.7 Hz, 1H), 7.42 (d, J = 2.5 Hz, 2H), 7.37 (d, J = 9.0 Hz, 2H), 4.66 (d, J = 7.5 Hz, 2H), 4.40 (s, 2H), 4.24 (s, 2H), 4.14 (bs, 4H), 3.40 (s, 2H), 3.06 (s, 3H), 1.82 (s, 3H)
1349		MS (ESI) m/z 715.66 [M+1]+; ; 1H NMR (400 MHz, DMSO-d6) δ 8.89 (s, 1H), 8.82 (d, J = 4.8 Hz, 1H), 8.41 (s, 1H), 7.58 (dd, J = 8.8 Hz, 2.8 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.4 Hz, 1H), 7.34 (d, J = 8.8 Hz, 1H), 4.38 (s, 2H), 4.22 (s, 2H), 4.05 (s, 1H), 3.40-3.32 (m, 2H), 2.93 (s, 2H), 2.66-2.61 (m, 2H), 2.11-2.09 (m, 2H), 1.74 (s, 5H)	1352		MS (ESI) m/z 652.12 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (s, 1H), δ 8.74 (d, J = 4.8 Hz, 1H), 8.64 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.69-7.66 (m, 2H), 7.53 (d, J = 4.4 Hz, 1H), 4.83 (s, 2H), 4.76 (s, 4H), 4.37 (bs, 4H), 4.04 (bs, 1H), 3.34-2.82 (m, 4H), 2.12 (s, 3H)

1353		MS (ESI) m/z 692.45 [M+1] +; 1H NMR (400 MHz, DMSO-d6) δ 13.05 (bs, 1H), 8.83 (s, 1H), 8.75 (d, J = 4.6 Hz, 1H), 8.64 (s, 1H), 7.75 (d, J = 8.2 Hz, 1H), 7.69 (s, 1H), 7.66 (s, 1H), 7.52 (d, J = 4.6 Hz, 1H), 4.83 (s, 2H), 4.31 (bs, 1H), 3.43 (bs, 7H), 2.85 (s, 4H), 2.11 (s, 3H)	1356		MS (ESI) m/z 660.27 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.05 (bs, 1H), 8.79 (s, 1H), 8.75 (d, J = 4.6 Hz, 1H), 8.65 (s, 1H), 7.75 (d, J = 8.1 Hz, 1H), 7.68 (m, 2H), 7.53 (d, J = 4.6 Hz, 1H), 6.34 (m, 1H), 4.82 (s, 2H), 3.76-2.66 (m, 10H), 2.09 (s, 1H)
1354		MS (ESI) m/z 636.25 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.18 (bs, 1H), 8.84 (s, 1H), 8.75 (d, J = 4.8 Hz, 1H), 8.65 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.70-7.65 (m, 2H), 7.53 (d, J = 4.8 Hz, 1H), 4.84 (s, 2H), 4.38 (m, 2H), 3.79 (m, 2H,), 3.49 (m, 4H), 3.03 (m, 1H), 2.14 (s, 3H), 0.93 (m, 4H)	1357		MS (ESI) m/z 658.37 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.8 Hz, 1H), 8.61 (s, 1H), 8.46 (s, 1H), 7.60 (dd, J = 8.8, 2.4 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.6 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 6.33 (t, J = 53.6 Hz, 1H), 5.09 (s, 1H), 4.38 (t, J = 4.3 Hz, 2H), 4.21 (t, J = 5.7, 2H), 4.15-3.80 (m, 7H), 2.21 (bs, 2H), 1.76 (s, 3H)
1355		MS (ESI) m/z 686.0 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.03 (s, 1H), 8.83 (s, 1H), 8.75 (d, J = 4.8 Hz, 1H), 8.64 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.70-7.66 (m, 1H), 7.53 (d, J = 4.8 Hz, 1H), 4.72 (s, 2H), 3.80 (bs, 4H), 3.39 (bs, 4H), 3.05-3.02 (m, 5H), 2.16 (s, 3H)	1358		MS (ESI) m/z 716.50 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.8 Hz, 1H), 8.68 (s, 1H), 8.45 (s, 1H), 7.60 (dd, J = 8.8 Hz, 2.4 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.37-7.33 (m, 2H), 5.77 (d, J = 46 Hz, 1H), 4.39 (s, 2H), 4.22 (s, 2H), 3.24 (bs, 2H), 3.29-3.15 (m, 8H), 1.79 (s, 3H)

1359		1362	
MS (ESI) m/z 766.56 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4 Hz, 1H), 8.66 (s, 1H), 8.46 (s, 1H), 7.60 (dd, J = 2.4, 8.8 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.4 Hz, 1H), 7.36 (d, J = 8.8 Hz, 1H), 4.39 (bs, 2H), 4.21 (bs, 2H), 3.68 (bs, 4H), 2.96 (bs, 2H), 2.78 (bs, 4H), 2.46 (s, 1H) 1.77 (s, 3H)		MS (ESI) m/z 755.45 [M+1] +; 1H NMR (400 MHz, DMSO- d6) δ 12.44 (s, 1H), 8.83-8.79 (m, 3H), 7.76 (d, J = 8.4 Hz, 1H), 7.71- 7.67 (m, 2H), 7.61 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 3.75 - 3.60 (m, 4H), 3.56 (s, 3H), 3.31 (q, J = 10.0 Hz, 2H), 2.90 – 2.80 (m, 4H), 2.00 (s, 3H)	
1360		1363	
MS (ESI) m/z 726.51 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.53 (bs, 1H), 8.83 (d, J = 4.8 Hz, 1H), 8.61 (s, 1H), 8.40 (s, 1H), 7.59 (dd, J = 8.8 Hz, 2.4 Hz, 1H), 7.47 (d, J = 4.4 Hz, 1H), 7.42 (d, J = 2.4 Hz, 1H), 7.36 (d, J = 8.8 Hz, 1H), 4.49 (bs, 1H), 4.52 (bs, 1H), 4.21 (bs, 2H), 3.69 (d, J = 10.4 Hz, 2H), 3.50 (bs, 2H), 3.40 (bs, 2H), 3.21 (s, 3H), 2.89-2.85 (m, 2H), 2.11 (bs, 4H), 1.78 (s, 3H)		MS (ESI) m/z 668.48 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.21 (bs, 1H), 9.37 (bs, 1H), 8.82 (d, J = 4.8 Hz, 1H), 8.67 (s, 1H), 8.37 (s, 1H), 7.59 (dd, J = 8.8, 2.4 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.41 (d, J = 2.0 Hz, 1H), 7.36 (d, J = 9.2 Hz, 1H), 4.38 (s, 2H), 4.21 (s, 2H), 3.80-3.50 (m, 2H), 3.20-2.90 (m, 2H), 2.61 (s, 3H), 1.78 (s, 3H), 1.40-0.80 (m, 8H)	
1361		1364	
MS (ESI) m/z 724.51 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.8 Hz, 1H), 8.64 (s, 1H), 8.46 (s, 1H), 7.60 (dd, J = 8.8, 2.8 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.4 Hz, 1H), 7.35 (d, J = 8.8 Hz, 1H), 4.37 (s, 2H), 4.20 (s, 2H), 3.63 (bs, 4H), 2.84 (bs, 4H), 2.70-2.50 (m, 2H), 1.77 (s, 3H), 0.84-0.74 (m, 4H)		MS (ESI) m/z 642.35 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.8 Hz, 1H), 8.68 (s, 1H), 8.45 (s, 1H), 7.60 (dd, J = 8.8, 2.4 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.4 Hz, 1H), 7.36 (d, J = 8.8 Hz, 1H), 4.87-4.75 (m, 4H), 4.39 (bs, 2H), 4.22 (bs, 2H), 3.56-3.14 (m, 8H), 2.41 (s, 1H), 1.78 (s, 3H)	

1365		MS (ESI) m/z 656.52 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.30 (bs, 1H), 8.83 (d, J = 4.8 Hz, 1H), 8.69 (s, 1H), 8.41 (s, 1H), 7.62-7.59 (dd, J = 2.4, 8.8 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.41-7.36 (m, 2H), 4.40 (bs, 4H), 4.24 (bs, 2H), 3.48 (bs, 6H), 1.85 (s, 3H), 1.39 (s, 3H), 1.19 (bs, 2H), 0.82 (bs, 2H)	1368		MS (ESI) m/z 661.35 [M+1]+; ; 1H NMR (400 MHz, DMSO-d6) δ 8.78 (s, 1H), 8.77 (d, J = 3.2 Hz, 1H), 8.67 (s, 1H), 7.76 (d, J = 8.8 Hz, 1H), 7.71-7.65 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 3.67 (s, 4H), 2.82 (s, 4H) 2.07 (s, 3H), 1.32-1.27 (m, 2H), 1.17-1.09 (m, 2H)
1366		MS (ESI) m/z 686.46 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.79-8.73 (m, 2H), 8.66 (s, 1H), 7.75 (d, J = 9.2 Hz, 1H), 7.72-7.66 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 6.04 (t, J = 55.6 Hz, 1H), 4.82 (s, 2H), 3.59 (s, 4H), 3.02 (s, 4H), 2.06 (s, 3H), 0.90-0.78 (m, 4H)	1369		MS (ESI) m/z 682.51 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.81 (d, J = 4.4 Hz, 1H), 8.60 (s, 1H), 8.47 (s, 1H), 7.60 (dd, J = 9.2, 2.4 Hz, 1H), 7.46 (d, J = 4.4 Hz, 1H), 7.42 (d, J = 2.4 Hz, 1H), 7.35 (d, J = 9.2 Hz, 1H), 4.60 (s, 2H), 4.52 (s, 2H), 4.43-4.38 (m, 4H), 4.33-4.28 (m, 2H), 4.20 (bs, 2H), 3.79 (bs, 1H), 1.89 (t, J = 6.8 Hz, 2H), 1.80 (s, 3H), 1.67-1.58 (m, 4H), 1.47 (t, J = 6.4 Hz, 2H)
1367		MS (ESI) m/z 677.49 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.05 (bs, 1H), 9.99 (bs, 1H), 8.82 (s, 1H), 8.75 (d, J = 4.8 Hz, 1H), 8.65 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.71-7.66 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 4.83 (s, 2H), 4.45 (bs, 2H), 3.62 (bs, 4H), 3.27 (bs, 4H), 2.13 (s, 3H), 1.46 (bs, 6H)	1370		MS (ESI) m/z 684.53 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.9 Hz, 1H), 8.61 (s, 1H), 8.40 (s, 1H), 7.60 (dd, J = 2.4, 8.8 Hz, 1H), 7.46 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.4 Hz, 1H), 7.36 (d, J = 8.8 Hz, 1H), 4.51 (bs, 1H), 4.39 (s, 2H), 4.21 (s, 2H), 3.68 (d, J = 10.4 Hz, 2H), 3.21-3.16 (m, 2H), 3.09 (s, 3H), 3.01 (t, J = 5.6 Hz, 2H), 2.21-2.15 (m, 2H), 2.12-2.06 (m, 2H), 1.77 (s, 3H), 1.10 (bs, 1H), 0.67 (d, J = 7.2 Hz, 2H), 0.44-0.38 (m, 2H)

1371		MS (ESI) m/z 654.44 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 10.48 (bs, 1H), 8.82 (d, J = 4.8 Hz, 1H), 8.64 (s, 1H), 8.44 (s, 1H), 7.60 (dd, J = 9.2, 2.4 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.4 Hz, 1H), 7.36 (d, J = 8.8 Hz, 1H), 5.25-4.89 (m, 2H), 4.63 (d, J = 10.4 Hz, 2H), 4.38 (s, 2H), 4.21 (s, 2H), 3.98 (bs, 2H), 3.18 (bs, 1H), 2.75 (bs, 2H), 1.78 (s, 3H), 0.86 (bs, 4H)	1390		MS (ESI) m/z 650.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.93 (s, 1H), 8.39 (s, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.42 (d, J = 2.8 Hz, 2H), 7.35 (d, J = 9.0 Hz, 1H), 6.29 (s, 1H), 4.39 (d, J = 5.0 Hz, 2H), 4.26 (d, J = 4.9 Hz, 2H), 2.91 – 2.78 (m, 4H), 2.71 (s, 3H), 2.35 – 2.15 (m, 2H), 1.85 (s, 3H)
1378		MS (ESI) m/z 608.1	1395		MS (ESI) m/z 714.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.81 (d, J = 4.8 Hz, 1H), 8.54 (s, 1H), 8.48 (s, 1H), 7.61 (dd, J = 8.9, 2.7 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.7 Hz, 1H), 7.39 (d, J = 9.0 Hz, 1H), 4.54 (s, 2H), 4.43 (t, J = 5.1 Hz, 2H), 4.24 (t, J = 5.1 Hz, 2H), 3.82 – 3.40 (m, 10H), 1.83 (s, 3H)
1382		MS (ESI) m/z 608.0[M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 1H NMR (400 MHz, DMSO-d6) δ 9.05 (s, 1H), 8.44 (s, 1H), 7.94 – 7.86 (m, 2H), 7.64 – 7.54 (m, 4H), 7.46 – 7.40 (m, 2H), 7.37 (d, J = 9.0 Hz, 1H), 4.42 (d, J = 4.9 Hz, 2H), 4.29 (d, J = 4.9 Hz, 2H), 2.71 (s, 3H), 1.89 (s, 3H)	1396		MS (ESI) m/z 708.3 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.84 (s, 1H), 8.76 (d, J = 4.8 Hz, 1H), 8.65 (s, 1H), 7.76 (dd, J = 8.3, 0.5 Hz, 1H), 7.71 – 7.65 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 4.84 (s, 2H), 4.53 (s, 2H), 4.06 – 2.83 (m, 8H), 2.13 (s, 3H)

1397		1400	
MS (ESI) m/z 708.4 [M+1]+; ; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.8 Hz, 1H), 8.60 (s, 1H), 8.40 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.51 – 7.47 (m, 1H), 7.44 (d, J = 2.7 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 6.46 (t, J = 54.6 Hz, 1H), 4.54 (s, 4H), 4.41 (t, J = 4.9 Hz, 2H), 4.21 (t, J = 4.8 Hz, 2H), 4.10 (s, 4H), 2.75 (t, J = 4.7 Hz, 4H), 1.75 (s, 3H)		MS (ESI) m/z = 740.3 [M+1]+; 1H NMR (400 MHz, d6-DMSO) δ 9.59-9.49 (b, 1H), 8.83 (d, J = 4.6 Hz, 1H), 8.70 (s, 1H), 8.42 (s, 1H), 7.61 (dd, J = 8.9, 2.7 Hz, 1H), 7.49 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.7 Hz, 1H), 7.38 (d, J = 8.9 Hz, 1H), 4.43-4.36 (m, 2H), 4.24 (t, J = 4.8 Hz, 2H), 3.61-3.49 (m, 2H), 3.34-3.20 (m, 2H), 2.49-2.39 (m, 2H), 2.00-1.92 (m, 2H), 1.85 (s, 3H), 1.39 (s, 6H). Remaining protons partially obscured by water peak		
1398		1401	
MS (ESI) m/z 650.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.93 (s, 1H), 8.39 (s, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.42 (d, J = 2.8 Hz, 2H), 7.35 (d, J = 9.0 Hz, 1H), 6.29 (s, 1H), 4.39 (d, J = 5.0 Hz, 2H), 4.26 (d, J = 4.9 Hz, 2H), 2.91 – 2.78 (m, 4H), 2.71 (s, 3H), 2.35 – 2.15 (m, 2H), 1.85 (s, 3H)		MS (ESI) m/z = 738.3 [M+1]+; 1H NMR (400 MHz, d6-DMSO) δ 8.83 (d, J = 4.9 Hz, 1H), 8.67 (s, 1H), 8.42 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.48 (d, J = 4.7 Hz, 1H), 7.42 (d, J = 2.7 Hz, 1H), 7.37 (d, J = 8.9 Hz, 1H), 4.40 (t, J = 4.9 Hz, 2H), 4.23 (t, J = 4.9 Hz, 2H), 2.39-2.25 (m, 2H), 1.82 (s, 3H), 1.40-0.45 (b, 4H). Remaining protons appear as very broad signals and/or are partially obscured by water peak		
1399		1402	
MS (ESI) m/z 842.4 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.03 (s, 1H), 8.90 (d, J = 4.9 Hz, 1H), 8.72 (ddd, J = 4.6, 1.7, 0.9 Hz, 1H), 8.65 (s, 1H), 8.60 (s, 1H), 8.30 – 8.25 (m, 1H), 8.21 (td, J = 7.7, 1.7 Hz, 1H), 7.80 – 7.72 (m, 2H), 7.72 – 7.68 (m, 2H), 7.66 (d, J = 4.8 Hz, 1H), 4.83 (s, 2H), 3.09 (s, 3H), 1.94 (s, 3H), 1.77 (t, J = 18.9 Hz, 2H)		MS (ESI) m/z = 627.3 [M+1]+; 1H NMR (400 MHz, d6-DMSO) δ 10.20-10.10 ppm (b, 1H), 9.15 (s, 1H), 8.74 (d, J = 4.8 Hz, 1H), 8.61 (s, 1H), 7.78-7.75 (m, 1H), 7.71-7.68 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 15 Hz, 1H), 7.19 (dt, J = 7.3, 15 Hz, 1H), 4.97-4.79 (m, 2H), 4.88 (s, 2H), 4.35-4.13 (m, 2H), 3.75-3.53 (m, 2H), 2.91 (s, 3H), 2.15 (s, 3H)		

1403	Chiral	MS (ESI) m/z = 686.2 [M+1]+; 1H NMR (400 MHz, d6-DMSO) δ 8.77 (d, J = 4.8 Hz, 1H), 8.71 (s, 1H), 8.65 (s, 1H), 7.77-7.73 (m, 1H), 7.71-7.66 (m, 2H), 7.53 (d, J = 4.8 HZ, 1H), 6.37 (bt, J = 55 Hz, 1H), 4.81 (s, 2H), 3.25 (s, 3H), 2.37-2.18 (b, 2H), 2.11 (s, 3H). Remaining protons are (partially) obscured by water peak	1406	Chiral	MS (ESI) m/z = 714.5 [M+1]+; 1H NMR (400 MHz, d6-DMSO) δ 10.38-10.18 (b, 1H), 8.76 (d, J = 4.7 Hz, 1H), 8.75 (s, 1H), 8.66 (s, 1H), 7.78-7.66 (m, 3H), 7.55 (d, J = 4.7 Hz, 1H), 6.59 (t, J = 52.6 Hz, 1H), 4.82 (s, 2H), 4.78-4.68 (m, 1H), 4.24-4.14 (m, overlapping with water peak), 3.76-3.58 (m, overlapping with water peak), 3.12 (s, 3H), 2.47-2.37 (m, 2H), 2.37-2.26 (m, 2H), 2.21-2.13 (m, 2H), 2.10-2.01 (m, 2H)
1404		MS (ESI) m/z = 674.4 [M+1]+; 1H NMR (400 MHz, d6-DMSO) δ 8.75 (s, 1H), 8.75 (d, J = 4.7 Hz, 1H), 8.59 (s, 1H), 7.74 (dd, J = 8.1, 0.5 Hz, 1H), 7.69-7.64 (m, 2H), 7.43 (dd, J = 4.7, 0.3 Hz, 1H), 6.22 (tt, J = 55.7, 4.4 Hz, 1H), 4.81 (s, 2H), 3.85 (s, 3H), 3.71-3.67 (m, 4H), 2.84 (dt, J = 15.7, 4.2 Hz, 2H), 2.78-2.72 (m, 4H), 2.06 (s, 3H)	1407		MS (ESI) m/z = 686.1 [M+1]+; 1H NMR (400 MHz, d6-DMSO) δ 8.79 (b, 1H), 8.77 (d, J = 4.7 Hz, 1H), 8.67 (s, 1H), 7.79-7.74 (m, 1H), 7.71-7.67 (m, 2H), 7.54 (d, J = 4.7 Hz, 1H), 6.58-5.69 (b, 1H), 4.84 (s, 2H), 3.33 (t, J = 6.6 Hz, 1H), 3.28 (s, 3H), 2.08 (s, 3H). Remaining protons appear as broad signals and/or are (partially) obscured by water peak
1405		MS (ESI) m/z = 722.5 [M+1]+; 1H NMR (400 MHz, d6-DMSO) δ 8.82 (s, 1H), 8.74 (d, J = 4.7 Hz, 1H), 8.62 (s, 1H), 7.73 (d, J = 8.4 Hz, 1H), 7.67 (dd, J = 8.4, 2.2 Hz, 1H), 7.61 (dd, J = 2.2, 0.4, 1H), 7.43 (d, J = 4.7 Hz, 1H), 4.82 (s, 2H), 4.59-4.53 (m, 2H), 3.86 (s, 3H), 3.69-3.62 (m, 2H), 2.16 (s, 3H). Remaining protons appear as very broad signals and/or are partially obscured by water peak	1408		MS (ESI) m/z = 819.2 [M+1]+; 1H NMR (400 MHz, d6-DMSO) δ 12.98 (bs, 1H), 10.80-10.54 (b, 1H), 8.81 (d, J = 4.8 Hz, 1H), 8.79 (s, 1H), 8.75 (s, 1H), 7.77 (dd, J = 8.3, 0.5 Hz, 1H), 7.72-7.66 (m, 2H), 7.63 (d, J = 4.8 Hz, 1H), 6.40 (tt, J = 53.6, 2.8 Hz, 1H), 5.27-5.17 (m, 1H), 5.00-4.90 (m, 4H), 4.82 (s, 2H), 4.12 (bs, 2H), 3.99-3.85 (m, 2H), 3.76-3.55 (m, 4H), 2.11-1.93 (m, 4H), 1.96 (s, 3H)

1409		MS (ESI) m/z = 840.5 [M+1]+; 1H NMR (400 MHz, d6-DMSO) δ 13.15-12.95 (b, 1H), 10.75-10.55 (b, 1H), 9.26 (dd, J = 2.4, 0.7 Hz, 1H), 8.89 (dd, J = 4.8, 1.6 Hz, 1H), 8.81 (d, J = 4.8 Hz, 1H), 8.61 (s, 1H), 8.52 (ddd, J = 8.1, 2.4, 1.6 Hz, 1H), 8.46 (s, 1H), 7.74-7.64 (m, 3H), 7.62 (dd, J = 2.2, 0.5 Hz, 1H), 7.59 (d, J = 4.8 Hz, 1H), 6.37 (tt, J = 53.7, 3.1 Hz, 1H), 4.77 (s, 2H), 4.10 (bs, 4H), 3.97-3.82 (m, 2H), 3.72-3.50 (m, 4H), 2.07-1.94 (m, 4H), 1.87 (s, 3H)
1410		MS (ESI) m/z = 791.4 [M+1]+; 1H NMR (400 MHz, d6-DMSO) δ 12.44 (s, 1H), 10.60-10.50 (b, 1H), 8.80 (s, 1H), 8.80 (d, J = 4.8 Hz, 1H), 8.78 (s, 1H), 7.77 (dd, J = 8.3, 0.5 Hz, 1H), 7.70 (dd, J = 8.3, 2.1 Hz, 1H), 7.67 (dd, J = 2.1, 0.5 Hz, 1H), 7.62 (d, J = 4.8 Hz, 1H), 4.83 (s, 2H), 4.27-3.90 (m, 6H), 3.79-3.56 (m, 4H expected; partially obscured by water peak), 3.55 (s, 3H expected; partially obscured by water peak), 2.12-1.95 (m, 4H), 2.00 (s, 3H), 1.73 (t, J = 19 Hz, 3H)
1411		MS (ESI) m/z = 833.3 [M+1]+; 1H NMR (400 MHz, d6-DMSO) δ 12.65 (bs, 1H), 10.59 (bs, 1H), 8.78 (d, J = 4.8 Hz, 1H), 8.75 (s, 1H), 8.71 (s, 1H), 7.74 (dd, J = 8.3, 0.5 Hz, 1H), 7.67 (dd, J = 8.3, 2.1, 1H), 7.64 (dd, J = 2.1, 0.5 Hz, 1H), 7.59 (d, J = 4.8 Hz, 1H), 5.24-5.15 (m, 1H), 4.98-4.85 (m, 4H), 4.79 (s, 2H), 4.21-3.87 (m, 4H), 3.74-3.54 (m, 4H), 2.10-1.91 (m, 4H), 1.92 (s, 3H), 1.70 (t, J = 19.3 Hz, 3H)
1412		MS (ESI) m/z = 854.4 [M+1]+; 1H NMR (400 MHz, d6-DMSO) d/ppm = 13.13-13.93 (b, 1H), 10.65-10.49 (b, 1H), 9.26 (dd, J = 2.4, 0.8 Hz, 1H), 8.89 (dd, J = 4.9, 1.6 Hz, 1H), 8.81 (d, J = 4.8 Hz, 1H), 8.61 (s, 1H), 8.52 (ddd, J = 8.1, 2.4, 1.6 Hz, 1H), 8.46 (s, 1H), 7.73 (dd, J = 8.4, 0.4 Hz, 1H), 7.69 (ddd, J = 8.1, 3.3, 0.8 Hz, 1H), 7.66 (dd, J = 8.4, 2.2 Hz, 1H), 7.62 (dd, J = 2.2, 0.4 Hz, 1H), 7.59 (d, J = 4.8 Hz, 1H), 4.77 (s, 2H), 4.24-3.90 (m, 6H expected, overlapping with water peak), 3.71-3.51 (m, 4H), 2.08-1.93 (m, 4H), 1.87 (s, 3H), 1.70 (t, J = 19.4 Hz, 3H)
1413		MS (ESI) m/z 702.5 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 10.61 (s, 1H), 8.81 – 8.72 (m, 2H), 8.64 (s, 1H), 7.79 – 7.72 (m, 1H), 7.71 – 7.64 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 4.32 – 3.89 (m, 6H), 3.64 (m, 4H), 2.07 (d, J = 1.6 Hz, 6H), 2.00 (s, 3H), 1.74 (t, J = 19.6 Hz, 3H)
1414		LCMS (ESI) m/z 702.5 [M+1]+

1415		1421	
MS (ESI) m/z 629.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.23 (d, J = 22.2 Hz, 1H), 8.78 (m, 1H), 8.44 (d, J = 17.1 Hz, 1H), 8.11 (d, J = 57.3 Hz, 1H), 7.57 (m, 1H), 7.48 – 7.40 (m, 2H), 7.34 (dd, J = 12.2, 9.0 Hz, 1H), 4.39 (m, 2H), 4.26 (d, J = 5.4 Hz, 2H), 3.47 – 3.31 (m, 2H), 3.25 (dd, J = 13.1, 9.7 Hz, 1H), 2.29 (m, 1H), 2.22 – 2.11 (m, 1H), 2.11 – 2.01 (m, 1H), 1.99 (d, J = 2.0 Hz, 3H), 1.82 (d, J = 14.3 Hz, 1H), 1.46 (s, 1H), 1.26 (s, 3H)		MS (ESI) m/z 619.45 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.17 (bs, 1H), 7.92 (bs, 1H), 7.52 (d, J = 5.2 Hz, 1H), 7.34-7.27 (m, 2H), 7.14 (bs, 1H), 4.35 (bs, 2H), 4.26 (bs, 2H), 4.04-3.97 (m, 2H), 3.74-3.67 (m, 2H), 2.34 (s, 3H), 1.82 (s , 3H), 1.78 (s, 3H)	
1418		1422	
MS (ESI) m/z 644.0 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.86 (s, 1H), 8.71 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.40 (s, 1H), 7.39 (d, J = 2.7 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.40 (t, J = 5.1 Hz, 2H), 4.31 – 4.22 (m, 4H), 3.62 (d, J = 12.1 Hz, 2H), 3.40 (t, J = 13.0 Hz, 2H), 3.20 (q, J = 11.4 Hz, 2H), 2.90 (s, 3H), 2.70 (s, 3H), 2.53 (s, 3H), 2.00 (s, 3H)		MS (ESI) m/z 676.42 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.23 (bs, 1H), 8.82 (d, J = 4.8 Hz, 1H), 8.64 (s, 1H), 8.45 (s, 1H), 7.59-7.57 (m, 1H), 7.45 (d, J = 4.80, 1H), 7.42 (d, J = 2.0 Hz, 1H), 7.35 (d, J = 8.8 Hz, 1H), 4.38 (s, 2H), 4.20 (s, 2H), 3.65 (s, 4H), 2.67 (s, 4H), 2.60-2.48 (m, 2H), 1.74 (s, 3H), 1.35 (J = 21.6 Hz, 6H)	
1419		1423	
MS (ESI) m/z 588.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.90 (s, 1H), 8.63 (s, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.43 (d, J = 2.7 Hz, 1H), 7.41 (s, 1H), 7.36 (d, J = 9.0 Hz, 1H), 6.33 (q, J = 1.6 Hz, 1H), 5.97 (q, J = 1.9 Hz, 1H), 4.54 – 4.48 (m, 2H), 4.42 (t, J = 5.0 Hz, 2H), 4.28 (t, J = 5.1 Hz, 2H), 2.67 (s, 3H), 1.99 (s, 3H)		MS (ESI) m/z 660.27 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.05 (bs, 1H), 8.79 (s, 1H), 8.75 (d, J = 4.64 Hz, 1H), 8.65 (s, 1H), 7.75 (d, J = 8.12 Hz, 1H), 7.68 (m, 2H), 7.53 (d, J = 4.64 Hz, 1H), 6.34 (m, 1H), 4.82 (s, 2H), 3.76-2.66 (m, 10H), 2.09 (s, 1H)	

1424		1427	
MS (ESI) m/z 662.41 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.84 (d, J = 4.8 Hz, 1H), 8.70 (s, 1H), 8.42 (s, 1H), 7.61 (dd, J = 8.8 Hz, 2.8 Hz, 1H), 7.47 (d, J = 4.4 Hz, 1H), 7.41 (d, J = 2.8 Hz, 1H), 7.37 (d, J = 9.2 Hz, 1H), 4.96-4.67 (m, 2H), 4.40-4.21 (m, 5H), 3.57-3.36 (m, 8H), 1.84 (s, 3H), 1.37 (d, J = 6.0 Hz, 3H)		MS (ESI) m/z 697.51 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.01 (s, 1H), 8.82 (d, J = 4.4 Hz, 1H), 8.41 (s, 1H), 7.59 (dd, J = 8.8, 2.8 Hz, 1H), 7.46 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.4 Hz, 1H), 7.35 (d, J = 8.8 Hz, 1H), 4.39 (t, J = 4.4 Hz, 2H), 4.24 (t, J = 4.4 Hz, 2H), 3.81-3.75 (m, 1H), 3.31 (bs, 3H), 2.45 (s, 3H), 2.32-2.23 (m, 1H), 2.11-1.93 (m, 3H), 1.92-1.66 (m, 5H)
1425		1428	
MS (ESI) m/z 688.50 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.8 Hz, 1H), 8.67 (s, 1H), 8.44 (s, 1H), 7.60 (dd, J = 2.8, 8.8 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.41 (d, J = 2.8 Hz, 1H), 7.37 (d, J = 8.8 Hz, 1H), 4.58-4.48 (m, 1H), 4.44-4.41 (m, 2H), 4.39-4.36 (m, 2H), 3.56-3.53 (m, 4H), 3.30-3.28 (m, 1H), 3.17-2.95 (m, 4H), 2.22-2.19 (m, 2H), 1.84 (s, 3H), 1.14-0.77 (m, 4H)		MS (ESI) m/z 702.53 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.8 Hz, 1H), 8.59 (s, 1H), 8.42 (s, 1H), 7.59 (dd, J = 2.4, 8.8 Hz, 1H), 7.46 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.8 Hz, 1H) 7.36 (d, J = 9.2 Hz, 1H), 4.52 (s, 2H), 4.37-4.40 (m, 2H), 4.23-4.26 (m, 1H), 4.18-4.21 (m, 2H), 3.03 (s, 3H), 2.94-2.97 (m, 2H), 2.66-2.72 (m, 2H), 1.71-1.75 (m, 7H), 0.64-0.68 (m, 4H)	

1426		MS (ESI) m/z 724.56 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.8 Hz, 1H), 8.66 (s, 1H), 8.47 (s, 1H), 7.60 (dd, J = 2.4, 8.8 Hz, 1H), 7.49 (d, J = 4.8 Hz, 1H), 7.41 (d, J = 2.8 Hz, 1H), 7.35 (d, J = 9.2 Hz, 1H), 4.74 (s, 1H), 4.63 (s, 1H), 4.39 (t, J = 4.4 Hz, 2H), 4.21 (t, J = 4.4 Hz, 2H), 3.69 (bs, 4H), 2.88 (bs, 4H), 2.72 (bs, 4H), 1.7(s, 3H)	1429		MS (ESI) m/z 704.54 [M+1]; 1H NMR (400 MHz, DMSO-d6) δ 13.2 (bs, 1H), 9.11 (bs, 1H), 8.83 (d, J = 4.8 Hz, 1H), 8.61 (s, 1H), 8.38 (s, 1H), 7.60 (dd, J = 2.8, 8.8 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.8 Hz, 1H) 7.36 (d, J = 8.8 Hz, 1H), 4.74-4.62 (d, J = 46.8 Hz, 2H), 4.60-4.57 (m, 1H), 4.39 (bs, 2H), 4.21 (bs, 2H), 3.66-3.58 (m, 2H), 3.30-3.24 (m, 2H), 3.09 (s, 3H), 2.26-2.20 (m, 2H), 2.11-2.08 (m, 2H), 1.76 (s, 3H), 1.38 (s, 6H)
1430		MS (ESI) m/z 720.50 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.84 (d, J = 4.8 Hz, 1H), 8.59 (s, 1H), 8.44 (s, 1H), 7.60 (dd, J = 2.4, 6.4 Hz, 1H), 7.49 (d, J = 4.8 Hz, 1H), 7.44 (d, J = 2.8 Hz, 1H), 7.37 (d, J = 8.8 Hz, 1H), 6.08 (t, J = 55.6 Hz, 1H), 4.38 (d, J = 4.4 Hz, 2H), 4.25 (bs, 1H), 4.19 (bs, 2H), 3.08 (bs, 2H), 3.03 (s, 3H), 2.92 (bs, 2H), 1.77 (bs, 7H), 0.48-0.78 (m, 4H)	1433		MS (ESI) m/z 708.50 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.2 Hz, 1H), 8.65 (s, 1H), 8.41 (s, 1H), 7.59 (d, J = 8.6 Hz, 1H), 7.47-7.43 (m, 2H), 7.35 (d, J = 8.8 Hz, 1H), 6.51 (t, J = 53.4 Hz, 1H), 4.38 (s, 4H), 4.21 (s, 2H), 3.07 (bs, 5H), 2.52 (s, 2H), 2.17 (bs, 2H), 2.02 (bs, 2H), 1.75 (s, 3H), 1.11 (t, J = 6.3 Hz, 3H)
1431		MS (ESI) m/z 722.55 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.8 Hz, 1H), 8.61 (s, 1H), 8.39 (s, 1H) 7.61 (dd, J = 2.4, 9.2 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.42-7.35 (m, 2H), 6.52 (t, J = 52 Hz, 1H), 4.62-4.56 (m, 1H), 4.39 (bs, 2H), 4.21 (bs, 2H,), 3.38-3.34 (m, 4H), 3.09 (s, 3H), 2.32-2.26 (m, 2H), 2.12-2.09 (m, 2H), 1.76 (s, 3H), 1.44 (s, 6H)	1434		MS (ESI) m/z 667.18 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.32 (bs, 1H), 8.81 (d, J = 4.8 Hz, 1H), 8.60 (s, 1H), 8.46 (s, 1H), 7.60 (dd, J = 9.2, 2.8 Hz, 1H), 7.44 (dd, J = 15.6 Hz, 2H), 7.35 (d, J = 9.2 Hz, 1H), 4.59 (s, 2H), 4.53 (s, 2H), 4.38 (bs, 4H), 4.24- 4.20 (m, 4H), 3.91-3.88 (m, 1H), 2.17 (bs, 2H), 2.01 (t, J = 9.6 Hz, 2H), 1.82 (s, 3H), 1.78-1.71 (m, 2H)

1432		MS (ESI) m/z 708.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (dd, J = 4.8 Hz, 2 Hz, 1H), 8.61 (d, J = 2 Hz, 1H), 8.40 (s, 1H), 7.61 (d, J = 8.8 Hz, 1H), 7.46 (dd, J = 4.8 Hz, 2 Hz, 1H), 7.43 (d, J = 4.0 Hz, 1H), 7.36 (d, J = 7.2 Hz, 1H), 4.99 (bs, 4H), 4.58 (bs, 1H), 4.39 (s, 2H), 4.21 (s, 2H), 4.0 (bs, 2H), 3.70 (bs, 2H), 3.28 (bs, 1H), 3.09 (s, 3H), 2.33-2.00 (m, 4H), 1.76 (s, 3H)	1435		MS (ESI) m/z 718.48 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.8 Hz, 1H), 8.61 (s, 1H), 8.47 (s, 1H), 7.60 (dd, J = 9.2, 2.8 Hz, 1H), 7.46 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.8 Hz, 1H), 7.36 (d, J = 8.8 Hz, 1H), 4.78-4.59 (m, 4H), 4.40-4.30 (m, 6H), 4.23-4.18 (m, 2H), 3.35-3.15 (m, 2H), 2.80-2.65 (m, 2H), 1.80 (s, 3H), 1.47 (s, 3H)
1436		MS (ESI) m/z 682.52 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.5 (bs, 1H), 9.66 (bs, 1H), 8.80 (d, J = 4.8 Hz, 1H), 8.61 (s, 1H), 8.47 (s, 1H), 7.60 (dd, J = 9.2, 2.8 Hz, 1H), 7.46 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.4 Hz, 1H), 7.36 (d, J = 8.8 Hz, 1H), 4.65-4.45 (m, 8H), 4.40-4.35 (m, 2H), 4.25-4.15 (m, 2H), 2.91 (bs, 1H), 1.80 (s, 3H), 1.17 (s, 3H), 1.06 (s, 3H), 0.85-0.55 (m, 2H)	1439		MS (ESI) m/z 692.45 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.8 Hz, 1H), 8.67 (s, 1H), 8.44 (s, 1H), 7.59 (dd, J = 8.8, 2.4 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.4 Hz, 1H), 7.36 (d, J = 8.8 Hz, 1H), 6.54 (t, J = 54.8 Hz, 1H), 4.38 (d, J = 4.8 Hz, 2H), 4.22 (d, J = 4.8 Hz, 2H), 4.10 (d, J = 12 Hz, 1H), 3.93 (d, J = 12.4 Hz, 1H), 3.41-3.32 (m, 2H), 3.16-3.13 (m, 3H), 2.02 (bs, 1H),1.76 (s, 3H), 0.53-0.41 (m, 4H)
1437		MS (ESI) m/z 667.18 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.32 (bs, 1H), 8.81 (d, J = 4.8 Hz, 1H), 8.60 (s, 1H), 8.46 (s, 1H), 7.60 (dd, J = 9.2, 2.8 Hz, 1H), 7.44 (dd, J = 15.6 Hz, 2H), 7.35 (d, J = 9.2 Hz, 1H), 4.59 (s, 2H), 4.53 (s, 2H), 4.38 (bs, 4H), 4.24- 4.20 (m, 4H), 3.91-3.88 (m, 1H), 2.17 (bs, 2H), 2.01 (t, J = 9.6 Hz, 2H), 1.82 (s, 3H), 1.78-1.71 (m, 2H)	1440		MS (ESI) m/z 693.42 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.03 (s, 1H), 8.84 (d, J = 4.8 Hz, 1H), 8.33 (s, 1H), 7.65-7.58 (m, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.4 Hz, 1H), 7.36 (d, J = 8.8 Hz, 1H), 6.40 (t, J = 62.4 Hz, 1H), 4.41 (s, 2H), 4.28 (d, J = 5.2 Hz, 2H), 3.51-3.05 (m, 8H), 2.50 (bs, 2H), 1.82 (s, 3H), 1.77 (s, 1H)

1438		1441	
MS (ESI) m/z 710.17 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.8 Hz, 1H), 8.67 (s, 1H), 8.46 (s, 1H), 7.60 (dd, J = 8.8 Hz, 2.4 Hz, 1H), 7.49 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.8 Hz, 1H), 7.36 (d, J = 8.8 Hz, 1H), 4.39 (d, J = 4.8 Hz, 2H), 4.29 (bs, 2H), 3.96 (dd, J = 14, 5.2 Hz, 1H), 3.87 (bs, 2H), 3.71 (bs, 1H), 3.59 (t, J = 9.2 Hz, 1H), 3.27 (bs, 1H), 2.90 (d, J = 12.8 Hz, 1H), 2.26 (bs, 1H), 1.76 (s, 3H), 0.58 (d, J = 6.4 Hz, 2H), 0.46 (s, 2H)		MS (ESI) m/z 728.40 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.8 Hz, 1H), 8.59 (s, 1H), 8.44 (s, 1H), 7.60-7.58 (dd, J = 2.4, 8.8 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.4 Hz, 1H), 7.36 (d, J = 8.8 Hz, 1H), 4.38 (bs, 2H), 4.25-4.19 (m, 3H), 3.35-3.30 (m, 2H), 3.07(s, 5H), 2.66-2.59 (m, 2H), 1.92 (d, J = 9.2 Hz, 2H), 1.78-1.72 (m, 5H)	
1443		1446	
MS (ESI) m/z 656.45 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.07 (s, 1H), 8.75 (d, J = 4.8, 2H), 8.65 (s, 1H), 7.75 (d, J = 8.8 Hz, 1H), 7.68 (d, J = 6.8 Hz, 2H), 7.53 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 4.47 (d, J = 44 Hz, 2H), 3.66 (bs, 4H), 2.96 (bs, 1H), 2.74 (s, 3H), 2.07-2.08 (m, 4H), 1.23 (s, 3H)		MS (ESI) m/z 682.44 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.81 (s, 1H), 8.75 (d, J = 4.8 Hz, 1H), 8.66 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.70-7.67 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 4.83 (s, 2H), 4.56-4.41 (m, 2H), 3.77-3.06 (m, 8H), 2.23 (s, 3H), 1.23-0.72 (m, 6H)	
1444		1447	
MS (ESI) m/z 650.47 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.29 (bs, 1H), 8.83 (s, 1H), 8.76 (d, J = 4.8 Hz, 1H), 8.65 (s, 1H), 7.76 (d, J = 8.4 Hz, 1H), 7.70-7.65 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 4.83 (s, 2H), 4.46 (bs, 2H), 3.53 (bs, 6H), 2.14 (s, 3H), 1.39 (s, 3H), 1.20 (bs, 2H), 0.83 (bs, 2H)		MS (ESI) m/z 664.45 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.99 (bs, 1H), 9.00 (bs, 1H), 8.83 (bs, 1H), 8.75 (d, J = 4.8 Hz, 1H), 8.65 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.70-7.64 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 4.83 (s, 2H), 4.37 (bs, 2H), 3.85-3.40 (m, 6H), 2.90-2.80 (m, 1H), 2.13 (s, 3H), 1.38 (s, 3H), 1.07 (s, 3H), 0.95-0.75 (m, 2H)	

1445	MS (ESI) m/z 668.45 [M+1]+; 1; H NMR (400 MHz, DMSO-d6) δ 8.79 (s, 1H), 8.76 (d, J = 4.8 Hz, 1H), 8.66 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.69-7.67 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 4.83 (s, 2H), 4.60 (d, J = 48.4 Hz, 2H), 3.80-3.50 (m, 4H), 3.30-2.80 (m, 4H), 2.09 (s, 3H), 1.20-0.80 (m, 4H)	1448	MS (ESI) m/z 674.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.81 (s, 1H), 8.75 (d, J = 4.4 Hz, 1H), 8.65 (s, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.69-7.67 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 4.91-4.83 (m, 6H), 4.12 (bs, 1H), 3.79 (bs, 4H), 3.27 (bs, 4H), 2.10 (s, 3H)
1449	MS (ESI) m/z 688.47 [M+1]+; ; 1H NMR (400 MHz, DMSO-d6) δ 8.81 (s, 1H), 8.75 (d, J = 4.8 Hz, 1H), 8.65 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.69-7.67 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 4.83 (s, 2H), 4.72-4.54 (m, 2H), 4.32 (bs, 2H), 3.14-2.67 (m, 8H), 2.10 (s, 3H), 1.48-1.45 (m, 3H)	1452	MS (ESI) m/z 670.50 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.76 (bs, 1H), 8.84 (s, 1H), 8.76 (d, J = 4.4 Hz, 1H), 8.65 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.70-7.66 (m, 2H), 7.54 (d, J = 4.8 Hz, 2H), 4.83 (s, 2H), 4.72 (d, J = 46.8 Hz, 2H), 4.46 (d, J = 14.0 Hz, 2H), 3.85-3.50 (m, 4H), 3.40-3.30 (m, 2H), 2.15 (s, 3H), 1.40 (s, 6H)
1450	MS (ESI) m/z 668.42 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.74 (bs, 1H), 8.46 (s, 1H), 8.75 (d, J = 4.8 Hz, 1H), 8.65 (s, 1H), 7.76 (d, J = 8.4 Hz, 1H), 7.69-7.66 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 5.74 (d, J = 34.0 Hz, 2H), 5.10 (s, 1H), 4.98 (s, 1H), 4.83 (s, 2H), 4.40 (d, J = 20.8 Hz, 2H), 3.96 (bs, 2H), 3.65 (m, 2H), 3.54 (m, 2H), 3.29 (bs, 2H), 2.14 (s, 3H)	1453	MS (ESI) m/z 670.13 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.78 (bs, 1H), 8.83 (s, 1H), 8.75 (d, J = 4.8 Hz, 1H), 8.65 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.71-7.64 (m, 2H), 7.53 (d, J = 4.8 Hz, 1H), 4.83 (s, 2H), 4.32 (bs, 2H), 3.85-3.30 (m, 8H), 2.13 (s, 3H), 1.50 (d, J = 21.2 Hz, 6H)

1451		1454	
MS (ESI) m/z 664.24 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.84 (s, 1H), 8.75 (d, J = 4.8 Hz, 1H), 8.65 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.70-7.66 (m, 2H), 7.53 (d, J = 4.8 Hz, 1H), 4.83 (s, 2H), 4.36 (m, 2H), 3.71-3.57 (m, 4H), 3.30-3.18 (m, 4H), 2.15 (s, 3H), 2.21 (s, 3H), 0.60-0.51 (m, 4H)		MS (ESI) m/z 684.48 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.84 (s, 1H), 8.75 (d, J = 4.8 Hz, 1H), 8.65 (s, 1H), 7.75 (d, J = 8 Hz, 1H), 7.70-7.66 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 4.83 (s, 2H), 4.74-4.60 (m, 2H), 4.47 (d, J = 13.6 Hz, 2H), 3.75 (d, J = 11.2 Hz, 2H), 3.60-3.53 (m, 2H), 3.31-3.28 (m, 2H), 2.21-2.15 (m, 5H) 1.42 (s, 6H)	
1455		1458	
MS (ESI) m/z 688.32 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.80 (s, 1H), 8.75 (d, J = 4.8 Hz, 1H), 8.66 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.69-7.67 (m, 2H), 7.54 (d, J = 4.8, 1H), 6.45-6.14 (m, 1H), 4.82 (s, 2H), 3.98-3.69 (m, 4H), 3.17 (m, 4H), 2.11 (s, 3H), 1.29 (s, 6H)		MS (ESI) m/z 706.49 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.96 (bs, 1H), 8.84 (s, 1H), 8.76 (d, J = 4.8 Hz, 1H), 8.64 (s, 1H), 7.76 (d, J = 8.4 Hz, 1H), 7.69 (dd, J = 8.4, 2.0 Hz, 1H), 7.65 (d, J = 2.0 Hz, 1H), 7.53 (d, J = 4.8 Hz, 1H), 4.84 (s, 2H), 4.40-4.36 (m, 2H), 3.74-3.72 (m, 2H), 3.29 (bs, 6H), 2.45-2.38 (m, 2H), 2.14 (s, 3H), 1.98-1.93 (m, 2H)	
1456		1459	
MS (ESI) m/z 674.18 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.16 (bs, 1H), 8.84 (s, 1H), 8.75 (d, J = 4.8 Hz, 1H), 8.64 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.67 (t, J = 8.4 Hz, 2H), 7.53 (d, J = 4.8 Hz, 1H), 6.26 (t, J = 56 Hz, 1H), 4.83 (s, 2H), 4.36 (bs, 2H), 3.73 (bs, 2H), 3.37 (bs, 6H), 2.40 (bs, 2H), 2.13 (s, 3H)		MS (ESI) m/z 642.17 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.85 (s, 1H), 8.76 (d, J = 4.8 Hz, 1H), 8.65 (s, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.69 (dd, J = 8.4 Hz, 2.0 Hz, 1H), 7.65 (s, 1H), 7.53 (d, J = 4.8 Hz, 1H), 5.12-4.93 (m, 2H), 4.84 (s, 2H), 4.44 (dd, J = 42.4 Hz, 14.4 Hz, 1H), 3.54-3.51 (m, 4H), 3.00 (s, 3H), 2.50-2.43 (m, 1H), 2.14 (s, 3H)	

1457		1460	
MS (ESI) m/z 656.39 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.84 (s, 2H), 8.75 (d, J = 4.8 Hz, 1H), 8.64 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.70-7.65 (m, 2H), 7.53 (d, J = 4.8 Hz, 1H), 4.83 (s, 2H), 4.65-4.50 (m, 2H), 4.38 (d, J = 13.6 Hz, 2H), 3.46 (bs, 4H), 3.32 (bs, 4H), 2.19-2.06 (m, 5H)		MS (ESI) m/z 708.44 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.85 (s, 1H), 8.76 (d, J = 4.8 Hz, 1H), 8.65 (s, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.70-7.66 (m, 2H), 7.53 (d, J = 4.8 Hz, 1H), 4.84 (s, 2H), 4.66-4.36 (m, 5H), 3.91-3.78 (m, 4H), 2.95 (bs, 3H), 2.13 (s, 3H)	
1461		1464	
MS (ESI) m/z 633.40 [M+1] +; 1H NMR (400 MHz, DMSO-d6) δ 13.05 (bs, 1H), 9.51 (bs, 1H), 9.12 (s, 1H), 8.74 (d, J = 4.8 Hz, 1H), 8.61 (s, 1H), 7.76 (d, J = 9.1 Hz, 1H), 7.81-7.67 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 6.56 (s, 1H), 4.87 (s, 2H), 4.30-4.10 (m, 2H), 3.80 (bs, 1H), 3.01 (bs, 4H), 2.19 (s, 3H), 1.10-0.84 (m, 4H)		MS (ESI) m/z 690.43 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.04 (bs, 1H), 8.81-8.75 (m, 2H), 8.65 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.68 (d, J = 10.0 Hz, 1H), 7.53 (d, J = 4.4 Hz, 1H), 4.83 (s, 2H), 4.36-4.02 (m, 4H), 3.69-3.59 (m, 4H), 3.36-2.9 (m, 4H), 2.11 (s, 3H)	
1462		1465	
MS (ESI) m/z 639.37 [M+1]+; ; 1H NMR (400 MHz, DMSO-d6) δ 13.07 (bs, 1H), 10.26 (bs, 1H), 9.12 (s, 1H), 8.75 (d, J = 4.8 Hz, 1H), 8.61 (s, 1H), 7.76 (d, J = 8.8 Hz, 1H), 7.71-7.66 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 6.57 (s, 1H), 5.00-4.85 (m, 4H), 4.29-3.95 (m, 2H), 3.90-3.80 (m, 2H), 3.60-3.45 (m, 2H), 3.10-2.90 (m, 2H), 2.18 (s, 3H)		MS (ESI) m/z 680.51 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (s,1H), 8.76 (d, J = 4.8 Hz, 1H), 8.65 (s, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.70-7.67 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 4.83 (s, 2H), 4.49-4.43 (m, 2H), 3.76-3.46 (m, 8H), 3.26 (s, 3H), 2.49 (s, 1H), 2.12 (s, 3H), 1.25 (bs, 2H), 0.97 (bs, 2H)	

1463		1466	
MS (ESI) m/z 657.40 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.10 (s, 1H), 8.75 (d, J = 4.8 Hz, 1H), 8.62 (s, 1H), 7.76 (d, J = 9.2 Hz, 1H), 7.70-7.68 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 6.62-6.34 (m, 2H), 4.86 (s, 2H), 3.41-3.24 (m, 4H), 3.15-2.95 (m, 2H), 2.87 (bs, 2H), 2.16 (s, 3H)		MS (ESI) m/z 674.47 [M+1]+; 1; H NMR (400 MHz, DMSO-d6) δ 8.80 (s, 1H), 8.75 (d, J = 4.8 Hz, 1H), 8.65 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.69 (bs, 1H), 7.67 (s, 1H), 7.53 (d, J = 4.4 Hz, 1H), 6.31 (t, J = 53.2 Hz, 1H), 4.82 (s, 2H), 3.79 (bs, 4H), 3.11 (bs, 4H), 2.64-2.59 (m, 1H), 2.09 (s, 3H), 1.21 (bs, 3H)	
1467		1470	
MS (ESI) m/z 686.19 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.77-8.74 (m, 2H), 8.64 (s, 1H), 7.75 (d, J = 9.2 Hz, 1H), 7.69-7.67 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 4.57-4.55 (m, 4H), 4.24 (d, 2H), 3.21-3.15 (m, 2H), 2.41 (s, 1H), 2.08-2.04 (m, 5H), 1.55 (s, 2H)		MS (ESI) m/z 674.44 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.74 (bs, 1H), 8.83 (d, J = 4.8 Hz, 1H), 8.70 (s, 1H), 8.44 (s, 1H), 7.61-7.58 (dd, J = 2.4, 8.8 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.41 (d, J = 2.4 Hz, 1H), 7.38 (d, J = 8.8 Hz, 1H), 5.73 (d, J = 30.4 Hz, 2H), 5.09 (s, 1H), 4.98 (s, 1H), 4.40 (d, J = 4.8 Hz, 2H), 4.31 (bs, 2H), 4.24 (d, J = 4.8 Hz, 2H), 3.96 (bs, 2H), 3.63 (m, 2H), 3.32-3.18 (m, 4H), 1.84 (s, 3H)	
1468		1471	
MS (ESI) m/z 661.37 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.02 (bs, 1H), 9.07 (s, 1H), 8.76 (s, 1H), 8.61 (s, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.69 (s, 2H), 7.53 (s, 1H), 4.87 (s, 2H), 3.90 (s, 2H), 3.50-3.30 (m, merged, 2H), 2.55 (s, 3H), 2.09 (s, 3H)		MS (ESI) m/z 724.09 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.8 Hz, 1H), 8.70 (s, 1H), 8.45 (s, 1H), 7.60 (dd, J = 2.4, 8.8 Hz, 1H), 7.46 (d, J = 4.8 Hz, 1H), 7.41 (d, J = 2.4 Hz, 1H), 7.36 (d, J = 8.8 Hz, 1H), 4.39 (s, 2H), 4.32-4.23 (m, 4H), 3.28-2.86 (m, 4H), 1.83 (s, 3H), 1.30-1.21 (m, 4H)	

1469		1472	
MS (ESI) m/z 704.21 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.9 Hz, 1H), 8.70 (s, 1H), 8.40 (s, 1H), 7.55 (dd, J = 2.4, 8.8 Hz, 1H), 7.50 (d, J = 4.9 Hz, 1H), 7.31 (d, J = 2.8 Hz, 2H), 4.46 (t, J = 4.9 Hz, 2H), 4.34 (t, J = 4.9 Hz, 2H), 4.10 (bs, 4H), 3.72 (bs, 4H), 3.61 (s, 2H), 2.11 (s, 3H), 1.99-1.80 (m, 4H), 1.03 (t, J = 7.4 Hz, 6H)		MS (ESI) m/z 726.18 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.8 Hz, 1H), 8.66 (bs, 1H), 8.45 (s, 1H), 7.59 (dd, J = 2.4, 9.2 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.4 Hz, 1H), 7.36 (d, J = 9.2 Hz, 1H), 4.38 (s, 2H), 4.21 (s, 2H), 3.75 (bs, 8H), 2.71 (s, 2H), 1.76 (s, 3H), 1.15 (s, 6H)	
1473		1476	
MS (ESI) m/z 698.22 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.8 Hz, 1H), 8.69 (bs, 1H), 8.45 (s, 1H), 7.59 (dd, J = 2.4, 9.2 Hz, 1H), 7.45 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.4 Hz, 1H), 7.36 (d, J = 9.2 Hz, 1H), 4.39 (s, 2H), 4.22 (s, 4H), 3.54 (bs, 6H), 1.98-1.64 (m, 2H), 1.18 (d, J = 7.2 Hz, 2H), 1.10-1.05 (m, 12H)		MS (ESI) m/z 710.49 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.90 (bs, 1H), 8.81 (d, J = 5.2 Hz, 1H), 8.61 (s, H), 8.47 (s, 1H), 7.60 (dd, J = 8.8, 2.4 Hz, 1H), 7.46 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.8 Hz, 1H), 7.36 (d, J = 8.8 Hz, 1H), 4.63 (s, 2H), 4.59-4.47 (m, 6H), 4.38 (t, J = 4.4 Hz, 2H), 4.21 (d, J = 4.8 Hz, 2H), 2.70 (s, 1H), 1.81 (s, 3H), 1.09 (s, 6H), 1.07 (s, 6H)	
1474		1477	
MS (ESI) m/z 700.44 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 5.2 Hz, 1H), 8.60 (s, 1H), 8.43 (s, 1H), 7.59-7.57 (dd, J = 2.4, 10.8 Hz, 1H), 7.49 (d, J = 4.8 Hz, 1H), 7.39 (d, J = 2.4 Hz, 1H), 7.35 (d, J = 9.2 Hz, 1H), 4.36 (s, 2H), 4.19 (s, 2H), 3.65 (m, 4H), 4.44-3.38 (m, 2H), 2.87 (bs, 4H), 1.77 (s, 3H)		MS (ESI) m/z 720.50 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.35 (bs, 1H), 8.82 (d, J = 4.8 Hz, 1H), 8.61 (s, 1H), 8.40 (s, 1H), 7.59 (dd, J = 2.40, 8.8 Hz, 1H), 7.47 (d, J = 4.4 Hz, 1H), 7.42 (d, J = 2.8 Hz, 1H), 7.36 (d, J = 8.8 Hz, 1H), 4.53 (bs, 1H), 4.39 (bs, 2H), 4.21 (bs, 2H), 3.74 (bs, 1H), 3.58 (bs, 2H), 3.09 (bs, 9H), 2.10 (bs, 4H), 1.77 (s, 3H)	

1475		MS (ESI) m/z 704.47 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.81 (d, J = 4.8 Hz, 1H), 8.60 (s, 1H), 8.47 (s, 1H), 7.59 (dd, J = 9.2, 2.8 Hz, 1H), 7.46 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.4 Hz, 1H), 7.35 (d, J = 9.2 Hz, 1H), 4.53 (bs, 4H),4.45-4.35 (m, 2H), 4.25-4.15 (m, 2H), 3.60-3.45 (m, 1H), 3.20-2.70 (m, 4H), 2.60-2.40 (m, merged, 4H), 1.81 (s, 3H)	1478		MS (ESI) m/z 692.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.81 (d, J = 4.8 Hz, 1H), 8.62 (s, 1H), 8.47 (s, 1H), 7.60 (dd, J = 9.2, 2.8 Hz, 1H), 7.45 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.4 Hz, 1H), 7.36 (d, J = 9.2 Hz, 1H), 6.41 (t, J = 53.6 Hz, 1H), 4.38-4.37 (m, 2H), 4.21 (s, 2H), 3.91 (bs, 6H), 3.17 (s, 4H), 3.03-2.81 (m, 2H), 1.79 (s, 3H)
1479		MS (ESI) m/z 663.41 [M+1] +; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.8 Hz, 1H), 8.72 (s, 1H), 8.37 (s, 1H), 7.60 (d, J = 8.4 Hz, 1H), 7.47 (d, J = 4.4 Hz, 1H), 7.42 (bs, 1H), 7.36 (d, J = 8.8 Hz, 1H), 5.47 (d, J = 48.4 Hz, 1H), 4.93 (bs, 1H), 4.82 (bs, 1H), 4.39 (bs, 2H), 4.24 (bs, 2H), 3.68 (bs, 4H), 3.37-3.27 (m, 4H), 2.29-2.10 (m, 1H), 2.01-1.98 (m, 1H), 1.82-1.77 (m, 3H)	1482		MS (ESI) m/z 628.33 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.04 (bs, 1H), 9.07 (s, 1H), 8.76 (d, J = 4.8 Hz, 1H), 8.61 (s, 1H), 7.77 (d, J = 9.2 Hz, 1H), 7.69 (t, J = 3.2 Hz, 1H), 7.54 (d, J = 4.4 Hz, 1H), 6.33 (s, 1H), 4.86 (s, 2H), 2.89-2.84 (m, 4H), 2.29-2.22 (m, 2H), 2.14 (s, 3H)
1480		MS (ESI) m/z 691.44 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.00 (s, 1H), 8.84 (d, J = 4.8 Hz, 1H), 8.39 (s, 1H), 7.61-7.58 (dd, J = 2.8, 8.8 Hz, 1H), 7.48-7.45 (dd, J = 10.8, 8.8 Hz, 2H), 7.37 (d, J = 9.2 Hz, 1H), 6.46 (m, 1H), 4.40 (t, 2H), 4.25 (bs, 2H), 3.07-2.97 (m, 8H), 2.22 (m, 2H), 2.06 (s, 3H), 1.79 (s, 3H)	1483		MS (ESI) m/z 753.43 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.65 (s, 1H), 9.87 (bs, 1H), 8.90 (d, J = 4.8 Hz, 1H), 8.76 (s, H), 8.55 (s, 1H), 7.63 (dd, J = 8.8, 2.4 Hz, 1H), 7.57 (d, J = 4.8 Hz, 1H), 7.44-7.37 (m, 2H), 4.73 (d, J = 46.0 Hz, 2H), 4.50-4.35 (m, 4H), 4.23 (s, 2H), 3.80-3.50 (m, 7H), 3.45-3.22 (m, 2H), 1.85 (s, 3H), 1.42 (s, 6H)

1481		MS (ESI) m/z 630.38 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.11 (s, 1H), 8.57 (d, J = 4.8 Hz, 1H), 8.61 (s, 1H), 7.77-7.75 (m, 1H), 7.69 (dd, J = 2.0, 6.8 Hz, 2H), 7.54 (d, J = 4.8 Hz, 1H), 4.86 (s, 2H), 2.53 (s, 1H), 2.17-2.15 (m, 3H), 2.08-2.06 (m, 2H), 2.01 (d, J = 5.6 Hz, 6H)	1484		MS (ESI) m/z 679.16 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.85 (bs, 1H), 8.96 (s, 1H), 8.82 (d, J = 4.8 Hz, 1H), 8.33 (s, 1H), 7.60 (dd, J = 2.4, 8.8 Hz, 2H), 7.47-7.43 (m, 1H), 7.36 (d, J = 8.8 Hz, 1H), 6.66-6.39 (m, 1H), 4.39 (t, J = 4.4 Hz ,2H), 4.25 (bs, 2H), 3.66-3.51 (m, 4H), 3.05 (d, J = 5.6 Hz, 4H), 2.19 (bs, 1H), 1.80 (s, 6H), 1.63-1.60 (m, 2H)
1485		MS (ESI) m/z 639.38 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.96 (s, 1H), 8.82 (d, J = 4.4 Hz, 1H), 8.34 (s, 1H), 7.60 (dd, J = 9.2, 2.8 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.8 Hz, 1H), 7.36 (d, J = 9.2, 1H), 6.36 (t, J = 49.2 Hz, 1H), 4.40 (t, J = 4.8 Hz, 2H), 4.27-4.26 (m, 2H), 3.43 (bs, 4H), 2.73 (bs, 2H), 1.82 (s, 3H)	1488		MS (ESI) m/z 719.44 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.45 (s, 1H), 10.12 (bs, 1H), 8.89 (s, 1H), 8.82 (d, J = 4.8 Hz, 1H), 8.79 (s, 1H), 7.77 (d, J = 8.4 Hz, 1H), 7.72-7.69 (m, 1H), 7.66 (d, J = 1.6 Hz, 1H), 7.62 (d, J = 4.8 Hz, 1H), 5.00-4.80 (m, 2H), 4.35 (bs, 2H), 3.82-3.60 (m, 4H), 3.55 (s, 3H), 3.50-3.22 (m, 4H), 2.03 (s, 3H)
1486		MS (ESI) m/z 769.56 [M+1]+	1489		MS (ESI) m/z 698.22 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.80 (s, 1H), 8.75 (d, J = 4.8 Hz, 1H), 8.65 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.68 (d, J = 9.2 Hz, 2H), 7.53 (d, J = 4.4 Hz, 1H), 4.83 (s, 2H), 3.59 (bs, 2H), 3.09 (bs, 8H), 5.19 (s, 5H), 1.82 (bs, 1H)

1487		MS (ESI) m/z 737.44 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.44 (bs, 1H), 8.84-8.80 (m, 3H), 7.77 (d, J = 8.4 Hz, 1H), 7.71-7.66 (m, 2H), 7.61 (d, J = 4.8 Hz, 1H), 6.32 (t, J = 52.0 Hz, 1H), 4.83 (s, 2H), 3.75 (bs, 4H), 3.56 (bs, 3H), 2.95 (bs, 6H), 2.01 (s, 3H)	1490 MS (ESI) m/z 700.41 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 10.35 (s, 1H), 8.78 (s, 1H), 8.75 (d, J = 4.4 Hz, 1H), 8.64 (s, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.69 (d, J = 9.6 Hz, 2H), 7.54 (d, J = 4.8 Hz, 1H), 6.39 (bs, 1H), 4.83 (s, 2H), 4.37-4.08 (m, 4H), 3.87 (bs, 4H), 3.26 (bs, 2H), 2.18 (bs, 4H), 2.10 (s, 3H)
1491		MS (ESI) m/z 680.42 [M+1]+; 1H NMR (400 MHz, DMSO-d6) d 8.76 (d, J = 4.8 Hz, 1H), 8.68 (d, J = 8.8 Hz, 2H), 7.75 (d, J = 8.8 Hz, 1H), 7.68 (d, J = 6.4 Hz, 2H), 7.55 (d, J = 4.8 Hz, 1H), 4.81 (s, 2H), 3.82 (t, J = 6.8 Hz, 2H), 3.33-3.25 (m, 5H), 2.92 (t, J = 6.8 Hz, 2H), 2.45 (s, 3H), 2.04 (s, 3H)	1494 MS (ESI) m/z 689.42 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.77 (d, J = 4.8 Hz, 1H), 8.73 (s, 1H), 8.66 (s, 1H), 7.76 (d, J = 9.2 Hz, 1H), 7.69-7.68 (m, 2H), 7.55 (d, J = 4.4 Hz, 1H), 4.82 (s, 2H), 4.30 (s, 1H), 3.06-3.01 (m, 7H), 2.06 (s, 3H), 1.86-1.83 (m, 4H), 1.25 (dd, J = 8.0 Hz, 5.6 Hz, 2H), 1.05 (dd, J = 7.2, 4.8 Hz, 2H)
1492		MS (ESI) m/z 633.31 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.11 (s, 1H), 8.73 (d, J = 4.8 Hz 1H), 8.59 (s, 1H), 7.76 (d, J = 8.4 Hz, 1H), 7.70-7.67 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 6.40 (t, J = 50.8 Hz, 1H), 4.87 (s, 2H), 3.49 (bs, 4H), 3.12-2.77 (m, 5H), 2.17 (s, 3H)	1495 MS (ESI) m/z 638.41 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.79-8.74 (m, 2H), 8.65 (s, 1H), 7.78 (d, J = 8.0 Hz, 1H), 7.70-7.68 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 4.83 (s, 2H), 4.54-4.53 (m, 1H), 3.58-3.55 (m, 2H), 3.20 (bs, 2H), 3.01 (s, 3H), 2.83-2.82 (m, 3H), 2.10 (bs, 7H)

1493		MS (ESI) m/z 700.47 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (s, 1H), 8.75 (d, J = 4.8 Hz, 1H), 8.65 (s, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.70-7.67 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 4.83 (s, 2H), 4.43-3.90 (m, 4H), 3.22-2.87 (m, 8H), 2.13 (s, 3H), 1.46 (s, 3H)	1496		MS (ESI) m/z 690.46 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.75 (d, J = 4.7 Hz 1H), 8.72 (s, 1H), 8.69 (s, 1H), 7.74 (d, J = 8.2 Hz, 1H), 7.66-7.64 (m, 2H), 7.53 (d, J = 4.6 Hz, 1H), 4.83 (s, 2H), 4.60-4.58 (m, 1H), 3.18 (s, 3H), 3.10-3.00 (m, 1H), 2.27 (s, 3H), 1.60-1.57 (m, 1H), 1.30-1.24 (m, 5H), 0.87-0.67 (m, 8H)
1497		MS (ESI) m/z 694.46 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.76 (d, J = 4.8 Hz, 1H), 8.69 (d, J = 6.8 Hz, 1H), 7.76-7.43 (m, 1H), 7.68 (dd, J = 2.0, 4.0 Hz, 1H), 7.54 (d, J = 4.8 Hz, 1H), 4.81 (s, 2H), 3.73-3.70 (m, 2H), 3.27 (bs, 5H), 2.68-2.64 (m, 2H), 2.41 (s, 3H), 2.05 (s, 3H), 1.90 (t, J = 13.6 Hz, 2H)	1500		MS (ESI) m/z 700.47 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.74 (d, J = 4.8 Hz, 1H), 8.63 (s, 1H), 8.60 (s, 1H), 7.75 (d, J = 8 Hz, 1H), 7.68-7.66 (m, 2H), 7.51 (d, J = 4.8 Hz, 1H), 6.15 (tt, J = 4.0, 55.6 Hz, 1H), 4.79 (s, 2H), 4.53 (t, J = 7.2 Hz, 2H), 2.89 (d, J = 11.2 Hz, 2H), 2.77-2.67 (m, 4H), 2.21-2.16 (m, 4H), 2.03 (s, 3H), 1.81 (d, J = 11.6 Hz, 2H)
1498		MS (ESI) m/z 595.39 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.11 (bs, 1H), 9.73 (bs, 1H), 9.14 (s, 1H), 8.73 (d, J = 4.8 Hz, 1H), 8.60 (s, 1H), 7.76 (d, J = 9.2 Hz, 1H), 7.71-7.67 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 7.39 (d, J = 15.2 Hz, 1H), 7.20-7.10 (m, 1H), 4.88 (s, 2H), 4.16-4.08 (m, 2H), 2.87 (s, 6H), 2.15 (s, 3H)	1501		MS (ESI) m/z 783.47 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.47 (s, 1H), 8.81 (d ,J = 5.6 Hz, 2H), 8.75 (s, 1H), 7.78 (d, J = 8.4 Hz, 1H), 7.71-7.68 (dd, J = 2.0, 10.4 Hz, 2H), 7.62 (d, J = 4.4 Hz, 1H), 4.82 (s, 2H), 4.32 (bs, 1H), 3.55 (s, 3H), 3.31 (bs, 2H), 3.10 (bs, 5H), 2.51 (bs, 2H), 1.97 (bs, 5H), 1.82-1.79 (m, 2H)

1499	MS (ESI) m/z 672.39 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.26 (bs, 1H), 9.90 (bs, 1H), 8.89 (s, 1H), 8.75 (d, J = 4.8 Hz, 1H), 8.69 (s, 1H), 7.76 (d, J = 8.4 Hz, 1H), 7.71-7.66 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 6.48 (t, J = 53.2 Hz, 1H), 5.21-5.02 (m, 2H), 4.82 (s, 2H), 4.53 (bs, 4H), 4.20-3.80 (m, 2H), 2.78-2.63 (m, 2H), 2.18 (s, 3H)	1502	MS (ESI) m/z 716.50 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.75 (d, J = 4.8 Hz, 1H), 8.72 (s, 1H), 8.57 (s, 1H), 7.75 (d, J = 9.2 Hz, 1H), 7.68-7.66 (m, 2H), 7.50 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 4.28-4.22 (m, 1H), 3.09 (s, 3H), 3.01 (d, J = 11.2 Hz, 2H), 2.75 (t, J = 14.4 Hz, 2H), 2.38 -2.32 (m, 2H), 2.05 (s, 3H), 2.01-1.85 (m, 4H), 1.77 (d, J = 11.6 Hz, 2H), 0.96 (t, J = 7.2 Hz, 3H)
1503	MS (ESI) m/z 718.42 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.08 (bs, 1H), 8.76-8.74 (m, 2H), 8.65 (s, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.69-7.67 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 6.79 (t, J = 74.8 Hz, 1H), 4.82 (s, 2H), 4.56 (bs, 1H), 4.23 (s, 2H), 3.65 (bs, 2H), 3.46 (bs, 2H), 3.26-3.19 (m, 2H), 3.11 (s, 3H), 2.26-2.08 (m, 2H), 2.04 (s, 5H)	1506	MS (ESI) m/z 730.26 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.76-8.74 (m, 2H), 8.65 (s, 1H), 7.75 (d, J = 6.0 Hz, 1H), 7.70-7.67 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 4.65-4.60 (m, 1H), 3.91-3.78 (m, 2H), 3.41-3.39 (m, 2H), 3.22 (s, 3H), 2.32-2.26 (m, 2H), 2.24-2.08 (m, 5H), 1.84-1.79 (m, 3H), 1.51 (s, 6H)
1504	MS (ESI) m/z 744.4 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.75 (d, J = 4.8 Hz, 2H), 8.65 (s, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.70 (d, J = 2.0 Hz, 2H), 7.55 (d, J = 4.8 Hz, 1H), 6.73 (t, J = 75 Hz, 1H), 4.82 (s, 2H), 4.65 (bs, 1H), 4.21 (bs, 2H), 3.09 (s, 3H), 2.70-2.50 (m, 4H), 2.09 (bs, 7H), 1.33 (bs, 2H), 1.12 (bs, 2H)	1507	MS (ESI) m/z 734.30 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.76 (d, J = 4.8 Hz, 1H), 8.71 (s, 1H), 8.66 (s, 1H), 7.76 (d, J = 5.2 Hz, 1H), 7.70-7.67 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 4.81 (s, 2H), 4.30-4.06 (m, 2H), 3.53-3.37 (m, 2H), 3.08 (s, 3H), 2.05 (s, 3H), 1.90-1.86 (m, 4H), 1.33 (s, 6H)

1505	MS (ESI) m/z 671.41 [M+1] +; 1H NMR (400 MHz, DMSO-d6) δ 8.76 (d, J = 4.8 Hz, 1H), 8.68 (d, J = 1.6 Hz, 2H), 7.75 (d, J = 8.4 Hz, 1H), 7.70-7.67 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 4.82 (s, 3H), 3.38-3.28 (m, 4H), 3.11 (s, 9H), 2.02 (s, 3H), 1.97-1.91 (m, 2H), 1.89-1.83 (m, 2H)	1508 Chiral	MS (ESI) m/z, 684.48 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.76 (d, J = 4.8 Hz, 1H), 8.74 (s, 1H), 8.65 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.69 (d, J = 2.0 Hz, 1H), 7.67 (s, 1H), 7.55 (d, J = 4.8 Hz, 1H), 4.82 (bs, 4H), 4.68-4.62 (m, 2H), 3.60 (bs, 2H), 3.33 (bs, 2H), 3.11 (s, 3H), 2.24 (bs, 2H), 2.13 (bs, 2H), 2.09 (s, 3H), 1.33 (d, J = 6.8 Hz, 3H)
1509	MS (ESI) m/z 704.38 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.06 (bs, 1H), 9.76 (bs, 1H), 8.84 (s,1H), 8.75 (d, J = 4.8 Hz, 1H), 8.64 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.70-7.65 (m, 2H), 7.53 (d, J = 4.8 Hz, 1H), 6.71 (t, J = 75.6 Hz, 1H), 4.83 (s, 2H), 4.40-4.36 (m, 2H), 3.94 (t, J = 6.0 Hz, 2H), 3.74-3.71 (m, 2H), 3.60-3.20 (m, 6H), 2.14 (s, 3H), 2.10-2.05 (m, 2H)	1512	MS (ESI) m/z 745.4 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.65 (s, 1H), 10.01 (bs, 1H), 8.87 (d, J = 4.8 Hz, 1H), 8.62 (s, 1H), 8.60 (s, 1H), 7.61 (dd, J = 8.8, 4.8 Hz, 1H), 7.54 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.5 Hz, 1H), 7.38 (d, J = 9.0 Hz, 1H), 4.60 (s, 2H), 4.54 (s, 2H), 4.44-4.37 (m, 4H), 4.28-4.16 (m, 4H), 4.00-3.80 (m, 1H), 3.49 (s, 3H), 2.23-2.14 (m, 2H), 2.09-1.95 (m, 2H), 1.85-1.70 (m, 5H)
1510	MS (ESI) m/z 716.40 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.15 (bs, 1H), 8.79 (s, 1H), 8.75 (d, J = 4.8 Hz, 1H), 8.66 (s, 1H), 7.75 (d, J = 9.1 Hz, 1H), 7.69-7.67 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 6.68 (t, J = 75.9 Hz, 1H), 4.82 (s, 2H), 4.01 (bs, 2H), 3.40-2.80 (m, 8H), 2.08 (s, 3H), 1.05-0.65 (m, 4H)	1513	MS (ESI) m/z 724.49 [M+1]+; ; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.8 Hz, 1H), 8.61 (s, 1H), 8.40 (s, 1H), 7.60 (dd, J = 8.8, 2.4 Hz, 1H), 7.46 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.4 Hz, 1H), 7.36 (d, J = 9.2 Hz, 1H), 6.79 (t, J = 75.2 Hz, 1H), 4.54-4.51 (m, 1H), 4.38 (d, J = 4.4 Hz, 2H), 4.28 (d, J = 4.4 Hz, 4H), 3.67-3.63 (m, 2H), 3.45 (bs, 2H), 3.25-3.22 (m, 2H), 3.09 (s, 3H), 2.21-2.15 (m, 2H), 2.08-2.05 (m, 2H), 1.71 (s, 3H)

1511	MS (ESI) m/z 716.44 [M+1]+; ; 1H NMR (400 MHz, DMSO-d6) δ 13.01 (bs, 1H), 10.04 (bs, 1H), 8.84 (s, 1H), 8.75 (d, J = 4.8 Hz,1H), 8.64 (s,1H), 7.75 (d, J = 8.4 Hz, 1H), 7.70-7.60 (m, 2H), 7.52 (d, J = 4.4 Hz,1H), 6.71 (t, J = 75.2 Hz, 1H), 4.83 (s, 2H), 4.55-4.36 (m, 3H), 3.70-3.40 (m, 5H), 3.16 (bs, 2H), 2.77 (bs, 2H), 2.50-2.35 (m, 2H), 2.14 (s, 3H)	1514	MS (ESI) m/z 740.49 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.8 Hz, 1H), 8.59 (s, 1H), 8.43 (s, 1H), 7.60 (dd, J = 9.2, 2.8 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.4 Hz, 1H), 7.35 (d, J = 8.8 Hz, 1H), 4.38-4.37 (m, 2H), 4.26 (bs, 2H), 4.19 (s,2H), 3.36 (bs, 2H), 3.05 (s, 3H), 1.83 (bs, 4H), 1.73 (s, 4H), 1.33 (s, 6H)
1515	MS (ESI) m/z 744.51 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.8 Hz, 1H), 8.60 (s, 1H), 7.85 (dd, J = 8.8 Hz, 2.4 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.8 Hz, 1H), 7.36 (d, J = 9.2 Hz, 1H), 6.57 (t, J = 52 Hz, 1H), 4.38 (d, J = 4.8 Hz, 2H), 4.30-4.02 (m, 3H), 3.30-2.89 (m, 9H), 1.99 (bs, 2H), 1.82 (bs, 2H), 1.74 (s, 3H)	1519	MS (ESI) m/z 680.45 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.08 (bs, 1H), 8.75 (d, J = 4.8 Hz, 2H), 8.64 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.69 (d, J = 2 Hz, 2H), 7.5 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 4.57 (bs, 2H), 4.34 (bs, 2H), 3.23 (d, J = 11.6 Hz, 2H), 3.19 (s, 1H), 3.11 (s, 3H), 2.31 (m, 2H), 2.21 (s, 3H), 2.10-2.03 (m, 5H)
1516	MS (ESI) m/z 753.18 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.66 (s, 1H), 9.81 (bs, 1H), 8.89 (d, J = 4.4 Hz, 1H), 8.75 (s, 1H), 8.57 (s, 1H), 7.59 (dd, J = 2.8, 9.2 Hz, 1H), 7.56 (d, J = 4.8 Hz, 1H), 7.40 (d, J = 8.4 Hz, 2H), 2.26 (s, 2H), 4.23 (s, 4H), 3.80 (bs, 6H), 3.61 (s, 3 H), 3.42 (bs, 2H), 1.81 (s, 3H), 1.53-1.48 (m, 6H)	1520	MS (ESI) m/z 720.44 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.09 (bs, 1H), 8.77-8.75 (m, 2H), 8.65 (s, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.68 (d, J = 9.2 Hz, 2H), 7.55 (d, J = 4.4 Hz, 1H), 4.83 (s, 2H), 4.55 (bs, 1H), 3.70 (bs, 2H), 3.24 (bs, 4H), 3.11 (bs, 3H), 2.89 (bs, 2H), 2.15-2.11 (m, 7H)

1518	MS (ESI) m/z 702.43 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.75 (d, J = 4.8 Hz, 1H), 8.74 (s, 1H), 8.65 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.69 (s, 1H), 7.67 (s, 1H), 7.55 (d, J = 4.8 Hz, 1H), 6.53 (t, J = 50.0 Hz, 1H), 4.82 (bs, 2H), 4.57 (d, J = 2.4 Hz, 1H), 3.58 (bs, 2H), 3.36 (bs, 2H), 3.16 (s, 3H), 2.98 (bs, 1H), 2.24 (bs, 2H), 2.08 (bs, 5H), 1.35 (s, 3H)	1521	MS (ESI) m/z 784.45 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.76-8.75 (m, 2H), 8.65 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.70-7.67 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 4.56 (dt, J = 47.2, 5.6 Hz, 2H), 4.59-4.57 (m, 1H), 3.68-3.55 (m, 2H), 3.21-3.19 (m, 4H), 3.11 (s, 3H), 2.21-2.05 (m, 9H)
1522	MS (ESI) m/z 714.42 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.76 (d, J = 4.8 Hz, 1H), 8.71 (s, 1H), 7.66 (s, 1H), 7.75 (d, J = 9.2 Hz, 1H), 7.68 (t, J = 2.8 Hz, 2H), 7.55 (d, J = 4.8 Hz, 1H), 6.08 (t, J = 56.4 Hz, 1H), 4.81 (s, 2H), 4.09 (bs, 1H), 3.05 (bs, 5H), 2.92 (bs, 2H), 2.05 (s, 3H), 1.79-1.73 (m, 4H), 0.85-0.78 (m, 4H)	1525	MS (ESI) m/z 648.39 [M+1]; 1H NMR (400 MHz, DMSO-d6) δ 8.78 (s, 1H), 8.76 (d, J = 4.4 Hz, 1H), 8.65 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.70-7.67 (m, 1H), 7.55 (d, J = 4.8 Hz, 1H), 5.13 (bs, 1H), 4.81-4.67 (m, 6H), 3.97 (bs, 2H), 2.77 (bs, 2H), 2.10 (s, 3H), 0.85 (bs, 4H)
1523	MS (ESI) m/z 680.48 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.76 (d, J = 6.4 Hz, 2H), 8.64 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.70-7.67 (m, 2H), 7.55 (d, J = 4.4 Hz, 1H), 4.82 (s, 2H), 4.80-4.76 (m, 4H), 4.58 (bs, 1H), 4.37 (bs, 1H), 3.55 (d, J = 8.8 Hz, 2H), 3.12 (bs, 5H), 2.15-2.10 (m, 5H), remainder of protons are merged in moisture peak	1526 (Chiral)	MS (ESI) m/z 704.41 [M+1] +; 1H NMR (400 MHz, DMSO-d6) δ 13.16 (bs, 1H), 8.79 (s, 1H), 8.75 (d, J = 4.8 Hz, 1H), 8.65 (s, 1H), 7.75 (d, J = 8.3 Hz, 1H), 7.69-7.67 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 3.73 bs, 4H), 3.00 (bs, 4H), 2.70-2.50 (m, merged, 1H), 2.20-2.07 (m, 1H), 2.08 (s, 3H), 1.03-1.08 (m, 2H)

1524		1527	
MS (ESI) m/z 678.20 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.06 (bs, 1H), 8.75-8.74 (m, 2H), 8.65 (s, 1H), 7.75 (d, J = 8.4 Hz ,1H), 7.68 (d, J = 8.8 Hz ,2H), 7.54 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 4.64 (t, J = 8.4 Hz, 1H), 3.49 (s, 4H), 3.10 (s, 3H), 2.21-2.08 (m, 7H), 1.39 (s, 3H), 1.14 (bs, 2H), 0.81 (bs, 2H)		MS (ESI) m/z 664.45 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.05 (bs, 1H), 8.79 (s, 1H), 8.75 (d, J = 4.8 Hz, 1H), 8.65 (s, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.71-7.65 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 4.83 (s, 2H), 4.39 (d, J = 12.4 Hz, 2H), 3.19 (t, J = 12.0 Hz, 2H), 2.95-2.90 (m, 5H), 2.32-2.28 (m, 2H), 2.10 (s, 3H), 2.00-1.80 (m, 2H), 1.02-0.91 (m, 2H), 0.90-0.81 (m, 2H)
1528		1531 Chiral	
MS (ESI) m/z 625.37 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.77 (d, J = 4.8 Hz, 1H), 8.72 (s, 1H), 8.66 (s, 1H), 7.75 (d, J = 8.8 Hz, 1H), 7.70-7.65 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 4.81 (s, 2H), 4.60-4.45 (m, 1H), 4.05-3.95 (m, 2H), 3.65-3.40 (m, 2H), 3.11 (s, 3H), 2.06 (s, 3H), 2.00-1.85 (m, 2H), 1.78 (d, J = 10.8 Hz, 2H)		MS (ESI) m/z 714.45 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.06 (bs, 1H), 10.53 (bs, 1H), 8.77-8.70 (m, 2H), 8.65 (s, 1H), 7.75 (d, J = 4.4 Hz, 1H), 7.69-7.67 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 6.49 (t, J = 56.4 Hz, 1H), 4.82 (s, 2H), 4.57 (bs, 2H), 3.80-3.48 (m, 3H), 3.40-3.20 (m, 2H), 3.16 (s, 4H), 3.01-2.70 (m, 2H), 2.02-2.15 (m, 2H), 2.06 (s, 3H), 1.80-1.65 (m, 2H)
1529		1532 Chiral	
MS (ESI) m/z 696.48 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.00 (bs, 1H), 8.76-8.74 (m, 2H), 8.65 (s, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.70-7.67 (m, 2H), 7.75 (d, J = 4.8 Hz, 1H), 4.83 (s, 2H), 4.72-4.66 (m, 2H), 3.65 (bs, 4H), 3.09 (s, 3H), 2.71 (s, 1H), 2.12-2.08 (m, 7H), 1.35 (bs, 2H), 1.16 (bs, 2H)		MS (ESI) m/z 670.30 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 10.05 (bs, 1H), 8.76-8.70 (m, 2H), 8.65 (s, 1H), 7.75 (d, J = 8.8 Hz, 1H), 7.70-7.68 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 4.96- 4.68 (m, 4H), 4.01-3.95 (m, 1H), 3.65-3.28 (m, 3H), 3.22 (s, 3H), 2.82 (s, 3H), 2.80-2.55 (m, 4H), 2.08 (s, 3H)	

1530		1533 Chiral	
MS (ESI) m/z 732.40 [M+1]+; 1H NMR (400 MHz, DMSO- d6) δ 8.76 (d, J = 4.8, 1H), 8.70 (s, 1H), 8.65 (s, 1H), 7.79-7.73 (m, 1H), 7.71-7.65 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 4.81 (s, 2H), 4.32-4.20 (m, 1H), 3.12-3.10 (m, 5H), 2.81 (t, J = 11.2 Hz, 2H), 2.05 (s, 3H), 1.85-1.65 (m, 4H), 1.06-0.90 (m, 4H)		MS (ESI) m/z 698.43 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.19 (bs, 1H), 8.76-8.75 (m, 2H), 8.65 (s, 1H), 7.75 (d, J = 8.8 Hz, 1H), 7.70-7.68 (m, 2H), 7.55 (d, J = 8.8 Hz, 1H), 4.95-4.82 (m, 4H), 4.35-4.25 (m, 1H), 3.60-3.40 (m, 3H), 3.12 (s, 3H), 2.95-2.90 (m, 3H), 2.13-1.72 (m, 11H)	
1534		1537	
MS (ESI) m/z 597.28 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.35 (s, 1H), 8.79-8.75 (m, 2H), 7.75 (d, J = 8.0 Hz, 1H), 7.71-7.66 (m, 2H), 7.54 (d, J = 4.4 Hz, 1H), 5.00-4.97 (m, 1H), 4.88 (d, J = 18.4 Hz, 1H), 4.77-4.73 (m, 2H), 4.44 (bs, 1H), 3.89 (d, J = 12.0 Hz, 1H), 3.64 (d, J = 12.0 Hz, 1H), 3.57 (s, 3H), 2.13 (s, 3H)		MS (ESI) m/z 768.43 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.74 (d, J = 5.2 Hz, 1H), 8.70 (s, 1H), 8.63 (s, 1H), 7.83 (bs, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.70-7.69 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 6.74-6.60 (m, 1H), 6.48 (bs, 1H), 4.81 (s, 2H), 4.5-4.25 (m, 2H), 4.15-4.05 (bs, 2H), 3.90 (s, 3H), 3.45-3.3 (bs, 2H), 3.09 (s, 3H), 2.2-2.13 (bs, 2H), 2.06 (s, 3H), 2.05-1.9 (bs, 2H)	
1535		1538	
MS (ESI) m/z 702.43 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.77 (d, J = 4.4 Hz, 2H), 8.66 (s, 1H), 7.75 (d, J = 9.2 Hz, 1H), 7.70-7.68 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 6.51 (bs, 1H), 4.82 (s, 2H), 4.35 (bs, 1H), 3.66-3.51 (m, 6H), 3.06-2.97 (m, 2H), 2.16-2.02 (m, 7H), 1.13 (t, J = 6.8 Hz, 3H)		MS (ESI) m/z 811.19 [M+1]+; ; 1H NMR (400 MHz, DMSO-d6) δ 12.45 (s, 1H), 8.85 (d, J = 4.8 Hz 1H), 8.70 (s, 2H), 8.69 (s, 1H), 7.78-7.69 (m, 3H), 7.63 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 4.32 (t, J = 11.6 Hz, 1H), 3.94-3.87 (m, 2H), 3.31 (bs, 2H), 3.10-3.07 (m, 5H), 2.59 (m, 1H), 1.96 (d, J = 9.3 Hz, 2H), 1.90-1.77 (m, 5H), 1.44 (s, 6H)	

1536	MS (ESI) m/z 768.45 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.76 (d, J = 4.8 Hz, 1H), 8.74 (s, 1H), 8.65 (s, 1H), 7.90 (bs, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.70 (d, J = 2.0 Hz, 1H), 7.67 (s, 1H), 7.55 (d, J = 4.8 Hz, 1H), 6.61 (bs, 1H), 4.82 (s, 2H), 4.53-4.24 (m, 5H), 3.92 (s, 3H), 3.53 (m, 2H), 3.09 (s, 5H), 2.00 (s, 5H)	1539	MS (ESI) m/z 833.16 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.88 (bs, 1H), 8.84-8.83 (m, 2H), 8.73 (s, 1H), 7.77 (d, J = 4.4 Hz, 1H), 7.76-7.69 (m, 2H), 7.63 (d, J = 4.8 Hz, 1H), 6.73-6.46 (tt, J = 54.4, 4.4 Hz, 1H), 4.82 (s, 2H), 4.49 (dt, J = 14.8, 4.0 Hz, 2H), 4.36-4.30 (m, 1H), 3.36 (bs, 2H), 3.10 (s, 5H), 2.66-2.63 (m, 2H), 2.05-1.77 (m, 7H)
1540	MS (ESI) m/z 688.42 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.80-8.74 (m, 2H), 8.65 (s, 1H), 7.75 (d, J = 8.8 Hz, 1H), 7.70-7.66 (m, 1H), 7.55 (d, J = 4.8 Hz, 1H), 6.47 (t, J = 58.0 Hz, 1H), 4.83 (s, 2H), 4.68 (bs, 1H), 3.70-3.40 (m, 4H), 3.16 (s, 3H), 3.08-2.75 (m, 2H), 2.08 (s, 3H), 2.05-1.75 (m, 4H)	1543	MS (ESI) m/z 707.43 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.35 (bs, 1H), 8.38 (d, J = 4.8 Hz, 1H), 8.72 (s, 1H), 8.36 (s, 1H), 7.61 (dd, J = 2.4, 8.8 Hz, 1H), 7.59 (d, J = 2.4 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.37 (d, J = 8.8 Hz, 1H), 5.46-5.45 (m, 1H), 4.39 (bs, 2H), 4.24 (bs, 2H), 3.92 (m, 1H), 3.60-3.58 (m, 2H), 3.08-3.05 (m, 8H), 2.14-1.90 (m, 2H), 1.79-1.77 (m, 3H)
1541	MS (ESI) m/z 701.18 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.92 (bs, 1H), 8.76 (d, J = 4.8 Hz, 1H), 8.69-8.66 (m, 2H), 7.76 (d, J = 8.8 Hz, 1H), 7.68 (t, J = 3.6 Hz, 2H), 7.55 (d, J = 4.4 Hz, 1H), 6.59 (bs, 1H), 4.81 (s, 2H), 3.72 (d, J = 6.0 Hz, 2H), 3.40 (bs, 4H), 3.33 (s, 3H), 3.11-2.99 (m, 2H), 2.06 (s, 3H), 1.79 (bs, 4H), 1.47 (bs, 1H)	1544 Chiral	MS (ESI) m/z 714.18 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.76 (d, J = 4.8 Hz, 2H), 8.64 (s, 1H), 7.75 (d, J = 9.2 Hz, 1H), 7.69 (t, J = 8.8 Hz, 2H), 7.54 (d, J = 4.8 Hz, 1H), 6.49 (bs, 1H), 4.82 (s, 2H), 4.49 (s, 1H), 3.75 (bs, 8H), 2.97 (s, 2H), 2.08 (bs, 5H), 1.81 (s, 1H), 1.68 (d, J = 12.8 Hz, 2H)

1542		MS (ESI) m/z 674.40[M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.26 (s, 1H), 8.81 (d, J = 4.8 Hz, 1H), 8.73 (s, 1H), 7.77 (d, J = 8.4 Hz, 1H), 7.72-7.69 (m, 2H), 7.57 (d, J = 4.4 Hz, 1H), 6.42-6.15 (m, 1H), 4.90-4.80 (m, 3H), 4.51-4.46 (m, 1H), 3.87-3.84 (m, 2H), 3.68-3.61 (m, 3H), 3.58-3.37 (m, 2H), 3.25-3.17 (m, 2H), 2.87 (bs, 2H), 2.17 (s, 3H)	1545	Chiral	MS (ESI) m/z 714.45 [M+1]+; 1H NMR (400 MHz, DMSO-d6 at 353.1 K) δ 8.15 (s, 1H), 8.77 (d, J = 4.8 Hz, 1H), 8.68 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.67-7.64 (m, 2H), 7.53 (d, J = 4.8 Hz, 1H), 4.86-4.80 (m, 2H), 4.08-4.05 (m, 1H), 3.09 (s, 3H), 2.98 (m, 3H), 2.18 (s, 3H), 2.06-2.01 (m, 1H), 1.67 (t, J = 18.4 Hz, 3H), 1.38-1.26 (m, 4H)
1546		MS (ESI) m/z 811.16 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.43 (s, 1H), 8.82 (d, J = 4.8 Hz, 1H), 8.74 (d, J = 8.0 Hz, 2H), 7.78 (d, J = 8.8 Hz, 1H), 7.70 (d, J = 2.0 Hz, 1H), 7.68 (s, 1H), 7.61 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 4.29 (t, J = 23.2 Hz, 1H), 3.22 (q, J = 10.0 Hz, 2H), 3.09 (s, 3H), 3.04 (d, J = 19.2 Hz, 10H), 1.92 (d, J = 8.0 Hz, 5H), 1.78 (d, J = 9.6 Hz, 2H)	1549		MS (ESI) m/z 859.42 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.05 (bs, 1H), 8.93 (d, J = 4.8 Hz, 1H), 8.56 (s, 1H), 8.25 (s, 1H), 8.17 (d, J = 7.6 Hz, 1H), 7.77-7.55 (m, 1H), 7.70-7.63 (m, 4H), 7.55-7.51 (m, 1H), 7.45 (d, J = 7.6 Hz, 1H) 4.82 (s, 2H), 4.29 (bs, 1H), 3.31 (bs, 2H), 3.08 (bs, 5H), 2.67 (s, 3H), 2.63-2.58 (m, 2H), 1.94-1.88 (m, 2H). 1.83 (s, 3H), 1.79-1.76 (m, 2H)
1547		MS (ESI) m/z 809.16 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.52 (s, 1H), 8.79 (t, J = 8.0 Hz, 2H), 8.73 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.70 (d, J = 2 Hz, 2H), 7.60 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 4.31 (t, J = 21.2 Hz, 1H), 3.29-3.22 (m, 4H), 3.10 (bs, 5H), 2.50 (s, 1H), 1.94 (d, J = 11.7 Hz, 5H), 1.78 (s, 2H), 1.29 (d, J = 3.8 Hz, 2H), 1.26-1.14 (m, 2H)	1550		MS (ESI) m/z 881.42 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.28 (bs, 1H), 8.94 (d, J = 5.2 Hz, 1H), 8.58 (s, 1H), 8.28 (s, 1H), 8.24-8.19 (m, 1H), 7.77-7.75 (m, 1H), 7.70-7.68 (m, 2H), 7.66 (d, J = 4.8 Hz, 1H), 7.61-7.56 (m, 1H), 7.48-7.40 (m, 1H), 4.80 (s, 2H), 4.37-4.26 (m, 1H), 3.37 (bs, 2H), 3.12-3.10 (m, 2H), 3.07 (s, 3H), 2.66-2.63 (m, 2H), 1.99-1.88 (m, 2H), 1.85-1.74 (m, 5H)

1548	MS (ESI) m/z 845.44 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.09 (bs, 1H), 8.83 (d, J = 4.8 Hz, 1H), 8.67 (s, 1H), 8.45 (s, 1H), 8.15 (d, J = 7.2 Hz, 2H), 7.78-7.74 (m, 2H), 7.69-7.66 (m, 4H), 7.61 (d, J = 4.8 Hz, 1H), 4.80 (s, 2H), 4.31 (bs, 1H), 3.28 (bs, 2H), 3.09-3.06 (m, 5H), 2.58-2.50 (m, 2H), 1.94 (d, J = 11.2 Hz, 2H), 1.87 (s, 3H), 1.79 (d, 10.4 Hz, 2H)	1551	MS (ESI) m/z 859.42 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.05 (bs, 1H), 8.93 (d, J = 4.8 Hz, 1H), 8.56 (s, 1H), 8.25 (s, 1H), 8.17 (d, J = 7.6 Hz, 1H), 7.77-7.55 (m, 1H), 7.70-7.63 (m, 4H), 7.55-7.51 (m, 1H), 7.45 (d, J = 7.6 Hz, 1H) 4.82 (s, 2H), 4.29 (bs, 1H), 3.31 (bs, 2H), 3.08 (bs, 5H), 2.67 (s, 3H), 2.63-2.58 (m, 2H), 1.94-1.88 (m, 2H). 1.83 (s, 3H), 1.79-1.76 (m, 2H)
1553	MS (ESI) m/z 730.17 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.74 (s, 1H), 8.56 (s, 1H), 7.60-7.73 (m, 1H), 7.67-7.66 (m, 2H), 7.51 (d, J = 4.8 Hz, 1H), 6.14-5.56 (m, 1H), 4.82 (s, 2H), 4.59-4.55 (m, 2H), 4.48 (t, J = 6.4 Hz, 2H), 4.34-4.31 (m, 2H), 4.26-4.21 (m, 1H), 3.14-3.03 (m, 4H), 2.87 (t, J = 12.4 Hz, 1H), 2.07 (s, 3H), 1.76 (d, J = 12.0 Hz, 2H), 1.56-1.48 (m, 2H)	1556	Chiral MS (ESI) m/z 700.34 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 10.04 (s, 1H), 8.77-8.74 (m 2H), 8.65 (s, 1H), 7.76 (d, J = 8.4 Hz, 1H), 7.70-7.66 (dd, J = 2.0, 10.4 Hz, 2H), 7.55 (d, J = 4.4 Hz, 1H), 6.54 (bs, 1H), 4.82 (s, 2H), 4.42 (s, 1H), 4.19 (bs, 1H), 3.86-3.59 (bs, 4H), 3.16-2.74 (bs, 4H), 2.11 (s, 5H), 1.97-1.78 (bs, 2H)
1554	MS (ESI) m/z 757.34 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.89 (s, 1H), 8.79 (d, J = 4.8 Hz, 1H), 8.59 (s, 1H), 7.77 (s, 1H), 7.75 (s, 1H), 7.71 (d, J = 2.0 Hz, 1H), 7.68 (bs, 1H), 7.58 (d, J = 4.4 Hz, 1H), 6.29 (t, J = 61.2 Hz, 1H), 4.86 (s, 2H), 4.44 (bs, 2H), 4.04 (bs, 4H), 3.25 (bs, 2H), 2.16 (bs, 4H), 2.10 (bs, 3H)	1557	MS (ESI) m/z 702.35[M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.00 (bs, 1H), 10.03 (bs, 1H), 8.80-8.68 (m, 3H), 7.74-7.63 (m, 3H), 7.59 (d, J = 5.2 Hz, 1H), 6.53 (t, J = 54.4 Hz, 1H), 5.90-5.40 (m, 1H), 4.48 (bs, 1H), 3.81-3.41 (m, 4H), 3.38-3.10 (m, 2H), 3.09 (s, 3H), 2.40-1.95 (m, 7H), 1.47 (t, J = 6.8 Hz, 3H)

1555	MS (ESI) m/z 764.14 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 10.13 (bs, 1H), 8.77 (s, 1H), 8.75 (d, J = 7.2 Hz, 1H), 8.65 (s, 1H), 7.76 (s, 1H), 7.70 (d, J = 2.0 Hz, 2H), 7.67-7.54 (m, 6H), 4.82 (s, 2H), 4.56-4.22 (m, 5H), 3.01 (s, 5H), 2.97-2.87 (m, 2H), 2.09 (s, 5H)	1558	MS (ESI) m/z 707.32 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.18 (s, 1H), 8.79 (d, J = 4.8 Hz, 1H), 8.64 (s, 1H), 7.77 (d, J = 8.8 Hz, 1H), 7.70-7.68 (m, 2H), 7.56 (d, J = 4.8 Hz, 1H), 7.49-7.44 (m, 2H), 7.36 (bs, 1H), 6.42 (tt, J = 52.4, 7.4 Hz, 1H), 4.90 (s, 2H), 4.38 (bs, 2H), 3.48 (bs, 2H), 3.24 (bs, 2H), 2.86 (bs, 2H), 2.16 (s, 3H)
1559	MS (ESI) m/z 695.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.22 (bs, 1H), 8.78 (d, J = 4.7 Hz, 1H), 8.65 (s, 1H), 8.00-7.99 (m, 2H), 7.77 (d, J = 9.0 Hz, 1H), 7.70-7.66 (m, 4H), 7.56 (d, J = 4.7 Hz, 1H), 6.43 (t, J = 53.4 Hz, 1H), 4.90 (s, 2H), 4.23 (bs, 2H), 3.41 (bs, 2H), 2.66 (bs, 3H), 2.19 (s, 3H)	1562	MS (ESI) m/z 722.38 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.86 (bs, 1H), 8.81 (d, J = 4.8 Hz, 1H), 8.46 (s, 1H), 7.61-7.58 (m, 1H), 7.46 (d, J = 4.8 Hz, 1H), 7.41-7.36 (m, 2H), 4.50 (m, 1H), 4.41 (bs, 2H), 4.21 (bs, 2H), 3.65-3.37 (m, 4H), 3.06 (s, 3H), 2.62 (s, 3H), 2.25 (m, 2H), 2.00 (m, 2H), 1.79-1.69 (m, 8H)
1560	MS (ESI) m/z 703.32 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 11.40 (s, 1H), 9.44 (bs, 1H), 8.73 (s, 1H), 8.68 (d, J = 4.8 Hz, 1H), 8.48 (s, 1H), 7.74-7.72 (m, 1H), 7.66-7.64 (m, 2H), 7.48 (d, J = 4.8 Hz, 1H), 6.45 (b, 1H), 4.80 (s, 2H), 4.49 (bs, 1H), 3.35 (s, 4H), 3.08 (s, 3H), 2.50-2.47 (m, 2H), 2.08 (bs, 2H), 1.99 (s, 5H)	1563	MS (ESI) m/z 722.45 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.59 (s, 1H), 8.41 (bs, 1H), 7.59 (dd, J = 2.4, 8.8 Hz, 1H), 7.42-7.40 (m, 2H), 7.36 (d, J = 9.2 Hz, 1H), 4.53 (bs, 1H), 4.38 (bs, 2H), 4.21 (bs, 2H), 3.84 (bs, 4H), 3.08 (s, 3H), 3.54 (bs, 2H), 2.70 (s, 3H)), 1.99 (bs, 2H), 1.82 (bs, 5H), 1.76 (bs, 3H)

1561		MS (ESI) m/z 757.43 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.47 (s, 1H), 8.81-8.78 (m, 3H), 7.77 (d, J = 8.4, 1H), 7.72-7.67 (m, 2H), 7.62 (d, J = 4.8 Hz, 1H), 4.83 (s, 2H), 4.78 (t, J = 6.8 Hz, 4H), 4.60 (bs, 1H), 4.36 (bs, 1H), 3.58 (bs, 2H), 3.53 (s, 3H), 3.12 (s, 3H), 3.05 (d, J = 14.0 Hz, 2H), 2.14 (bs, 4H), 1.99 (s, 3H)	1564		MS (ESI) m/z 668.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.78 (s, 1H), 8.75 (d, J = 4.8 Hz, 1H), 8.64 (s, 1H), 7.75 (d, J = 9.2 Hz, 1H), 7.67-7.70 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 5.45 (d, J = 56.8 Hz, 1H), 4.83 (s, 2H), 4.54-4.29 (m, 5H), 3.52 (bs, 2H), 3.15-3.09 (m, 2H), 2.19-2.09 (m, 5H), 1.60-1.52 (m, 2H)
1565		MS (ESI) m/z 708.44 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.85 (s, 1H), 8.76 (d, J = 4.8 Hz, 1H), 8.65 (s, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.70-7.66 (m, 2H), 7.53 (d, J = 4.8 Hz, 1H), 4.84 (s, 2H), 4.66-4.36 (m, 5H), 3.91-3.78 (m, 4H), 2.95 (bs, 3H), 2.13 (s, 3H)	1569		MS (ESI) m/z 618.28 [M+1] +; 1H NMR (400 MHz, DMSO-d6) δ 14.24 (bs, 1H), 13.11 (bs, 1H), 9.17 (s, 1H), 8.79 (d, J = 4.80 Hz, 1H), 8.67 (s, 1H), 8.52 (d, J = 7.20 Hz, 2H), 7.76 (d, J = 8.00 Hz, 1H), 7.71-7.68 (m, 2H), 7.53 (d, J = 4.80 Hz, 1H), 7.38 (d, J = 7.20 Hz, 2H), 4.89 (s, 2H), 3.69 (s, 3H), 2.23 (s, 3H)
1566		MS (ESI) m/z 828.47 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.02 (s, 1H), 8.90 (d, J = 4.8 Hz, 1H), 8.71 (d, J = 4.4 Hz, 1H), 8.65 (s, 1H), 8.60 (s, 1H), 8.27-8.18 (m, 2H), 7.77-7.53 (m, 4H), 7.49 (d, J = 5.6 Hz, 1H), 6.66-6.29 (m, 1H), 4.82 (s, 2H), 4.60-4.45 (m, 1H), 3.50-3.15 (m, 6H), 3.09 (s, 3H), 2.30-1.80 (m, 7H)	1571		MS (ESI) m/z 665.43 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.00 (s, 1H), 8.82 (d, J = 4.4 Hz, 1H), 8.35 (s, 1H), 7.60 (dd, J= 8.8 Hz, 2.4 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.4 Hz, 1H), 7.36 (d, J = 8.8 Hz, 1H), 6.55 (t, J = 53.2 Hz, 1H), 4.40 (d, J = 4.4 Hz, 2H), 4.26 (s, 2H), 3.87 (bs, 1H), 3.47-3.24 (m, 4H), 2.00-1.89 (m, 4H),1.78 (s, 3H), 1.74-1.67 (m, 2H)

1568		MS (ESI) m/z 636.25 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.18 (bs, 1H), 8.84 (s, 1H), 8.75 (d, J = 4.8 Hz,1H), 8.65 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.70-7.65 (m, 2H), 7.53 (d, J = 4.8 Hz, 1H), 4.84 (s, 2H), 4.38 (m, 2H), 3.79 (m, 2H,), 3.49 (m, 4H), 3.03 (m, 1H), 2.14 (s, 3H), 0.93 (m, 4H)	
1572		MS (ESI) m/z 709.45 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.18 (s, 1H), 8.77 (d, J = 4.8 Hz, 1H), 8.63 (s, 1H), 7.76 (d, J = 9.2 Hz, 1H), 7.70 (dd, J = 6.4 Hz, 2.0 Hz, 2H), 7.55 (d, J = 4.8 Hz, 1H), 4.89 (s, 2H), 3.78-3.56 (m, 3H), 3.28-3.19 (m, 2H), 3.00-2.79 (m, 2H), 2.08 (s, 3H), 1.98-1.85 (m, 4H)	
1573		MS (ESI) m/z 685.39 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.06 (s, 1H), 8.75 (d, J = 4.8 Hz, 1H), 8.61 (s, 1H), 7.77-7.75 (m, 1H), 7.70-7.68 (m, 2H), 7.55 (d, J = 4.4 Hz, 1H), 6.60 (bs, 1H), 6.41 (s, 1H), 4.86 (s, 2H), 3.99-3.58 (m, 2H), 3.03-2.76 (m, 4H), 2.54 (s, 3H), 2.29-2.14 (m, 5H), 1.77-1.75 (m, 1H)	
1576	Chiral	[02041] MS (ESI) m/z 714.55 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 8.80 (s, 1H), 8.76 (d, J = 4.8 Hz, 1H), 8.64 (s, 1H), 7.75 (d, J = 8.8 Hz, 1H), 7.68-7.67 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 3.81-3.38 (m, 5H), 3.08 (s, 3H), 2.82-2.70 (m, 2H), 2.43-2.33 (m, 2H), 2.06 (s, 3H),1.68-1.53 (m, 7H)	
1574		MS (ESI) m/z 659.38 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.14 (s, 1H), 8.77 (d, J = 4.8 Hz, 1H), 8.60 (s, 1H), 7.76 (d, J = 18.4 Hz, 1H), 7.70 (d, J=2.0 Hz, 1H), 7.55 (d, J = 4.8 Hz, 2H), 6.55 (t, J = 54.4 Hz, 1H), 4.87 (s, 2H), 3.60-2.87 (m, 7H), 2.17 (s, 3H), 2.04-1.73 (m, 4H)	
1577	Chiral	MS (ESI) m/z 714.49 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 8.80 (s, 1H), 8.76 (d, J = 4.8 Hz, 1H), 8.64 (s, 1H), 7.75 (d, J = 8.8 Hz, 1H), 7.68-7.67 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 3.81-3.38 (m, 5H), 3.08 (s, 3H), 2.82-2.70 (m, 2H), 2.43-2.33 (m, 2H), 2.06 (s, 3H), 1.68-1.53 (m, 7H)	

1575	Chiral		MS (ESI) m/z 728.08 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 8.80 (s, 1H), 8.76 (d, J = 4.8 Hz, 1H), 8.64 (s, 1H), 7.75 (d, J = 8.8 Hz, 1H), 7.68-7.67 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 3.81-3.38 (m, 5H), 3.08 (s, 3H), 2.82-2.70 (m, 2H), 2.43-2.33 (m, 2H), 2.06 (s, 3H), 1.68-1.53 (m, 7H)	1578		MS (ESI) m/z 771.57 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.48 (s, 1H), 8.82 (d, J = 4.4 Hz, 2H), 8.78 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.72-7.67 (m, 2H), 7.63 (d, J = 4.8 Hz, 1H), 4.83 (s, 2H), 4.77-4.75 (m, 4H), 4.44-4.35 (m, 2H), 3.76-3.59 (m, 3H), 3.54 (s, 3H), 3.28-3.19 (m, 1H), 3.02 (bs, 2H), 2.15 (s, 4H), 1.99 (s, 3H), 1.15 (t, J = 6.8 Hz, 3H)
1579	Chiral		MS (ESI) m/z 760.64 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.76 (d, J = 4.8 Hz, 1H), 8.17 (s, 1H), 8.66 (s, 1H), 7.76-7.74 (m, 1H), 7.70-7.68 (m, 2H), 7.56 (d, J = 4.8 Hz, 1H), 6.43-4.15 (m, 1H), 4.81 (s, 2H), 4.30 (bs, 1H), 3.54 (bs, 4H), 3.08 (s, 3H), 2.05 (bs, 7H), 1.83-1.67 (m, 6H), 1.17 (bs, 3H)	1583	Chiral	MS (ESI) m/z 744.52 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.76 (d, J = 4.8 Hz, 1H), 8.70 (s, 1H), 8.66 (s, 1H), 7.75 (d, J = 9.2 Hz, 1H), 7.69-7.68 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 4.81 (s, 2H), 4.26-4.23 (m, 1H), 3.12-3.09 (m, 4H), 2.93 (bs, 3H), 2.57-2.52 (m, 2H), 2.06 (s, 3H), 1.89 (bs, 4H), 1.75-1.72 (m, 7H), 1.22 (bs, 2H)
1581	Chiral		MS (ESI) m/z 702.52 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.74-8.70 (m, 2H), 8.37 (s, 1H), 7.74 (d, J = 8.4 Hz, 1H), 7.67-7.64 (m, 2H), 7.44 (d, J = 4.4 Hz, 1H), 6.16 (t, J = 55.6 Hz, 1H), 4.89-4.84 (m, 3H), 3.081 (bs, 4H), 2.80-2.72 (m, 2H), 2.33 (bs, 3H), 2.07-1.98 (m, 4H), 1.90 (bs, 3H), 1.75-1.71 (m, 1H), 1.41 (t, J = 7.2 Hz, 1H)	1584		MS (ESI) m/z 724.3 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.01 (bs, 1H), 8.76-8.74 (m, 2H), 8.64 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.70-7.67 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 4.74-7.56 (m, 3H), 3.52-3.49 (m, 2H), 3.32-3.26 (m, 4H), 3.11 (s, 3H), 2.26-2.21 (m, 2H), 2.10 (s, 3H), 2.03-1.91 (m, 8H)

1582		MS (ESI) m/z 778.66 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.76 (d, J = 4.8 Hz, 1H), 8.73 (s, 1H), 8.65 (s, 1H), 7.75 (d, J = 8.8 Hz, 1H), 7.70-7.67 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 4.58 (bs, 2H), 4.24 (bs, 2H), 3.11 (s, 3H), 2.94-2.67 (m, 6H), 2.32-2.08 (m, 9H)	1585		MS (ESI) m/z 722.42 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.77 (d, J = 4.8 Hz, 1H), 8.71 (s, 1H), 8.66 (s, 1H), 7.76-7.74 (m, 1H), 7.69-7.68 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 4.81 (s, 2H), 4.29-4.27 (m, 1H), 3.44 (bs, 2H), 3.17-3.09 (m, 5H), 2.66 (bs, 2H), 2.05 (s, 3H), 1.94 (d, J = 10.4 Hz, 2H), 1.80 (d, J = 10.8 Hz, 2H)
1586		MS (ESI) m/z 748.52 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.76 (d, J = 4.8 Hz, 1H), 8.72 (s, 1H), 8.70 (s, 1H), 7.74 (d, J = 8.0 Hz, 1H), 7.70-7.62 (m, 2H), 7.53 (d, J = 4.8 Hz, 1H), 4.84 (s, 2H), 4.48-4.30 (m, 1H), 3.40-2.85 (m, 9H), 2.20-1.75 (m, 7H), 1.20 (s, 6H)	1589		MS (ESI) m/z 791.49 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.47 (s, 1H), 9.72 (bs, 1H), 8.81-8.78 (m, 3H), 7.77 (d, J = 8.4 Hz, 1H), 7.72-7.67 (m, 2H), 7.62 (d, J = 4.8 Hz, 1H), 4.83 (s, 2H), 4.59 (bs, 1H), 3.82-3.45 (m, 6H), 3.30-2.95 (m, 9H), 2.20-2.14 (m, 4H), 1.99 (s, 3H)
1587		MS (ESI) m/z 746.54 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.13 (bs, 1H), 8.75 (d, J = 4.8 Hz, 1H), 8.70 (s, 1H), 8.65 (s, 1H), 7.75 (d, J = 9.2 Hz, 1H), 7.68-7.67 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 4.81 (s, 2H), 4.26 (bs, 1H), 3.09 (s, 3H), 3.04 (d, J = 10.8 Hz, 2H), 2.70-2.50 (merged, 2H), 2.10-2.00 (m, 5H), 1.88-1.81 (m, 4H), 0.97 (s, 2H), 0.74 (s, 2H)	1590		MS (ESI) m/z 807.10 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.47 (s, 1H), 8.80 (d, J = 5.2 Hz 1H), 8.78 (s, 1H), 8.75 (s, 1H), 7.77 (d, J = 8.4 Hz, 1H), 7.70 (dd, J = 10.4 Hz, 2 Hz, 2H), 7.62 (d, J = 4.8 Hz, 1H), 6.45 (t, J = 54.8 Hz, 1H), 4.82 (s, 2H), 4.50 (d, J = 6.8 Hz, 2H), 4.45 (d, J = 6.8 Hz, 2H), 4.34-4.29 (m, 1H), 3.55 (s, 3H), 3.11 (s, 3H), 2.91 (d, J = 10.8 Hz, 2H), 2.60-2.53 (m, 2H),1.96-1.85 (m, 7H)

1588		MS (ESI) m/z 760.61 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.05 (bs, 1H), 9.09 (bs, 1H), 8.80-8.70 (m, 2H), 8.65 (s, 1H), 7.75 (d, J = 8.40 Hz, 1H), 7.71-7.63 (m, 2H), 7.54 (d, J = 4.00 Hz, 1H), 4.82 (s, 2H), 4.56 (bs, 1H), 3.70-3.50 (m, 4H), 3.20-3.20 (merged, 2H), 3.11 (s, 3H), 2.41-2.20 (m, 6H), 2.18-1.94 (m, 7H)	1591		MS (ESI) m/z 857.53 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.85 (d, J = 5.2 Hz, 1H), 8.81 (s, 1H), 8.75 (s, 1H), 7.78 (d, J = 8.8 Hz, 1H), 7.71-7.69 (m, 2H), 7.64 (d, J = 4.8 Hz, 1H), 6.73-6.58 (m, 1H), 6.15-5.87 (m, 1H), 4.82 (s, 2H), 4.59-4.55 (m, 2H), 4.52-4.47 (m, 4H), 4.35-4.22 (m, 4H), 3.16-3.04 (m, 3H), 2.86 (m, 1H), 1.92 (s, 3H), 1.76 (d, J = 11.2 Hz, 2H), 1.56-1.48 (m, 2H)
1592		MS (ESI) m/z 714.10 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 13.09 (bs, 1H), 8.75-8.74 (m, 2H), 8.64 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.69-7.67 (m, 2H), 7.53 (d, J = 4.8 Hz, 1H), 4.82 (s, 2H), 4.39 (bs, 2H), 4.01 (bs, 1H), 3.66 (bs, 1H), 3.20-2.95 (m, 5H), 2.72-2.66 (m, 2H), 2.08 (bs, 5H), 1.90-1.60 (m, 4H)	1595		MS (ESI) m/z 847.0 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 13.06 (bs, 1H), 8.85 (d, J = 4.8 Hz, 1H), 8.83 (s, 1H), 8.75 (s, 1H), 7.78 (d, J = 8.80 Hz, 1H), 7.71 (bs, 2H), 7.65 (d, J = 4.80 Hz, 1H), 5.04 (q, J = 9.60 Hz, 2H), 4.83 (s, 2H), 4.59 (bs, 1H), 3.77 (bs, 4H), 3.37 (bs, 2H), 3.11 (s, 3H), 2.26 (bs, 2H), 2.02 (bs, 2H), 1.95 (s, 3H), 1.76 (t, J = 17.6Hz, 3H)
1593		MS (ESI) m/z 851.58 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 13.03 (bs, 1H), 8.87 (d, J = 4.80 Hz, 1H), 8.84 (s, 1H), 8.73 (s, 1H), 7.77 (d, J = 9.20 Hz, 1H), 7.71-7.69 (m, 2H), 7.65 (d, J = 4.80 Hz, 1H), 5.06 (q, J = 9.60 Hz, 2H), 4.82 (s, 2H), 4.32-4.29 (m, 1H), 3.33 (bs, 2H), 3.09 (bs, 5H), 2.58 (bs, 2H), 1.96 (bs, 2H), 1.92 (s, 3H), 1.80 (d, J = 11.2 Hz, 2H)	1596		MS (ESI) m/z 701.0 [M+1]+; 1H-NMR (400 MHz, DMSO-d6 with D2O) δ 8.68 (s, 1H), 8.67 (s, 1H), 8.39 (s, 1H), 7.71 (d, J = 8.4 Hz, 1H), 7.65-7.63 (m, 1H), 7.57 (d, J = 1.6 Hz, 1H), 7.41 (d, J = 4.8 Hz, 1H), 4.73 (s 2H), 4.55-4.49 (m, 1H), 3.80-3.72 (m, 2H), 3.62-3.57 (m, 2H), 3.28 (t, J = 11.6 Hz, 2H), 3.09 (s, 1H), 2.53 (bs, 1H), 2.32-2.20 (m, 2H), 2.06 (bs, 6H), 1.74 (t, J = 19.6 Hz, 3H)

1594		MS (ESI) m/z 705.48 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 8.68 (s, 1H), 8.67 (s, 1H), 8.45 (s, 1H), 7.72 (d, J = 8.00 Hz, 1H), 7.65 (d, J = 8.40 Hz, 1H), 7.61 (bs, 1H), 7.44 (d, J = 2.40 Hz, 1H), 4.76 (s, 2H), 4.32 (t, J = 12.00 Hz, 1H), 3.49 (d, J = 8.80 Hz, 2H), 3.18 (d, J = 10.80 Hz, 2H), 3.07 (s, 3H), 2.73 (t, J = 11.2 Hz, 2H), 2.02 (s, 3H), 1.96 (d, J = 13.2 Hz, 2H), 1.85 (d, J = 10.8 Hz, 2H)	1597		MS (ESI) m/z 833.52 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 13.08 (bs, 1H), 8.86-8.84 (m, 2H), 7.79-7.769 (m, 1H), 7.71 (t, J = 2.0 Hz, 2H), 7.66 (d, J = 5.2 Hz, 1H), 6.51 (bs, 1H), 5.08-5.01 (m, 2H), 4.83 (s, 2H), 4.52 (bs, 1H), 3.94 (bs, 2H), 3.41 (bs, 4H), 3.21 (s, 3H), 2.15 (bs, 2H), 2.07 (s, 5H)
1598		MS (ESI) m/z 758.69 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.94 (bs, 1H), 8.77 (d, J = 4.8 Hz, 1H), 8.64 (s, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.69-7.67 (m, 2H), 7.55 (d, J = 4.4 Hz, 1H), 6.43 (bs, 1H), 4.82 (s, 2H), 4.53 (bs, 1H), 3.79 (bs, 4H), 3.39-3.35 (m, 2H), 3.11 (s, 3H), 2.41 (bs, 2H), 2.32-2.26 (m, 2H), 2.09 (s, 7H), 1.86-1.82 (m, 1H), 1.65-1.60 (m, 1H)	1601		MS (ESI) m/z 805.69 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 12.47 (bs, 1H), 8.81 (d, J = 4.8 Hz, 1H), 8.78 (bs, 2H), 7.79 (d, J = 11.6 Hz, 1H), 7.70 (bs, 1H), 7.68 (bs, 1H), 7.63 (d, J = 4.80 Hz, 1H), 4.82 (s, 2H), 4.20 (bs, 1H), 3.65 (q, J = 6.80 Hz, 2H), 3.54 (s, 3H), 2.93-2.90 (m, 2H), 2.69-2.66 (m, 4H), 2.42-2.32 (m, 3H), 1.94 (s, 3H), 1.92-1.89 (m, 4H) 1.11 (t, J = 6.8 Hz, 3H)
1599		[0025] MS (ESI) m/z 638.41 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.79-8.74 (m, 2H), 8.65 (s, 1H), 7.78 (d, J = 8.0 Hz, 1H), 7.70-7.68 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 4.83 (s, 2H), 4.54-4.53 (m, 1H), 3.58-3.55 (m, 2H), 3.20 (bs, 2H), 3.01 (s, 3H), 2.83-2.82 (m, 3H), 2.10 (bs, 7H)	1602	Chiral	MS (ESI) m/z 773.67 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.47 (s, 1H), 9.72 (bs, 1H), 8.81-8.78 (m, 3H), 7.77 (d, J = 8.36 Hz, 1H), 7.72-7.67 (m, 2H), 7.62 (d, J = 4.80 Hz, 1H), 5.33-5.14 (dm, 1H), 4.83 (s, 2H), 4.63-4.55 (m, 1H), 4.03-3.97 (m, 1H), 3.60-3.50 (merged, 3H), 3.11 (s, 3H), 3.09-3.02 (m, 2H), 2.76-2.50 (m, 6H), 2.12-2.07 (m, 4H), 1.99 (s, 3H)

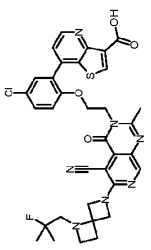
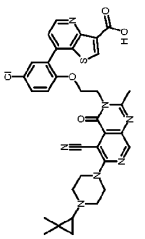
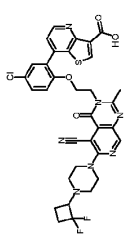
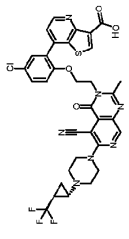
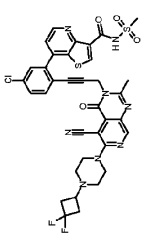
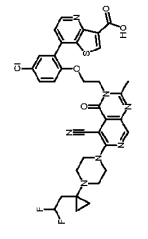
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MS (ESI) m/z 678.56 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.12 (bs, 1H), 8.83-8.73 (m, 3H), 8.66 (s, 1H), 7.76 (d, J = 8.8 Hz, 1H), 7.70-7.68 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 4.83 (s, 2H), 4.40 (bs, 1H), 3.71-3.57 (m, 4H), 3.40-3.20 (merged, 2H), 2.85 (bs, 1H), 2.18-2.00 (m, 7H), 1.14 (t, J = 6.4 Hz, 3H), 0.98-0.79 (m, 4H)		MS (ESI) m/z 833.74 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 9.86 (bs, 1H), 8.80-8.78 (d, J = 8.80 Hz, 2H), 8.68 (s, 1H), 7.80-7.67 (m, 4H), 4.88 (s, 2H), 4.54 (bs, 1H), 3.66-3.38 (m, 4H), 3.33-3.27 (m, 2H), 3.09 (s, 3H), 2.40-2.25 (m, 2H), 2.12 (s, 3H), 2.10-1.99 (m, 2H), 1.76 (t, J = 19.2 Hz, 3H)	
1604		1607	
MS (ESI) m/z 793.67 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 12.45 (s, 1H), 8.83 (d, J = 4.8 Hz, 1H), 8.73 (bs, 2H), 7.78 (d, J = 8.4 Hz, 1H), 7.71-7.69 (m, 2H), 7.63 (d, J = 4.8 Hz, 1H), 4.83 (s, 2H), 4.61 (bs, 1H), 3.84 (bs, 1H), 3.69-3.65 (m, 2H), 3.11 (s, 3H), 2.02-1.91 (m, 6H), 1.76 (bs, 4H), 1.38 (t, J = 14.4 Hz, 3H)		MS (ESI) m/z 829.71 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.49 (s, 1H), 8.81 (d, J = 4.8 Hz, 1H), 8.78 (d, J = 3.0 Hz, 2H), 7.77 (d, J = 8.16 Hz, 1H), 7.70-7.68 (m, 2H), 7.49 (d, J = 6.36 Hz, 1H), 6.56 (tt, J = 4.16 Hz, J = 88.08 Hz, 1H), 4.82 (s, 2H), 4.22-4.16 (m, 1H), 3.65 (d, J = 6.88 Hz, 2H), 3.55 (s, 3H) 3.04-2.94 (m, 4H), 2.49-2.41 (m, 2H), 1.99-1.89 (m, 5H), 1.78 (d, J = 10.68 Hz, 2H), 1.11 (t, J = 6.72 Hz, 3H)	
1605		1608	
MS (ESI) m/z 793.67 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 12.45 (s, 1H), 8.83 (d, J = 4.8 Hz, 1H), 8.73 (bs, 2H), 7.78 (d, J = 8.4 Hz, 1H), 7.71-7.69 (m, 2H), 7.63 (d, J = 4.8 Hz, 1H), 4.83 (s, 2H), 4.61 (bs, 1H), 3.84 (bs, 1H), 3.69-3.65 (m, 2H), 3.11 (s, 3H), 2.02-1.91 (m, 6H), 1.76 (bs, 4H), 1.38 (t, J = 14.4 Hz, 3H)		MS (ESI) m/z 871.79 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.71 (s, 1H), 8.83 (d, J = 4.8 Hz, 1H), 8.78 (s, 1H), 8.72 (s, 1H), 7.77 (d, J = 8.16 Hz, 1H), 7.71-7.69 (m, 2H), 7.64 (d, J = 4.84 Hz, 1H), 6.58 (tt, J = 52.56 Hz, 5.4 Hz, 1H), 5.25-5.20 (m, 1H), 4.98-4.92 (m, 4H), 4.82 (s, 2H), 4.24 (bs, 1H), 3.95 (bs, 2H), 3.68-3.62 (m, 2H), 3.50-3.10 (m, 4H), 2.01-1.97 (m, 2H), 1.90 (s, 3H), 1.86 (bs, 2H), 1.12 (t, J = 6.8 Hz, 3H)	

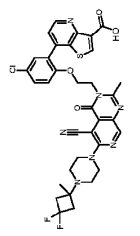
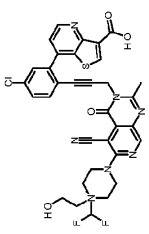
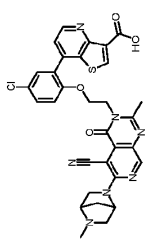
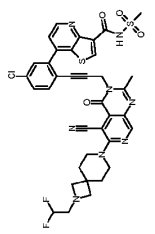
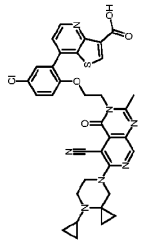
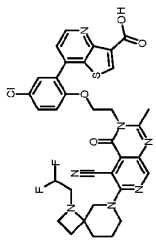
1606		1609	
MS (ESI) m/z 821.52 [M+1]+; ; 1H-NMR (400 MHz, DMSO-d6) δ 12.48 (s, 1H), 8.80 (d, J = 4.84 Hz, 1H), 8.78 (d, J = 2.6 Hz, 2H), 7.77 (d, J = 8.31 Hz, 1H), 7.71-7.67 (m, 2H), 7.62 (d, J = 4.80 Hz, 1H), 4.76 (s, 2H), 4.60-4.57 (m, 1H), 3.85-3.58 (m, 4H), 3.49 (s, 3H), 3.32 (t, J = 12 Hz, 2H), 3.10 (s, 3H), 2.32-2.02 (m, 4H), 1.98 (s, 3H), 1.80-1.70 (m, 3H)		MS (ESI) m/z 892.75 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.05 (s, 1H), 8.91 (d, J = 4.4 Hz, 1H), 8.72 (d, J = 3.6 Hz, 1H), 8.65 (s, 1H), 8.60 (s, 1H), 8.28 (d, J = 8.0 Hz, 1H), 8.21 (t, J = 7.6 Hz, 1H), 7.77-7.75 (m, 2H), 7.70-7.66 (m, 3H), 6.58 (t, J = 52.8 Hz, 1H), 4.82 (s, 2H), 4.23 (bs, 1H), 3.62 (d, J = 7.2 Hz, 2H), 3.16-3.12 (m, 4H), 2.53 (s, 2H), 2.01 (bs, 2H), 1.90-1.84 (m, 5H), 1.09 (t, J = 6.4 Hz, 3H)	
1610 Chiral		1617	
MS (ESI) m/z 881.27 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 12.71 (s, 1H), 8.81 (d, J = 4.84 Hz, 1H), 8.77 (s, 1H), 8.76 (s, 1H), 7.77 (d, J = 8.36 Hz, 1H), 7.72-7.67 (m, 2H), 7.62 (d, J = 4.84 Hz, 1H), 5.20-5.16 (m, 1H), 4.97-4.89 (m, 4H), 4.82 (s, 2H), 4.75-4.70 (m, 1H), 4.61-4.57 (m, 1H), 3.54-3.51 (m, 2H), 3.54-3.43 (m, 3H), 3.11 (s, 3H), 3.08-3.06 (m, 2H), 2.87-2.83 (m, 2H), 2.11-2.08 (m, 4H), 1.95 (s, 3H)		MS (ESI) m/z 730.46 [M+1]+; 1H NMR (400 MHz, DMSO-d6 with D2O) δ 8.67 (bs, 2H), 7.95 (d, J = 7.6 Hz, 1H), 7.50 (d, J = 8.4 Hz, 1H), 7.28 (s, 1H), 7.21 (bs, 2H), 6.28 (m, J = 53.6 Hz, 1H), 4.30 (bs, 2H), 4.21-4.00 (m, 3H), 3.29-3.19 (m, 4H), 2.99 (s, 3H), 2.80 (bs, 2H), 2.03 (bs, 2H), 1.86 (bs, 2H), 1.64 (s, 3H)	
1611 Chiral		1618	
MS (ESI) m/z 902.74 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 13.02 (s, 1H), 8.89 (d, J = 4.80 Hz, 1H), 8.72 (d, J = 4.40 Hz, 1H), 8.64 (s, 1H), 8.61 (s, 1H), 8.27-8.25 (m, 1H), 8.22-8.18 (m, 1H), 7.77-7.73 (m, 2H), 7.71-7.69 (m, 2H), 7.65 (d, J = 4.80 Hz, 1H), 4.83 (s, 2H), 4.75-4.70 (m, 1H), 4.58 (bs, 1H), 3.67 (bs, 3H), 3.54 (d, J = 10.80 Hz, 2H), 3.42-3.38 (m, 1H), 2.86-2.84 (m, 2H), 2.85 (bs, 2H), 2.45-2.40 (m, 2H), 2.08 (bs, 4H), 1.95 (s, 3H)		MS (ESI) m/z 791.49 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.47 (s, 1H), 9.72 (bs, 1H), 8.81-8.78 (m, 3H), 7.77 (d, J = 8.4 Hz, 1H), 7.72-7.67 (m, 2H), 7.62 (d, J = 4.8 Hz, 1H), 4.83 (s, 2H), 4.59 (bs, 1H), 3.82-3.45 (m, 6H), 3.30-2.95 (m, 9H), 2.20-2.14 (m, 4H), 1.99 (s, 3H)	

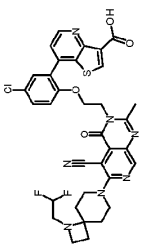
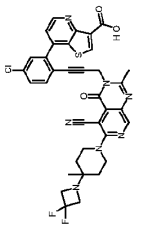
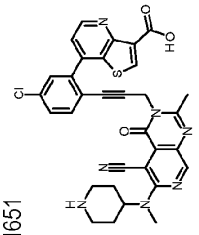
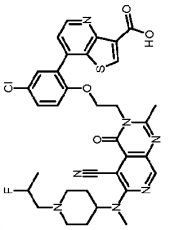
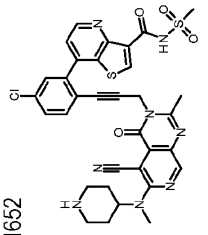
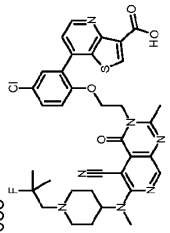
1616		MS (ESI) m/z 786.58 [M+1]+ ; 1H NMR (400 MHz, DMSO-d6 with D2O) δ 8.77 (d, J = 4.40 Hz, 1H), 8.68 (s, 1H), 8.19 (d, J = 9.60 Hz, 1H), 7.52 (dd, J = 2.2, 8.8 Hz, 1H), 7.35-7.26 (m, 3H), 6.24 (t, J = 54.4 Hz, 1H), 4.33-4.17 (m, 10H), 3.21 (bs, 3H), 3.03 (s, 3H), 2.70 (bs, 1H), 2.58 (bs, 1H), 1.97 (bs, 2H), 1.82 (bs, 2H), 1.55 (s, 3H), 1.28 (t, J = 6.8 Hz, 6H)
1620		MS (ESI) m/z 726.41 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 8.81 (d, J = 4.0 Hz, 1H), 8.57 (s, 1H), 8.34 (s, 1H), 7.58 (d, J = 7.2, 1H), 7.39-7.33 (m, 3H), 4.37 (bs, 2H), 4.25 (bs, 3H), 3.91 (s, 3H), 3.3; 2-3.30 (m, 2H), 3.07-2.72 (m, 5H), 2.44-2.32 (m, 2H), 1.93-1.74 (bs, 4H), 1.69 (s, 3H)
1621		LCMS: 603.6 [M+H]+; 1H NMR (400 MHz, Methanol-d4) δ 8.31 (s, 1H), 7.54 (dd, J = 8.9, 2.6 Hz, 1H), 7.41 (s, 1H), 7.36 – 7.25 (m, 2H), 4.46 (t, J = 5.1 Hz, 2H), 4.34 (t, J = 5.1 Hz, 2H), 3.13 (s, 6H), 2.89 (s, 3H), 2.83 (s, 3H), 2.24 (s, 3H)
1624		LCMS (ESI) m/z 662.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.79 (d, J = 4.8 Hz, 1H), 8.46 (s, 1H), 7.57 (dd, J = 9.0, 2.6 Hz, 1H), 7.44 (d, J = 4.8 Hz, 1H), 7.39 – 7.32 (m, 2H), 4.98 – 4.74 (m, 2H), 4.40 (t, J = 5.1 Hz, 2H), 4.29 (s, 1H), 4.21 (t, J = 5.1 Hz, 2H), 3.64 (s, 3H), 3.56 (s, 1H), 3.47 (s, 1H), 3.31 (s, 2H), 2.63 (s, 3H), 1.86 (s, 3H)
1622		LCMS (ESI) m/z 658.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.62 (s, 1H), 7.69 (tt, J = 8.5, 6.6 Hz, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.48 – 7.43 (m, 2H), 7.40 – 7.32 (m, 3H), 4.43 (t, J = 5.0 Hz, 2H), 4.27 (t, J = 4.9 Hz, 2H), 2.81 (s, 3H), 2.69 (s, 3H), 1.88 (s, 3H)
1625		MS (ESI) m/z 805.29 [M+1]+

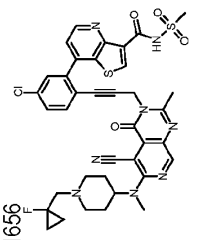
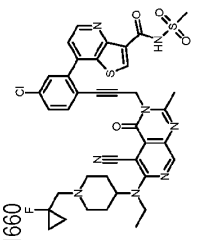
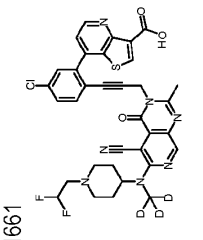
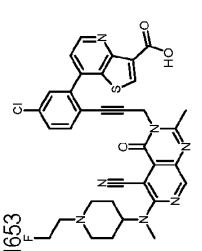
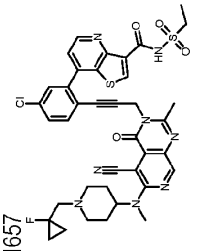
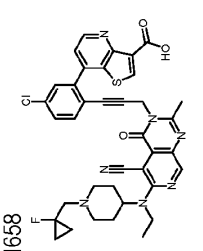
1623		1626	LCMS (ESI) m/z 599.2 [M+1]+
	LCMS (ESI) m/z 644.1 [M+1]+; 1H NMR (400 MHz, Chloroform-d) δ 8.48 (s, 1H), 7.61 (dd, J = 8.9, 2.7 Hz, 1H), 7.43 (s, 1H), 7.42 – 7.37 (m, 2H), 4.42 (d, J = 5.3 Hz, 2H), 4.33 (s, 1H), 4.30 (s, 1H), 4.25 (d, J = 5.0 Hz, 2H), 3.61 (d, J = 12.2 Hz, 2H), 3.44 (d, J = 13.6 Hz, 4H), 3.24 (d, J = 11.0 Hz, 1H), 2.92 (d, J = 4.4 Hz, 3H), 2.73 (s, 3H), 2.66 (s, 4H), 1.98 (s, 3H)		
1627		1630	MS (ESI) m/z 618.09 [M+1]+
	MS (ESI) m/z 602.29 [M+1]+		
1628		1631	
	MS (ESI) m/z 608.3 [M+1]+		

1629		1632	LCMS (ESI) m/z 469.5 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.77 – 8.71 (m, 2H), 8.66 (s, 1H), 7.75 (dd, J = 8.1, 0.8 Hz, 1H), 7.72 – 7.64 (m, 2H), 7.54 (d, J = 4.9 Hz, 1H), 4.81 (s, 2H), 4.63 (s, 2H), 4.53 (s, 2H), 4.44 (s, 2H), 4.39 (s, 2H), 3.36 (s, 4H), 2.73 – 2.62 (m, 1H), 2.10 (s, 3H)
1633	LCMS (ESI) m/z 608.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.70 (d, J = 4.7 Hz, 2H), 8.63 (s, 1H), 8.47 (s, 2H), 7.72 (dd, J = 8.1, 0.8 Hz, 1H), 7.68 – 7.61 (m, 2H), 7.50 (d, J = 4.8 Hz, 1H), 4.77 (s, 2H), 4.54 (s, 4H), 4.20 (t, J = 6.2 Hz, 4H), 2.06 (s, 3H), 1.20 (s, 1H)	1636	MS (ESI) m/z 619.45 [M+1]+
1634	MS (ESI) m/z 678.5 [M+1]+	1637	MS (ESI) m/z 638.39 [M+1]+

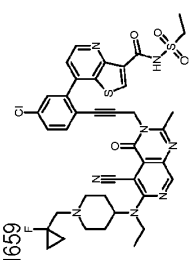
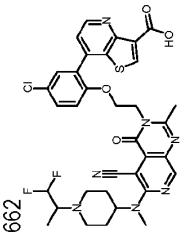
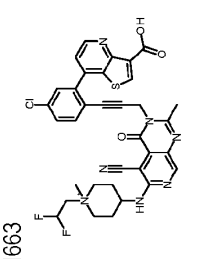
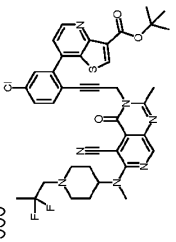
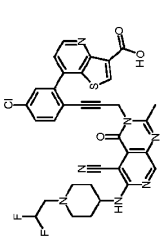
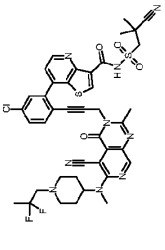
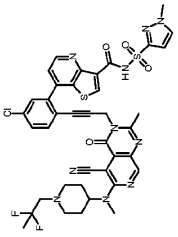
1635 	MS (ESI) m/z 688.48 [M+1]+	1638 	MS (ESI) m/z 670.50 [M+1]+
1639 	MS (ESI) m/z 706.46 [M+1]+	1642 	MS (ESI) m/z 710.46 [M+1]+
1640 		1643 	MS (ESI) m/z 706.47 [M+1]+

1641 	MS (ESI) m/z 706.55 [M+1]	1644 	MS (ESI) m/z 690.47 [M+1]+
1645 	MS (ESI) m/z 628.46 [M+1]+	1648 	LCMS: 2.01 Min, 777.3 [M+H]+
1646 	MS (ESI) m/z 668.45 [M+1]+	1649 	MS (ESI) m/z = 706.48 [M+1]+

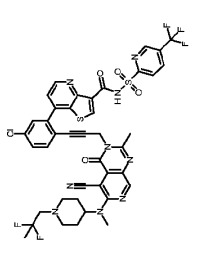
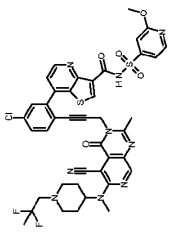
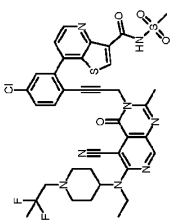
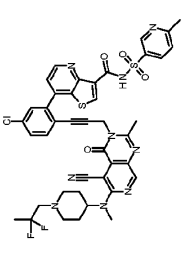
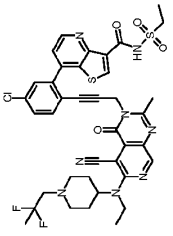
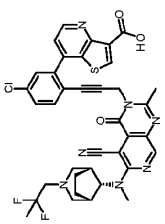
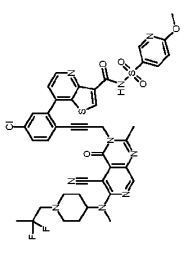
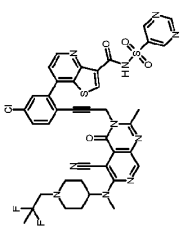
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1651 		1654 	MS (ESI) m/z, 690.46 [M+1]+
1652 		1655 	MS (ESI) m/z 704.57 [M+1]+

1656 		
1660 		
1661 		
1653 	1657 	1658 

MS (ESI) m/z 670.43 [M+1]+

1659 		1662 	MS (ESI) m/z 708.54 [M+1]+
1663 	MS (ESI) m/z 688.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.72 (d, J = 4.8 Hz, 1H), 8.70 (s, 1H), 8.61 (s, 1H), 7.74 – 7.71 (m, 1H), 7.67 – 7.63 (m, 2H), 7.52 (d, J = 4.8 Hz, 1H), 7.03 (d, J = 8.5 Hz, 1H), 6.80 (tt, J = 52.4, 3.5 Hz, 1H), 4.78 (s, 2H), 4.55 – 4.40 (m, 1H), 4.02 (td, J = 14.3, 3.9 Hz, 2H), 3.69 – 3.60 (m, 4H), 3.25 (s, 3H), 2.32 – 2.18 (m, 2H), 2.10 – 2.01 (m, 2H), 2.00 (s, 3H).	1666 	
1664 		1672 	1676 

1665	MS (ESI) m/z = 714.5 [M+1]+	1673	1677
1669	1667	1671	1674
1670	1668	1675	1678

1679 	1683 	1686 	
1680 	1687 	1690 Chiral 	MS (ESI) m/z 728.47 [M+1]+
1681 	1684 		

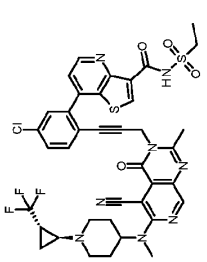
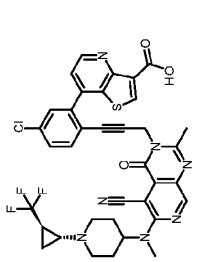
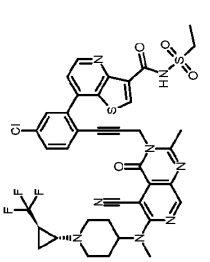
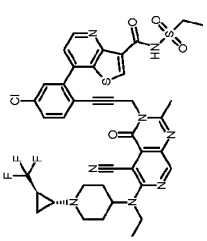
1682	1685		
1688 Chiral	MS (ESI) m/z 720.47 [M+1]+	1691 Chiral	MS (ESI) m/z 714.55 [M+1]+
1689 Chiral	MS (ESI) m/z 714.45 [M+1]+	1697	1700

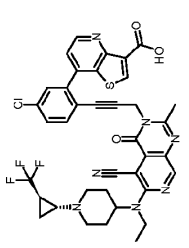
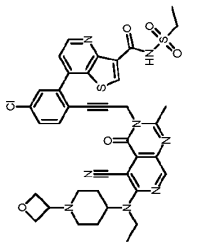
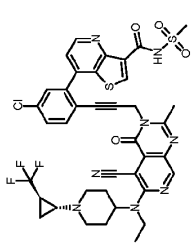
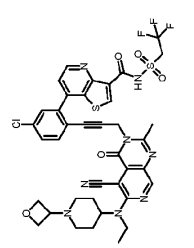
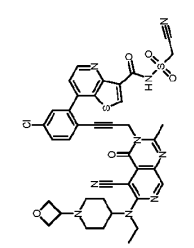
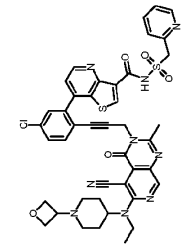
1693	1692	1695	1701 Chiral
1694	1696	1699	1698
1702 Chiral		1706	MS (ESI) m/z 878.31 [M+1]+

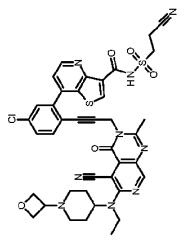
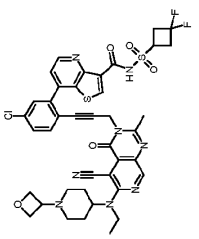
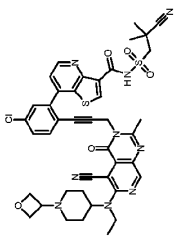
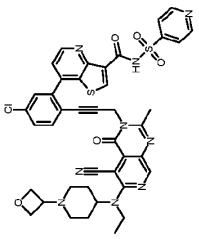
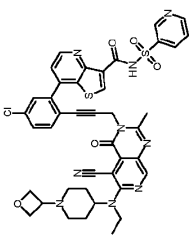
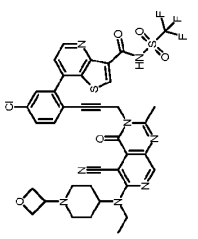
1703	MS (ESI) m/z 815.32 [M+1]+	1707	1709
1704	MS (ESI) m/z 857.25 [M+1]+	1711	1710
1705	MS (ESI) m/z 878.28 [M+1]+	1708	1714

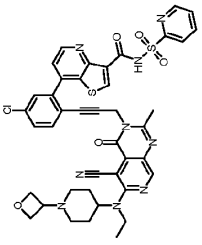
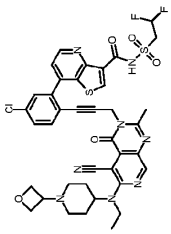
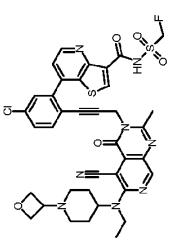
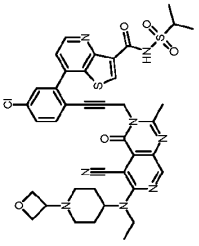
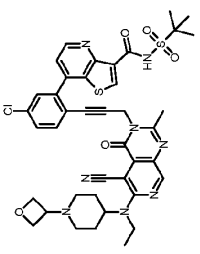
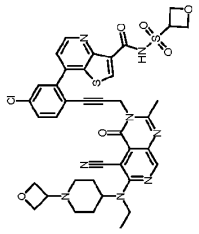
1712	1715	1721	
1713	1716	1719	
1717	MS (ESI) m/z 762.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.77 (d, J = 4.8 Hz, 1H), 8.75 (s, 1H), 8.65 (s, 1H), 7.76 (d, J = 8.2 Hz, 1H), 7.71 – 7.66 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 7.26 (s, 1H), 4.83 (s, 2H), 4.68 – 4.55 (m, 1H), 4.22 (d, J = 13.7 Hz, 1H), 3.99 – 3.71 (m, 7H), 3.20 (s, 3H), 2.70 – 2.61 (m, 2H), 2.42 – 2.30 (m, 2H), 2.18 – 2.00 (m, 5H)	1723	MS (ESI) m/z 726.28 [M+1]+

1718	1720	1724 Chiral	MS (ESI) m/z 732.18 [M+1]+
1725 Chiral	MS (ESI) m/z 732.19 [M+1]+	1728 Chiral	MS (ESI) m/z 809.32 [M+1]+
1722	MS (ESI) m/z 817.25 [M+1]+		

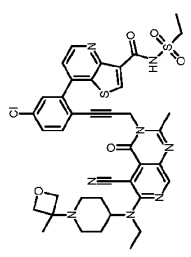
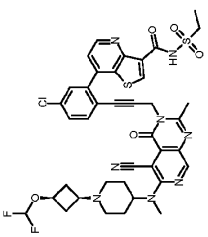
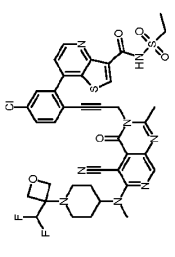
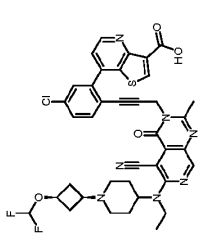
1726	Chiral		MS (ESI) m/z 823.30 [M+1]+		
1727	Chiral		MS (ESI) m/z 732.19 [M+1]+		
1729	Chiral		MS (ESI) m/z 823.3 [M+1]+	1732	Chiral  MS (ESI) m/z 837.31 [M+1]+

1730	Chiral		MS (ESI) m/z 746.28 [M+1]+	1733		MS (ESI) m/z 785.26 [M+1]+	
1731	Chiral		MS (ESI) m/z 823.27 [M+1]+	1734		MS (ESI) m/z 839.26 [M+1]+	
1735			MS (ESI) m/z 796.33 [M+1]+	1738		MS (ESI) m/z 848.33 [M+1]+	

1736		MS (ESI) m/z 810.23 [M+1]+	1739		MS (ESI) m/z 847.32 [M+1]+
1737		MS (ESI) m/z 838.32 [M+1]+	1740		MS (ESI) m/z 834.36 [M+1]+
1741		MS (ESI) m/z 834.32 [M+1]+	1744		MS (ESI) m/z 825.21 [M+1]+

1742		MS (ESI) m/z 834.31 [M+1]+	1745		MS (ESI) m/z 821.25 [M+1]+
1743		MS (ESI) m/z 788.18 [M+1]+	1746		MS (ESI) m/z 799.24 [M+1]+
1747		MS (ESI) m/z 813.29 [M+1]+	1750		MS (ESI) m/z 813.22 [M+1]+

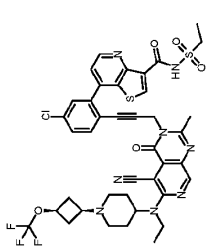
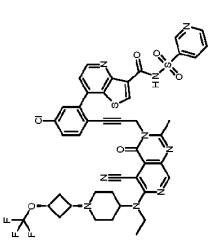
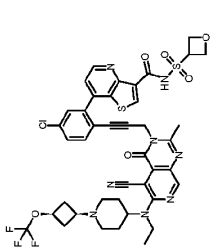
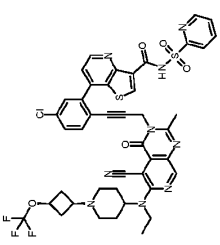
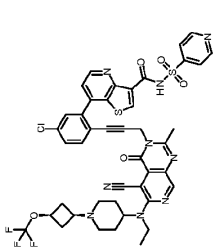
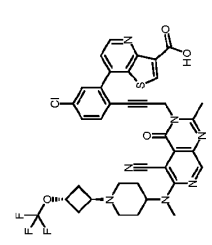
1748	MS (ESI) m/z 811.27 [M+1]+	1751	MS (ESI) m/z 771.31 [M+1]+
1749	MS (ESI) m/z 797.29 [M+1]+	1752	MS (ESI) m/z 708.23 [M+1]+
1753	MS (ESI) m/z 785.32 [M+1]+	1756	MS (ESI) m/z 821.28 [M+1]+

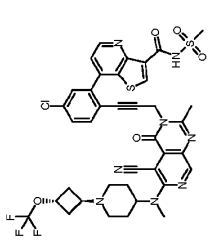
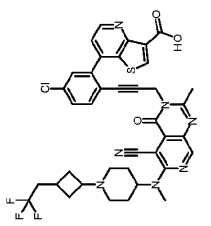
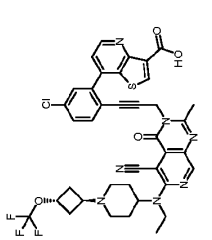
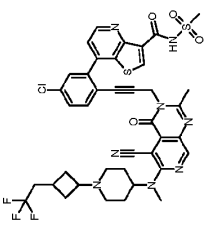
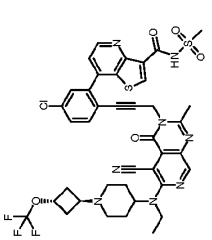
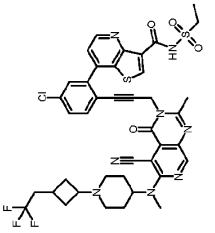
1754		1757 Chiral	
MS (ESI) m/z 799.34 [M+1]+		MS (ESI) m/z 835.45 [M+1]+	
1755		1758 Chiral	
MS (ESI) m/z 821.31 [M+1]+		MS (ESI) m/z 758.28 [M+1]+	

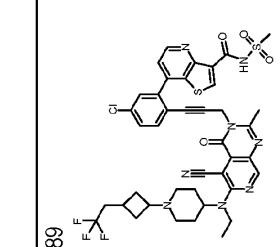
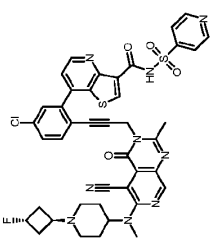
1759 Chiral	MS (ESI) m/z 835.26 [M+1]+	1762	LCMS (ESI) m/z 863.3 [M+1]+ ; 1H NMR (400 MHz, DMSO-d6) δ 12.72 (s, 1H), 9.53 (d, J = 9.3 Hz, 1H), 8.83 (d, J = 4.9 Hz, 1H), 8.78 (d, J = 6.8 Hz, 2H), 7.78 (dd, J = 8.3, 0.5 Hz, 1H), 7.77 – 7.66 (m, 2H), 7.64 (d, J = 4.9 Hz, 1H), 6.73 (t, J = 21 Hz, 1H), 5.21 (tt, J = 7.8, 6.2 Hz, 1H), 5.00 – 4.89 (m, 4H), 4.84 (s, 2H), 4.82 – 4.74 (m, 1H), 4.60 (p, J = 8.0 Hz, 1H), 3.94 (q, J = 7.8 Hz, 1H), 3.58 (d, J = 11.8 Hz, 2H), 3.13 (s, 3H), 3.05 (s, 2H), 2.78 – 2.68 (m, 1H), 2.72 (s, 1H), 2.17 – 2.06 (m, 4H), 1.97 (s, 3H)
1760 Chiral	MS (ESI) m/z 849.43 [M+1]+	1763 Chiral	LCMS (ESI) m/z 884.5 [M+1]+ ; 1H NMR (400 MHz, DMSO-d6) δ 13.02 (s, 1H), 8.90 (d, J = 4.9 Hz, 1H), 8.72 (ddd, J = 4.7, 1.7, 1.0 Hz, 1H), 8.63 (d, J = 13.4 Hz, 2H), 8.27 (dt, J = 7.9, 1.1 Hz, 1H), 8.24 – 8.16 (m, 1H), 7.80 – 7.67 (m, 4H), 7.66 (d, J = 4.8 Hz, 1H), 6.72 (t, J = 76 Hz, 1H), 4.83 (s, 2H), 4.78 (dt, J = 7.3, 3.8 Hz, 1H), 4.58 (d, J = 5.8 Hz, 1H), 3.93 (q, J = 7.6 Hz, 1H), 3.56 (d, J = 11.8 Hz, 2H), 3.04 (s, 1H), 2.72 (dd, J = 14.6, 7.1 Hz, 2H), 2.09 (s, 3H), 1.97 (s, 3H)
1761	LCMS (ESI) m/z 821.4 [M+1]+	1764 Chiral	LCMS (ESI) m/z 884.5 [M+1]+ ; 1H NMR (400 MHz, DMSO-d6) δ 8.95 – 8.89 (m, 2H), 8.82 (d, J = 4.9 Hz, 1H), 8.65 (s, 1H), 8.47 (s, 1H), 8.07 – 8.01 (m, 2H), 7.77 – 7.58 (m, 3H),6.68 (t, J = 76 Hz, 1H) 4.81 – 4.71 (m, 2H), 4.55 (p, J = 8.0 Hz, 1H), 3.93 – 3.85 (m, 1H), 3.53 (d, J = 11.7 Hz, 2H), 3.01 (s, 1H), 2.77 – 2.63 (m, 2H), 2.07 (s, 3H), 1.90 (s, 2H), 1.90 (d, J = 16.7 Hz, 0H)

1765	Chiral	LCMS (ESI) m/z 884.5 [M+1]+ ; 1H NMR (400 MHz, DMSO-d6) δ 9.24 (dd, J = 2.5, 0.8 Hz, 1H), 8.89 (dd, J = 4.8, 1.6 Hz, 1H), 8.81 (d, J = 4.9 Hz, 1H), 8.63 (s, 1H), 8.50 (ddd, J = 8.2, 2.4, 1.6 Hz, 1H), 8.46 (s, 1H), 7.76 – 7.64 (m, 3H), 7.64 – 7.57 (m, 2H), 6.69 (t, J = 76 Hz, 1H), 4.76 (d, J = 10.9 Hz, 3H), 4.55 (t, J = 8.0 Hz, 1H), 3.94 – 3.85 (m, 1H), 3.52 (s, 1H), 3.08 (s, 3H), 3.02 (s, 1H), 2.74 – 2.64 (m, 2H), 2.08 (s, 4H), 1.88 (s, 3H)	1768	Chiral	MS (ESI) m/z 877.29 [M+1]+
1766	Chiral	MS (ESI) m/z 758.34 [M+1]+	1769	Chiral	MS (ESI) m/z 898.4 [M+1]+
1767	Chiral	MS (ESI) m/z 835.33 [M+1]+	1770	Chiral	MS (ESI) m/z 898.26 [M+1]+

1771	MS (ESI) m/z 898.29 [M+1]+	1774	MS (ESI) m/z 902.23 [M+1]+
1772	MS (ESI) m/z 839.28 [M+1]+	1775	MS (ESI) m/z 776.35 [M+1]+
1773	MS (ESI) m/z 902.19 [M+1]+	1776	MS (ESI) m/z 853.3 [M+1]+

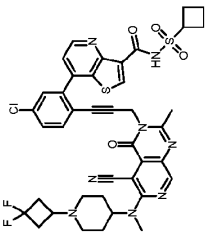
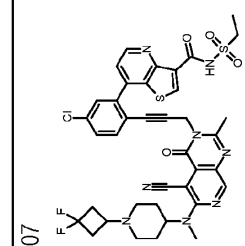
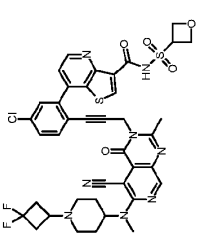
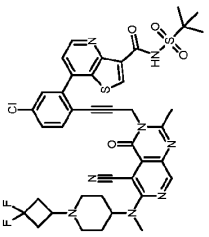
1777 Chiral 	MS (ESI) m/z 819.33 [M+1]+	1780 Chiral 	MS (ESI) m/z 916.27 [M+1]+
1778 Chiral 	MS (ESI) m/z 895.27 [M+1]+	1781 Chiral 	MS (ESI) m/z 916.27 [M+1]+
1779 Chiral 	MS (ESI) m/z 916.3 [M+1]+	1782 Chiral 	MS (ESI) m/z 762.31 [M+1]+

1783 Chiral 	MS (ESI) m/z 839.26 [M+1]+	1786 	MS (ESI) m/z 760.31 [M+1]+
1784 Chiral 	MS (ESI) m/z 776.29 [M+1]+	1787 	MS (ESI) m/z 837.35 [M+1]+
1785 Chiral 	MS (ESI) m/z 853.37 [M+1]+	1788 	MS (ESI) m/z 851.42 [M+1]+

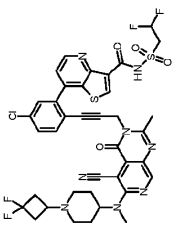
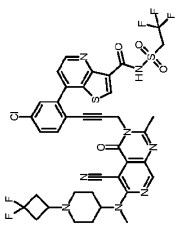
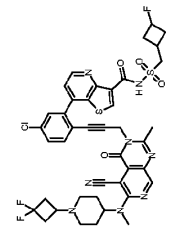
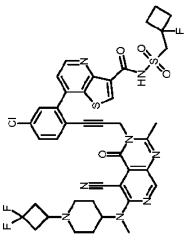
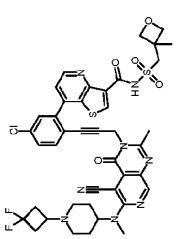
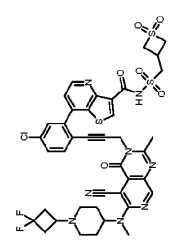
1789 	MS (ESI) m/z 851.41 [M+1]+	1792 Chiral 	MS (ESI) m/z 836.27 [M+1]+
1790	MS (ESI) m/z 865.46 [M+1]+	1793 Chiral	MS (ESI) m/z 836.3 [M+1]+
1791 Chiral	MS (ESI) m/z 815.24 [M+1]+	1794 Chiral	MS (ESI) m/z 836.33 [M+1]+

1795	Chiral		MS (ESI) m/z 710.25 [M+1]+	1798	Chiral		MS (ESI) m/z 850.31 [M+1]+
1796	Chiral		MS (ESI) m/z 787.34 [M+1]+	1799	Chiral		MS (ESI) m/z 850.34 [M+1]+
1797	Chiral		MS (ESI) m/z 829.34 [M+1]+	1800	Chiral		MS (ESI) m/z 850.25 [M+1]+

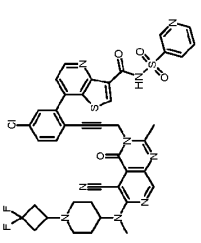
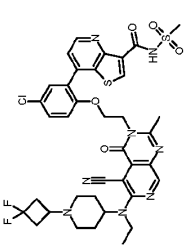
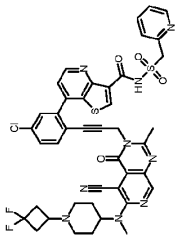
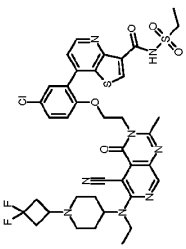
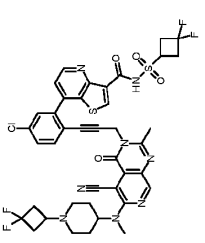
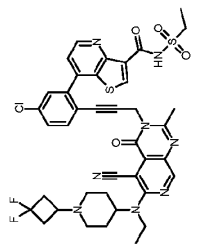
1801	MS (ESI) m/z 710.28 [M+1]+	1804	MS (ESI) m/z 797.32 [M+1]+
1802	MS (ESI) m/z 787.28 [M+1]+	1805	MS (ESI) m/z 811.3 [M+1]+
1803	MS (ESI) m/z 801.44 [M+1]+	1806	MS (ESI) m/z 770.31 [M+1]+

1807	MS (ESI) m/z 805.28 [M+1]+	1810 	MS (ESI) m/z 831.26 [M+1]+
1808 	MS (ESI) m/z 819.358 [M+1]+	1811 	MS (ESI) m/z 833.22 [M+1]+
1809	MS (ESI) m/z 817.27 [M+1]+	1812 	MS (ESI) m/z 833.39 [M+1]+

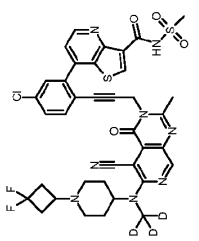
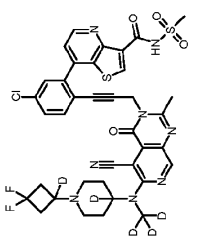
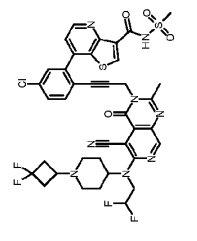
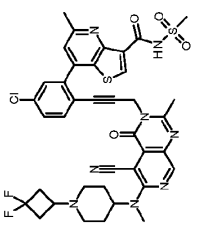
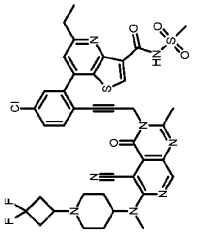
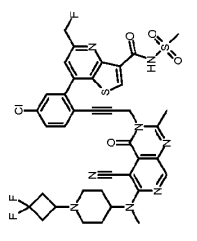
1813	MS (ESI) m/z 624.2 [M+1]+	1816	MS (ESI) m/z 850.31 [M+1]+
1814	MS (ESI) m/z 843.32 [M+1]+	1817	MS (ESI) m/z 809.22 [M+1]+
1815	MS (ESI) m/z 787.34 [M+1]+	1818	MS (ESI) m/z 845.26 [M+1]+

1819		MS (ESI) m/z 841.17 [M+1]+	
1820		MS (ESI) m/z 817.25 [M+1]+	
1821		MS (ESI) m/z 863.33 [M+1]+	
1822		MS (ESI) m/z 863.38 [M+1]+	
1823		MS (ESI) m/z 861.36 [M+1]+	
1824		MS (ESI) m/z 895.39 [M+1]+	

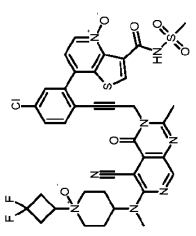
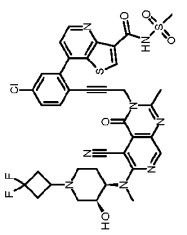
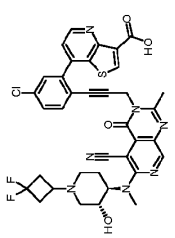
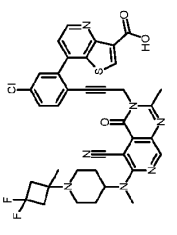
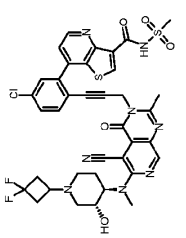
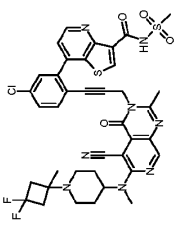
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1826	MS (ESI) m/z 830.3 [M+1]+	1829	MS (ESI) m/z 854.26 [M+1]+
1827	MS (ESI) m/z 858.28 [M+1]+	1830	MS (ESI) m/z 854.26 [M+1]+

1831 	MS (ESI) m/z 854.22 [M+1]+	1834 	MS (ESI) m/z 811.4 [M+1]+
1832 	MS (ESI) m/z 868.26 [M+1]+	1835 	MS (ESI) m/z 825.41 [M+1]+
1833 	MS (ESI) m/z 867.24 [M+1]+	1836 	MS (ESI) m/z 819.33 [M+1]+

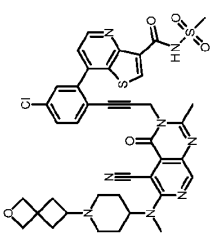
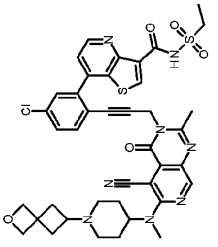
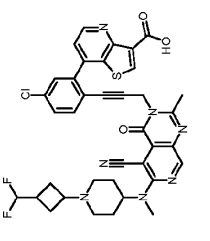
1837	MS (ESI) m/z 847.35 [M+1]+	1840	MS (ESI) m/z 868.29 [M+1]+
1838	MS (ESI) m/z 868.26 [M+1]+	1841	MS (ESI) m/z 700.33 [M+1]+
1839	MS (ESI) m/z 868.26 [M+1]+	1842	MS (ESI) m/z 777.26 [M+1]+

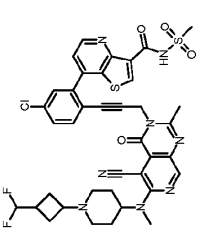
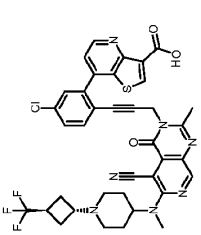
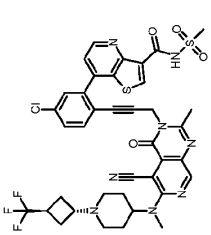
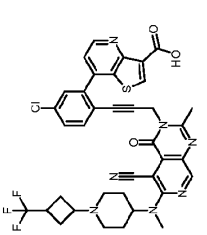
1843		MS (ESI) m/z 794.33 [M+1]+	
1844		MS (ESI) m/z 796.44 [M+1]+	
1845		MS (ESI) m/z 841.34 [M+1]+	
1846		MS (ESI) m/z 805.38 [M+1]+	
1847		MS (ESI) m/z 819.34 [M+1]+	
1848		MS (ESI) m/z 823.3 [M+1]+	

1849	MS (ESI) m/z 835.36 [M+1]+	1852	MS (ESI) m/z 730.36 [M+1]+
1850	MS (ESI) m/z 730.34 [M+1]+	1853	MS (ESI) m/z 807.18 [M+1]+
1851	MS (ESI) m/z 807.33 [M+1]+	1854	MS (ESI) m/z 746.16 [M+1]+

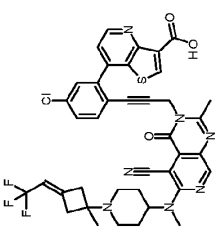
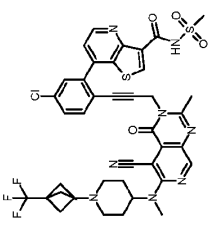
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1856	Chiral 	MS (ESI) m/z 730.37 [M+1]+	1859		MS (ESI) m/z 728.3 [M+1]+
1857	Chiral 	MS (ESI) m/z 807.4 [M+1]+	1860		MS (ESI) m/z 805.32 [M+1]+

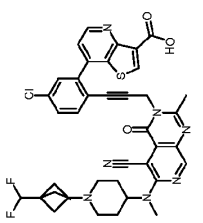
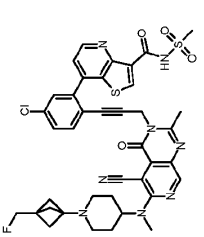
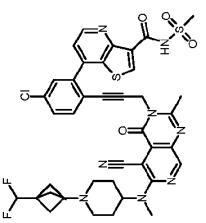
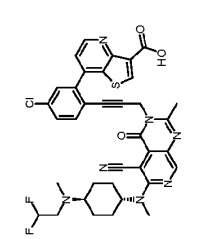
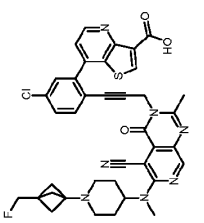
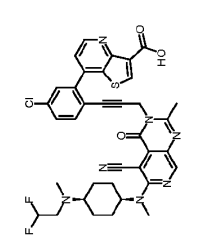
1861	MS (ESI) m/z 746.31 [M+1]+	1864	MS (ESI) m/z 781.26 [M+1]+
1862	MS (ESI) m/z 823.39 [M+1]+	1865	MS (ESI) m/z 795.37 [M+1]+
1863	MS (ESI) m/z 704.27 [M+1]+	1866	MS (ESI) m/z 718.34 [M+1]+

1867	MS (ESI) m/z 795.35 [M+1]+	1870 	MS (ESI) m/z 797.35 [M+1]+
1868	MS (ESI) m/z 809.44 [M+1]+	1871 	MS (ESI) m/z 811.4 [M+1]+
1869	MS (ESI) m/z 720.3 [M+1]+	1872 	MS (ESI) m/z 728.26 [M+1]+

1873 	MS (ESI) m/z 805.26 [M+1]+	1876 Chiral 	MS (ESI) m/z 746.28 [M+1]+
1874	MS (ESI) m/z 819.46 [M+1]+	1877 Chiral 	MS (ESI) m/z 823.3 [M+1]+
1875	MS (ESI) m/z 819.33 [M+1]+	1878 	MS (ESI) m/z 746.34 [M+1]+

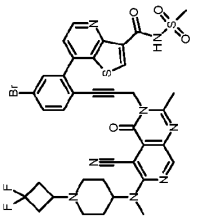
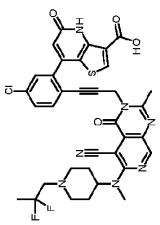
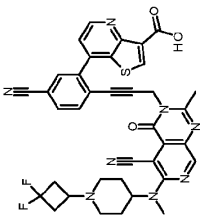
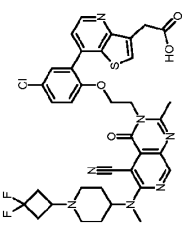
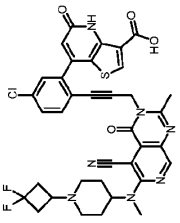
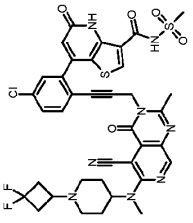
1879	MS (ESI) m/z 823.33 [M+1]+	1882	MS (ESI) m/z 738.34 [M+1]+
1880 Chiral	MS (ESI) m/z 756.29 [M+1]+	1883	MS (ESI) m/z 815.4 [M+1]+
1881 Chiral	MS (ESI) m/z 833.32 [M+1]+	1884	MS (ESI) m/z 692.31 [M+1]+

1885 	MS (ESI) m/z 772.35 [M+1]+	1888 	MS (ESI) m/z 835.26 [M+1]+
1886	MS (ESI) m/z 849.4 [M+1]+	1889	MS (ESI) m/z 754.34 [M+1]+
1887	MS (ESI) m/z 758.28 [M+1]+	1890	MS (ESI) m/z 831.29 [M+1]+

1891 	MS (ESI) m/z 740.33 [M+1]+	1894 	MS (ESI) m/z 799.27 [M+1]+
1892 	MS (ESI) m/z 817.32 [M+1]+	1895 Chiral 	MS (ESI) m/z 716.5 [M+1]+
1893 	MS (ESI) m/z 722.34 [M+1]+	1896 Chiral 	MS (ESI) m/z 716.33 [M+1]+

1897	Chiral	MS (ESI) m/z 702.46 [M+1]+	1983	MS (ESI) m/z 497.0 [M+1]+
1898		LCMS 1.90 (ESI) m/z 669.3 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.97 (s, 1H), 8.83 (d, J = 4.8 Hz, 1H), 8.40 (s, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.50 – 7.41 (m, 2H), 7.36 (s, 1H), 7.23 – 7.09 (m, 2H), 4.40 (t, J = 5.0 Hz, 2H), 4.24 (t, J = 4.9 Hz, 2H), 3.55 (d, J = 4.8 Hz, 2H), 3.38 – 3.24 (m, 3H), 2.71 – 2.62 (m, 2H), 2.46 (s, 3H), 2.33 (p, J = 1.9 Hz, 1H), 1.75 (s, 3H)	1984	MS (ESI) m/z 655.19 [M+1]+
1982		MS (ESI) m/z 461.0 [M+1]+	1985	MS (ESI) m/z 734.34 [M+1]+

2020	MS (ESI) m/z 627.43 [M+1]+	2023	MS (ESI) m/z 790.3 [M+1]+
2021	MS (ESI) m/z 806.23 [M+1]+	2024	MS (ESI) m/z 713.31 [M+1]+
2022	MS (ESI) m/z 731.29 [M+1]+	2025	MS (ESI) m/z 789.36 [M+1]+
2029	MS (ESI) m/z 746.25 [M+1]+	2032	

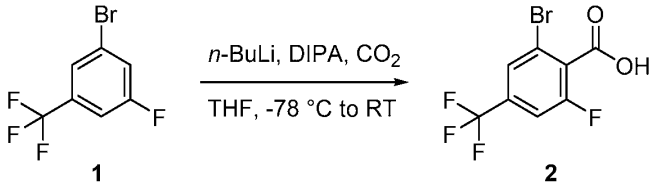
2030		2038	
MS (ESI) m/z 837.28 [M+1]+		MS (ESI) m/z 718.1 [M+1]+	
2031		2039	
MS (ESI) m/z 705.34 [M+1]+		MS (ESI) m/z 734.37 [M+1]+	
2041		2042	
MS (ESI) m/z 807.38 [M+1]+		MS (ESI) m/z 807.38 [M+1]+	

[0311] Example 2. General Methods for Synthesizing 7-CF_3-Thienylpyridine and Derivative Compounds

[0312] The 7-CF3-thienylpyridine and derivative compounds in Table 2 can be synthesized using methods described in Example 2. Many of the reactions described in Example 1 were used to synthesize compounds in Table 2. For some compounds, some of the reactions described in Example 3, below, can be used to prepare the compounds.

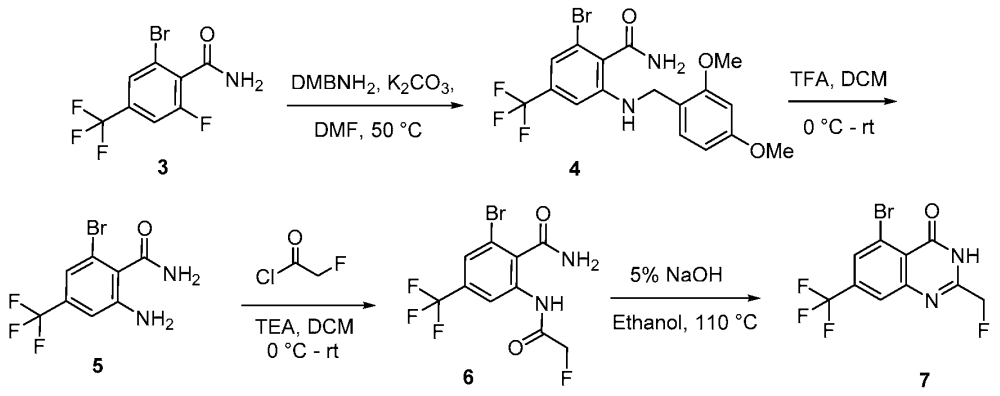
Example 2A. Methods of synthesizing the left-hand side

Example 2A.1



[0313] To a solution of diisopropyl amine (17.8 mL, 0.123 mol) in dry tetrahydrofuran (200 mL) is added *n*-butyllithium (1.6 M, 66.5 mL, 0.113 mol) drop wise at -78 °C under argon atmosphere. The reaction mixture is warmed to -10 °C and stirred for 30 min. A solution of 1-bromo-3-fluoro-5-(trifluoromethyl)benzene (1, 25.0 g, 0.102 mol) in dry tetrahydrofuran (50 mL) is added at -78 °C and mixture stirred for 45 min at -78°C. To this reaction mixture carbon dioxide gas is purged for 15 min and the temperature is gradually increased to room temperature in 2 h. After completion, the reaction mixture is cooled to -78 °C and quenched with ice water. The mixture is basified with 1 N aqueous sodium hydroxide solution and washed with diethyl ether. The aqueous layer is acidified with 2 N hydrochloric acid to pH~1 and extracted with ethyl acetate. The organic layer is separated, dried over anhydrous sodium sulphate, filtered and concentrated to afford 2-bromo-6-fluoro-4-(trifluoromethyl)benzoic acid (2).

Example 2A.2



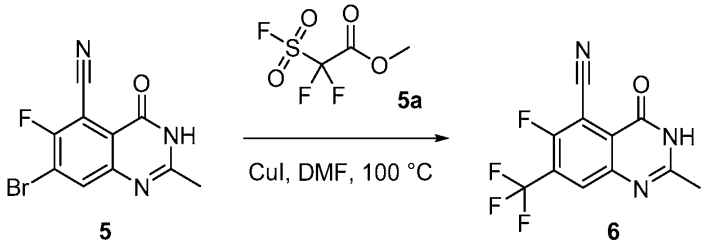
[0314] To a solution 2-bromo-6-fluoro-4-(trifluoromethyl)benzamide (3, 4.5 g, crude, 15.7 mmol) in *N,N*-dimethylformamide (40 mL), potassium carbonate (6.5 g, 47.2 mmol) and (2,4-dimethoxyphenyl)methanamine (3.1 mL, 20.45 mmol) are added at room temperature. The reaction mixture is heated to 50 °C and stirred for 16 h. After completion of reaction, the reaction mixture is poured into ice water and extracted with ethyl acetate The organic layer is washed with brine solution, dried over anhydrous sodium sulphate, filtered, concentrated under reduced pressure to get crude. The crude is purified by column chromatography using 5 % methanol in dichloromethane as eluent. The desired fractions are concentrated under reduced pressure to afford 2-bromo-6-((2,4-dimethoxybenzyl)amino)-4-(trifluoromethyl)benzamide (4).

[0315] To a solution of 2-bromo-6-((2,4-dimethoxybenzyl)amino)-4-(trifluoromethyl)benzamide (4, 1.0 g, 2.30 mmol) in dichloromethane (10 mL) is added trifluoroacetic acid (1.8 mL, 23.0 mmol), and the mixture is stirred for 30 min. After completion of reaction, the reaction mixture is concentrated, and the resulting crude is diluted with dichloromethane and washed with saturated sodium bicarbonate solution, brine solution, dried over anhydrous sodium sulphate and concentrated under reduced pressure to get crude. The crude is purified by column chromatography using 5 % methanol in dichloromethane as eluent. The desired fractions are concentrated under reduced to afford 2-amino-6-bromo-4-(trifluoromethyl)benzamide (5).

[0316] To a solution of 2-amino-6-bromo-4-(trifluoromethyl)benzamide (5, 2.0 g, 7.06 mmol) in dichloromethane (20 mL) are added triethylamine (2.93 mL, 21 mmol) and 2-fluoroacetyl chloride (1.0 mL, 14.1 mmol) at 0 °C, and the reation mixture is stirred for 30 min at same temperature. After completion of reaction, the reaction mixture is diluted with ice water and extracted with dichloromethane. The organic layer is washed with saturated brine solution, dried over anhydrous sodium sulphate and concentrated under reduced pressure to afford 2-bromo-6-(2-fluoroacetamido)-4-(trifluoromethyl)benzamide (6).

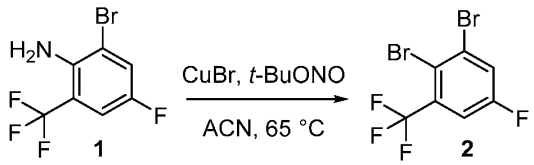
[0317] To a solution of 2-bromo-6-(2-fluoroacetamido)-4-(trifluoromethyl)benzamide (6, 0.600 g, 1.749 mmol) in ethanol (5 mL) is added 5 % sodium hydroxide (4.0 mL). The mixture is heated to 110 °C and stirred for 30 min. After completion of reaction, the reaction mixture is neutralized with 1 N hydrochloric acid and extracted with ethyl acetate. The organic layer is washed with saturated brine solution, dried over anhydrous sodium sulphate and concentrated under reduced pressure to get crude product. The crude product is purified by column chromatography using silica gel (100-200 mesh) and 0-5 % methanol in dichloromethane as eluent. The desired fractions are concentrated under reduced pressure to afford 5-bromo-2-(fluoromethyl)-7-(trifluoromethyl)quinazolin-4(3H)-one (7).

Example 2A.3



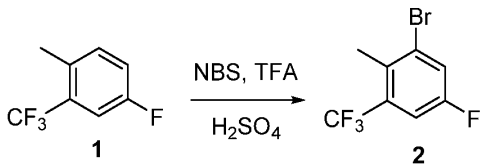
[0318] To a solution of 7-bromo-6-fluoro-2-methyl-4-oxo-3,4-dihydroquinazoline-5-carbonitrile (5, 0.200 g, 0.7 mmol) in *N,N*-dimethylformamide (2 mL), copper(I) iodide (0.159 g, 0.84 mmol) and methyl 2,2-difluoro-2-(fluorosulfonyl)acetate (5a, 0.403 g, 2.1 mmol) are added and reaction mixture is heated at 100 °C for 16 h. After completion, reaction mixture is cooled; water is added to reaction mixture and extracted with ethyl acetate. The organic layer is dried over anhydrous sodium sulphate, filtered and concentrated to afford 6-fluoro-2-methyl-4-oxo-7-(trifluoromethyl)-3,4-dihydroquinazoline-5-carbonitrile (6).

Example 2A.4



[0319] A suspension of copper(I) bromide (89.8 g, 620.1 mmol) and *tert*-butyl nitrite (63.8 mL, 620.1 mmol) in acetonitrile (2500 mL) is heated at 65 °C for 15 min. A solution of 2-bromo-4-fluoro-6-(trifluoromethyl)aniline (1, 100 g, 387.6 momol) in acetonitrile is added and heated the reaction mixture at 65 °C for 1 h. After completion, the reaction mass is quenched with water and extracted with ethyl acetate. The organic layer is dried over anhydrous sodium sulphate, filtered and concentrated under reduced pressure to get the crude material. The crude compound is purified by column chromatography using 0-5 % ethyl acetate in hexanes over silica gel (100-200 mesh) to afford 1,2-dibromo-5-fluoro-3-(trifluoromethyl)benzene (2).

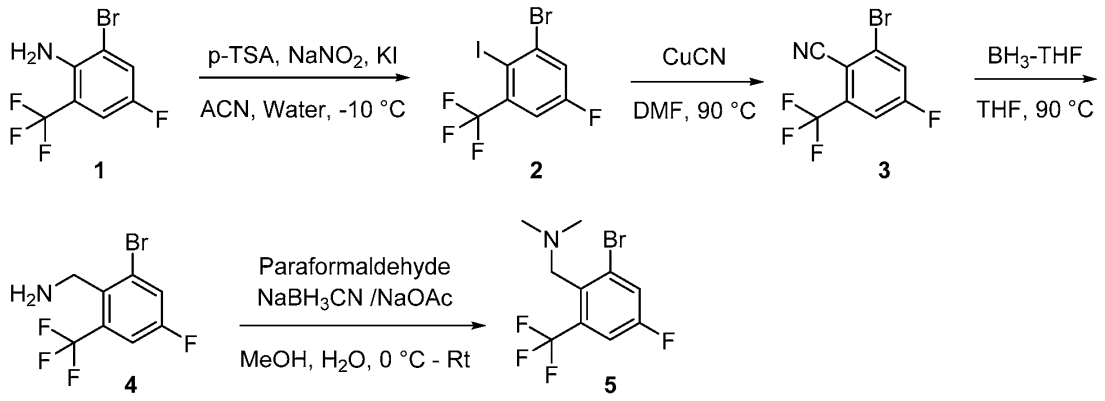
Example 2A.5



[0320] To a stirred solution of 4-fluoro-1-methyl-2-(trifluoromethyl)benzene (1, 1.05 g, 5.89 mmol) in TFA (4 mL) is added sulfuric acid (1.25 mL) and then *N*-bromosuccinimide (1.05 g,

5.89 mmol). The resulting mixture is capped, covered in aluminum foil to keep light out, and stirred at room temperature overnight. The reaction mixture is poured into vigorously stirred ice water and then extracted with hexanes. The organics are washed with brine, then saturated aqueous sodium bicarbonate. The organics are dried over magnesium sulfate, filtered, concentrated on a rotary evaporator, and purified via silica gel chromatography (100 % hexanes) to afford 1-bromo-5-fluoro-2-methyl-3-(trifluoromethyl)benzene (2).

Example 2A.6



[0321] To a solution of 2-bromo-4-fluoro-6-(trifluoromethyl)aniline (1, 100.0 g, 389.2 mmol) in acetonitrile (2500 mL) is added p-toluenesulfonic acid (220.9 g, 1160.1 mmol) portion wise at -10 °C. A solution of sodium nitrite (51.68 g, 750 mmol) and potassium iodide (157.7 g, 949.2 mmol) in water (100 mL) is added at -10 °C and the mixture is stirred for 45 min at -10 °C. After completion, the reaction mixture is quenched with water & extracted with ethyl acetate (5000 mL). The organic layer is washed with aqueous saturated sodium thiosulphate (500 mL). Organic layer is separated, dried over anhydrous sodium sulphate, filtered and concentrated to afford 1-bromo-5-fluoro-2-iodo-3-(trifluoromethyl)benzene (2).

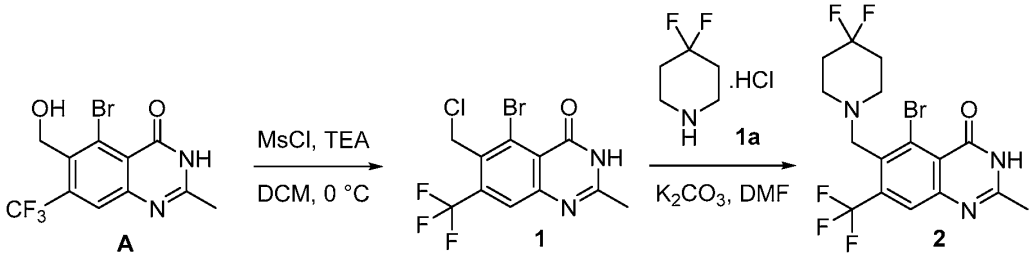
[0322] To a solution of 1-bromo-5-fluoro-2-iodo-3-(trifluoromethyl) benzene (2, 80.0 g, 217.3 mmol) in *N,N*-dimethylformamide (500 mL), copper(I) cyanide (19.4 g, 217.2 mmol) is added at room temperature. The reaction mixture is stirred at 90 °C for 12 h. After completion, it is cooled to room temperature, poured into ice water and extracted with ethyl acetate (2.0 L). The organic layer is washed with brine solution, dried over anhydrous sodium sulphate and concentrated under reduced pressure to get crude. The crude compound is purified by flash column chromatography using 0-5 % ethyl acetate in hexanes to afford 2-bromo-4-fluoro-6-(trifluoromethyl)benzonitrile (3).

[0323] To a solution 2-bromo-4-fluoro-6-(trifluoromethyl)benzonitrile (3, 12.0 g, 44.9 mmol) in tetrahydrofuran (200 mL), borane in tetrahydrofuran (1 M, 67 mL, 67.1 mmol) is added drop

wise wise at 0 °C. The reaction mixture is allowed to stir at 90 °C for 12 h. After completion, the reaction mixture is poured into chilled methanol and concentrated under reduced pressure. The crude compound is purified by flash column chromatography using 0-15 % ethyl acetate in hexanes to afford (2-bromo-4-fluoro-6-(trifluoromethyl) phenyl)methanamine (4).

[0324] To a solution of (2-bromo-4-fluoro-6-(trifluoromethyl) phenyl)methanamine (4, 6.0 g, 22.6 mmol) in methanol (100 mL), paraformaldehyde (6.0 g, 200.0 mmol) and solution of sodium acetate (5.4 g, 66.0 mmol) in water (10 mL) are added and stirred at room temperature for 1 h. Sodium cyanoborohydride (4.03 g, 66.1 mmol) is added portion wise at 0 °C. The reaction mixture is allowed to stir at room temperature for 12 h. After completion, the reaction mixture is concentrated under reduced pressure. Crude residue is diluted with water and extracted with diethyl ether (100 mL). The crude compound is purified by flash column chromatography using 0-15 % ethyl acetate in hexanes to afford 1-(2-bromo-4-fluoro-6-(trifluoromethyl)phenyl)-*N,N*-dimethylmethanamine (5).

Example 2A.7

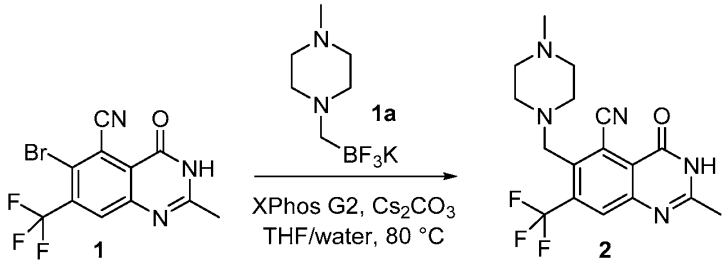


[0325] To a solution of 5-bromo-6-(hydroxymethyl)-2-methyl-7-(trifluoromethyl)quinazolin-4(3H)-one (**A**, 0.32 g, 0.94 mmol) in dichlomethane (6 mL) at 0 °C, triethyl amine (0.39 mL, 2.84 mmol) and methanesulfonyl chloride (0.11 mL, 1.42 mmol) are added and stirred at 0 °C for 1 h. After completion, the reaction mixture is diluted with water and extracted with dichloromethane. The organic layer is washed with water, saturated brine, dried over anhydrous sodium sulfate and concentrated under reduced pressure to afford 5-bromo-6-(chloromethyl)-2-methyl-7-(trifluoromethyl)quinazolin-4(3H)-one (**1**)

[0326] To a solution of 4,4-difluoro piperidine (1a, 2.0 g, 12.7 mmol) in *N,N*-dimethylformamide (10.0 mL) is added potassium carbonate (1.06 g, 7.62 mmol) at room temperature and the mixture is stirred for 20 min. Then 5-bromo-6-(chloromethyl)-2-methyl-7-(trifluoromethyl)quinazolin-4(3H)-one (1, 0.9 g, 2.54 mmol) is added to the reaction mixture at room temperature and stirring is continued for 24 h. After completion, the reaction mixture is diluted with water and extracted with ethyl acetate. The organic layer is washed with water and saturated brine solution, dried over anhydrous sodium sulphate, filtered and concentrated. The

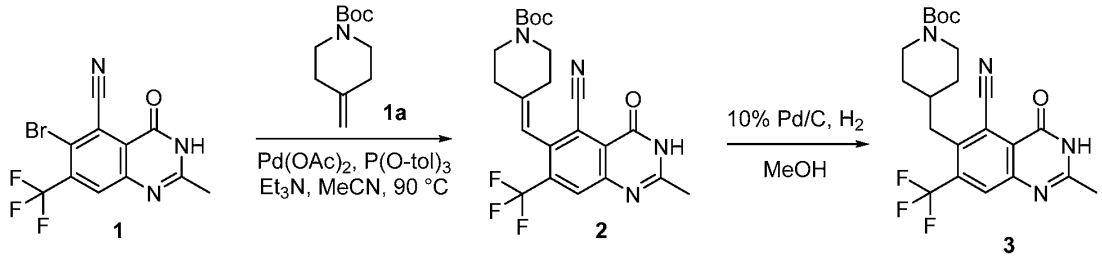
crude product is purified by column chromatography using silica gel (100-200 mesh) and 50 % ethyl acetate in hexane as eluent. The desired fractions are concentrated under reduced pressure to afford 5-bromo-6-((4,4-difluoropiperidin-1-yl)methyl)-2-methyl-7-(trifluoromethyl)quinazolin-4(3H)-one (2).

Example 2A.8



[0327] To a solution of 6-bromo-2-methyl-4-oxo-7-(trifluoromethyl)-3,4-dihydroquinazoline-5-carbonitrile (1, 50 mg, 0.151 mmol) in tetrahydrofuran (3 mL) and water (0.75 mL) are added 1-methyl-4-((trifluoro-λ^4-boranyl)methyl)piperazine, potassium salt (1a, 497 mg, 2.25 mmol), cesium carbonate (196 mg, 0.602 mmol) and XPhos Chloro(2-dicyclohexylphosphino-2′,4′,6′-triisopropyl-1,1′-biphenyl)[2-(2′-amino-1,1′-biphenyl)]palladium(II) (24 mg, 0.0301 mmol) and the mixture is sparged with argon for 5 min, then it is sealed and heated to 80 °C for 15 h. After completion, the mixture is concentrated under reduced pressure to get crude product. The crude product obtained is purified by prep-HPLC to afford 2-methyl-6-((4-methylpiperazin-1-yl)methyl)-4-oxo-7-(trifluoromethyl)-3,4-dihydroquinazoline-5-carbonitrile (2).

Example 2A.9

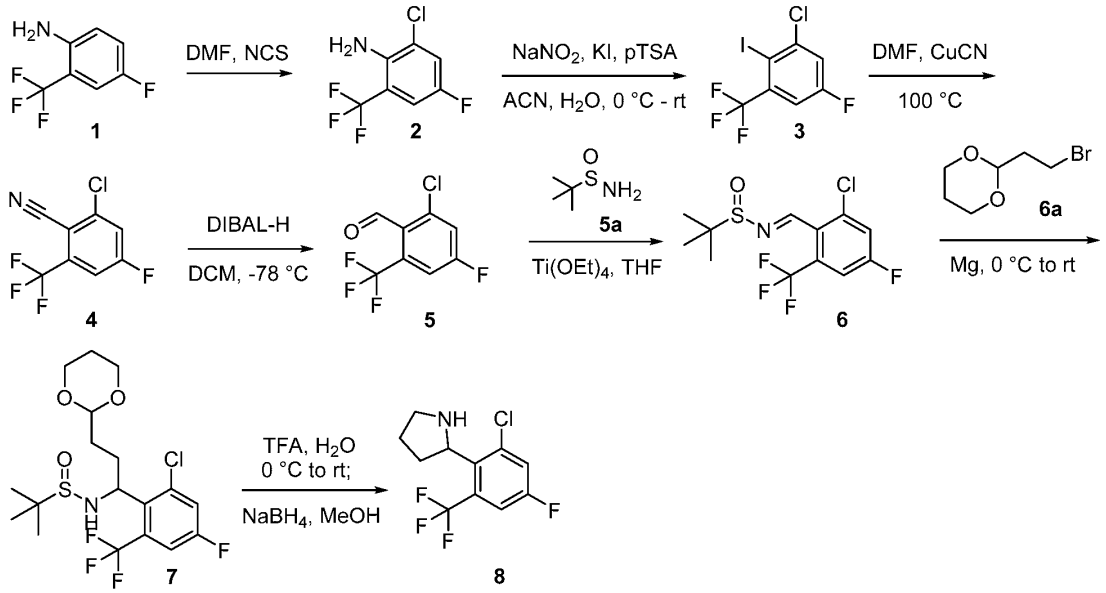


[0328] A solution of 6-bromo-2-methyl-4-oxo-7-(trifluoromethyl)-3,4-dihydroquinazoline-5-carbonitrile (**1**, 1.00 g, 3.02 mmol), *tert*-butyl 4-methylenepiperidine-1-carboxylate (**1a**, 5.90 g, 30.1 mmol), triethylamine (1.20 mL, 9.03 mmol), and tri (o-tolyl)phosphine (0.366 g, 1.23 mmol) in acetonitrile (10.0 mL) is degassed with argon for 10 min. Palladium (II) acetate (0.134 g, 0.60 mmol) is then added to the reaction mixture and degassing is continued for 5 min. The reaction mixture is heated at 90 °C for 24 h. After this time, the reaction mixture is cooled to room temperature, diluted with ethyl acetate, and concentrated to dryness under reduced

pressure. The crude product is purified by silica gel (100-200 mesh) column chromatography using 30-50 % ethyl acetate in hexanes as eluent. The desired fractions are concentrated under reduced pressure to afford *tert*-butyl 4-((5-cyano-2-methyl-4-oxo-7-(trifluoromethyl)-3,4-dihydroquinazolin-6-yl)methylene)piperidine-1-carboxylate (**2**).

[0329] To a solution of *tert*-butyl 4-((5-cyano-2-methyl-4-oxo-7-(trifluoromethyl)-3,4-dihydroquinazolin-6-yl)methylene)piperidine-1-carboxylate (**2**, 0.90 g, 2.0 mmol) in methanol (20 mL) is added 10 % palladium on carbon (1.35 g) at room temperature. The reaction mixture is stirred at room temperature for 2 h under hydrogen atmosphere. Then, the reaction mixture is filtered with Celite. The filtrate is washed with ethyl acetate and concentrated to dryness under reduced pressure to obtain a crude product. The crude product is purified by silica gel (100-200 mesh)column chromatography using 3-5 % methanol in dichloromethane as eluent. The desired fractions are concentrated under reduced pressure to afford *tert*-butyl 4-((5-cyano-2-methyl-4-oxo-7-(trifluoromethyl)-3,4-dihydroquinazolin-6-yl)methyl)piperidine-1-carboxylate (**3**).

Example 2A.10



[0330] To a solution of 4-fluoro-2-(trifluoromethyl)aniline (**1**, 100.0 g, 558.66 mmol) in *N*,*N*-dimethylformamide (500 mL), *N*-chlorosuccinamide (78.7 g, 558.66 mmol) is added at room temperature. This reaction mixture is stirred for 16 h. After this time, the mixture is diluted with water and extracted with ethyl acetate. The organic layer is washed with water and then brine, dried over anhydrous sodium sulfate, filtered, and concentrated. The crude product is purified by silica gel (100-200 mesh) column chromatography using hexanes as eluent. The desired fractions

are concentrated under reduced pressure to afford 2-chloro-4-fluoro-6-(trifluoromethyl)aniline (**2**).

[0331] To a solution of 2-chloro-4-fluoro-6-(trifluoromethyl)aniline (**2**, 43.0 g, 201.87 mmol) in acetonitrile (200 mL) at -10 °C, p-toluenesulfonic acid monohydrate (115.0 g, 605.63 mmol) is added. This reaction mixture is stirred for 15 min at the same temperature. A solution of sodium nitrite (27.85 g, 403.74 mmol) and potassium iodide (83.77 g, 504.67 mmol) in water (50 mL) is added dropwise to the reaction mixture as it is stirred at -10 °C for 30 min. Next, the reaction mixture is diluted with water and extracted with ethyl acetate. The organic layer is washed with aqueous saturated sodium thiosulfate solution and then brine, dried over anhydrous sodium sulfate, filtered, and concentrated. The crude product is purified by silica gel (100-200 mesh) column chromatography using hexanes as eluent. The desired fractions are concentrated under reduced pressure to afford 1-chloro-5-fluoro-2-iodo-3-(trifluoromethyl)benzene (**3**).

[0332] To a solution of 1-chloro-5-fluoro-2-iodo-3-(trifluoromethyl)benzene (**3**, 30 g, 92.6 mmol) in *N,N*-dimethylformamide (200 mL), copper(I) cyanide (12.36 g, 138.88 mmol) is added. This reaction mixture is heated at 100 °C for 16 h. After this time, the mixture is diluted with water and extracted with ethyl acetate. The organic layer is washed with water and brine, dried over anhydrous sodium sulfate, filtered, and concentrated. The crude product is purified by silica gel (100-200 mesh) column chromatography using 3 % ethyl acetate in hexanes as eluent. The desired fractions are concentrated under reduced pressure to afford 2-chloro-4-fluoro-6-(trifluoromethyl)benzonitrile (**4**).

[0333] To a solution of 2-chloro-4-fluoro-6-(trifluoromethyl)benzonitrile (**4**, 15.0 g, 67.26 mmol) in dry dichloromethane (150 mL) at -78 °C, diisobutylaluminiumhydride (1.0 M in toluene, 134.52 mL, 134.52 mmol) is added dropwise. The mixture is stirred at same temperature for 30 min. Next, the reaction mixture is quenched with 1 N aqueous hydrochloric acid and extracted with dichloromethane. The organic layer is dried over anhydrous sodium sulfate, filtered, and concentrated to dryness under reduced pressure to afford 2-chloro-4-fluoro-6-(trifluoromethyl)benzaldehyde (**5**).

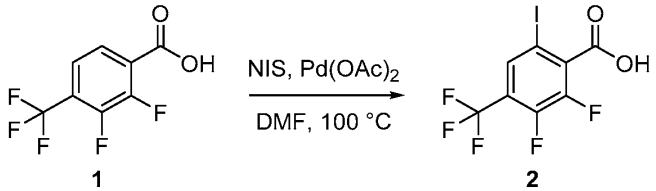
[0334] To a solution of 2-chloro-4-fluoro-6-(trifluoromethyl)benzaldehyde (**5**, 17.00 g, 75.22 mmol) in tetrahydrofuran (100 mL), 2-methylpropane-2-sulfinamide (**5a**, 13.65 g, 112.83 mmol) and titanium ethoxide (34.30 mL, 150.44 mmol) are added dropwise at room temperature. This reaction mixture is stirred at the same temperature for 16 h. After this time, the reaction mixture is quenched with aqueous ammonium chloride solution, filtered with Celite, and washed with ethyl acetate. The filterate is concentrated and the crude residue is purified by Combi-flash (40 g,

Redi-Sep column) using 20 % ethyl acetate in hexanes as eluent. The desired fractions are concentrated under reduced pressure to afford (E)-*N*-(2-chloro-4-fluoro-6-(trifluoromethyl)benzylidene)-2-methylpropane-2-sulfinamide (**6**).

[0335] Magnesium turnings (5.0 g) are added to dry tetrahydrofuran (50 mL) followed by iodine (0.002 g) and the mixture is heated to just above room temperature. Then, 2-(2-bromoethyl)-1,3-dioxane (**6a**, 9.8 mL, 72.94 mmol) is added and the mixture is heated till it became colorless. Then, this mixture is added dropwise to a solution of (E)-*N*-(2-chloro-4-fluoro-6-(trifluoromethyl)benzylidene)-2-methylpropane-2-sulfinamide (**6**, 12.00 g, 36.47 mmol) in tetrahydrofuran (50 mL) at room temperature. The resulting mixture is stirred at room temperature for 1 h. Next, the reaction mixture is quenched with aqueous ammonium chloride solution and extracted with ethyl acetate. The organic layer dried over anhydrous sodium sulfate and concentrated. The crude residue is purified by Combi-flash (40 g, Redi-Sep column) using 30 % ethyl acetate in hexanes as eluent. The desired fractions are concentrated under reduced pressure to afford *N*-(1-(2-chloro-4-fluoro-6-(trifluoromethyl)phenyl)-3-(1,3-dioxan-2-yl)propyl)-2-methylpropane-2-sulfinamide (**7**).

[0336] A solution mixture of *N*-(1-(2-chloro-4-fluoro-6-(trifluoromethyl)phenyl)-3-(1,3-dioxan-2-yl)propyl)-2-methylpropane-2-sulfinamide (**7**, 12.00 g, 26.96 mmol) in trifluroacetic acid in water (3:1, 180 mL) is stirred at room temperature for 16 h. After this time, the reaction mixture is quenched with aqueous sodium bicarbonate solution and extracted with ethyl acetate. The organic layer is dried over anhydrous sodium sulfate, filtered, and concentrated. The solid residue is dissolved in methanol, after which sodium borohydrate (8.00 g, 269.66 mmol) is added at 0 °C and the mixture is stirred at room temperature for 8 h. After this time, the reaction mixture is quenched with ice-cold water and extracted with ethyl acetate. The organic layer is dried over anhydrous sodium sulfate, filtered, and concentrated to dryness under reduced pressure to afford 2-(2-chloro-4-fluoro-6-(trifluoromethyl)phenyl)pyrrolidine (**8**).

Example 2A.11



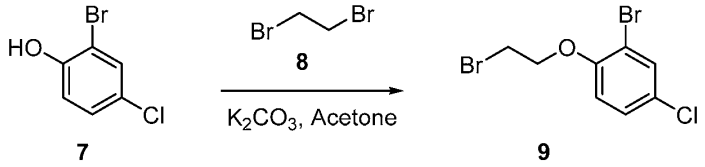
1 2

[0337] To a solution of 2,3-difluoro-4-(trifluoromethyl)benzoic acid (1, 5 g, 22.123 mmol) in *N,N*-dimethylformamide (50 mL), *N*-iodosuccinimide (7.43 g, 33.185 mmol) is added and purged with argon for 20 min. Then, palladium acetate (1.48 g, 6.637 mmol) is added and

reaction mixture is heated at 100 °C for 48 h. After completion, the reaction mixture is cooled, diluted with water and extracted with ethyl acetate. The combined organic layer is washed with cold water and brine solution, dried over anhydrous sodium sulphate, filtered and concentrated under reduced pressure to afford 2,3-difluoro-6-iodo-4-(trifluoromethyl)benzoic acid (2).

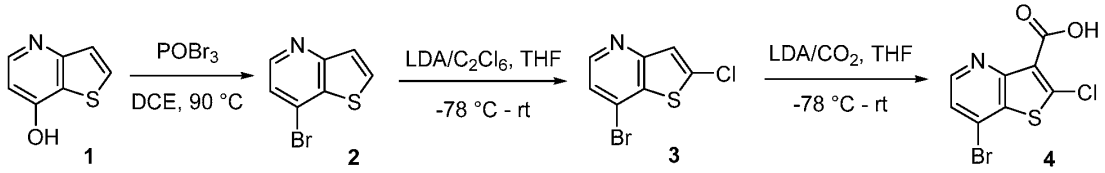
Example 2B. Methods of synthesizing the right-hand side

Example 2B.1



[0338] To a solution 2-bromo-4-chlorophenol (7, 50.0 g, 241.0 mmol) in aqueous sodium hydroxide (1 M) (1.0 L), tetra-*n*-butylammonium bromide (11.64 g, 36.15 mmol) and potassium iodide (6.00 g, 36.15 mmol) are added. 1,2-dibromoethane (8,165.6 g, 891.7 mmol) is added at 85 °C and stirred for 16 h at the same temperature. After completion, the reaction mixture is poured into water and extracted with ethyl acetate. Combined organic layer are washed with water, brine, dried over anhydrous sodium sulfate and concentrated under reduced pressure to get crude; the crude compound is purified by flash column chromatography (using 0-5 % ethyl acetate in hexanes) to afford 2-bromo-1-(2-bromoethoxy)-4-chlorobenzene (9).

Example 2B.2



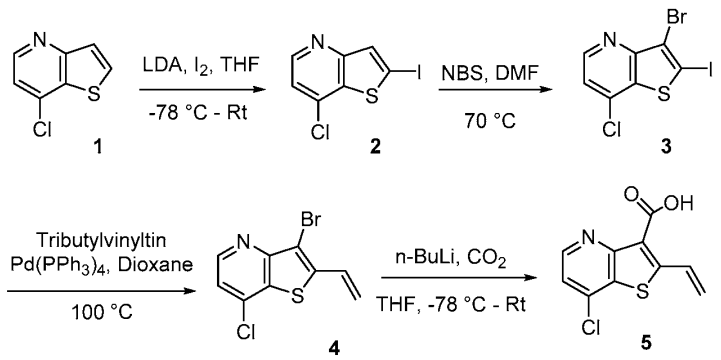
[0339] A stirred solution of thieno[3,2-b]pyridin-7-ol (1, 2.0 g, 13.2 mmol) in phosphorous oxybromide (7.5 g, 26.4 mmol) and 1,2-dichloroethane is heated at 90 °C for 12 h. After completion of the reaction, the mixture is cooled to room temperature and quenched with saturated aqueous solution of sodium bicarbonate and extracted with ethyl acetate. The organic layer is washed with brine, dried over anhydrous sodium sulphate, filtered and concentrated to afford 7-bromothieno[3,2-b]pyridine (2).

[0340] To a stirred solution of 7-bromothieno[3,2-b]pyridine (2, 1.5 g, 7.04 mmol) in dry tetrahydrofuran (20 mL), freshly prepared lithium diisopropylamide (2.0 M in hexane, 8.75 mL, 17.5 mmol) is added at -78 °C and the mixture is stirred at same temperature for 1 h. Hexachloroethane (2.0 mL, 8.44 mmol) is added drop wise and the reaction mixture is allowed

to warm up to room temperature over 3 h. The reaction is quenched with aqueous ammonium chloride solution, diluted with water and extracted with ethyl acetate. The organic layer is washed with water and saturated brine solution, dried over anhydrous sodium sulphate, filtered and concentrated. The crude product is purified over a plug of silica gel eluting the compound with ethyl acetate in hexanes (0-10 %). The desired fractions are concentrated under reduced pressure to afford 7-bromo-2-chlorothieno[3,2-b]pyridine (3).

[0341] To a solution of 7-bromo-2-chlorothieno[3,2-b]pyridine (3, 0.5 g, 2.02 mmol) in dry tetrahydrofuran (10 mL) and the mixture is cooled to -78 °C. Lithium diisopropylamide (2 M, 1.5 mL, 3.03 mmol) is added drop wise and the reaction mixture is stirred at -78 °C for 1 h. Carbon dioxide gas is purged through the reaction mass for 20 min at same temperature and is stirred for 1 h at -78 °C. The reaction mixture is slowly warmed to 0 °C and stirred for 30 min. After completion, reaction mixture is quenched with water and washed with ethyl acetate. Ethyl acetate layer is discarded and aqueous layer is acidified with aqueous solution of citric acid. It is then extracted with ethyl acetate. The organic layer is separated, dried over anhydrous sodium sulphate, filtered and concentrated under reduced pressure to afford 7-bromo-2-chlorothieno[3,2-b]pyridine-3-carboxylic acid (4).

Example 2B.3



[0342] To a stirred solution of 7-chlorothieno[3,2-b]pyridine (1, 1.5 g, 8.9 mmol) in dry tetrahydrofuran (50 mL) is added drop wise lithium diisopropylamide (11.7 mL, 19.5 mmol) at -78 °C and the mixture is stirred at same temperature for 1 h. Iodine (2.25 g, 8.87 mmol dissolved in tetrahydrofuran, 10 mL) is added drop wise and the reaction mixture is allowed to warm up to room temperature over 4 h. It is quenched with aqueous solution of ammonium chloride and extracted with ethyl acetate. The organic layer is washed with water and saturated brine solution, dried over anhydrous sodium sulphate, filtered and concentrated to dryness under reduced pressure. The crude product is purified by Combiflash (12 g, RediSep column) using 5-10 %

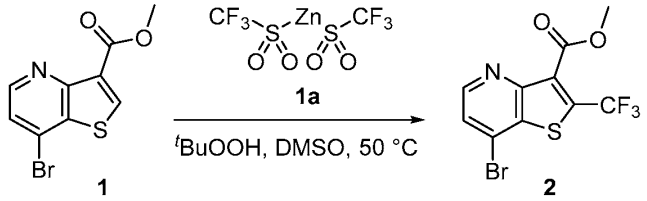
ethyl acetate in hexanes as eluent. The desired fractions are concentrated under reduced pressure to afford 7-chloro-2-iodothieno[3,2-b]pyridine (2).

[0343] To a solution of 7-chloro-2-iodothieno[3,2-b]pyridine (2, 1.0 g, 3.4 mmol) in *N,N*-dimethylformamide (10 mL), *N*-bromo succinamide is added at room temperature. The reaction mixture is heated and stirred at 70 °C for 12 h. After completion of the reaction, the mixture is diluted with water and extracted with ethyl acetate. The organic layer is washed with water and saturated brine solution, dried over anhydrous sodium sulphate, filtered and concentrated under reduced pressure. The crude product is purified by Combiflash (12 g, RediSep column) using 5-10 % ethyl acetate in hexanes as eluent. The desired fractions are concentrated under reduced pressure to afford 3-bromo-7-chloro-2-iodothieno[3,2-b]pyridine (3).

[0344] A suspension 3-bromo-7-chloro-2-iodothieno[3,2-b]pyridine (3, 1.0 g, 2.7 mmol) and tributyl vinyl tin (1.01 mL, 3.21 mmol) in 1,4-dioxane (10 mL) is degassed using argon for 10 min. Tetrakis(triphenylphosphine)palladium(0) (0.21 g, 0.19 mmol) is added to the reaction mixture at room temperature and the mixture is heated at 100 °C for 1 h. After completion, the reaction mixture is cooled to room temperature, diluted with water and extracted with ethyl acetate. The ethyl acetate layer is dried over sodium sulfate and concentrated to dryness under reduced pressure. The crude product is purified over a plug of silica gel eluting the compound with ethyl acetate:hexanes (1-10 %). The desired fractions are concentrated under reduced pressure to afford 3-bromo-7-chloro-2-vinylthieno[3,2-b]pyridine (4).

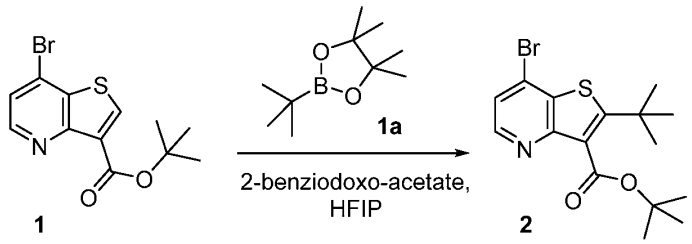
[0345] To a solution of 3-bromo-7-chloro-2-vinylthieno[3,2-b]pyridine (4, 0.6 g, 2.19 mmol) in dry tetrahydrofuran (20 mL) is added drop wise n-Butyl lithium (1.7 mL 1.3 M in hexanes, 2.19 mmol) at -78 °C and reaction mixture is stirred at the same temperature for 2 h. Carbon dioxide gas is purged through the reaction mixture at -78 °C for 30 min and the reaction mixture is stirred for 1 h at the same temperature. The reaction mixture is slowly warmed to 0 °C and stirred for 30 min. After completion, reaction mixture is quenched with water and washed with ethyl acetate. Ethyl acetate layer is discarded and aqueous layer is acidified with aqueous solution of citric acid and extracted with ethyl acetate. The organic layer is separated, dried over anhydrous sodium sulphate, filtered and concentrated under reduced pressure to afford 7-chloro-2-vinylthieno[3,2-b]pyridine-3-carboxylic acid (5).

Example 2B.4



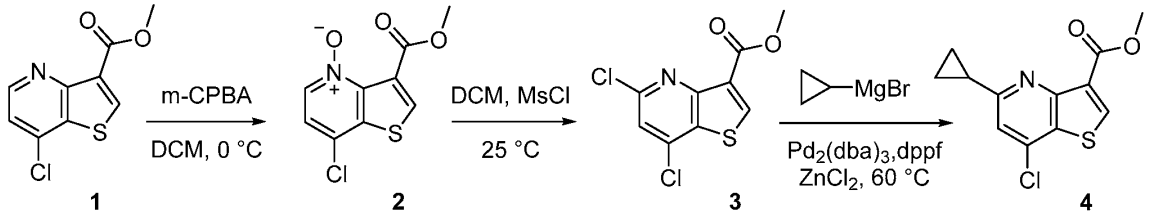
[0346] Methyl 7-bromothieno[3,2-b]pyridine-3-carboxylate (1, 68.0 mg, 0.25 mmol) and bis(trifluoromethylsulfinyloxy)zinc (1a, 139.8 mg, 0.50 mmol) are dissolved in dimethylsulfoxide (1.71 mL) in an oven-dried screw capped vial equipped with a stir bar. The mixture is stirred vigorously at 0 °C while *tert*-butyl hydroperoxide (0.09 mL, 0.92 mmol) is added slowly. After completion of addition the ice bath is removed and the reaction mixture is heated to 50 °C in a heating block for 2.5 h before being cooled to room temperature. The reaction mixture is diluted with saturated aqueous sodium bicarbonate and ethyl acetate. The layers are separated and the aqueous phase extracted with ethyl acetate three times. The combined organic material is washed with brine and dried over magnesium sulfate. The solids are filtered and solvent removed *in vacuo* to afford a crude residue that is purified via silica gel chromatography (5 to 40 % ethyl acetate in hexanes), affording methyl 7-bromo-2-(trifluoromethyl)thieno[3,2-b]pyridine-3-carboxylate (2).

Example 2B.5



[0347] A solution of *tert*-butyl 7-bromothieno[3,2-b]pyridine-3-carboxylate (1, 150.0 mg, 0.480 mmol), (3-oxo-1λ^{3},2-benziodoxol-1-yl) acetate (417.5 mg, 0.950 mmol), 2-(*tert*-butyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1a, 132.0 mg, 0.720 mmol) and tris(2,2'-bipyridyl)dichloro-ruthenium(II)hexahydrate (35.7 mg, 0.048 mmol) in hexafluoroisopropanol (1.25 mL) is stirred at room temperature and irradiated with a 60 watt household lamp positioned 10 cm away from the vial for 24 h. After completion, reaction mixture is diluted with dichloromethane and silica gel is added. The solvent is evaporated. The crude silica mixture is purified by flash chromatography using silica gel (100-200 mesh) using 0-10 % methanol in dichloromethane as eluent. The desired fractions are concentrated under reduced pressure to afford *tert*-butyl 7-bromo-2-(*tert*-butyl)thieno[3,2-b]pyridine-3-carboxylate (2).

Example 2B.6

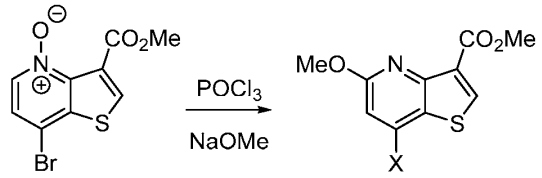


[0348] Methyl 7-chlorothieno[3,2-b]pyridine-3-carboxylate (1, 0.2 g, 0.88 mmol) is dissolved in dichloromethane (2.2 mL) in an oven-dried screw capped vial equipped with a stir bar. The reaction mixture is stirred at room temperature while 3-chloroperbenzoic acid (0.24 g, 1.41 mmol) is added in 4 portions over 2 min. After 24 h the reaction mixture is poured onto silica gel and purification via silica gel chromatography (50-100 % ethyl acetate in hexanes, then 10 % methanol in ethyl acetate) afforded 7-chloro-3-(methoxycarbonyl)thieno[3,2-b]pyridine 4-oxide (2).

[0349] 7-chloro-3-(methoxycarbonyl)thieno[3,2-b]pyridine 4-oxide (2, 0.12 g, 0.47 mmol) is dissolved in dichloromethane (3.3 mL) in an oven-dried screw capped vial equipped with a stir bar. The mixture is stirred at room temperature while methanesulfonyl chloride (0.18 mL, 2.36 mmol) dropwise. After 3 h more methanesulfonyl chloride (0.18 mL, 2.36 mmol) is added dropwise. After 4.5 h the reaction mixture is warmed to 40 °C and stirred an additional 16 h before being cooled to room temperature. The reaction mixture is poured onto silica gel and purification via silica gel chromatography (0-50 % ethyl acetate in hexanes) afforded methyl 5,7-dichlorothieno[3,2-b]pyridine-3-carboxylate (3).

[0350] Zinc chloride solution (0.5 M, 0.59 mL, 0.29 mmol) is dissolved in tetrahydrofuran (1.0 mL) in an oven-dried screw capped vial equipped with a stir bar. The reaction mixture is stirred at room temperature while bromo(cyclopropyl)magnesium (0.59 mL, 0.29 mmol) solution is added slowly. After 45 min a solution of methyl 5,7-dichlorothieno[3,2-b]pyridine-3-carboxylate (3, 67.0 mg, 0.25 mmol) in tetrahydrofuran (1.5 mL) is added slowly. After 1 min $Pd_2(dba)_3$ (28.4 mg, 0.03 mmol) and dppf (30.4 mg, 0.06 mmol) are added and the reaction mixture subsequently heated to 60 °C for 1 h. The reaction mixture is cooled to room temperature and poured onto saturated aqueous NH_4Cl. The aq. phase is extracted with ethyl acetate three times. The combined organic material is washed with brine and dried over magnesium sulfate, filtered and solvent removed *in vacuo* to provide a brown oil. Purification via silica gel chromatography (8-29 % ethyl acetate in hexanes) afforded methyl 7-chloro-5-cyclopropylthieno[3,2-b]pyridine-3-carboxylate (4).

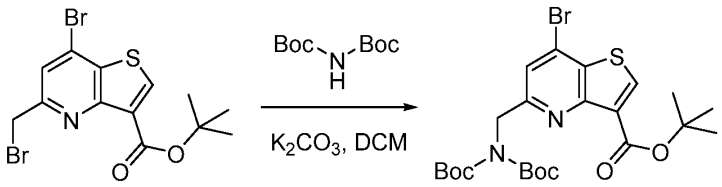
Example 2B.7



2 **3** (X=Br)/**3'** (X=Cl)
(ratio 3':3 ca. 3:1)

[0351] 7-bromo-3-(methoxycarbonyl)thieno[3,2-b]pyridine 4-oxide (2, 148 mg, 0.514 mmol) is dissolved in chloroform (10 mL) and $POCl_3$ (0.48 mL, 0.79 g, 5.1 mmol) is added. The vial is sealed and the mixture is stirred at 60 °C for 4 h, then over night at room temperature. Then the mixture is concentrated, taken up in DCM, washed with $NaHCO_3$(aq), dried (Na_2SO_4), filtered, and concentrated. The crude product (140 mg) is dissolved in THF (9 mL) and sodium methanolate (25 % in MeOH, 0.12 mL, 0.12 g, 0.52 mmol) is added. The mixture is stirred at room temperature for 2.75 h, and another 0.13 mL NaOMe sln (25 % in MeOH) are added. After 30 min another 0.04 mL NaOMe sln (25 % in MeOH) are added. After another 10 min another 0.04 mL NaOMe sln (25 % in MeOH) are added. Then the mixture is diluted with DCM and washed with water. The organic phase is dried (Na_2SO_4), filtered, concentrated. Purification by column chromatography yielded 23.9 mg of a 3:1 mixture of 3' and 3.

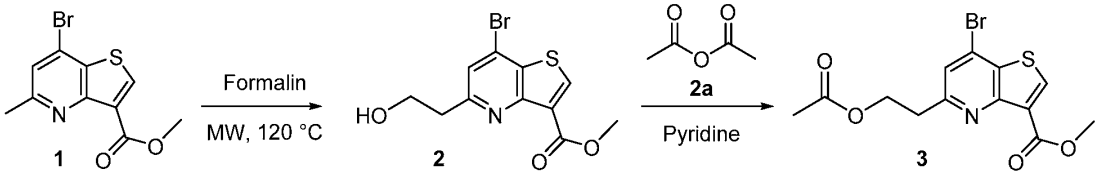
Example 2B.8



2 **3**

[0352] To a solution of *tert*-butyl 7-bromo-5-(bromomethyl)thieno[3,2-b]pyridine-3-carboxylate (2, 200.0 mg, 0.491 mmol) in *N,N*-dimethylpyrrolidone (3 mL) is added *tert*-butyl *N*-*tert*-butoxycarbonylcarbamate (160.1 mg, 0.736 mmol) and potassium carbonate (203.6 mg, 1.473 mmol) and the reaction mixture is stirred at room temperature for 24 h. After completion, reaction mixture is diluted with dichloromethane and silica gel is added. The solvent is evaporated. The crude silica mixture is purified by Isco column chromatography using 0-10 % methanol in dichloromethane as eluent. The desired fractions are concentrated under reduced pressure to afford *tert*-butyl 5-[[bis(*tert*-butoxycarbonyl)amino]methyl]-7-bromo-thieno[3,2-b]pyridine-3-carboxylate (3).

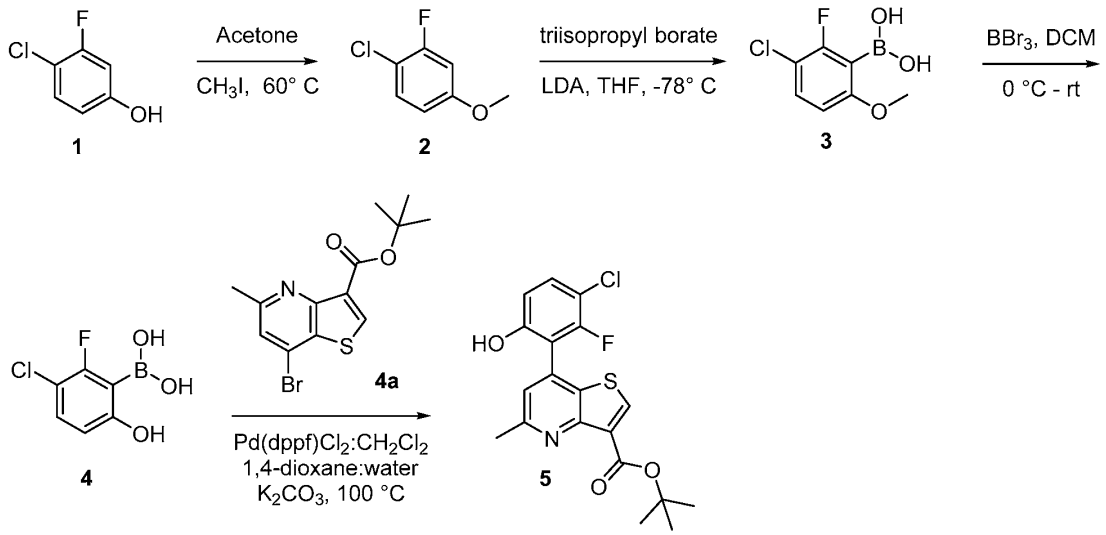
Example 2B.9



[0353] A suspension of methyl 7-bromo-5-methylthieno[3,2-b]pyridine-3-carboxylate (1, 3.50 g, 12.3 mmol) in formalin (37-40 %) 10 mL is irradiated in microwave at 120 °C for 1 h. After 1 h, the reaction mass is cooled and extracted with ethyl acetate. The starting material is not consumed in 1 h, reaction is irradiated again after work-up 3 times under microwave. The reaction is monitored by LCMS, still 50 % starting material is remaining. The reaction mass is cooled and extracted with ethyl acetate. The organic layer is dried over anhydrous sodium sulfate and concentrated to dryness under reduced pressure. The residue is purified by column chromatography using silica (100-200 mesh) and 0-40 % ethyl acetate in hexane to afford methyl 7-bromo-5-(2-hydroxyethyl)thieno[3,2-b]pyridine-3-carboxylate (2).

[0354] To a solution of methyl 7-bromo-5-(2-hydroxyethyl)thieno[3,2-b]pyridine-3-carboxylate (2, 0.32 g, 1.01 mmol) in pyridine (10 mL), acetic anhydride (0.115 mL, 1.22 mmol) is added to the reaction mixture. The reaction mixture is stirred at room temperature for 16 h. After completion of reaction as confirmed on thin layer chromatography and LCMS, reaction mixture is diluted with water and extracted with ethyl acetate. The organic layer is dried over anhydrous sodium sulfate and concentrated to dryness under reduced pressure. The crude is purified by combi flash (4 g, Redi Sep column) using 50 % ethyl acetate in hexanes as eluent to afford methyl 5-(2-acetoxyethyl)-7-bromothieno[3,2-b]pyridine-3-carboxylate (3).

Example 2B.10



[0355] To a solution of 4-chloro-3-fluorophenol (1, 3.0 g, 20.59 mmol) in acetone (30 mL) iodomethane (5.2 mL, 82.00 mmol) and potassium carbonate (5.6 g,41.00 mmol) are added at room temperature and reaction mixture is stirred at 60 °C for 12 h. After completion of reaction as confirmed on thin layer chromatography, reaction mass is evaporated and reaction mixture is diluted with water and extracted with ethyl acetate. The organic layer is dried over anhydrous sodium sulphate, filtered and concentrated to get afford 1-chloro-2-fluoro-4-methoxybenzene (2).

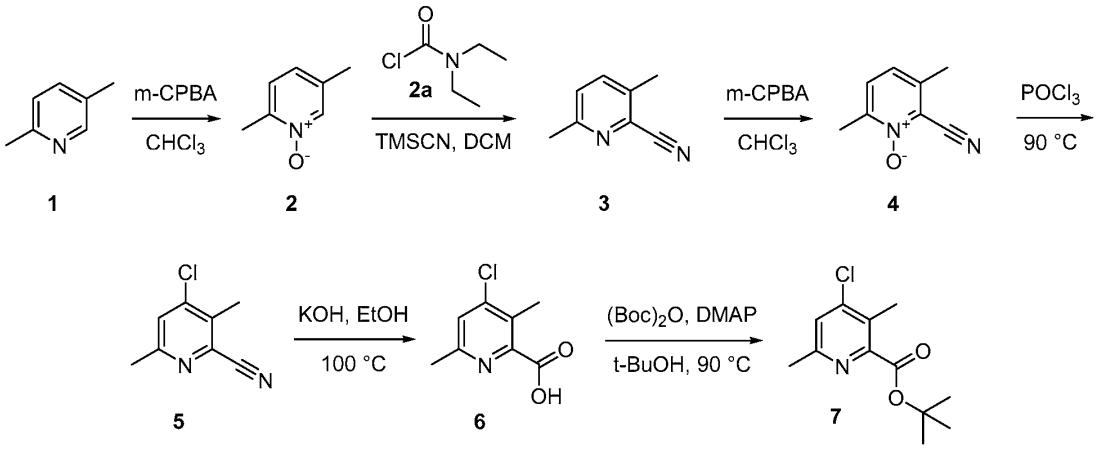
[0356] To a solution of 1-chloro-2-fluoro-4-methoxybenzene (2, 1.9 g, 11.84 mmol) in tetrahydrofuran (20 mL), lithium di-isopropylamide (2 M in tetrahydrofuran) (11.8 mL, 23.75 mmol) is added drop wise at -78 °C and reaction mixture is stirred at same temperature for 1 h. Then Tri-Iso propyl Borate (3.26 mL, 14.16 mmol) is added dropwise at -78 °C. The reaction mixture is stirred for 2 h at room temperature. After completion reaction, reaction mixture is quenched with saturated solution of ammonium chloride and extracted with ethyl acetate. The organic layer is dried over anhydrous sodium sulphate, filtered and concentrated to get crude compound. The crude compound obtained is purified by combi flash chromatography using 12 gm redisep column eluting with 80 % ethyl acetate in hexane to afford of (3-chloro-2-fluoro-6-methoxyphenyl)boronic acid (3).

[0357] To a solution of (3-chloro-2-fluoro-6-methoxyphenyl)boronic acid (3, 0.35 g, 1.71 mmol) in dichloromethane (5 mL) Boron tribromide (0.324 mL, 3.43 mmol) is added drop wise at 0 °C and reaction mixture is stirred at room temperature for 1 h. After completion of reaction as confirmed on thin layer chromatography the reaction mixture is quenched with ice cold water.

The solid precipitated is filtered and washed with pentane to afford as (3-chloro-2-fluoro-6-hydroxyphenyl)boronic acid (4).

[0358] A suspension of *tert*-butyl 7-bromo-5-methylthieno[3,2-b]pyridine-3-carboxylate (4a, 0.230 g 0.8 mmol), (3-chloro-2-fluoro-6-hydroxyphenyl)boronic acid (4, 0.30 g, 1.6 mmol) and potassium carbonate (0.334 g,2.4 mmol) in 1,4-dioxane (2.0 mL) and water (0.5 mL) is degassed with argon gas 10 min. [1,1′-Bis(diphenylphosphino)ferrocene]dichloropalladium(II),complex with dichloromethane (0.03 g, 0.04 mmol) is added to above suspension and reaction mixture is stirred for 3 h at 90 °C. The reaction mixture is monitored with LCMS and thin layer chromatography reaction mixture. After completion, the reaction mass is filtered through Celite bed and washed with ethyl acetate. The crude compound obtained is purified through combi flash chromatography using 4 gm redisep column by eluting with 90 % ethyl acetate in hexane to afford *tert*-butyl 7-(3-chloro-2-fluoro-6-hydroxyphenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (5).

Example 2B.11



[0359] To a solution of 2,5-dimethylpyridine (1, 10.0 g, 93.4 mmol) in Chloroform (100 mL) is added to metachloroperbenzoic acid (19.3 g, 112.1 mmol) at 0 °C under argon atmosphere and mixture is stirred at room temperature for 16 h. After completion, the reaction mixture is diluted with 10% calcium hydroxide solution and the solution is filtered through celite, filtrate is concentrated and dried to afford 2,5-dimethylpyridine 1-oxide (2).

[0360] To a solution of 2,5-dimethylpyridine 1-oxide (2, 10.0 g, 81.3 mmol) in dichloromethane (100 ml) is added to Trimethylsilylcyanide (11.2 g, 89.4 mmol) at 0 °C under argon atmosphere and stirred at room temperature for 30 minute, diethylcarbamic chloride (2a, 11.3 mL, 89.4 mmol) is added and stirring continued at room temperature for 24 h. After completion, the reaction mixture is quenched with 10% potassium carbonate solution and extracted with ethyl

acetate. Organic layer is dried over anhydrous sodium sulfate and concentrated to dryness under reduced pressure. The crude product is purified by column chromatography using silica (100-200 mesh) using 30-40% ethyl acetate in hexanes as eluent. The desired fractions are concentrated under reduced pressure to afford 3,6-dimethylpicolinonitrile (3).

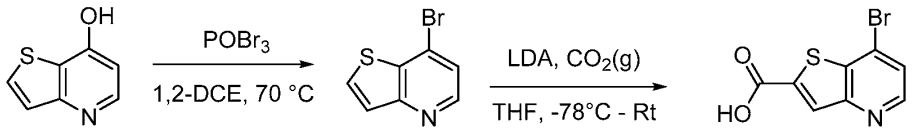
[0361] To a solution of 3,6-dimethylpicolinonitrile (3, 7.00 g, 46.9 mmol) in Chloroform (70 mL) is added to metachloroperbenzoic acid (8.75 g, 56.6 mmol) at 0 °C under argon atmosphere and stirring continued at room temperature for 16 h. After completion, the reaction mixture is diluted with 10% calcium hydroxide solution and filtered through celite, filtrate is concentrated and dried to afford 2-cyano-3,6-dimethylpyridine 1-oxide (4).

[0362] A solution of 2-cyano-3,6-dimethylpyridine 1-oxide (4, 7.0 g, 46.9 mmol) in phosphoryl chloride (50 mL) is stirred at 90 °C for 4 h. After completion, the reaction mixture is concentrated and purified by column chromatography using silica (100-200 mesh) using 20-30% ethyl acetate in hexanes as eluent. The desired fractions are concentrated under reduced pressure to afford 4-chloro-3,6-dimethylpicolinonitrile (5).

[0363] A solution of 4-chloro-3,6-dimethylpicolinonitrile (5, 4.0 g, 24.0 mmol) in ethanol (20 mL) and 10% Potassium hydroxide solution (20 mL) is stirred at 100 °C for 16 h. After completion, the reaction mixture is cooled and acidified with 2M hydrochloric acid solution up to pH 5 and extracted with ethyl acetate. Organic layer is dried over anhydrous sodium sulfate, filtered and concentrated to dryness under reduced pressure. To afford 4-chloro-3,6-dimethylpicolinic acid (6).

[0364] To a solution of 4-chloro-3,6-dimethylpicolinic acid (6, 1.50 g, 8.10 mmol) in tert-butyl alcohol (9.0 ml) is added di-tert-butyl dicarbanate (0.75 mL, 3.56 mmol) and 4-dimethylamino pyridine (1.48 g, 12.1 mmol) at 0 °C under argon atmosphere and stirred at 90 °C for 4 h. After completion, the reaction mixture is concentrated under reduced pressure. The crude compound is purified by flash column chromatography using 20-30% ethyl acetate in hexane to afford tert-butyl 4-chloro-3,6-dimethylpicolinate (7).

Example 2B.12



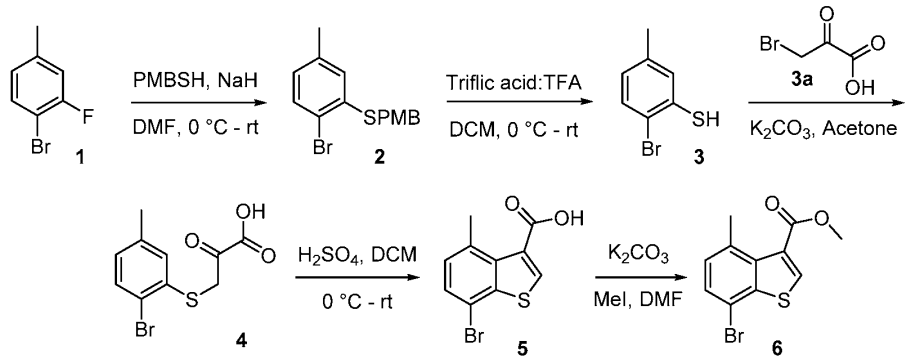
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[0365] To a stirred solution of thieno [3,2-b]pyridin-7-ol (1, 5.0 g, 33.07 mmol) in 1,2-dichloroethane (50 mL) is added phosphorous oxybromide (143.21 g, 496.09 mmol) portion-

wise at room temperature and the mixture is stirred at 70 °C for 10 h. The reaction mixture is cooled at 0 °C, basified with 10 % aqueous solution of sodium htdroxide and extracted with dichloromethane. The organic layer is washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated to dryness under reduced pressure to afford 7-bromothieno[3,2-b]pyridine (2).

[0366] To a stirred solution of 7-bromothieno[3,2-b]pyridine (2, 4.0 g, 18.78 mmol) in dry tetrahydrofuran (40 mL) is added lithium diisopropylamide solution (2.0 M in hexanes, 26.30 mL, 53.60 mmol) drop wise at -78 °C and the mixture is stirred at same temperature for 1 h. Carbon dioxide gas is purged through the reaction mass for 15 min and the reaction mixture is allowed to warm up to room temperature over 4 h. The reaction is quenched with aqueous ammonium chloride solution, diluted with water and extracted with ethyl acetate. The organic layer is washed with saturated brine, dried over anhydrous sodium sulphate, filtered and concentrated to afford 7-bromothieno[3,2-b]pyridine-2-carboxylic acid (3).

Example 2B.12



[0367] To a stirred solution of (4-methoxyphenyl)methanethiol (12.3 g, 87.77 mmol) in *N,N*-dimethylformamide (150 mL) is added sodium hydride (4.60 g, 119.69 mmol) portion wise at 0 °C. After 10 min, 1-bromo-2-fluoro-4-methylbenzene (1, 15.0 g, 79.79 mmol) is added and the reaction is stirred at room temperature for 2 h. After completion, the reaction is poured into ice water and extracted with ethyl acetate. The organic layer is washed with water, brine, dried over anhydrous sodium sulfate and concentrated under reduced pressure to get the crude. The crude product is purified by Combiflash (40 g, RediSep column) using 0-5 % ethyl acetate in hexanes as eluent. The desired fractions are concentrated under reduced pressure to afford (2-bromo-5-methylphenyl)(4-methoxybenzyl)sulfane (2).

[0368] To a solution of (2-bromo-5-methylphenyl)(4-methoxybenzyl)sulfane (2, 18.0 g, 55.90 mmol) in dichloromethane (140 mL) is added a mixture of trifluoroacetic acid (20 mL) and triflic acid (5 mL) in dichloromethane (40 mL) at 0 °C drop wise and the reaction mixture is stirred at

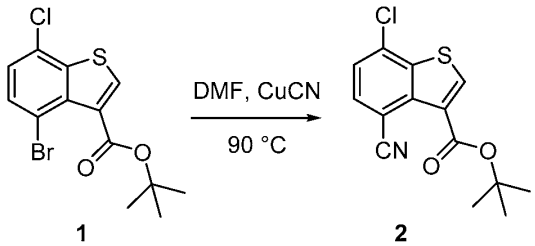
room temperature for 2 h. After completion, the reaction is poured into ice-water and extracted with dichloromethane. The organic layer is washed with water, brine, dried over anhydrous sodium sulfate and concentrated under reduced pressure to get the crude product 2-bromo-5-methylbenzenethiol (3).

[0369] To a solution 2-bromo-5-methylbenzenethiol (3, 4.7 g, 23.27 mmol) in acetone (47.0 mL) is added potassium carbonate (16.0 g, 116.35 mmol) at room temperature and the mixture is stirred for 10 min. 3-Bromo-2-oxopropanoic acid (3a, 11.6 g, 69.80 mmol) is added to the reaction mixture and stirred for 5 h at room temperature. After completion, the acetone is evaporated under reduced pressure; the residue is diluted with water and extracted with ethyl acetate. The organic layer is washed with water, brine, dried over anhydrous sodium sulfate and concentrated under reduced pressure to get 3-((2-bromo-5-methylphenyl)thio)-2-oxopropanoic acid (4).

[0370] To a solution of 3-((2-bromo-5-methylphenyl)thio)-2-oxopropanoic acid (4, 4.0 g, 13.89 mmol) in dichloromethane (40.0 mL) is added sulfuric acid(10.0 mL) and the reaction mixture is stirred at room temperature for 5 h. After completion, the reaction mixture is poured into ice water, extracted with dichloromethane. The organic layer is washed with water, brine, dried over anhydrous sodium sulfate and concentrated under reduced pressure to get 7-bromo-4-methylbenzo[b]thiophene-3-carboxylic acid (5).

[0371] To a solution 7-bromo-4-methylbenzo[b]thiophene-3-carboxylic acid (5, 3.0 g, 11.11 mmol) in *N,N*-dimethylformamide (30.0 mL) is added potassium carbonate (4.6 g, 33.33 mmol) and iodomethane (1.4 mL, 22.22 mmol) at 0 °C and the reaction mixture is stirred at room temperature for 4 h. After completion, the reaction mass is poured into water and extracted with ethyl acetate. The organic layer is washed with water, brine, dried over anhydrous sodium sulfate and concentrated under reduced pressure; the crude product is purified by flash column chromatography using 5 % ethyl acetate in hexanes as eluent. The desired fractions are concentrated under reduced pressure to afford methyl 7-bromo-4-methylbenzo[b]thiophene-3-carboxylate (6).

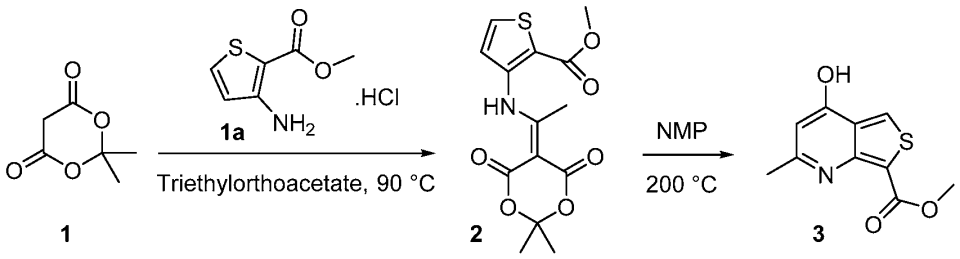
Example 2B.13



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[0372] To a solution of *tert*-butyl 4-bromo-7-chlorobenzo[b]thiophene-3-carboxylate (**1**, 0.7 g, 2.01 mmol) in *N*,*N*-dimethylformamide (2 mL), copper(I) cyanide (0.180 g, 2.01 mmol) is added. This reaction mixture is heated at 90 °C for 2 h. After this time, the reaction mixture is filtered with Celite and washed with ethyl acetate. The filtrate is washed with water and then brine solution, dried over anhydrous sodium sulfate, and concentrated under reduced pressure to obtain the crude product. This is purified by column chromatography using silica gel (100-200 mesh) and 30-50 % ethyl acetate in hexane as eluent. The desired fractions are concentrated under reduced pressure to afford *tert*-butyl 7-chloro-4-cyanobenzo[b]thiophene-3-carboxylate (**2**).

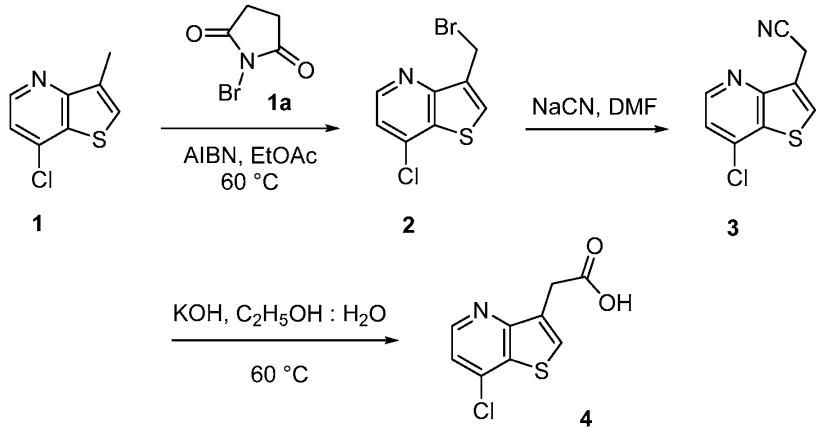
Example 2B.14



[0373] A solution of 2,2-dimethyl-1,3-dioxane-4,6-dione (1, 0.41 g, 2.84 mmol) and diethoxymethoxyethane (50.0 mL) is stirred and heated at 90 °C for 2 h in a closed vessel. Methyl 3-aminothiophene-2-carboxylate hydrochloride (1a, 0.5 g, 2.58 mmol) is added portion wise at 90 °C under argon atmosphere and continued heating at 90 °C for 12 h. After completion, the reaction mass is cooled to room temperature, added water and extracted with ethyl acetate. The organic layer is dried over anhydrous sodium sulfate, filtered and concentrated under vacuo to get crude. The crude is triturated with diethyl ether to afford methyl 3-((1-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)ethyl)amino)thiophene-2-carboxylate (2).

[0374] A solution of methyl 3-((1-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)ethyl)amino)thiophene-2-carboxylate (2, 0.200 g, 0.61 mmol) in *N*-methyl pyrrolidone (15 mL) is heated in microwave at 200 °C for 30 min. After completion, the reaction mass is cooled to room temperature, filtered and the crude solid is purified by prep-HPLC to afford methyl 4-hydroxy-2-methylthieno[3,4-b]pyridine-7-carboxylate (3).

Example 2B.15

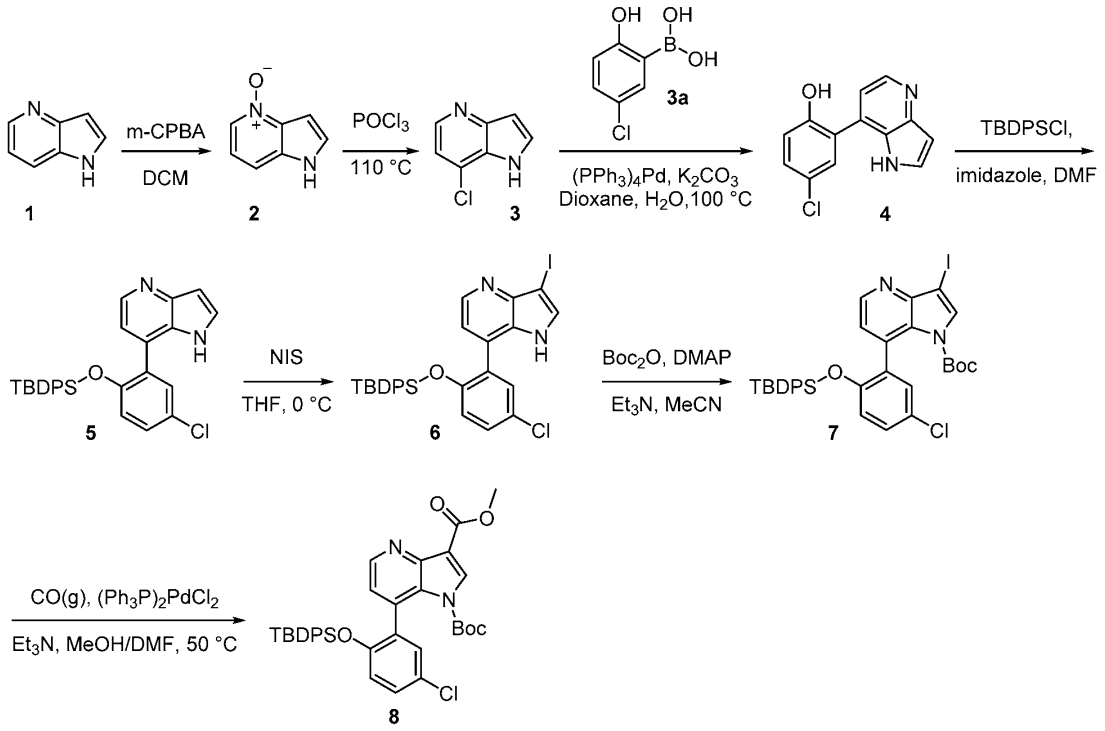


[0375] To a stirred solution of 7-chloro-3-methylthieno[3,2-b]pyridine (1, 1.0 g, 5.44 mmol) in ethyleacetate (10 mL) are added 1-bromopyrrolidine-2,5-dione (1a, 1.93 g, 10.8 mmol) and azobisisobutyronitrile (0.088 g, 0.540 mmol) at room temperature. The reaction is stirred at 60 °C for 4 h. After completion, the reaction mixture is quenched with water and extracted with ethyl acetate. The organic layer is washed with brine solution, dried over anhydrous sodium sulfate, filtered and concentrated to dryness under reduced pressure. The crude product is purified by Combiflash (12 g, RediSep column) using 1-5 % ethylacetate in hexanes as eluent to afford 3-(bromomethyl)-7-chlorothieno[3,2-b]pyridine (2).

[0376] To a solution of 3-(bromomethyl)-7-chlorothieno[3,2-b]pyridine (2, 1.50 g, 5.70 mmol) in *N,N*-dimethylformamide (15 mL) is added sodium cyanide (0.561 g, 11.40 mmol) and the mixture is stirred at room temperature for 3 h. After completion, the reaction is quenched with ice cold water and extracted with ethyl acetate. The organic layer is washed with cold water, dried over anhydrous sodium sulfate, filtered and concentrated to dryness under reduced pressure to afford 2-(7-chlorothieno[3,2-b]pyridin-3-yl)acetonitrile (3).

[0377] To a solution of 2-(7-chlorothieno[3,2-b]pyridin-3-yl)acetonitrile (3, 1.10 g, 5.20 mmol) in a mixture of ethanol and water (1:1, (20 mL) is added potassium hydroxide (2.96 g, 52.8 mmol) and the mixture is stirred at 60 °C for 10 h. After completion, the reaction mixture is concentrated and extracted with diethyl ether. The aqueous layer is acidified with 1 N aqueous hydrochloric acid solution, and extracted with ethyl acetate. The organic layer is washed with saturated brine solution, dried over anhydrous sodium sulphate, filtered and concentrated to afford 2-(7-chlorothieno[3,2-b]pyridin-3-yl)acetic acid (4).

Example 2B.16



[0378] To a solution of 1H-pyrrolo[3,2-b]pyridine (1, 2.5 g, 21 mmol) in DCM (75 mL) at 0 °C is slowly added *m*-CPBA (5.69 g, 25.4 mmol). The mixture is stirred from 0 °C to rt. After 16 h the reaction is complete as judged by TLC (SiO_2, 10 % MeOH/DCM). The mixture is concentrated and the residue purified by column chromatography (SiO_2, 0-20 % MeOH/DCM). The product is isolated as a mixture with m-CBA (ratio ca. 1:0.7 by ^{1}H-NMR). The so-obtained material 1H-pyrrolo[3,2-b]pyridine 4-oxide (2).

[0379] 1H-pyrrolo[3,2-b]pyridine 4-oxide (2, 3.64 g) in $POCl_3$ (30 mL, 50 g, 0.32 mol) are refluxed overnight under argon (oil-bath, 130 °C). Then the mixture is carefully transferred into an Erlenmeyer flask with crushed ice with stirring. The mixture is then basified with NaOH (aq, 12.5 %) to pH ca. 8, and the precipitated material is collected by filtration. The aq. phase is extracted (3 x EtOAc), and the combined organic phases are dried (Na_2SO_4), filtered and concentrated. The precipitated and extracted material are combined, dissolved in DCM and washed with $NaHCO_3$(aq). The organic phase is dired (Na_2SO_4), filtered and concentrated to afford 7-chloro-1H-pyrrolo[3,2-b]pyridine (3).

[0380] The reaction is run in two batches (0.80 g of (3) per batch), and the two batches are combined for purification purposes. To a solution of 7-chloro-1H-pyrrolo[3,2-b]pyridine (3, 0.80 g, 5.2 mmol) in 1,4-dioxane (14 mL) and water (3.5 mL) are added (5-chloro-2-

hydroxyphenyl)boronic acid (3a,1.4 g, 8.1 mmol) and potassium carbonate (2.2 g, 16 mmol) and the mixture is degassed by bubbling argon through it for 5 min. $Pd(PPh_3)_4$ (0.61 g, 0.53 mmol) is added, and the mixture is degassed for another 5 min, then placed in a preheated heating block (100 °C) and stirred for 20 h. Then the mixture is cooled down to room temperature. The two batches are combined, diluted with water, extracted with EtOAc. The organic phase is dried (Na_2SO_4), filtered, and concentrated. Purification by column chromatography (SiO_2, 0-20 % MeOH/DCM) to afford 4-chloro-2-(1H-pyrrolo[3,2-b]pyridin-7-yl)phenol (4).

[0381] To a solution of 4-chloro-2-(1H-pyrrolo[3,2-b]pyridin-7-yl)phenol (4, 37 mg, 0.15 mmol) in DMF (0.7 mL) at 0 °C are added imidazole (23 mg, 0.34 mmol) and *tert*-butyl-chloro-diphenyl-silane (0.05 mL, 0.05 g, 0.2 mmol), and the mixture is stirred at rt. After 3 h the mixture is diluted with water and EtOAc, and the aq. phase is extracted (3 x EtOAc). The combined organic phases are dried (Na_2SO_4), filtered and concentrated. Purification by column chromatography (SiO_2, 0-40 % EtOAc/hexane) to afford 7-(2-((*tert*-butyldiphenylsilyl)oxy)-5-chlorophenyl)-1H-pyrrolo[3,2-b]pyridine (5).

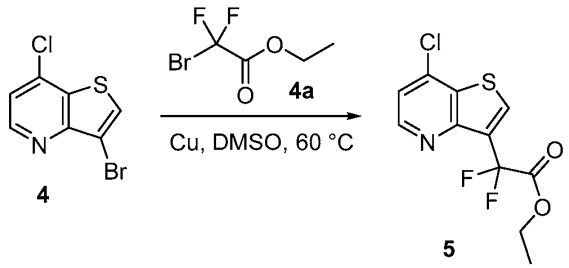
[0382] To a solution of 7-(2-((*tert*-butyldiphenylsilyl)oxy)-5-chlorophenyl)-1H-pyrrolo[3,2-b]pyridine (5; 1.08 g, 2.24 mmol) in THF (20 mL) at 0 °C is added *N*-Iodosuccinimide (503 mg, 2.24 mmol) and the mixture is stirred for 10 min. Then the reaction is diluted with EtOAc, quenched with $Na_2S_2O_3$(aq) and water, and extracted (2 x EtOAc). The combined organic phases are dried, filtered and concentrated. Purification by column chromatography (SiO_2, 0-40 % EtOAc/hexane) afforded to afford 7-(2-((*tert*-butyldiphenylsilyl)oxy)-5-chlorophenyl)-3-iodo-1H-pyrrolo[3,2-b]pyridine (6).

[0383] To a solution of 7-(2-((*tert*-butyldiphenylsilyl)oxy)-5-chlorophenyl)-3-iodo-1H-pyrrolo[3,2-b]pyridine (6, 990 mg, 1.63 mmol) in MeCN (11 mL) at 0 °C are added triethylamine (0.45 mL, 0.33 g, 3.2 mmol), di-*tert*-butyl dicarbonate (531 mg, 2.43 mmol) in 2 mL MeCN and 4-dimethylaminopyridine (40 mg, 0.33 mmol) and the mixture is stirred at rt. After 1 h water is added, and the mixture is extracted with DCM (3 x). The combined organic phases are dried (Na_2SO_4), filtered and concentrated. Purification by column chromatography (SiO_2, 0-20 % EtOAc/hexane) to afford *tert*-butyl 7-(2-((*tert*-butyldiphenylsilyl)oxy)-5-chlorophenyl)-3-iodo-1H-pyrrolo[3,2-b]pyridine-1-carboxylate (7).

[0384] To a solution of *tert*-butyl 7-(2-((*tert*-butyldiphenylsilyl)oxy)-5-chlorophenyl)-3-iodo-1H-pyrrolo[3,2-b]pyridine-1-carboxylate (7, 1.06 g, 1.49 mmol) in methanol (11 mL) and DMF (4 mL) are added triethylamine (0.43 mL, 0.31 g, 3.1 mmol) and $(Ph_3P)_2PdCl_2$ (105 mg, 0.149 mmol). Then the mixture is stirred at 50 °C under a CO atmosphere. After 18 h the mixture is

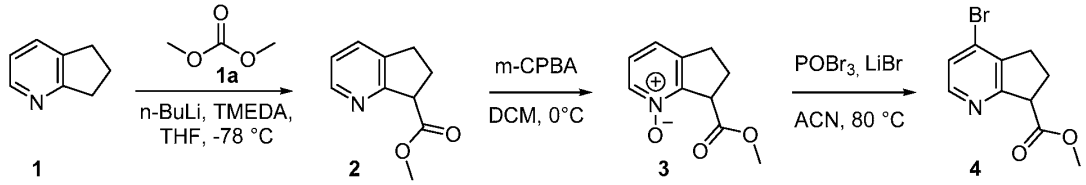
concentrated and purified by column chromatography (SiO_2, 0-50 % EtOAc/hexane) to afford 1-(*tert*-butyl) 3-methyl 7-(2-((*tert*-butyldiphenylsilyl)oxy)-5-chlorophenyl)-1H-pyrrolo[3,2-b]pyridine-1,3-dicarboxylate (8).

Example 2B.17



[0385] To a solution of 3-bromo-7-chlorothieno[3,2-b]pyridine (4, 0.30 g, 1.21 mmol), and ethyl 2-bromo-2,2-difluoroacetate (4a, 0.73 g, 3.62 mmol) in dimethylsulfoxide (12.0 mL), cupper powder (0.11 g, 1.81 mmol) is added at room temperature and the mixture is heated at 60 °C for 16 h. After completion, reaction mass is diluted with ethyl acetate and filtered through Celite. The filterate is washed with water and brine solution, dried over sodium sulfate filtered and concentrated. The crude is purified by flash column chromatography using silica gel (100-200 mesh) and 20-30 % ethyl acetate in hexane as eluent. The desired fractions are concentrated under reduced pressure to afford ethyl 2-(7-chlorothieno[3,2-b]pyridin-3-yl)-2,2-difluoroacetate (5).

Example 2B.18



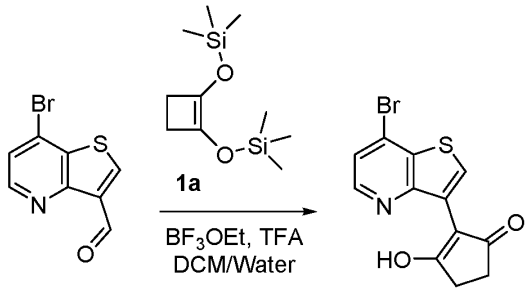
[0386] To a solution of *N,N*,N',N'-tetramethylethylenediamine (11.69 g, 100.42 mmol) in tetrahydrofuran (100 mL), *n*-butyllithium (1.3 M in hexane, 71.1 mL, 92.43 mmol) is added at -78°C, then 6,7-dihydro-5H-cyclopenta[b]pyridine (1, 10.0 g, 84.03 mmol) is added dropwise and the mixture is stirred at -78 °C for 45 min. Then, a solution of dimethyl carbonate (1a, 8.31 g, 92.43 mmol) in tetrahydrofuran (10 mL) is added drop wise and the mixture is allowed to room temperature over an 1 h. The reaction mixture is quenched with saturated ammonium chloride solution and extracted with ethyl acetate. The combined organic layer is dried over anhydrous sodium sulphate, filtered and concentrated. The crude is purified by column chromatography

using silica gel (100-200 mesh) and 0-25 % ethyl acetate in hexane as eluent to afford methyl 6,7-dihydro-5H-cyclopenta[b]pyridine-7-carboxylate (2).

[0387] To a solution of methyl 6,7-dihydro-5H-cyclopenta[b]pyridine-7-carboxylate (2, 2.5 g, 14.12 mmol) in dichloromethane (30 mL), 3-chloroperbenzoic acid (4.85 g, 28.24 mL) is added at 0 °C and the mixture is stirred at the same temperature for 30 min. After completion, the reaction mixture is quenched with saturated sodium bicarbonate solution (10 mL) and extracted with dichloromethane. The combined organic layer is washed brine, dried over anhydrous sodium sulphate, filtered and concentrated. The crude is purified by column chromatography using silica gel (100-200 mesh) and 0-10 % methanol in dichloromethane as eluent. The desired fractions are concentrated under reduced pressure to afford 7-(methoxycarbonyl)-6,7-dihydro-5H-cyclopenta[b]pyridine 1-oxide (3).

[0388] To a solution of 7-(methoxycarbonyl)-6,7-dihydro-5H-cyclopenta[b]pyridine 1-oxide (3, 1.5 g, 7.77 mmol) in acetonitrile (25 mL), lithium bromide (0.67 g, 7.77 mmol) and phosphorus bromide (22.3 g, 77.72 mmol) are added and the reaction mixture is heated at 80 °C for 24 h. After completion, the reaction mixture is cooled to 0 °C, quenched with saturated sodium bicarbonate solution (50 mL) and extracted with ethyl acetate. The combined organic layer is dried over anhydrous sodium sulphate, filtered and concentrated. The crude is purified by column chromatography using silica gel (100-200 mesh) and 0-25 % ethyl acetate in hexane to afford methyl 4-bromo-6,7-dihydro-5H-cyclopenta[b]pyridine-7-carboxylate (4).

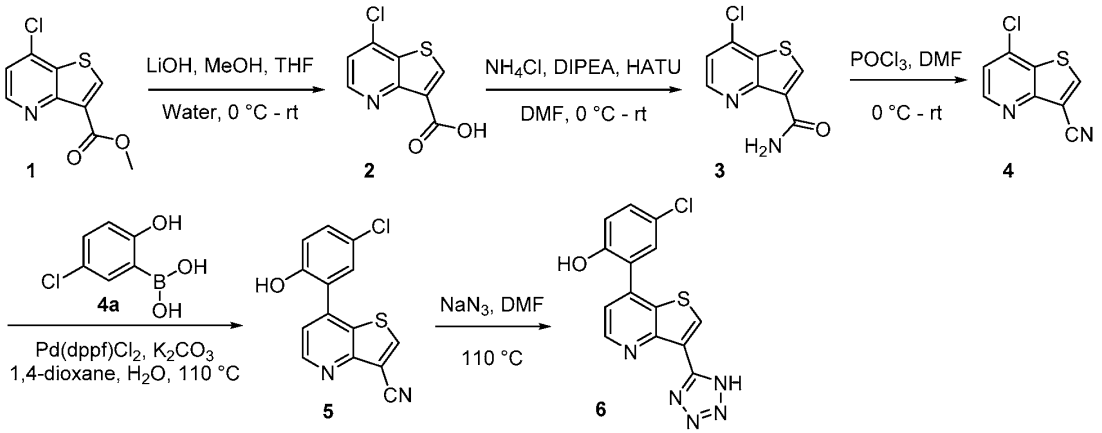
Example 2B.19



[0389] To a solution of 7-bromothieno[3,2-b]pyridine-3-carbaldehyde (1, 36 mg, 0.148 mmol) in DCM (1 mL) in an oven-dried screw capped vial is equipped with a stir bar. To the mixture is added ethoxyethane trifluoroborane (0.02 mL, 0.163 mmol) with constant stirring at room tem added slowly. Then 1,2-bis((trimethylsilyl)oxy)cyclobut-1-ene (1a, 0.06 mL, 0.222 mmol) is added dropwise and the clear yellow mixture continued to stir at room temperature for 40 min. Water (0.030 mL) is added followed by ethoxyethane; trifluoroborane (0.27 mL, 2.22 mmol) and

the reaction is allowed to stir at room temperature overnight. No conversion to pinacol rearrangement product observed so water and DCM added and the aqueous phase extracted with dichloromethane three times. The combined organic material is washed with brine and dried over magnesium sulfate. The solids are filtered and solvent removed *in vacuo* to afford a crude yellow residue. Aqueous layer is concentrated in vaccum. Both aqueous and organic layer combined and is taken up in TFA (3.5 mL, 0.1480 mmol) and placed in a vial that is sealed and stirred in a heating block at 70 °C for 3 h. The reaction is cooled to room temperature and solvent removed *in vacuo*. Preparatory HPLC (water with 0.1 % TFA) afforded the product 2-(7-bromothieno[3,2-b]pyridin-3-yl)-3-hydroxycyclopent-2-en-1-one (2).

Example 2B.20



[0390] To a stirred solution of methyl 7-chlorothieno[3,2-b]pyridine-3-carboxylate (1, 15.0 g, 65.88 mmol) in methanol, tetrahydrofuran and water (2:1:1, 225 mL) is added lithium hydroxide (13.82 g, 329.43 mmol) at 0 °C and reaction mixture is stirred at room temperature for 16 h. After completion, the solvents are concentrated under reduced pressure and the aqueous layer is acidified with 1 N aqueous hydrochloric acid solution up to pH-3. Solid precipitate obtained is filtered and washed with n-pentane to afford 7-chlorothieno[3,2-b]pyridine-3-carboxylic acid (2).

[0391] To a solution of 7-chlorothieno[3,2-b]pyridine-3-carboxylic acid (2, 12.20 g, 57.10 mmol) in *N,N*-dimethylformamide (50 mL) is added 1-[bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxide hexafluorophosphate (32.5 g, 85.65 mmol) and reaction mixture is stirred for 10 min. The reaction mixture is then cooled to 0 °C and *N,N*-diisopropylethylamine (29.841 mL, 171.316 mmol) and ammonium chloride (15.2 g, 285.52 mmol) are added and reaction mixture is allowed to warm to room temperature and stirred for 16 h. After completion, the reaction is quenched with ice cold water and extracted with ethyl acetate. The organic layer is washed with cold water, dried over anhydrous sodium sulfate,

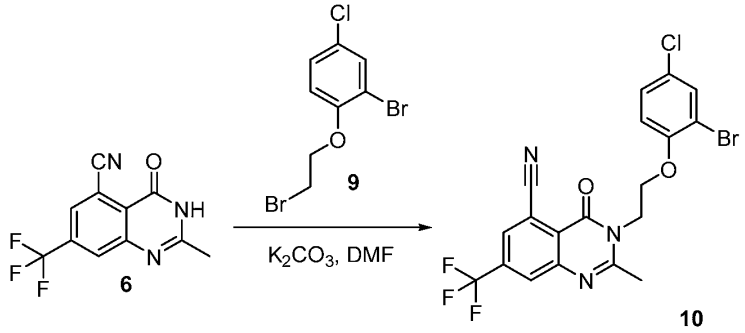
filtered and concentrated to dryness under reduced pressure. The crude product is triturated with pentane and dried to afford 7-chlorothieno[3,2-b]pyridine-3-carboxamide (3).

[0392] To a solution of 7-chlorothieno[3,2-b]pyridine-3-carboxamide (3, 10.0 g, 51.37 mmol) in *N,N*-dimethylformamide (100 mL) at 0 °C is added phosphorus oxytrichloride (48.0 mL, 513.76 mmol). The reaction is allowed to warm up to room temperature and stirred for 16 h. After completion, reaction mixture concentrated to dryness under reduced pressure. The reaction mixture is basified with saturated sodium bicarbonate solution up to pH-8 and extracted with ethyl acetate. The organic layer is washed with brine solution, dried over anhydrous sodium sulfate, filtered and concentrated to dryness under reduced pressure. The crude product is purified by Combiflash (40 g, RediSep column) using 0-20 % ethyl acetate in hexanes as eluent. The desired fractions are concentrated under reduced pressure to afford 7-chlorothieno[3,2-b]pyridine-3-carbonitrile (4).

[0393] To a solution of 7-chlorothieno[3,2-b]pyridine-3-carbonitrile (4, 8.0 g, 41.10 mmol), and (5-chloro-2-hydroxyphenyl)boronic acid (4a, 14.1 g, 82.20 mmol) in 1,4-dioxane (120.0 mL) is added 2 M solution of potassium carbonate (14.2 g, 102.7 mmol) reaction mixture is degassed with argon gas for 10 min. [1,1'-Bis(diphenylphosphino)ferrocene]palladium(II) dichloride (3.0 g, 4.11 mmol) is then added to reaction mixture and reaction mixture is stirred at 110 °C for 2 h. After completion, reaction mixture is cooled to room temperature, diluted with water and extracted with ethyl acetate. The organic layer is washed with brine solution, dried over anhydrous sodium sulfate, filtered and concentrated to dryness under reduced pressure. The crude product is purified by column chromatography using silica gel (100-200 mesh) and 0-50 % ethyl acetate in hexanes as eluent. The desired fractions are concentrated under reduced pressure to afford 7-(5-chloro-2-hydroxyphenyl)thieno[3,2-b]pyridine-3-carbonitrile (5).

[0394] To a solution of 7-(5-chloro-2-hydroxyphenyl)thieno[3,2-b]pyridine-3-carbonitrile (5, 5.1 g, 17.78 mmol) in *N,N*-dimethylformamide (50.0 mL) is added sodium azide (5.8 g, 88.93 mmol) at room temperature and the reaction mixture is heated to 110 °C for 36 h. After completion, reaction mixture is concentrated to dryness under reduced pressure. The crude product obtained is triturated with n-pentane to afford 2-(3-(1H-tetrazol-5-yl)thieno[3,2-b]pyridin-7-yl)-4-chlorophenol (6).

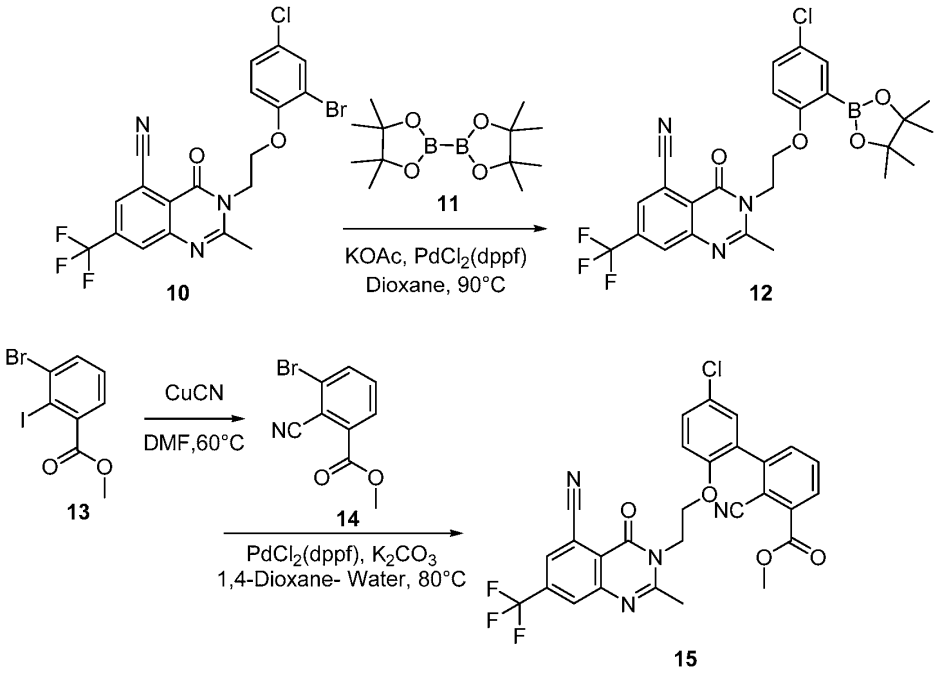
Example 2C. General Coupling methods



[0395] To a solution 2-methyl-4-oxo-7-(trifluoromethyl)-3,4-dihydroquinazoline-5-carbonitrile (6, 0.20 g, 0.79 mmol) in *N,N*-dimethylformamide (5 mL), potassium carbonate (0.33 g, 2.37 mmol) is added at room temperature. After 10 min, 2-bromo-1-(2-bromoethoxy)-4-chloro-benzene (9, 0.25 g, 0.79 mmol) is added and stirred for 16 h at room temperature. After completion, the reaction mixture is poured into water and extracted with ethyl acetate. Combined organic layer is washed with water, brine, dried over anhydrous sodium sulfate and concentrated under reduced pressure to get crude; the crude compound is purified by flash column chromatography (using 10-70 % ethyl acetate in hexanes) to afford 3-(2-(2-bromo-4-chloro-phenoxy)ethyl)-2-methyl-4-oxo-7-(trifluoromethyl)-3,4-dihydroquinazoline-5-carbonitrile (10).

Example 2D. Post Coupling modification methods

Example 2D.1

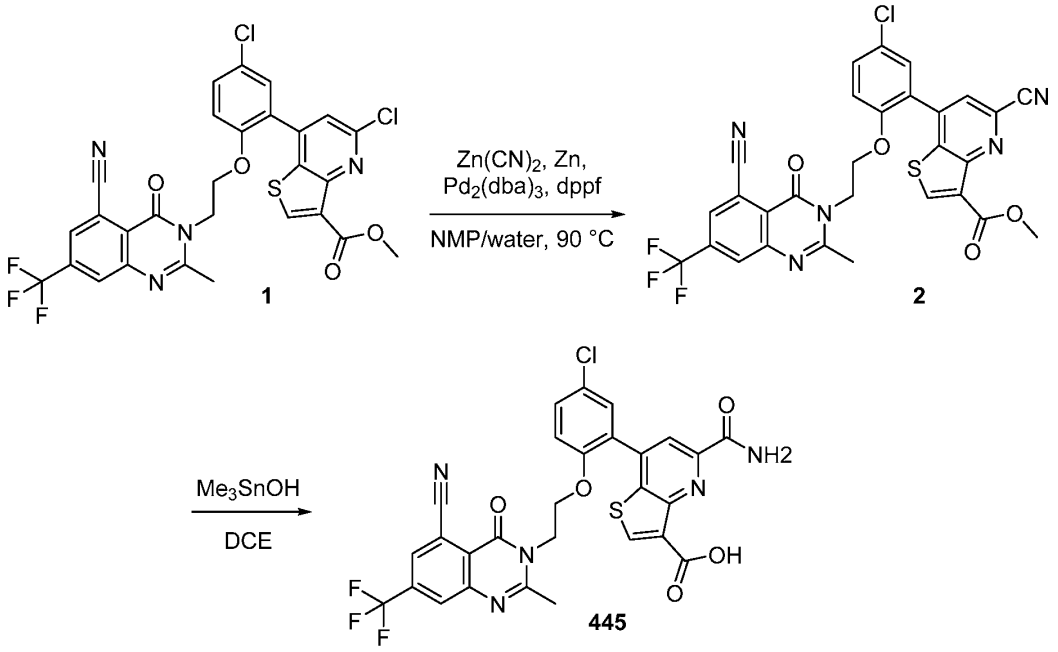


[0396] A solution of 3-(2-(2-bromo-4-chlorophenoxy)ethyl)-2-methyl-4-oxo-7-(trifluoromethyl)-3,4-dihydroquinazoline-5-carbonitrile (10, 1.8 g, 3.71 mmol), 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (11, 1.13 g, 4.45 mmol) and potassium acetate (0.73 g, 7.42 mmol) in 1,4-dioxane (35 mL) is degassed using argon gas for 10 min. 1,1'-Bis(diphenylphosphino)ferrocene-palladium(II)dichloride (0.217 g, 0.296 mmol) is added and the reaction mixture is degassed for another 10 min. The reaction mixture is heated and stirred at 90 °C for 6 h. After completion, the reaction mixture is diluted with water and extracted with ethyl acetate. The organic layer is dried over anhydrous sodium sulfate, filtered and concentrated to dryness under reduced pressure. The crude compound is purified by flash column chromatography 40 % ethyl acetate in hexanes as eluent to afford 3-(2-(4-chloro-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy)ethyl)-2-methyl-4-oxo-7-(trifluoromethyl)-3,4-dihydroquinazoline-5-carbonitrile (12).

[0397] To a solution methyl 3-bromo-2-iodobenzoate (13, 2.0 g, 5.88 mmol) *N,N*-dimethylformamide (20 mL), copper(I) cyanide (0.58 g, 6.47 mmol) is added and heated at 60 °C for 4 h. After completion, the reaction mass is diluted with water (100 mL) and extracted with ethyl acetate. Combined organic layer are washed with water, brine, dried over anhydrous sodium sulfate and concentrated under reduced pressure to get crude. The crude compound is purified by flash column chromatography (using 0-10 % ethyl acetate in hexane) to afford methyl 3-bromo-2-cyanobenzoate (14).

[0398] To a solution of 3-(2-(4-chloro-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenoxy)ethyl)-2-methyl-4-oxo-7-(trifluoromethyl)-3,4-dihydroquinazoline-5-carbonitrile (12, 0.40 g, 0.75 mmol) and methyl 3-bromo-2-cyanobenzoate (14, 0.215 g, 0.90 mmol) in 1,4-dioxane (8 mL) and water (2 mL), potassium carbonate (0.313 g, 2.25 mmol) is added at room temperature. The reaction mass is degassed by purging argon gas through the reaction mass for 10 min. 1,1'-Bis(diphenylphosphino)ferrocene-palladium(II)dichloride (0.055 g, 0.075 mmol) is added under argon atmosphere, heated and stirred the reaction mixture at 90 °C for 3 h. After completion, the reaction mass is diluted with water, extracted with ethyl acetate; combined organic layer is washed with water, brine and dried over anhydrous sodium sulfate and concentrated under reduced pressure to get crude. The crude compound is purified by flash column chromatography (using 0-50 % ethyl acetate in hexane) to afford methyl 5'-chloro-2-cyano-2'-(2-(5-cyano-2-methyl-4-oxo-7-(trifluoromethyl)quinazolin-3(4*H*)-yl)ethoxy)-[1,1'-biphenyl]-3-carboxylate (15).

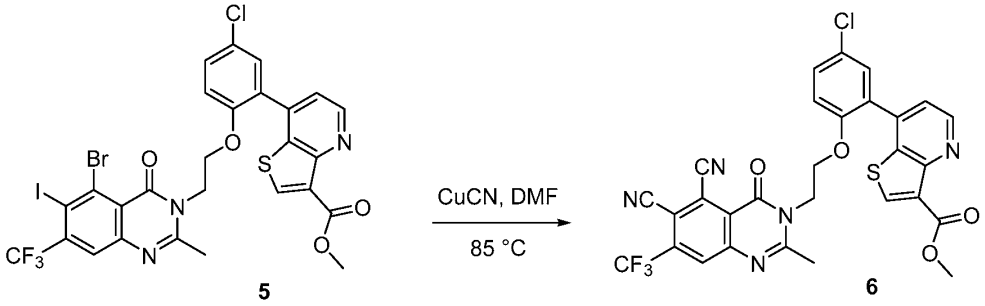
Example 2D.2



[0399] To a stirred solution of methyl 5-chloro-7-[5-chloro-2-[2-[5-cyano-2-methyl-4-oxo-7-(trifluoromethyl)quinazolin-3-yl]ethoxy]phenyl]thieno[3,2-b]pyridine-3-carboxylate (0.050 g, 0.079 mmol) in *N*-methyl-2-pyrrolidone and water (9:1, 2 mL) in a microwave vial, zinc cyanide (0.011 g, 0.095 mmol) and zinc dust (0.030 mg, 0.034 mmol) are added and the mixture is degassed with argon for 30 min. After adding 1,1'-bis(diphenylphosphino)ferrocene (0.0131 g, 0.023 mmol) and tris(dibenzylideneacetone)dipalladium(0) (10.8 mg, 0.012 mmol), the vial is sealed and then placed in a preheated heating block at 80 °C for 30 min. After completion of the reaction, the reaction mixture loaded on the Isco silica column. Purification by column chromatography eluting with 0 to 5 % methanol/dichloromethane to afford methyl 7-(5-chloro-2-(2-(5-cyano-2-methyl-4-oxo-7-(trifluoromethyl)quinazolin-3(4H)-yl)ethoxy)phenyl)-5-cyanothieno[3,2-b]pyridine-3-carboxylate (2).

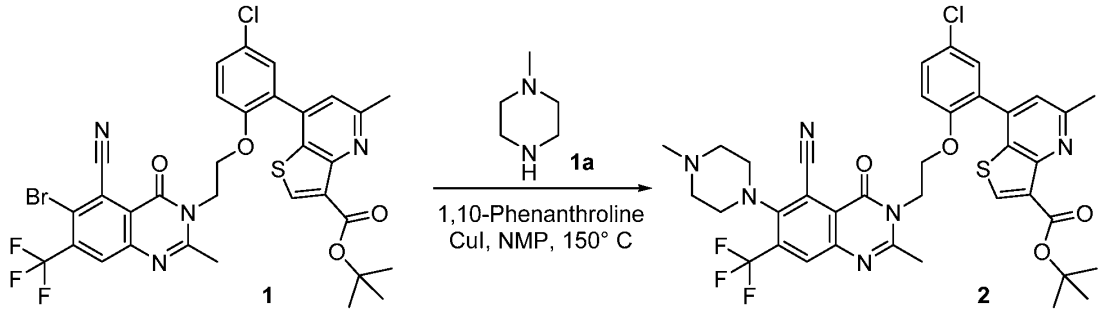
[0400] To a solution of methyl 7-(5-chloro-2-(2-(5-cyano-2-methyl-4-oxo-7-(trifluoromethyl)quinazolin-3(4H)-yl)ethoxy)phenyl)-5-cyanothieno[3,2-b]pyridine-3-carboxylate (2, 25.0 mg, 0.040 mmol) in 1,2-dichloroethane (2 mL), trimethyltin hydroxide (0.029 g, 0.160 mmol) is added at room temperature. The reaction mixture is heated at 90 °C for 16 h. After completion of the reaction, the organic solvent is evaporated and the crude is diluted with 50 % dimethyl sulfoxide/methanol. The crude product is purified by prep-HPLC to afford 5-carbamoyl-7-(5-chloro-2-(2-(5-cyano-2-methyl-4-oxo-7-(trifluoromethyl)quinazolin-3(4H)-yl)ethoxy)phenyl)thieno[3,2-b]pyridine-3-carboxylic acid (Cpd. No. 445F).

Example 2D.3



[0401] To a solution of methyl 7-(2-(2-(5-bromo-6-iodo-2-methyl-4-oxo-7-(trifluoromethyl)quinazolin-3(4H)-yl)ethoxy)-5-chlorophenyl)thieno[3,2-b]pyridine-3-carboxylate (5, 0.20 g, 0.256 mmol) in *N,N*-dimethylformamide is added copper(I) cyanide (0.069 g, 0.770 mmol) and stirred at 85 °C for 2 h. After completion, the reaction mixture is cooled to room temperature and poured into ice-water. The precipitate formed is collected by filtration and dried. The solid is dissolved in 10 % methanol in dichloromethane and passed through Celite bed. The filtrate is concentrated under reduced pressure to afford methyl 7-(5-chloro-2-(2-(5,6-dicyano-2-methyl-4-oxo-7-(trifluoromethyl)quinazolin-3(4H)-yl)ethoxy)phenyl)thieno[3,2-b]pyridine-3-carboxylate (6).

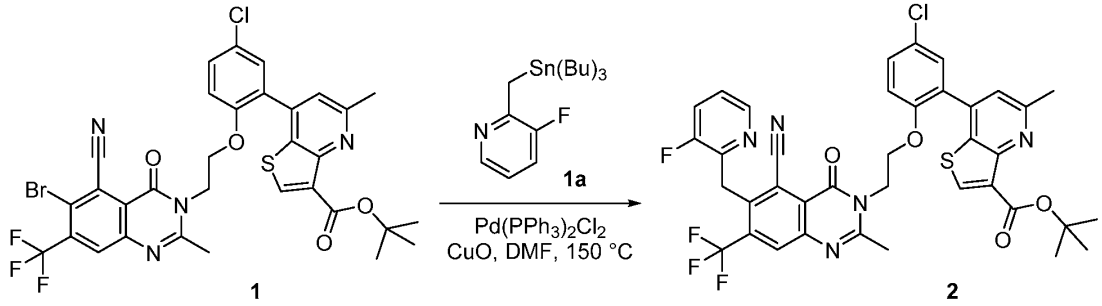
Example 2D.3



[0402] To a solution of *tert*-butyl 7-(2-(2-(6-bromo-5-cyano-2-methyl-4-oxo-7-(trifluoromethyl)quinazolin-3(4H)-yl)ethoxy)-5-chlorophenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (1, 0.20 g, 0.273 mmol) in *N*-Methyl-2-pyrrolidone (5.0 mL) is added 1-methylpiperazine (1a, 0.06 mL, 0.546 mmol) and the reaction mixture is degassed by argon for 10 min. Then copper(I) iodide (0.005 g, 0.027 mmol) and 1,10-phenanthroline (0.009 g, 0.054 mmol) is added and reaction mixture is heated at 150 °C for 6 h. After completion reaction mixture is diluted with water and extracted with ethyl acetate. The organic layer is dried over anhydrous sodium sulphate, filtered and concentrated to get crude compound. Crude compound obtained is purified by column chromatography using silica gel (100-200 mesh) and 3-4 %

methanol in dichloromethane to afford *tert*-butyl 7-(5-chloro-2-(2-(5-cyano-2-methyl-6-(4-methylpiperazin-1-yl)-4-oxo-7-(trifluoromethyl)quinazolin-3(4H)-yl)ethoxy)phenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (2).

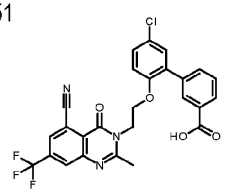
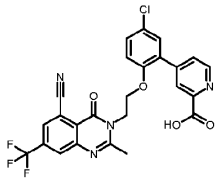
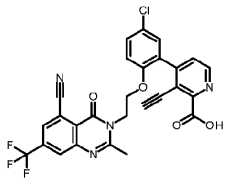
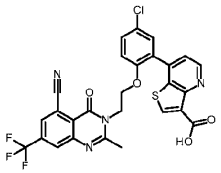
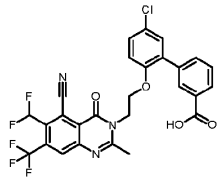
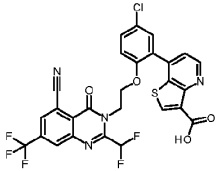
Example 2D.4



[0403] To a solution of *tert*-butyl 7-(2-(2-(6-bromo-5-cyano-2-methyl-4-oxo-7-(trifluoromethyl)quinazolin-3(4H)-yl)ethoxy)-5-chlorophenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (1, 50 mg, 0.0681 mmol) and 3-fluoro-2-((tributylstannyl)methyl)pyridine (1a, 190 mg, 0.476 mmol) in *N,N*-dimethylformamide (2 mL), is added copper(II) oxide (11 mg, 0.136 mmol) at room temperature. The reaction mixture is purged with argon gas for 5 min, added bis(triphenylphosphine)palladium(II) dichloride (9.6 mg, 0.0136 mmol) and the vessel is then sealed, microwaved for 1 h at 150 °C. After completion, the reaction mixture is then directly loaded on an Isco loading column. Purified by column chromatography using 5 to 80 % ethyl acetate in hexane as eluent and product eluted around 60 % ethylacetate/hexane. The desired fractions are concentrated under reduced pressure to afford *tert*-butyl 7-(5-chloro-2-(2-(5-cyano-6-((3-fluoropyridin-2-yl)methyl)-2-methyl-4-oxo-7-(trifluoromethyl)quinazolin-3(4H)-yl)ethoxy)phenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (2).

[0404] Compounds made using one or more of the general methods described above are shown in Table 2. Where provided, characterization data is to the right of the compounds.

Table 2. 7-CF3-Thienylpyridine and Derivative Compounds

Compound	Characterization	Compound	Characterization
51 	MS (ESI) m/z 528.44 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.931 (s, 1H), 8.359 (s, 1H), 8.194 (s, 1H), 7.8409 (d, J = 11.6 Hz, 2H), 7.528 (d, J = 7.6 Hz, 1H), 7.412 (m, 2H), 7.278 (d, J = 2.6 Hz, 1H), 7.212 (d, J = 8.8 Hz, 1H), 4.359 (s, 4H), 2.208 (s, 3H)	60 	MS (ESI) m/z 527.02 [M-1]-. 1H NMR (400 MHz, DMSO-d6) δ 8.63 (bs, 1H), 8.37(s, 1H), 8.19 (s, 1H), 7.98 (bs, 1H), 7.61 (bs, 1H), 7.48 (d, J = 8.68 Hz, 1H), 7.42 (s, 1H), 7.26 (d, J = 8.92 Hz, 1H), 4.39 (s, 4H), 2.20 (s, 3H)
58 	MS (ESI) m/z 553.34 [M+1]+; UPLC: 98.94 %; 1H NMR (400 MHz, DMSO-d6) δ 8.44 (d, J = 3.96, 1H), 8.36 (s, 1H), 8.22 (s, 1H), 7.43 (dd, J = 2.48, 8.88 Hz, 1H), 7.23-7.18 (m, 3H), 4.33 (m, 4H), 4.03 (s, 1H), 2.09 (s, 3H)	61 	MS (ESI) m/z 585.13 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.27 (s, 1H), 8.84 (d, J = 4.76, 1H), 8.37 (d, J = 0.96 Hz, 1H), 8.26 (s, 1H), 8.00 (s, 1H), 7.59 (dd, J = 2.64, 8.92 Hz, 1H), 7.48 (d, J = 4.76 Hz, 1H), 7.43 (d, J = 2.6 Hz, 1H), 7.36 (d, J = 8.96, 1H), 4.42-4.23 (m, 4H), 1.74 (s, 3H)
59 	MS (ESI) m/z 578.08 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.91 (s, 1H), 8.28 (s, 1H), 7.84-7.81 (m, 2H), 7.6-7.2 (m, 6H), 4.37 (s, 4H), 2.21 (s, 3H)	65 	MS (ESI) m/z 621.17 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.7935 (d, J = 4.8 Hz, 1H), 8.568 (s, 1H), 8.338 (s, 1H), 8.236 (s, 1H), 7.610 (dd, J = 8.8 Hz, 1H), 7.487 (d, J = 4.8 Hz, 1H), 7.441 (d, J = 2.8 Hz, 1H), 7.372 (d, J = 9 Hz, 1H),6.687-6.429 (m, 1H), 4.431-4.355 (m, 4H)

120		MS (ESI) m/z 579.15 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.75(d, J = 4.48 Hz, 1H), 8.59 (s, 1H), 8.41 (s, 1H), 8.14 (s, 1H), 7.76 (d, J = 8.8 Hz, 1H), 7.69 (d, J = 6.04 Hz, 2H), 7.56 (d, J = 4.48 Hz, 1H), 4.88(s, 2H), 2.10 (s, 3H)	
121		MS (ESI) m/z 599.14 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.55 (s, 1H), 8.36 (s, 1H), 8.27 (s, 1H), 7.97(s, 1H), 7.60-7.57 (dd, J = 2.52 Hz, 1H), 7.41 (s, 2H), 7.35 (d, J = 8.96 Hz, 1H), 4.40 (t, J = 4.6 Hz, J = 4.48 Hz, 2H), 4.25 (t, J = 4.04 Hz, J = 5.0 Hz, 2H), 2.69 (s, 3H), 1.81 (s, 3H)	
122		MS (ESI) m/z 601.98 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.93 (bs, 1H), 8.35 (s, 1H), 8.06 (s, 1H), 7.77 (s, 1H), 7.51(dd, J = 8.88, 2.6 Hz, 1H), 7.29-7.22 (m, 4H), 4.35 (t, J = 4.4 Hz, 2H), 4.24 (t, J = 4.84 Hz, 2H), 1.77 (s, 3H)	
145		MS (ESI) m/z 524.41 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.05 (s, 1H), 8.37 (s, 1H), 8.19 (s, 1H), 7.8480-7.726 (m, 3H), 7.4848-7.454 (m, 3H), 7.36 (s, 1H), 6.43 (d, J = 15.68 Hz, 1H), 6.15 (d, J = 15.68 Hz, 1H), 4.83 (d, J = 3.4 Hz, 2H), 2.56 (s, 3H)	
146		MS (ESI) m/z 526.46 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.98 (bs, 1H), 8.35 (d, J = 1.36 Hz, 1H), 8.177 (s, 1H), 7.767 (s, 1H), 7.744 (s, 1H), 7.58-7.557 (m, 1H), 7.467-7.382 (m, 3H), 7.229 (d, J = 6.4 Hz , 1H), 3.933 (t, J = 7.04 Hz, 2H), 2.611 (t, J = 8.44 Hz, 2H), 2.447 (s, 3H), 1.768 (m, 2H)	
156		MS (ESI) m/z 552.22 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.92 (bs, 1H), 8.34 (s, 1H), 8.18 (s, 1H), 7.83 (dd, J = 7.64, 1.0 Hz, 1H), 7.44-7.34 (m, 3H), 7.16-7.14 (m, 2H), 4.31 (bs, 4H), 3.73 (s, 1H), 1.98 (s, 3H)	

158		MS (ESI) m/z 572.49 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.15 (bs, 1H), 8.36 (s, 1H), 8.21 (s, 1H), 7.63 (s, 1H), 7.58 (d, J = 8 Hz, 1H), 7.51 (d, J = 7.6 Hz, 1H), 7.429-7.401 (dd, J = 2.4 Hz, J' = 8.72 Hz, 1H), 7.33 (d, J = 2.4 Hz, 1H), 7.21 (d, J = 8.8 Hz, 1H), 4.37 (s, 4H), 2.25(s, 3H)	164		MS (ESI) m/z 571 [M+1]; 1H NMR (400 MHz, DMSO-d6) δ 8.79(s, 1H), 8.43(d, J = 16.6 Hz, 2H), 8.11(s, 1H), 7.79 (bs, 1H), 7.60(s, 1H), 7.46(m, 2H), 7.35(m, 1H), 4.40(s, 2H), 4.20(s, 2H), 3.89(s, 1H)
159		MS (ESI) m/z 538 [M+1]+. 1H NMR (400 MHz, DMSO-d6) δ 8.43 (s, 1H), 8.29(s, 1H), 8.01 (s, 1H), 7.59 (bs, 1H), 7.38-7.36 (m , 1H), 7.32-7.30 (m, 1H), 7.20 (d, J = 2.56 Hz, 2H), 7.16 (d, J = 8.76 Hz, 1H), 4.26 (s, 4H), 3.8 (s, 1H)	168		MS (ESI) m/z 553.20 [M+1]+. UPLC: 98.95 %; 1H NMR (400 MHz, DMSO-d6) δ 13.65 (s, 1H), 8.37(s, 1H), 8.19 (s, 1H), 8.08 (d, J = 7.68 1H), 7.78-7.76 (t, J = 7.76 Hz, 1H), 7.61 (d, J = 7.24 Hz, 1H), 7.49 (dd, J = 2.4, 8.84 Hz, 1H), 7.28 (d, J = 2.52 Hz, 1H), 7.25 (d, J = 8.92 Hz 1H), 4.32 (m, 4H), 1.95 (s, 3H)
162		MS (ESI) m/z 515.10 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.63 (d, J = 5.04 Hz, 1H), 8.43 (d, J = 1.08 Hz, 1H), 8.27 (s, 1H), 8.23 (s, 1H), 8.03 (s, 1H), 7.67-7.65 (dd, J = 1.52, 4.96 Hz, 1H), 7.49 (d, J = 2.72 Hz, 1H), 7.47 (s, 1H), 7.25 (d, J = 9.28 Hz, 1H), 4.40-4.37 (m, 4H)	169		MS (ESI) m/z 554.24 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.77 (bs, 1H), 8.36 (s, 1H), 8.17 (s, 1H), 7.71 (d, J = 7.32 Hz, 1H), 7.36-7.28 (m, 2H), 7.23 (d, J = 7.8 Hz, 1H), 7.10 (d, J = 9.56 Hz, 2H), 6.57-6.50 (q, J = 6.32, 11.64 Hz, 1H), 4.88 (d, J = 11.32 Hz, 1H), 4.64 (d, J = 17.52 Hz, 1H), 4.30 (s, 4H), 2.02 (s, 3H)

181		MS (ESI) m/z 603.04 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 8.83 (s, 1H), 8.50 (s, 1H), 8.33 (s, 1H), 8.15 (s, 1H), 7.60-7.36 (m, 4H), 4.72 (d, J = 44 Hz, 2H), 4.39 (bs, 2H), 4.12 (bs, 2H)	
182		MS (ESI) m/z 546.08 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.40 (s, 1H), 8.30 (s, 1H), 7.87-7.83 (m, 2H), 7.55 (d, J = 7.50 Hz, 1H), 7.45-7.39 (m, 2H), 7.30 (d, J=2.48 Hz, 1H), 7.20 (d, J = 8.0 Hz, 1H), 5.10 (d, J = 45 Hz, 2H), 4.39 (bs, 4H)	
185		MS (ESI) m/z 539.07 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.82 (s, 1H), 8.60 (s, 1H), 8.50 (s, 1H), 7.87-7.71 (m, 2H), 7.53-7.51 (d, J = 8 Hz, 1H), 7.43-7.37 (m, 2H), 7.35-7.20 (m, 2H), 4.53 (t, J = 4 Hz, 2H), 4.39 (t, J = 4 Hz, 2H)	
		186	
		187	
		199	
			MS (ESI) m/z 530.11 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.43 (s, 1H), 8.08 (s, 1H), 7.88 (s, 1H), 7.73 (d, J =7.2 Hz, 1H), 7.65 (s, 2H), 7.41-7.33 (m, 3H), 7.22 (d, J=8.72, 1H), 4.30-4.27 (t, J =6 Hz, 2H), 4.22-4.20 (t, J = 5.54 Hz, 2H)
			MS (ESI) m/z 548.03 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.91 (s, 1H), 8.47 (s, 1H), 8.29 (s, 1H), 7.88 (s, 1H), 7.77 (d, J = 7.50 Hz, 1H), 7.59 (d, J = 7.90 Hz, 1H), 7.42-7.38 (m, 2H), 7.31 (d, J = 2.48 Hz, 1H), 7.22 (d, J = 9.0 Hz, 1H), 4.52 (d, J = 4.72 Hz, 2H), 4.38 (d, J = 4.8 Hz, 2H)
			MS (ESI) m/z 584.69 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.50 (s, 1H), 8.72 (d, 4.08 Hz, 1H), 8.29 (s, 1H), 8.08 (s, 1H), 7.70 (s, 1H), 7.58 (dd, J = 2.32, 8.52 Hz, 1H), 7.40 (d, J = 2.36 Hz, 1H), 7.35 (d, J = 8.96 Hz, 2H), 4.42 (s, 2H), 4.26 (s, 2H), 1.81 (s, 3H)

201		MS (ESI) m/z 585.16 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 14.04 (b, 1H), 8.30 (s, 1H), 8.25 (d, J = 5.56 Hz, 1H), 7.96 (d, J = 6.4 Hz, 2H), 7.60-7.58 (m, 2H), 7.50 (dd, J = 8.8 Hz, 1H), 7.30 (d, J = 8.84 Hz, 1H), 4.45 (t, J = 4.72 Hz, 2H), 4.36 (t, J = 4.6 Hz, 2H), 2.18 (s, 1H)	205		MS (ESI) m/z 599.18 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.79 (d, J = 4.96 Hz, 1H), 8.38 (s, 1H), 7.98 (s, 1H), 7.60 (dd, J = 8.88, 2.6 Hz, 1H), 7.53 (d, J = 4.88 Hz, 1H), 7.43 (d, J = 2.56 Hz, 1H), 7.36 (d, J = 8.96 Hz, 1H), 4.43 (s, 2H), 4.27 (s, 2H), 2.34 (s, 3H), 1.85 (s, 3H)
202		MS (ESI) m/z 599.18 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.41 (s, 1H), 8.66 (d, 4.56 Hz, 1H), 8.37 (s, 1H), 8.17 (s, 1H), 7.56 (m, 2H), 7.40 (d, J = 2.44 Hz, 1H), 7.33 (d, J = 9.04 Hz, 1H), 7.26 (d, J = 4.6 Hz, 1H), 4.38 (s, 2H), 4.25 (s, 2H), 3.84 (s, 2H), 1.78 (s, 3H)	206		MS (ESI) m/z 619.24 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.64 Hz, 1H), 8.36 (s, 1H), 8.07 (s, 1H), 7.60 (d, J = 8.84 Hz, 1H), 7.52 (d, J = 4.4 Hz, 1H), 7.41 (s, 1H), 7.34 (d, J = 8.92 Hz, 1H), 4.44 (s, 2H), 4.28 (s, 2H), 1.81 (s, 3H)
203		MS (ESI) m/z 589.91 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.88 (s, 1H), 8.29 (s, 1H), 8.04 (s, 1H), 8.01 (s, 1H), 7.92 (s, 1H), 7.48-7.44 (m, 2H), 7.29 (d, J = 8.8 Hz, 1H), 4.50 (m, 2H), 4.25 (s, 2H), 2.08 (s, 3H)	210		MS (ESI) m/z 610.15 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.16 (s, 1H), 8.82 (d, J = 4.64 Hz ,1H), 8.41 (d, J = 9.8 Hz , 2H), 7.6 (dd, J =8.92, 2.48 Hz, 1H), 7.45 (dd, J = 9.68 , 4.72 Hz, 2H), 7.37 (d, J = 8.88 Hz, 1H), 4.42 (t, J =5.04 Hz , 2H), 4.27 (t, J= 5.2 Hz , 2H), 1.96 (s, 3H)

214		MS (ESI) m/z 609.05 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.16 (bs, 1H), 8.86 (d, J = 4.6 Hz, 1H), 8.16 (s, 1H), 8.11 (s, 1H), 7.60 (d, J = 8.96 Hz, 1H), 7.49 (d, J = 4.44 Hz, 1H), 7.42 (s, 1H), 7.36 (d, J = 9.04, 1H), 4.42 (bs, 2H), 4.28 (bs, 2H), 1.74 (s, 3H)	226		MS (ESI) m/z 585.39 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.54 (s, 1H), 8.38 (s, 1H), 8.18 (s, 1H), 7.97 (t, J = 6.30 Hz, 2H), 7.55-7.52 (dd, J = 2.24, 2.32 Hz, 1H), 7.46 (d, J = 7.8 Hz, 1H), 7.30-7.25 (m, 2H), 4.45-4.29 (m, 4H), 1.98 (s, 3H)
215		MS (ESI) m/z 585 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.10 (bs, 1H), 9.33 (s, 1H), 8.38 (s, 2H), 7.98 (s, 1H), 7.64 (dd, J = 8.8, 2.4 Hz, 1H), 7.45 (d, J = 2.4 Hz, 1H), 7.38 (d, J = 9.2 Hz, 1H), 4.45 (s, 2H), 4.27 (s, 2H), 1.77 (s, 3H)	227		MS (ESI) m/z 551.14 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.96 Hz, 1H), 8.38 (s, 1H), 8.32 (s, 1H), 8.01 (s, 1H), 7.55 (t, J = 7.16 Hz, 1H), 7.50 (d, J = 4.48 Hz, 1H), 7.34 (t, J = 5.6 Hz, 2H), 7.16 (t, J = 7.40 Hz, 1H), 4.41 (s, 2H), 4.27 (s, 2H), 1.80 (s, 3H)
225		MS (ESI) m/z 585.16 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.19 (s, 1H), 8.59 (d, J = 5.56 Hz, 1H), 8.35-8.32 (m, 2H), 8.05 (s, 1H), 7.93 (s, 1H), 7.55 (dd, J = 9.0, 2.56 Hz, 1H), 7.33-7.30 (m, 1H), 4.38 (s, 2H), 4.22 (s, 2H), 1.69 (s, 3H)	246		MS (ESI) m/z 603.15 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.77 (d, J = 4.84 Hz, 1H), 8.64 (s, 1H), 8.40 (d, J = 9.16 Hz, 1H), 7.60 (dd, J = 8.92 Hz, 2.6 Hz, 1H), 7.49 (d, J = 4.84 Hz, 1H), 7.45 (d, J = 2.6 Hz, 1H), 7.37 (d, J = 8.96 Hz, 1H), 4.44 (t, J = 4.8 Hz, 2H), 4.29 (t, J = 4.64 Hz, 2H), 1.99 (s, 3H)

255		MS (ESI) m/z 581.20 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.16 (bs, 1H), 8.83 (s, 1H), 7.77 (d, J = 4.4 Hz, 1H), 8.35 (s, 1H), 8.14 (s, 1H), 7.87 (d, J = 8.8 Hz, 1H), 7.61 (d, J = 8.4 Hz, 1H), 7.53 (s, 1H), 7.42 (d, J = 4.4 Hz, 1H), 6.50-6.44 (m, 1H), 5.98 (d, J = 16.0, 1H), 4.73 (d, J = 4.0, 2H), 2.38 (s, 3H)	
259		MS (ESI) m/z 586.14 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.91 (s, 1H), 8.80 (d, J = 4.92 Hz, 1H), 8.39 (d, J = 1.12 Hz, 1H), 8.35 (d, J = 2.80 Hz, 1H), 8.25 (s, 1H), 7.98 (d, J = 2.80 Hz, 1H), 7.49 (d, J = 4.88 Hz, 1H), 4.53 (t, J=5.4 Hz, 2H), 4.41 (t, J = 5.2 Hz, 2H), 2.62 (s, 3H)	266	MS (ESI) m/z 619.24 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.64 Hz, 1H), 8.36 (s, 1H), 8.07 (s, 1H), 7.60 (d, J = 8.84 Hz, 1H), 7.52 (d, J = 4.4 Hz, 1H), 7.41 (s, 1H), 7.34 (d, J = 8.92 Hz, 1H), 4.44 (s, 2H), 4.28 (s, 2H), 1.81 (s, 3H)
261		MS (ESI) m/z 644.23 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83-8.79 (m, 3H), 8.29 (s, 1H), 8.22 (s, 1H), 7.93 (s, 1H), 7.84 (d, J = 5.68 Hz, 2H), 7.59 (dd, J = 2.56, J=8.84 Hz, 1H), 7.51 (d, J = 4.8 Hz, 1H), 7.44 (d, J=2.60 Hz, 1H), 7.34 (d, J=8.96 Hz, 1H) 4.38 (t, J = 5.76 Hz, 2H), 4.22 (t, J = 4.60 Hz, 2H), 1.69 (s, 3H)	267	MS (ESI) m/z 609.20 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.04 (bs, 1H), 8.88 (d, J = 4.8 Hz, 1H), 8.30 (d, J = 1.2 Hz, 1H), 8.03 (d, J = 1.4 Hz, 1H), 7.61-7.56 (m, 2H), 7.42 (d, J = 2.8 Hz, 1H), 7.35 (d, J = 8.8 Hz, 1H), 4.91 (s, 1H), 4.44 (t, J = 4.4 Hz, 2H), 4.26 (d, J = 4.4 Hz, 2H), 1.73 (s, 3H)

272		287	
MS (ESI) m/z 586.17 [M+1]+. 1H NMR (400 MHz, DMSO-d6) δ 13.95 (bs, 1H), 8.98 (d, J = 4.4 Hz, 1H), 8.38 (s, 1H), 8.11 (s, 1H), 7.66 (d, J = 4.0 Hz, 1H), 7.60 (d, J = 9.6 Hz, 1H) 7.49 (s, 1H), 7.36 (d, J = 9.2 Hz, 1H), 4.45 (s, 2H), 4.28 (s, 2H), 1.74 (s, 3H)		MS (ESI) m/z 576.26 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.28 (bs, 1H), 8.84 (d, J = 4.8 Hz, 1H), 8.38 (s, 1H), 8.26 (s, 1H), 8.05 (dd, J = 8.6, 2.0 Hz, 1H), 8.01 (s, 1H), 7.89 (d, J = 2.0 Hz, 1H), 7.52 (d, J = 3.4 Hz, 1H), 7.5 (s, 1H), 4.51 (t, J = 4.8 Hz, 2H), 4.26 (t, J = 5.9 Hz, 2H), 1.7 (s, 3H)	
275		289	
MS (ESI) m/z 601.13 [M+1]+; 1H NMR (400 MHz, DMSO-d6) 8.85 (d, J = 4.80 Hz, 1H), 8.39 (s, 1H), 7.89 (s, 1H), 7.60 (dd, J = 8.88, 2.36 Hz, 1H), 7.50 (d, J = 4.80 Hz, 1H), 7.42 (d, J = 2.44 Hz, 1H), 7.35 (d, J = 8.96 Hz, 1H), 4.40 (t, J = 5.28 Hz, 2H). 4.23 (t, J = 4.40 Hz, 2H), 1.71 (s, 3H)		MS (ESI) m/z 594.14 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.85 (d, J = 4.5 1H), 8.39 (s, 1H), 8.28 (s, 1H), 8.00 (d, J=8.52, 2H), 7.63 (d, J = 11.4 Hz, 1H), 7.49 (d, J = 4.28 Hz, 1H), 4.527 (s, 2H), 4.26 (s, 2H), 1.683 (s, 3H)	
285		291	
MS (ESI) m/z 552.20 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.91 (d, J = 4.8 Hz, 1H), 8.79 (d, J = 6.2 Hz, 1H), 8.64 (s, 1H), 8.40 (s, 1H), 8.34 (s, 1H), 8.05 (s, 1H), 7.61 (d, J = 3.1 Hz, 1H), 7.55 (d, J = 4.7 Hz, 1H), 4.62 (t, J = 4.2 Hz, 2H), 4.31 (t, J = 4.7 Hz, 2H), 1.75 (s, 3H)		MS (ESI) m/z 577.06 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.15 (s, 1H), 8.91 (d, J = 4.72 Hz, 1H), 8.87 (s, 1H), 8.39 (s, 1H), 8.35 (s, 1H), 8.17 (s, 1H), 8.05 (s, 1H), 7.54 (d, J = 4.72 Hz, 1H), 4.66 (s, 2H), 4.27 (s, 2H), 1.79 (s, 3H)	

292		MS (ESI) m/z 577.0 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.88 (s, 1H), 8.87 (s, 1H), 8.38 (s, 1H), 8.27 (d, J = 8.7 Hz, 1H), 8.22 (s, 1H), 8.1 (d, J = 4.9 Hz, 1H), 8.04 (d, J = 8.7 Hz, 1H), 4.68 (t, J = 4.2 Hz, 2H), 4.55 (t, J = 4.4 Hz, 2H), 2.37 (s, 3H)
294		MS (ESI) m/z 603.17 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.84 Hz, 1H), 8.45 (s, 1H), 8.37 (d, J = 5.28 Hz, 1H), 7.60 (dd, J = 8.56, 6.72, Hz, 1H), 7.49 (d, J = 4.56 Hz 1H), 7.43 (d, J = 2.04 Hz, 1H), 7.37 (d, J = 8.88 Hz, 1H), 4.42 (t, J = 4.90, 2H), 4.27 (t, J = 4.40 Hz, 2H), 1.86 (s, 3H)
295		MS (ESI) m/z 634.99 [M+1]+;1H NMR (400 MHz, DMSO-d6), δ 8.76 (d, J = 2.68 Hz 1H), 8.35 (s, 1H), 8.10 (s, 1H), 7.74 (s, 1H), 7.58 (dd, J = 9.24, 2.81 Hz, 1H), 7.42 (d, J = 2.80 Hz, 1H), 7.40 (d, J = 4.40 Hz, 1H), 7.34 (d, J = 8.96 Hz, 1H), 4.45-4.37 (m, 2H), 4.30-4.22 (m, 2H), 1.82 (s, 3H)
296		MS (ESI) m/z 599.14 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.55 (s, 1H), 8.36 (s, 1H), 8.27 (s, 1H), 7.97(s, 1H), 7.60-7.57 (dd, J = 2.52, 8.8 Hz, 1H), 7.41 (m, 2H), 7.35 (d, J = 8.96 Hz, 1H), 4.40 (t, J = 5 Hz, 2H), 4.25 (t, J = 5.0 Hz, 2H), 2.69 (s, 3H), 1.82 (s, 3H)
299		MS (ESI) m/z 585.17 [M+1]+. 1H NMR (400 MHz, DMSO-d6) δ 14.22 (bs, 1H), 8.37 (s, 1H), 8.34 (d, J = 4.8 Hz, 1H), 8.18 (s, 1H), 7.98 (s, 1H), 7.47-7.44 (m, 2H), 7.38 (d, J = 2.4 Hz, 1H), 7.25 (d, J = 9.2 Hz, 1H), 4.34 (t, 4.8 Hz, 2H), 4.25 (t, J = 4.4, 2H), 1.97 (s, 3H)
300		MS (ESI) m/z 568.19 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.19 (s, 1H), 8.33 (s,1H), 8.20 (s, 1H), 8.06 (s, 1H), 7.61 (d, J = 7.28 Hz, 1H), 7.51 (d, J = 7.56 Hz, 1H), 7.47 (d, J = 2.32 Hz, 1H), 7.43 (d, J = 2.2 Hz, 1H), 7.28 (d, J = 8.8 Hz, 1H), 6.97 (t, J = 7.56 Hz, 1H,), 4.43(s, 2H), 4.32(s,2H), 2.10 (s, 3H)

301		319	
MS (ESI) m/z 583.99 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.46 (bs, 1H), 8.35 (s, 1H), 7.94 (s, 1H), 7.79 (s, 1H), 7.55 (d, J = 7.32 Hz, 1H), 7.49 (dd, J = 8.80, 2.68 Hz, 1H), 7.32-7.27 (m, 3H), 6.89 (t, J = 7.64 Hz, 1H), 4.30 (t, J = 5.08 Hz, 2H), 4.16 (t, J = 5.12 Hz, 2H), 1.92 (s, 3H)		MS (ESI) m/z 585.2 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) / ppm = 13.31 (bs, 1H), 9.59 (s, 1H), 8.37 (s, 1H), 8.34 (d, J = 1.9 Hz, 1H), 7.95-7.94 (m, 1H), 7.91 (s, 1H), 7.54 (dd, J = 8.9, 2.6 Hz, 1H), 7.38 (d, J = 2.6 Hz, 1H), 7.30 (d, J = 8.9 Hz, 1H), 4.36 (t, J = 4.7 Hz, 2H), 4.21 (t, J = 4.7 Hz, 2H), 1.70 (s, 3H)
314		320	
MS (ESI) m/z 585.94 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.25 (s, 1H), 9.18 (s, 1H), 8.33 (s, 1H), 8.24 (s, 1H), 7.97 (s, 1H), 7.62 (dd, J = 8.8, 2.7 Hz, 1H), 7.49 (d, J = 2.32 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.44 (t, J = 4.96 Hz, 2H), 4.27 (t, J = 4.96 Hz, 2H), 1.71 (s, 3H)		MS (ESI) m/z 582.1 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) / ppm = 8.49 (d, J = 5.1 Hz, 1H), 8.39 (d, J = 1.5 Hz, 1H), 8.15-8.02 (m, 2H), 7.60 (dd, J = 9.1, 2.6 Hz, 1H), 7.41 (d, J = 2.6 Hz, 1H), 7.30 (d, J = 9.1 Hz, 1H), 7.34-7.20 (m, 1H), 4.46-4.33 (m, 2H), 4.28-4.20 (m, 2H), 3.16 (s, 3H), 1.66 (s, 3H)
315		321	
MS (ESI) m/z 591.15 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.54 (s, 1H), 8.33 (s, 1H), 8.11 (s, 1H), 8.01 (s, 1H), 7.67 (d, J = 2.64 Hz, 1H), 7.59 (dd, J = 8.92, 2.68 Hz, 1H), 7.38 (d, J = 9 Hz, 1H), 4.60 (t, J = 5.24 Hz, 2H), 4.37 (t, J = 5.36 Hz, 2H), 2.14 (s, 3H)		MS (ESI) m/z 700.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 10.16 (s, 1H), 8.87 – 8.81 (m, 1H), 8.24 – 8.17 (m, 1H), 7.98 (s, 1H), 7.61 (dd, J = 8.9, 2.7 Hz, 1H), 7.49 (dd, J = 4.9, 2.0 Hz, 1H), 7.43 (d, J = 2.6 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 4.77 – 4.71 (m, 1H), 4.66 – 4.59 (m, 1H), 4.42 (t, J = 5.0 Hz, 2H), 4.32 – 4.11 (m, 6H), 3.70 – 3.53 (m, 2H), 3.23 – 3.11 (m, 2H), 1.81 (s, 3H)

322		[0503] MS (ESI) m/z 567.2 [M+1]+; 1H NMR (400 MHz, d6-DMSO) δ / ppm = 11.04 (d, J = 3.2 Hz, 1H), 8.38-8.37 (m, 1H), 8.10-8.08 (m, 1H), 8.02 (d, J = 8.1 Hz, 1H), 7.45 (dd, J = 8.9 Hz, 2.8 Hz, 1H), 7.25-7.15 (m, 4H), 7.02 (dd, J = 7.2, 1.2 Hz, 1H), 4.40-4.35 (m, 2H), 4.22-4.18 (m, 2H), 1.61 (s, 3H)
323		MS (ESI) m/z 568.0 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ / ppm = 13.49 (b, 1H), 8.59 (d, J = 5.6 Hz, 1H), 8.40-8.39 (m, 1H), 8.07-8.05 (m, 1H), 7.87-7.77 (m, 1H), 7.62 (dd, J = 8.9, 2.6 Hz, 1H), 7.60-7.49 (m, 1H), 7.42 (d, J = 2.6 Hz, 1H), 7.34 (d, J = 8.9 Hz, 1H), 4.45 (t, J = 4.6 Hz, 2H), 4.25 (t, J = 4.6 Hz, 2H), 1.76 (s, 3H)
324		MS (ESI) m/z 569.0 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ / ppm = 8.80 (s, 1H), 8.65 (d, J = 4.9 Hz, 1H), 8.53 (d, J = 2.7 Hz, 1H), 8.33 (bd, J = 1.7 Hz, 1H), 8.15-8.14 (m, 1H), 7.69 (d, J = 4.9 Hz, 1H), 7.43 (dd, J = 8.9, 2.7 Hz, 1H), 7.30 (d, J = 8.9 Hz, 1H), 4.55-4.52 (m, 4H), 2.45 (s, 3H)
325		MS (ESI) m/z 569.0 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ / ppm = 8.98-8.90 (m, 1H), 8.54-8.45 (m, 1H), 8.36-8.31 (m, 1H), 8.23-8.18 (m, 1H), 7.64-7.51 (m, 3H), 7.34-7.27 (m, 1H), 4.43-4.34 (m, 2H), 4.34-4.23 (m, 2H), 1.77 (s, 3H)
326		[0506] MS (ESI) m/z 535.1 [M+1]+
327		MS (ESI) m/z 616.4 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ / ppm = 8.33 (bd, J = 1.7 Hz, 1H), 8.24 (dd, J = 7.8, 0.9 Hz, 1H), 7.95 (s, 1H), 7.76 (dd, J = 7.8, 7.8 Hz, 1H), 7.50 (dd, J = 8.9, 2.6 Hz, 1H), 7.45 (bd, J = 7.8 Hz, 1H), 7.23-7.20 (m, 2H), 7.14 (s, 1H), 4.36-4.21 (m, 4H), 1.84 (s, 3H)

328		331	
MS (ESI) m/z 549.3 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ / ppm = 8.39 (bd, J = 1.7 Hz, 1H), 8.24-8.22 (m, 1H), 7.01-6.87 (m, 3H), 4.52 (t, J = 4.8 Hz, 2H), 4.35 (t, J = 4.8 Hz, 2H), 3.22-3.16 (m, 2H), 2.80 (s, 3H), 2.50-2.43 (m, 2H), 2.13-2.09 (m, 2H), 1.74-1.57 (m, 3H), 1.27-1.11 (m, 2H)		MS (ESI) m/z 601.6 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ / ppm = 10.48 (s, 1H), 8.37-8.36 (m, 1H), 7.95 (bs, 1H), 7.78 (bs, 1H), 7.56 (dd, J = 8.7, 2.6, 1H), 7.38 (d, J = 2.6 Hz, 1H), 7.31 (d, J = 8.7 Hz, 1H), 6.36 (bs, 1H), 4.41 (bt, 2H), 4.32 (bt, 2H), 2.15 (s, 3H)	
329		332	
MS (ESI) m/z 615.0 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ / ppm = 8.36 (bd, J = 1.6 Hz, 1H), 8.12 (s, 1H), 8.01-8.00 (m, 1H), 7.57 (dd, J = 8.9, 2.7 Hz, 1H), 7.39 (d, J = 2.7 Hz, 1H), 7.33 (d, J = 8.9 Hz, 1H), 6.90 (d, J = 0.3 Hz, 1H), 4.40 (t, J = 5.0 Hz, 2H), 4.26 (t, J = 5.0 Hz, 1H), 4.03 (s, 3H), 1.87 (s, 3H)		MS (ESI) m/z 615.1 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ / ppm = 13.35 (b, 1H), 8.32 (d, J = 1.2 Hz, 1H), 8.06-8.04 (m, 1H), 7.68 (s, 1H), 7.51 (dd, J = 8.8, 2.7 Hz, 1H), 7.32 (d, J = 2.7 Hz, 1H), 7.26 (d, J = 8.8 Hz, 1H), 6.35 (s, 1H), 4.35 (bt, 1H), 4.28 (bt, 1H), 3.65 (s, 3H), 2.06 (s, 3H)	
330		333	
MS (ESI) m/z 613.1 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ / ppm = 8.37 (bs, 1H), 8.24 (s, 1H), 7.95 (bs, 1H), 7.60 (dd, J = 8.8, 2.6, 1H), 7.47 (s, 1H), 7.43 (d, J = 2.6 Hz, 1H), 7.35 (d, J = 8.8 Hz, 1H), 4.41 (bt, 2H), 4.25 (bt, 2H), 3.01 (q, J = 7.6 Hz, 2H), 1.78 (s, 3H), 1.34 (t, J = 7.6 Hz, 3H)		MS (ESI) m/z 616.2 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ / ppm = 12.89 (b, 1H), 8.35 (d, J = 1.5 Hz, 1H), 8.07 (bs, 1H), 7.77 (bs, 1H), 7.50 (dd, J = 8.9, 2.7 Hz, 1H), 7.30-7.26 (m, 2H), 7.19 (d, J = 6.0 Hz, 1H), 4.35 (bt, 2H), 4.25 (bt, 2H), 2.33 (s, 3H), 1.83 (s, 3H)	

341		344	
MS (ESI) m/z 690.1 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ / ppm = 8.75 (d, J = 5.3 Hz, 1H), 8.28 (s, 1H), 8.06 (s, 1H), 7.60 (dd, J = 8.9, 2.8 Hz, 1H), 7.59 (s, 1H), 7.52 (bd, J = 5.3 Hz, 1H), 7.45 (s, 1H), 7.42 (d, J = 2.8 Hz, 1H), 7.37 (d, J = 8.9 Hz, 1H), 4.42 (t, J = 5.2 Hz, 2H), 4.28 (t, J = 5.2 Hz, 2H), 2.73 (s, 3H), 2.64 (s, 3H), 1.87 (s, 3H)		MS (ESI) m/z 694.2 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ / ppm = 8.87 (s, 1H), 8.71 (d, J = 4.7 Hz, 1H), 8.34 (s, 1H), 8.14 (s, 1H), 7.74-7.70 (m, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.45 (s, 1H), 7.43 (d, J = 2.7 Hz, 1H), 7.36 (d, J = 8.9 Hz, 1H), 4.48-4.20 (m, 4H), 2.72 (s, 3H), 1.87 (s, 3H)
342		347	
MS (ESI) m/z 694.2 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ / ppm = 8.82 (d, J = 2.8 Hz, 1H), 8.60-8.59 (m, 1H), 8.28 (s, 1H), 8.11-8.06 (m, 1H), 8.07 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.45 (s, 1H), 7.42 (d, J = 2.7 Hz, 1H), 7.37 (d, J = 8.9 Hz, 1H), 4.43 (t, J = 4.9 Hz, 2H), 4.29 (t, J = 4.9 Hz, 2H), 2.73 (s, 3H), 1.89 (s, 3H)		MS (ESI) m/z 682.5 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ / ppm = 9.32 (s, 1H), 8.71 (s, 1H), 8.30 (s, 1H), 8.05 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.44 (s, 1H), 7.42 (d, J = 2.7 Hz, 1H), 7.37 (d, J = 8.9 Hz, 1H), 4.42 (t, J = 4.7 Hz, 2H), 4.28 (t, J = 4.7 Hz, 2H), 2.72 (s, 3H), 1.88 (s, 3H)
343		348	
MS (ESI) m/z 694.5 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ / ppm = 8.85 (dd, J = 7.5, 5.8 Hz, 1H), 8.79 (d, J = 9.9 Hz, 1H), 8.35 (s, 1H), 8.12 (s, 1H), 7.64 (dd, J = 9.8, 5.8 Hz, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.47 (s, 1H), 7.43 (d, J = 2.7 Hz, 1H), 7.37 (d, J = 8.9 Hz, 1H), 4.49-4.19 (m, 4H), 2.73 (s, 3H), 1.87 (s, 3H)		MS (ESI) m/z 682.4 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ / ppm = 8.74 (d, J = 1.7 Hz, 1H), 8.31 (s, 1H), 8.06 (s, 1H), 7.67 (d, J = 1.7 Hz, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.47 (s, 1H), 7.43 (d, J = 2.7 Hz, 1H), 7.36 (d, J = 8.6 Hz, 1H), 4.42 (t, J = 4.9 Hz, 2H), 4.28 (t, J = 4.9 Hz, 2H), 2.74 (s, 3H), 1.86 (s, 3H)

349		354	
MS (ESI) m/z 704.3 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ / ppm = 8.28 (s, 1H), 8.08 (s, 1H), 7.83-7.77 (m, 1H), 7.60 (dd, J = 9.0, 2.8 Hz, 1H), 7.46 (s, 1H), 7.44 (d, J = 2.8 Hz, 1H), 7.43-7.38 (m, 1H), 7.37 (d, J = 9.0 Hz, 1H), 4.47-4.38 (m, 2H), 4.33-4.19 (m, 2H), 2.73 (s, 3H), 2.59 (s, 3H), 2.22 (s, 3H), 1.84 (s, 3H)		MS (ESI) m/z 615.0 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.87 – 8.84 (m, 2H), 7.61 – 7.57 (m, 2H), 7.53 – 7.51 (m, 2H), 7.38 (d, J = 9.0 Hz, 1H), 7.35 (s, 1H), 4.23 (t, J = 5.5 Hz, 2H), 3.74 (t, J = 5.4 Hz, 2H), 2.75 (s, 3H), 1.07 (s, 6H)	
350		356	
MS (ESI) m/z 704.5 [M+1]+; 1H-NMR (400 MHz, d_6-DMSO) / ppm = 8.47-8.37 (m, 1H), 8.29 (s, 1H), 8.08 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.46 (s, 1H), 7.44 (d, J = 2.7 Hz, 1H), 7.43-7.39 (m, 1H), 7.37 (d, J = 8.9 Hz, 1H), 4.47-4.43 (m, 2H), 4.34-4.18 (m, 2H), 2.73 (s, 3H), 2.57 (s, 3H), 2.06 (s, 3H), 1.84 (s, 3H)		MS (ESI) m/z 602.3 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.34 (s, 1H), 8.82 (d, J = 4.9 Hz, 1H), 8.45 (s, 1H), 8.37 – 8.36 (m, 1H), 8.05 – 8.04 (m, 1H), 7.95 (s, 1H), 7.52 (d, J = 4.9 Hz, 1H), 4.63 (t, J = 5.0 Hz, 2H), 4.31 (t, J = 5.0 Hz, 2H), 1.90 (s, 3H)	
352		363	
MS (ESI) m/z 599.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.68 (d, J = 4.7 Hz, 1H), 8.38 (dd, J = 1.8, 0.6 Hz, 1H), 8.22 (dt, J = 1.8, 0.8 Hz, 1H), 7.53 (dd, J = 8.9, 2.7 Hz, 1H), 7.42 (s, 1H), 7.39 (d, J = 2.7 Hz, 1H), 7.29 (d, J = 9.0 Hz, 1H), 7.21 (d, J = 4.7 Hz, 1H), 5.43 (s, 1H), 4.37 (t, J = 4.9 Hz, 2H), 4.24 (t, J = 4.9 Hz, 2H), 1.75 (s, 6H), 1.65 (s, 3H)		MS (ESI) m/z 613.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.25 (s, 1H), 7.92 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.43 (s, 1H), 7.41 (d, J = 2.7 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.41 (t, J = 5.0 Hz, 2H), 4.25 (t, J = 5.0 Hz, 2H), 2.71 (s, 3H), 2.70 (s, 3H), 1.85 (s, 3H)	

364		MS (ESI) m/z 613.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.41 (s, 1H), 8.16 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.43 (s, 1H), 7.41 (d, J = 2.7 Hz, 1H), 7.38 (d, J = 9.0 Hz, 1H), 4.44 (t, J = 5.0 Hz, 2H), 4.26 (t, J = 5.0 Hz, 2H), 2.68 (s, 3H), 2.69 – 2.63 (m, 3H), 1.93 (s, 3H)	375		MS (ESI) m/z 619.4 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.25 (s, 1H), 7.92 – 7.85 (m, 2H), 7.84 (t, J = 1.8 Hz, 1H), 7.54 (dt, J = 7.8, 1.6 Hz, 1H), 7.45 (d, J = 7.6 Hz, 1H), 7.43 – 7.37 (m, 3H), 7.29 (d, J = 2.6 Hz, 1H), 7.21 (d, J = 8.9 Hz, 1H), 4.40 – 4.33 (m, 4H), 2.52 (s, 3H), 2.24 (s, 3H)
373		MS (ESI) m/z 694.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 10.09 (s, 1H), 8.25 (d, J = 5.1 Hz, 1H), 7.98 (d, J = 5.3 Hz, 1H), 7.60 (dd, J = 8.9, 2.6 Hz, 1H), 7.44 (s, 1H), 7.42 (d, J = 2.6 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 5.95 (s, 1H), 4.41 (t, J = 5.4 Hz, 2H), 4.26 (t, J = 5.1 Hz, 2H), 4.13 (d, J = 17.4 Hz, 1H), 3.84 (d, J = 17.8 Hz, 1H), 3.02 – 2.88 (m, 5H), 2.73 – 2.66 (m, 5H), 1.87 (s, 3H)	376		MS (ESI) m/z 717.9 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.84 (d, J = 4.8 Hz, 1H), 8.22 (s, 1H), 7.98 (s, 1H), 7.61 (dd, J = 8.9, 2.7 Hz, 1H), 7.49 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.6 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 6.38 (tt, J = 53.3, 3.0 Hz, 1H), 4.42 (t, J = 5.1 Hz, 2H), 4.31 – 4.25 (m, 6H), 3.87 (td, J = 16.3, 3.0 Hz, 2H), 3.41 (s, 2H), 3.24 (s, 1H), 1.81 (s, 3H)
374		MS (ESI) m/z 626.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.74 (s, 1H), 8.15 (s, 1H), 7.83 (dt, J = 7.7, 1.5 Hz, 1H), 7.80 (t, J = 1.8 Hz, 1H), 7.50 (dt, J = 7.7, 1.6 Hz, 1H), 7.45 – 7.38 (m, 2H), 7.28 (d, J = 2.7 Hz, 1H), 7.21 (d, J = 8.9 Hz, 1H), 3.85 (t, J = 12.3 Hz, 2H), 3.54 (d, J = 11.7 Hz, 2H), 3.19 (d, J = 12.8 Hz, 2H), 3.12 – 2.99 (m, 2H), 2.89 (s, 3H), 2.21 (s, 3H)	377		MS (ESI) m/z 676.3 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.13 (s, 1H), 7.85 – 7.78 (m, 2H), 7.51 (dt, J = 7.7, 1.5 Hz, 1H), 7.44 – 7.37 (m, 2H), 7.28 (d, J = 2.7 Hz, 1H), 7.21 (d, J = 8.9 Hz, 1H), 6.38 (t, J = 54.0 Hz, 1H), 2.20 (s, 3H). Note: some aliphatic signals were very broad and could not be integrated

378		381	
MS (ESI) m/z 654.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.12 (s, 1H), 7.85 – 7.79 (m, 2H), 7.51 (dt, J = 7.7, 1.6 Hz, 1H), 7.44 – 7.37 (m, 2H), 7.27 (d, J = 2.6 Hz, 1H), 7.21 (d, J = 8.9 Hz, 1H), 4.34 (s, 4H), 3.06 – 2.76 (m, 2H), 2.20 (s, 3H), 2.06 (s, 3H) Note: some aliphatic signals were very broad and could not be integrated		MS (ESI) m/z 640.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.13 (s, 1H), 7.84 (dt, J = 7.7, 1.5 Hz, 1H), 7.80 (t, J = 1.8 Hz, 1H), 7.51 (dt, J = 7.7, 1.5 Hz, 1H), 7.45 – 7.38 (m, 2H), 7.27 (d, J = 2.6 Hz, 1H), 7.21 (d, J = 8.9 Hz, 1H), 4.35 (s, 4H), 2.92 (s, 3H), 2.19 (s, 3H). Note: some aliphatic signals were very broad and could not be integrated
379		382	
MS (ESI) m/z 689.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.15 (s, 1H), 8.11 (dd, J = 5.6, 1.9 Hz, 1H), 7.87 – 7.79 (m, 3H), 7.51 (dt, J = 7.7, 1.6 Hz, 1H), 7.45 – 7.38 (m, 2H), 7.28 (d, J = 2.7 Hz, 1H), 7.21 (d, J = 8.9 Hz, 2H), 6.85 (t, J = 6.3 Hz, 1H), 4.35 (s, 4H), 2.20 (s, 3H). Note: some aliphatic signals were very broad and could not be integrated		MS (ESI) m/z 688.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.13 (s, 1H), 7.87 – 7.80 (m, 2H), 7.52 (dt, J = 7.7, 1.5 Hz, 1H), 7.45 – 7.37 (m, 2H), 7.30 – 7.19 (m, 4H), 7.05 – 6.99 (m, 2H), 6.83 (t, J = 7.3 Hz, 1H), 4.35 (s, 4H), 2.20 (s, 3H). Note: some aliphatic signals were very broad and could not be integrated
380		383	
MS (ESI) m/z 689.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.51 (d, J = 2.9 Hz, 1H), 8.22 (d, J = 5.3 Hz, 1H), 8.15 (s, 1H), 8.08 (dd, J = 8.8, 2.8 Hz, 1H), 7.85 (dt, J = 7.7, 1.5 Hz, 1H), 7.83 – 7.78 (m, 2H), 7.51 (dt, J = 7.7, 1.6 Hz, 1H), 7.45 – 7.38 (m, 2H), 7.28 (d, J = 2.7 Hz, 1H), 7.21 (d, J = 8.9 Hz, 1H), 4.35 (s, 4H), 2.20 (s, 3H). Note: some aliphatic signals were very broad and could not be integrated		MS (ESI) m/z 711.0 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.26 (s, 1H), 7.92 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.43 (s, 1H), 7.42 (d, J = 2.6 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.40 (t, J = 5.1 Hz, 2H), 4.24 (t, J = 5.0 Hz, 2H), 2.94 (s, 3H), 2.72 (s, 3H), 1.82 (s, 3H). Note: some aliphatic signals were very broad and could not be integrated

386		389	
MS (ESI) m/z 605.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.80 (d, J = 5.1 Hz, 2H), 8.29 (s, 1H), 7.86 (dt, J = 7.6, 1.6 Hz, 1H), 7.82 (t, J = 1.8 Hz, 1H), 7.55 – 7.50 (m, 3H), 7.47 – 7.39 (m, 2H), 7.28 (d, J = 2.7 Hz, 1H), 7.22 (d, J = 8.9 Hz, 1H), 4.43 – 4.31 (m, 4H), 2.24 (s, 3H)		MS (ESI) m/z 703.9 [M+1]+; ; 1H NMR (400 MHz, DMSO-d6) δ 8.58 (s, 1H), 8.27 (s, 1H), 8.06 (s, 1H), 8.00 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.46 (s, 1H), 7.42 (d, J = 2.7 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 4.43 (t, J = 5.0 Hz, 2H), 4.28 (t, J = 4.9 Hz, 2H), 2.73 (s, 3H), 2.64 (s, 3H), 2.42 (s, 3H), 1.88 (s, 3H)
387		398	
MS (ESI) m/z 689.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.24 (d, J = 7.4 Hz, 2H), 7.88 (s, 1H), 7.45 – 7.34 (m, 5H), 7.26 (d, J = 2.7 Hz, 1H), 7.19 (d, J = 8.9 Hz, 1H), 7.13 (d, J = 7.1 Hz, 2H), 4.31 (s, 4H), 3.85 – 3.49 (m, 8H), 2.20 (s, 3H)		MS (ESI) m/z 656.0 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 10.16 (t, J = 5.4 Hz, 1H), 8.34 (d, J = 1.7 Hz, 1H), 8.14 (s, 1H), 8.05 (dd, J = 1.8, 0.8 Hz, 1H), 7.58 (dd, J = 8.9, 2.7 Hz, 1H), 7.39 (d, J = 2.7 Hz, 1H), 7.34 (d, J = 9.0 Hz, 1H), 7.33 (s, 1H), 4.40 (t, J = 5.0 Hz, 2H), 4.26 (t, J = 5.0 Hz, 2H), 4.21 (d, J = 5.4 Hz, 2H), 2.69 (s, 3H), 1.84 (s, 3H)
388		401	
MS (ESI) m/z 605.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.75 (dd, J = 4.9, 1.6 Hz, 1H), 8.62 (s, 1H), 8.28 (s, 1H), 7.91 (dt, J = 7.9, 1.9 Hz, 1H), 7.86 (dt, J = 7.6, 1.5 Hz, 1H), 7.82 (t, J = 1.8 Hz, 1H), 7.62 (dd, J = 7.8, 4.8 Hz, 1H), 7.53 (dt, J = 7.7, 1.5 Hz, 1H), 7.48 – 7.38 (m, 2H), 7.28 (d, J = 2.6 Hz, 1H), 7.22 (d, J = 8.9 Hz, 1H), 4.42 – 4.32 (m, J = 2.5 Hz, 4H), 2.24 (s, 3H)		MS (ESI) m/z 568.2 [M+H]+; 1H NMR (400 MHz, CD3OD) δ 8.16-8.13 (m, 1H), 8.05-8.02 (m, 1H), 7.97 (s, 1H), 7.90 (dd, J = 7.9, 1.3 Hz, 1H), 7.41 (dd, J = 8.8, 2.7 Hz, 1H), 7.31 (t, J = 7.6 Hz, 1H), 7.23 (d, J = 2.7 Hz, 1H), 7.20 (dd, J = 7.4, 1.3 Hz, 1H), 7.19 (d, J = 8.9 Hz, 1H), 4.40-4.30 (m, 4H), 1.98 (s, 3H)	

402		MS (ESI) m/z 584.3 [M+H]+; 1H NMR (400 MHz, Methanol-d4) δ 8.52 (dd, J = 8.3, 1.1 Hz, 1H), 8.15 (dd, J = 1.8, 0.6 Hz, 1H), 8.01 (dd, J = 1.7, 0.8 Hz, 1H), 7.77 (s, 1H), 7.51 (dd, J = 8.2, 7.2 Hz, 1H), 7.45 (dd, J = 8.9, 2.7 Hz, 1H), 7.30 – 7.25 (m, 1H), 7.22 (s, 1H), 7.21 – 7.16 (m, 1H), 4.40 (t, J = 4.8 Hz, 2H), 4.31 (t, J = 4.8 Hz, 2H), 1.82 (s, 3H)
410		MS (ESI) m/z 543.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.37 (d, J = 1.7 Hz, 1H), 8.17 (bs, 1H), 7.77 (bd, J = 1.6 Hz, 1H), 7.48 (bd, J = 1.4 Hz, 1H), 7.47 (dd, J = 8.9, 2.7 Hz, 1H), 7.36 (d, J = 2.7 Hz, 1H), 7.25 (d, J = 8.9 Hz, 1H), 4.39 (bs, 4H), 2.51 (s, 3H), 2.24 (s, 3H)
411		MS (ESI) m/z 557.6 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.40 (d, J = 1.7 Hz, 1H), 8.20 (d, J = 1.7 Hz, 1H), 7.49 (dd, J = 8.9, 2.7 Hz, 1H), 7.46-7.40 (br, 2H), 7.37 (d, J = 2.7 Hz, 1H), 7.26 (d, J = 8.9 Hz, 1H), 4.49-4.35 (m, 4H), 3.86 (s, 2H), 2.53 (s, 3H), 2.31 (s, 3H)
414		MS (ESI) m/z 583.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.38 (d, J = 1.8 Hz, 1H), 8.10 (br, 1H), 7.97 (s, 1H), 7.62 (dd, J = 8.9, 2.7 Hz, 1H), 7.53 (d, J = 2.7 Hz, 1H), 7.32 (d, J = 9.0 Hz, 1H), 7.15 (s, 1H), 4.37 (t, J = 4.9 Hz, 2H), 4.25 (t, J = 4.9 Hz, 2H), 2.59 (s, 3H), 1.85 (s, 3H)
415		MS (ESI) m/z 599.0 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (bs, 1H), 8.24 (s, 1H), 7.95 (s, 1H), 7.61 (d, J = 8.8 Hz, 1H), 7.50 (bs, 1H), 7.42 (bs, 1H), 7.36 (d, J = 7.8 Hz), 4.40 (bs, 2H), 4.25 (bs, 2H), 2.72 (s, 3H), 1.76 (s, 3H)
416		MS (ESI) m/z 599.0 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.81 (d, J = 4.6 Hz, 1H), 8.42 (s, 1H), 8.17 (s, 1H), 7.60 (dd, J = 9.4, 2.6 Hz, 1H), 7.49 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.7 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 4.44 (t, J = 4.8 Hz, 2H), 4.26 (t, J = 4.8 Hz, 2H), 2.67 (s, 3H), 1.84 (s, 3H)

417		MS (ESI) m/z 725.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 7.94 (s, 1H), 7.60 (dd, J = 8.8, 2.6 Hz, 1H), 7.44 (s, 1H), 7.42 (d, J = 2.7 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.42 (t, J = 5.0 Hz, 2H), 4.27 (t, J = 5.0 Hz, 2H), 3.94 (s, 2H), 3.43-3.29 (m, 4H), 2.99-2.82 (m, 4H), 2.78 (d, J = 4.3 Hz, 3H), 2.70 (s, 3H), 2.31 (s, 3H), 1.91 (s, 3H)	423		MS (ESI) m/z 682.6 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.32 (s, 1H), 7.89 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.44 (s, 1H), 7.42 (d, J = 2.6 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 5.04 (br, 6H), 4.39 (t, J = 5.0 Hz, 2H), 4.23 (t, J = 5.0 Hz, 2H), 3.21 (br, 4H), 2.71 (s, 3H), 1.80 (s, 3H)
421		MS (ESI) m/z 690.7 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.75 (dt, J = 4.8, 1.4 Hz, 1H), 8.08 – 7.99 (m, 2H), 7.65 – 7.53 (m, 3H), 7.45 (s, 1H), 7.42 (d, J = 2.6 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.42 (t, J = 4.9 Hz, 2H), 4.28 (br, 2H), 2.72 (s, 3H), 2.48 (s, 3H), 1.94 (s, 3H)	424		MS (ESI) m/z 668.3 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.18 (s, 1H), 7.95 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.43 (s, 1H), 7.42 (d, J = 2.7 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 4.41 (t, J = 5.0 Hz, 2H), 4.26 (t, J = 5.0 Hz, 2H), 4.11– 3.92 (m, 4H), 3.39 (br, 2H), 3.35-3.21 (m, 1H), 2.71 (s, 3H), 1.85 (s, 3H)
422		MS (ESI) m/z 668.4 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.35 (s, 1H), 7.92 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.43 (dd, J = 4.3, 1.8 Hz, 2H), 7.36 (d, J = 9.0 Hz, 1H), 4.40 (t, J = 5.0 Hz, 2H), 4.24 (t, J = 5.0 Hz, 2H), 3.37 – 3.28 (m, 4H), 2.70 (s, 3H), 2.10 – 1.99 (m, 4H), 1.82 (s, 3H)	425		MS (ESI) m/z 682.5 [M+1]+; 1H NMR (400 MHz, CDCl3) δ 8.35 (s, 1H), 8.12 (s, 1H), 7.47 (dd, J = 8.9, 2.6 Hz, 1H), 7.26 (s, 1H), 7.18 (s, 1H), 7.03 (d, J = 8.9 Hz, 1H), 4.56 (t, J = 9.0 Hz, 2H), 4.40 (t, J = 4.8 Hz, 2H), 4.29 (t, J = 4.9 Hz, 2H), 3.84 (t, J = 9.6 Hz, 2H), 3.49 (d, J = 6.6 Hz, 2H), 3.45 – 3.29 (m, 1H), 2.89 (s, 3H), 2.80 (s, 3H), 1.89 (s, 3H)

428		431	
MS (ESI) m/z 747.7 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.27 (s, 1H), 7.91 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.43 (s, 1H), 7.42 (d, J = 2.7 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 6.38 (br, 1H), 4.40 (t, J = 5.0 Hz, 2H), 4.24 (t, J = 5.0 Hz, 3H), 4.06-2.83 (br, 10H), 2.71 (s, 3H), 1.83 (s, 3H)		MS (ESI) m/z 683.4 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.57 (s, 1H), 8.50 (s, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.44 (d, J = 2.6 Hz, 1H), 7.40 (s, 1H), 7.37 (d, J = 9.0 Hz, 1H), 4.35 (t, J = 5.1 Hz, 2H), 4.26 (t, J = 5.1 Hz, 2H), 3.98 (dd, J = 11.3, 4.0 Hz, 2H), 3.43 (t, J = 11.3 Hz, 2H), 3.22 (m, 1H), 2.72 (s, 3H), 2.08 (s, 3H), 2.03 – 1.88 (m, 2H), 1.59 (d, J = 12.6 Hz, 2H)
429		433	
MS (ESI) m/z 681.7 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.31 (s, 1H), 7.96 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.43 (dd, J = 7.3, 2.1 Hz, 2H), 7.36 (d, J = 9.0 Hz, 1H), 5.92 (s, 1H), 4.41 (t, J = 5.0 Hz, 2H), 4.29 – 4.15 (m, 4H), 3.86 (m, 4H), 2.71 (s, 3H), 1.85 (s, 3H)		MS (ESI) m/z 712.4 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.80 (d, J = 2.4 Hz, 1H), 8.42 (s, 1H), 8.33 (td, J = 9.1, 2.4 Hz, 1H), 8.17 (s, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.45 (d, J = 2.4 Hz, 1H), 7.44 (s, 1H), 7.35 (d, J = 9.0 Hz, 1H), 4.40 (t, J = 5.0 Hz, 2H), 4.27 (t, J = 5.1 Hz, 2H), 2.70 (s, 3H), 1.84 (s, 3H)
430		434	
MS (ESI) m/z 729.5 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.25 (s, 1H), 7.93 (s, 1H), 7.61 (dd, J = 8.9, 2.7 Hz, 1H), 7.43 (s, 1H), 7.42 (d, J = 2.7 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 4.95 (t, J = 4.4 Hz, 1H), 4.82 (d, J = 4.6 Hz, 1H), 4.41 (t, J = 5.0 Hz, 2H), 4.25 (t, J = 5.0 Hz, 2H), 3.65-3.03 (br, 10H), 2.72 (s, 3H), 1.85 (s, 3H)		MS (ESI) m/z 708.6 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.46 (s, 1H), 8.15 (s, 1H), 7.89 (t, J = 8.9 Hz, 1H), 7.62 – 7.53 (m, 2H), 7.45 (s, 1H), 7.44 (d, J = 2.6, 0.9 Hz, 1H), 7.35 (d, J = 9.0 Hz, 1H), 4.40 (t, J = 5.0 Hz, 2H), 4.28 (d, J = 5.0 Hz, 2H), 2.71 (s, 3H), 2.52 (s, 3H), 1.82 (s, 3H)

437		MS (ESI) m/z 705.0 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.67 (s, 1H), 8.27 (s, 1H), 8.10 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.46 (s, 1H), 7.43 (d, J = 2.7 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 4.43 (t, J = 5.1 Hz, 2H), 4.28 (tt, J = 9.5, 5.0 Hz, 2H), 2.74 (s, 3H), 2.71 (s, 3H), 2.23 (s, 3H), 1.85 (s, 3H)
442		MS (ESI) m/z 691.3 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.27 (d, J = 2.1 Hz, 1H), 8.26 (s, 1H), 8.08 (s, 1H), 7.85 (d, J = 2.1 Hz, 1H), 7.60 (dd, J = 8.9, 2.6 Hz, 1H), 7.45 (s, 1H), 7.42 (d, J = 2.7 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 4.43 (t, J = 5.0 Hz, 2H), 4.29 (t, J = 5.0 Hz, 2H), 2.77 (s, 3H), 2.73 (s, 3H), 1.89 (s, 3H)
443		MS (ESI) m/z 604.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.58 (d, J= 4.8 Hz, 1H), 8.36 – 8.32 (m, 1H), 8.15 – 8.11 (m, 1H), 7.52 (dd, J= 8.9, 2.7 Hz, 1H), 7.38 (d, J = 2.7 Hz, 1H), 7.29 (d, J = 9.0 Hz, 1H), 7.23 (d, J = 4.8 Hz, 1H), 4.36 (t, J= 5.0 Hz, 2H), 4.25 (d, J= 5.0 Hz, 2H), 1.88 (s, 3H), 1.33 (s, 9H)
444		MS (ESI) m/z 619.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.34 (d, J = 1.9 Hz, 1H), 8.22 (s, 1H), 7.97 (dd, J = 1.9, 0.8 Hz, 1H), 7.56 (dd, J = 8.9, 2.7 Hz, 1H), 7.48 (s, 1H), 7.42 (d, J = 2.7 Hz, 1H), 7.31 (d, J = 9.0 Hz, 1H), 4.37 (t, J = 5.0 Hz, 2H), 4.23 (t, J = 5.0 Hz, 2H), 1.79 (s, 3H)
445		MS (ESI) m/z 628.7 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.32 (d, J = 1.8 Hz, 1H), 8.25 (s, 1H), 8.01 (d, J = 3.1 Hz, 1H), 7.94 (dd, J = 1.8, 0.9 Hz, 1H), 7.89 (s, 2H), 7.57 (dd, J = 8.9, 2.7 Hz, 1H), 7.43 (d, J = 2.6 Hz, 1H), 7.32 (d, J = 9.0 Hz, 1H), 4.37 (t, J = 5.0 Hz, 2H), 4.20 (t, J = 5.0 Hz, 2H), 1.65 (s, 3H)
446		MS (ESI) m/z 610.7 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.41 (d, J = 1.1 Hz, 1H), 8.35 (d, J = 1.7 Hz, 1H), 8.01 – 7.97 (m, 2H), 7.58 (ddd, J = 9.1, 2.7, 1.0 Hz, 1H), 7.44 (dd, J = 2.6, 1.0 Hz, 1H), 7.33 (d, J = 9.0 Hz, 1H), 4.38 (t, J = 5.0 Hz, 2H), 4.23 (t, J = 5.0 Hz, 2H), 1.71 (s, 3H)

447		MS (ESI) m/z 599.14 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.37 – 8.31 (m, 1H), 7.97 (d, J = 1.3 Hz, 1H), 7.95 (dt, J = 1.8, 0.8 Hz, 1H), 7.55 (dd, J = 8.9, 2.7 Hz, 1H), 7.35 – 7.28 (m, 2H), 7.17 (d, J = 0.9 Hz, 1H), 4.36 (t, J = 5.0 Hz, 2H), 4.20 (t, J = 5.0 Hz, 2H), 2.65 (d, J= 0.7 Hz, 3H), 1.86 (s, 3H)	454		MS (ESI) m/z 587.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.99 (s, 1H), 8.96 (s, 1H), 8.93 (d, J = 5.0 Hz, 1H), 8.39 – 8.37 (m, 1H), 8.26 (d, J = 5.0 Hz, 1H), 8.24 (dd, J = 1.7, 0.8 Hz, 1H), 4.77 (t, J = 5.1 Hz, 2H), 4.62 (t, J = 5.1 Hz, 2H), 2.53 (s, 3H)
452		MS (ESI) m/z 614.5 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.86 (s, 1H), 8.50 – 8.37 (m, 4H), 8.30 (s, 1H), 8.01 (s, 1H), 7.62 (dd, J = 8.9, 2.7 Hz, 1H), 7.57 (s, 1H), 7.40 – 7.35 (m, 2H), 4.44 (q, J = 6.1 Hz, 4H), 4.27 (t, J = 5.2 Hz, 2H), 1.77 (s, 3H)	455		MS (ESI) m/z 578.3 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.15 (s, 1H), 8.92 (s, 2H), 8.35 (s, 1H), 8.20 (d, J = 4.9 Hz, 2H), 4.83 (s, 2H), 4.60 (s, 2H), 2.56 (2, 3H)
453		MS (ESI) m/z 552.9 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.18 (dd, J = 6.2, 0.7 Hz, 1H), 8.89 – 8.84 (m, 2H), 8.37 – 8.33 (m, 1H), 8.20 (dt, J = 1.8, 0.8 Hz, 1H), 8.07 – 8.03 (m, 1H), 7.66 (dd, J = 6.2, 0.8 Hz, 1H), 4.63 (t, J = 5.0 Hz, 2H), 4.53 (t, J = 5.0 Hz, 2H), 3.88 (s, 1H), 2.33 (s, 3H)	465		LCMS: 704.5 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ 8.25 (s, 1H), 8.05 (s, 1H), 7.61 (dd, J = 8.9, 2.7 Hz, 1H), 7.50 – 7.33 (m, 4H), 4.42 (t, J = 5.0 Hz, 2H), 4.28 (t, J = 5.0 Hz, 2H), 2.73 (s, 3H), 2.62 (s, 6H), 1.87 (s, 3H)

466		470	
LCMS: 704.5 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ 8.74 – 8.65 (m, 1H), 8.32 (s, 1H), 8.09 (s, 1H), 7.80 (d, J = 7.8 Hz, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.49 – 7.41 (m, 3H), 7.37 (d, J = 9.0 Hz, 1H), 4.52 – 4.10 (m, 2H), 2.73 (s, 3H), 2.45 – 2.35 (m, 2H), 1.85 (s, 3H), 1.15 (t, J = 7.5 Hz, 3H)		LCMS: 708.5 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ 8.70 – 8.65 (m, 1H), 8.27 (d, J = 0.9 Hz, 1H), 8.10 (s, 1H), 7.91 (dd, J = 9.0, 2.9 Hz, 1H), 7.60 (ddd, J = 8.9, 2.6, 1.0 Hz, 1H), 7.47 – 7.41 (m, 2H), 7.37 (d, J = 8.9 Hz, 1H), 4.43 (d, J = 4.8 Hz, 2H), 4.37 – 4.17 (m, 2H), 2.74 (d, J = 0.9 Hz, 3H), 2.21 (s, 3H), 1.86 (s, 3H)	
468		471	
LCMS: 704.5 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ 8.75 (d, J = 5.2 Hz, 1H), 8.29 (s, 1H), 8.06 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.57 (s, 1H), 7.52 – 7.47 (m, 1H), 7.45 (s, 1H), 7.42 (d, J = 2.6 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 4.42 (t, J = 5.1 Hz, 2H), 4.29 (d, J = 5.2 Hz, 2H), 2.91 (q, J = 7.5 Hz, 2H), 2.73 (s, 3H), 1.87 (s, 3H), 1.29 (t, J = 7.6 Hz, 3H)		LCMS: 708.6 [M+H]+; 1H NMR (400 MHz, DMSO-d6); 1H NMR (400 MHz, DMSO-d6) δ 8.69 (d, J = 0.8 Hz, 1H), 8.30 (s, 1H), 8.11 (s, 1H), 7.61 – 7.57 (m, 1H), 7.55 (d, J = 5.6 Hz, 1H), 7.45 – 7.42 (m, 2H), 7.36 (d, J = 9.0 Hz, 1H), 4.54 – 4.10 (m, 1H), 2.72 (s, 3H), 2.58 (d, J = 1.0 Hz, 3H), 1.86 (s, 3H)	
469		472	
LCMS: 704.5 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ 8.72 (s, 1H), 8.25 (s, 1H), 8.11 (s, 1H), 7.63 – 7.58 (m, 2H), 7.47 (s, 1H), 7.44 (d, J = 2.6 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 4.43 (h, J = 5.9 Hz, 2H), 4.27 (dd, J = 11.3, 5.7 Hz, 1H), 2.74 (s, 3H), 2.64 (s, 3H), 2.08 (s, 3H), 1.84 (s, 3H)		LCMS: 708.6 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ 8.54 (d, J = 4.8 Hz, 1H), 8.33 (s, 1H), 8.12 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.51 (t, J = 5.1 Hz, 1H), 7.46 – 7.41 (m, 2H), 7.36 (d, J = 9.0 Hz, 1H), 4.57 – 4.15 (m, 2H), 2.72 (s, 3H), 2.56 (d, J = 3.0 Hz, 3H), 1.87 (s, 3H)	

473		LCMS: 708.6 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ 8.27 (s, 1H), 8.17 (dt, J = 4.7, 1.4 Hz, 1H), 7.99 (s, 1H), 7.77 (ddd, J = 9.8, 8.3, 1.3 Hz, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.45 – 7.40 (m, 2H), 7.36 (dt, J = 8.4, 1.9 Hz, 2H), 4.66 (s, 2H), 4.42 (t, J = 5.0 Hz, 2H), 4.26 (t, J = 5.1 Hz, 2H), 2.70 (s, 3H), 1.86 (s, 3H)	485		MS (ESI) m/z 711.6 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.48 (s, 1H), 8.22 (s, 1H), 7.96 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.43 (d, J = 2.5 Hz, 2H), 7.36 (d, J = 9.0 Hz, 1H), 4.41 (t, J = 5.1 Hz, 2H), 4.26 (d, J = 5.0 Hz, 2H), 3.95 (s, 2H), 3.38 (d, J = 11.4 Hz, 2H), 2.92 (d, J = 11.8 Hz, 4H), 2.78 (d, J = 4.5 Hz, 3H), 2.70 (s, 3H), 1.85 (s, 3H)
483		MS (ESI) m/z 711.6 [M+1]+; ; 1H NMR (400 MHz, DMSO-d6) δ 9.36 (s, 1H), 8.38 (s, 1H), 8.27 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.46 – 7.34 (m, 3H), 4.43 (d, J = 5.3 Hz, 2H), 4.27 (s, 2H), 4.14 (s, 2H), 3.30 (d, J = 11.8 Hz, 2H), 2.77 (d, J = 20.8 Hz, 7H), 2.68 (s, 3H), 1.88 (s, 3H)	486		MS (ESI) m/z 711.6 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.27 (s, 1H), 7.96 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.43 (d, J = 2.5 Hz, 2H), 7.36 (d, J = 9.0 Hz, 1H), 4.41 (t, J = 5.0 Hz, 2H), 4.25 (t, J = 5.0 Hz, 2H), 3.89 (s, 2H), 3.53 (s, 4H), 2.70 (s, 3H), 1.83 (s, 3H)
484		MS (ESI) m/z 615.6 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.37 (d, J = 1.7 Hz, 1H), 8.24 (s, 1H), 7.98 – 7.94 (m, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.53 (s, 1H), 7.41 (d, J = 2.6 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.81 (s, 2H), 4.41 (t, J = 5.1 Hz, 2H), 4.25 (t, J = 5.1 Hz, 2H), 1.77 (s, 3H)	487		MS (ESI) m/z 791.5 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.75 (d, J = 5.0 Hz, 1H), 8.50 (s, 1H), 8.33 (d, J = 1.8 Hz, 1H), 7.96 – 7.93 (m, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.49 (d, J = 5.0 Hz, 1H), 7.44 (d, J = 2.6 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.42 (t, J = 5.0 Hz, 2H), 4.26 (t, J = 5.1 Hz, 2H), 2.61 (s, 4H), 1.86 (s, 3H)

489		MS (ESI) m/z 741.8 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.47 (s, 1H), 8.21 (s, 1H), 7.97 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.48 – 7.41 (m, 2H), 7.36 (d, J = 9.0 Hz, 1H), 4.74 (s, 2H), 4.41 (t, J = 5.0 Hz, 2H), 4.25 (t, J = 5.0 Hz, 2H), 3.94 (s, 2H), 2.92 (d, J = 12.0 Hz, 5H), 2.78 (d, J = 4.2 Hz, 3H), 1.77 (s, 3H)
494		MS (ESI) m/z 735.9 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.85 (d, J = 4.8 Hz, 1H), 8.23 (s, 1H), 7.98 (s, 1H), 7.61 (dd, J = 8.9, 2.7 Hz, 1H), 7.51 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.6 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 4.42 (t, J = 4.9 Hz, 2H), 4.26 (t, J = 5.0 Hz, 2H), 4.08 – 3.82 (m, 4H), 3.38 (d, J = 6.2 Hz, 2H), 3.16 – 3.02 (m, 1H), 1.79 (s, 3H)
495		MS (ESI) m/z: 599.01; 1H-NMR (400 MHz, DMSO-d6) δ 8.70 (s, 1H), 8.36 (s, 1H), 8.22 (s, 1H), 8.01 (s, 1H), 7.59-7.56 (m, 1H), 7.37-7.35 (m, 2H), 4.48-4.44 (m, 1H), 4.27-4.20 (m, 3H), 2.08 (s, 3H), 1.17 (s, 3H)
496		MS (ESI) m/z 569.23 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.39 (s, 1H), 8.34 (d, J = 4.28 Hz, 1H), 8.23 (s, 1H), 7.44 (dd, J = 8.80, 2.40 Hz, 1H), 7.25 (d, J = 2.16 Hz, 1H), 7.21 (d, J = 8.84 Hz, 1H), 7.10 (s, 1H), 4.41-4.29 (m, 4H), 4.08 (t, J= 8.48, 1H), 2.12-2.10 (m, 4H), 2.03 (s, 3H)
501		MS (ESI) m/z 684.11 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.84 (d, J= 4.8 Hz, 1H), 8.28(s, 1H), 7.99 (s, 1H), 7.61 (dd, J= 8.92, 2.6 Hz, 1H), 7.51 (d, J= 4.76 Hz, 1H), 7.44 (d, J= 2.6 Hz, 1H), 7.37 (d, J= 9.00 Hz, 1H), 4.42 (t, J= 5.76 Hz, 2H), 4.26 (t, J= 4.36 Hz, 2H), 3.95 (bs, 2H), 3.55 (bs, 4H), 2.56 (bs, 4H), 1.76 (s, 3H)
502		MS (ESI) m/z 697.15 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.84 (d, J= 4.76, 1H), 8.23 (s, 1H), 7.98 (s, 1H), 7.61 (dd, J= 8.84, 2.56 Hz, 1H), 7.48 (d, J= 4.76 Hz, 1H), 7.44 (d, J= 2.6 Hz, 1H), 7.37 (d, J= 9.00 Hz, 1H), 4.42 (t, J= 3.8 Hz, 2H), 4.26 (t, J= 5.8, 2H), 3.94 (bs, 2H), 3.40 (d, J=10.68 Hz, 2H), 2.94 (d, J =10.68 Hz, 4H), 2.79 (d, J=3.4 Hz, 3H), 2.50 (m, 2H), 1.77 (s, 3H)

503		521	
MS (ESI) m/z 660.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.86 (d, J = 4.68 Hz, 1H), 8.11 (s, 1H), 8.07 (s,1H), 7.63 (d, J = 8.36, 1H), 7.57 (d, J = 11.32 Hz, 1H), 7.49 (d, J = 4.72 Hz, 1H), 4.63 (bs, 2H), 4.46 (t, J = 4.64 Hz, 2H), 4.28 (t, J = 4.72 Hz, 2H), 2.89 (bs, 6H), 1.75 (s, 3H)		MS (ESI) m/z 648.07 [M+1]+. 1H NMR (400 MHz, DMSO-d6) δ 12.10 (s, 1H), 8.84 (d, J = 4.80 Hz, 1H), 8.12 (s, 1H), 8.09 (S, 1H), 7.59 (dd, J = 8.88, 2.80 1H), 7.46 (d, J = 4.76 Hz, 1H), 7.41 (d, J = 2.60 Hz, 1H), 7.34 (d, J = 9.04 Hz, 1H), 4.42-4.38 (m, 2H), 4.28-4.21 (m, 2H), 3.88 (s, 3H), 1.66 (s, 3H)
505		522	
MS (ESI) m/z 637.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.86 (d, J = 4.76 Hz, 1H), 8.25 (s, 1H), 8.08 (s, 1H), 7.63 (d, J = 8.32 Hz, 1H), 7.55 (d, J = 11.2 Hz, 1H), 7.50 (d, J = 4.68 Hz, 1H), 4.43 (t, J = 5.00 Hz, 2H), 4.26 (t, J = 4.44 Hz, 2H), 1.68 (s, 3H)		MS (ESI) m/z 718.18 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.84 (d, J = 4.16 Hz, 1H), 8.27 (s, 1H), 8.98 (s, 1H), 7.59 (d, J = 8.52 Hz, 1H), 7.50 (d, J = 4.4 Hz, 1H), 7.43 (s, 1H), 7.36 (d, J = 9.08 Hz, 1H), 4.41 (bs, 2H), 4.24 (bs, 2H), 3.94 (s, 2H), 2.61 (s, 4H), 1.92 (s, 4H), 1.76 (s, 3H)	
519		523	
MS (ESI) m/z 696.3 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.69 (s, 1H), 8.92 (d, J = 4.44 Hz, 1H), 8.34 (s, 1H), 8.09 (s, 1H), 7.65-7.54 (m, 2H), 7.45 (d, J = 1.84 Hz, 1H), 7.36 (d, J = 8.84 Hz, 1H), 4.42 (t, J = 4.68 Hz, 2H), 4.24 (t, J = 5.24 Hz, 2H), 3.56 (s, 3H), 1.65 (s, 3H)		MS (ESI) m/z 710.21 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 13.23 (bs, 1H), 8.82 (d, J = 3.2 Hz, 1H), 8.27 (s, 1H), 7.99 (s, 1H), 7.59 (d, J = 8.88 Hz, 1H), 7.50-7.42 (m, 1H), 7.43 (s, 1H) 7.35 (d, J = 8.24 Hz, 1H), 4.41 (s, 2H), 4.24 (s, 2H), 3.84 (s, 1H), 3.50-3.30 (m, 4H), 3.07 (s, 2H), 2.02 (s, 2H), 1.85-1.70 (m, 5H)	

524		MS (ESI) m/z 616.13 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 13.27 (bs, 1H), 8.82 (s, J = 4.72 Hz, 1H), 8.17 (s, 1H), 8.00 (s, 1H), 7.58 (dd, J = 8.80, 2.44 Hz, 1H), 7.46 (d, J = 4.76 Hz, 1H), 7.40 (d, J = 2.52 Hz, 1H), 7.35 (d, J = 8.8 Hz, 1H), 5.52 (s, 2H), 4.40 (t, J = 4.28 Hz, 2H), 4.23 (t, J = 5.2 Hz, 2H), 1.73 (s, 3H)	
525		MS (ESI) m/z 692.27 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (s, 1H), 8.23 (s, 1H), 7.97 (s, 1H), 7.65-7.26 (m, 4H), 6.16 (t, J = 56.26 Hz, 1H), 4.40 (s, 2H), 4.24 (s, 2H), 4.04 (s, 2H), 2.94 (t, J = 14.2 Hz, 2H), 2.28 (s, 3H), 1.75 (s, 3H)	
526		MS (ESI) m/z 668.20 [M+1]+; 1H-NMR (400 MHz, CD3OD) δ 8.80 (d ,J = 4.84 Hz, 1H), 8.27 (s, 1H), 8.19 (s, 1H), 7.57 (dd, J = 2.96, 9.76 Hz, 1H), 7.49 (d, J = 4.84 Hz, 1H), 7.36 (d, J = 2.36 Hz, 1H), 7.31 (d, J = 8.88 Hz, 1H), 4.98 (s, 2H), 4.46 (t, J = 2.36, 2H), 4.37 (t, J = 4.6 Hz, 2H),.3.74 (s, 4H), 2.20 (s, 4H), 2.03 (s, 3H)	
527		MS (ESI) m/z 670.40 [M+1]+; 1H-NMR (400 MHz CD3OD) δ 8.78 (d, J = 4.88 Hz, 1H), 8.27 (s, 1H), 8.20 (s, 1H), 7.57 (dd, J = 2.56, 8.92 Hz, 1H), 7.49 (d, J = 4.92 Hz, 1H), 7.36 (d, J = 2.48 Hz, 1H), 7.32 (d, J = 8.84 Hz, 1H), 4.98 (s, 2H), 4.46 (t, J = 4.76, 2H), 4.37 (t, J = 4.5 Hz, 2H),.3.52-3.47 (m, 4H), 2.03 (s, 3H), 1.48-1.29 (m, 6H)	
528		MS (ESI) m/z 682.19 [M+1]+; 1H NMR (400 MHz, DMSO-d6 + D2O) δ 8.83 (d, J= 4.80 Hz, 1H), 8.21 (s, 1H), 8.06 (s, 1H), 7.61-7.57 (dd, J = 2.48, 8.80 Hz, 1H), 7.48 (d, J = 4.68 Hz, 1H), 7.44 (d, J = 2.48 Hz, 1H), 7.36 (d, J = 8.92 Hz, 1H), 4.58 (m, 2H), 4.40 (t, J = 6.36 Hz, 2H), 4.26 (t, J = 4.52 Hz, 2H),, 3.29 (m, 4H), 1.75 (m, 7H), 1.54 (m, 2H)	
535		MS (ESI) m/z 537.11 [M+1] +. 1H NMR (400 MHz, DMSO-d6) δ 12.77 (bs, 1H), 8.39 (s, 1H), 7.23 (s, 1H), 7.03 (d, J = 8.9 Hz), 6.92 (s, 1H), 4.51 (m, 2H), 4.38 (t, J = 4.8 Hz, 3H), 4.19-4.16 (m, 2H), 3.95 (d, J = 11.2 Hz, 1H), 3.63-3.59 (m, 1H), 3.27 (d, J = 9.6 Hz, 1H), 2.94-2.79 (m, 5H)	

549	MS (ESI) m/z 651.08 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.84 (d, J = 4.72 Hz, 1H), 8.22 (s, 1H), 8.07 (s, 1H), 7.61-7.23 (m, 5H), 4.41 (t, J=4.2 Hz, 2H), 4.26 (t, J=4.2 Hz, 2H), 1.72 (s, 3H)	555	MS (ESI) m/z 633. [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.78 (d, J = 4.88, 1H), 8.089 (s, 1H), 7.615 (dd, J=8.92, 8.96, 1H), 7.519 (d, J = 4.88 Hz, 1H), 7.414 (d, J= 2.6, 1H), 7.37 (d, J = 8.96 Hz, 1H), 4.43 (bs, 2H), 4.29 (bs, 2H), 2.41 (s, 3H), 1.89 (s, 3H)
553	MS (ESI) m/z 636.0 [M+1]+;; 1H NMR (400 MHz, DMSO-d6) δ 8.74 (d, J = 4.7 Hz, 1H), 8.53 (s, 1H), 8.21 (s, 1H), 7.77 (d, J = 8.1 Hz, 1H), 7.7 (d, J = 2.0 Hz, 1H), 7.68 (s, 1H), 7.54 (d, J = 4.7 Hz, 1H), 4.91 (s, 2H), 4.63 (bs, 2H), 2.87 (bs, 6H), 2.11 (s, 3H)	556	MS (ESI) m/z 656.21 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.79 (d, J=4.76, 1H), 8.088 (s,1H), 7.618 (dd, J=8.84, 8.72, 1H), 7.517 (d, J= 4.84 Hz, 1H), 7.44 (d, J= 2.16, 1H), 7.36 (d, J=8.88 Hz, 1H), 4.602 (bs, 2H), 4.419 (bs, 2H), 4.28 (bs, 2H), 2.84 (bs, 6H), 2.34 (s, 3H), 1.83 (s, 3H)
554	MS (ESI) m/z 613.04 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.77 (d, J = 4.8 Hz, 1H), 8.55 (s, 1H), 8.22 (s, 1H), 7.76 (d, J = 8.2 Hz, 1H), 7.7 (d, J = 2.0 Hz, 1H), 7.67 (s, 1H), 7.55 (d, J = 4.7 Hz, 1H), 4.88 (s, 2H), 2.07 (s, 3H)	558	MS (ESI) m/z 633.10 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 8.24 (s, 1H), 8.03 (s, 1H), 7.61-7.58 (dd, J = 2.52,J = 8.84 Hz, 1H), 7.44 (s, 1H),-7.41 (d, J = 2.52, 1H),7.37 (d, J= 8.92, 1H), 4.42 (t, J = 5.46 Hz, 2H), 4.27 (t, J = 4.32 Hz, 2H), 2.71 (s, 3H),1.79 (s, 3H)

559		MS (ESI) m/z 656.15 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.48 (s, 1H), 8.06 (bs, 1H), 8.03 (s, 1H), 7.62 (dd, J = 8.92 Hz, 2.52 Hz, 1 H), 7.45-7.34 (m, 2 H), 7.36 (d, J = 8.32 Hz, 1H), 4.75 (s, 2 H), 4.44 (t, J = 3.6 Hz, 2H), 4.29 (t, J = 5.6 Hz, 2 H), 2.99 (s, 6H), 2.72 (s, 3 H), 1.82 (s, 3 H)	562		MS (ESI) m/z 650.17 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.34 (bs, 1H), 8.73 (d, J = 4.7 Hz, 1H), 8.66 (s, 1H), 8.13 (d, J = 9.7 Hz, 1H), 7.76 (d, J = 9.0 Hz, 1H), 7.68 (m, 1H), 7.53 (d, J = 4.7 Hz, 1H), 7.37 (t, J = 53.7 Hz, 1H), 4.88 (s, 2H), 2.22 (s, 3H)
560		MS (ESI) m/z: 593 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 13.24 (s, 1H), 8.59 (s, 1H), 8.42 (s, 1H), 8.12 (s, 1H), 7.75 (d, J = 8.24 Hz, 1H), 7.68-7.64 (m, 2H), 7.46 (s, 1H), 4.87 (s, 2H), 2.59 (s, 3H), 2.14 (s, 3H)	563		MS (ESI) m/z 635.09 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.98 (bs, 1H), 8.37 (s, 1H), 8.28 (s, 1H), 8.00 (s, 1H), 7.67 (s, 1H), 7.60 (dd, J = 1.68, 8.56 Hz, 1H), 7.45 (bs, 1H), 7.35 (d, J = 8.88 Hz, 1H), 7.18 (t, J = 54.84 Hz, 1H), 4.39-4.35 (m, 2H), 4.23-4.20 (m, 2H), 1.67 (s, 3H)
561		MS (ESI) m/z 627.06 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) 13.23 (bs, 1H), 8.54 (s, 1H), 8.20 (s, 1H), 7.75 (d, J = 8.32 Hz, 1H), 7.69 (dd, J = 8.24, 1.96 Hz, 1H), 7.64 (s, 1H), 7.47 (s, 1H), 4.87 (s, 2H). 2.64 (s, 3H), 2.14 (s 3H)	564		MS (ESI) m/z 655.21 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.06 (s, 1H), 9.45 (s, 1H), 8.18 (s, 1H), 7.50 (dd, J=2.52 Hz, J=9.12 Hz, 2H), 7.28-7.25 (m, 2H), 7.15 (d, J = 7.28 Hz, 1H), 4.75 (s, 2H), 4.36 (bs, 2H), 4.24 (bs, 2H), 2.98 (s, 6H), 2.68 (s, 3H), 1.72 (s, 3H)

565		MS (ESI) m/z 676.11 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.02 (bs, 1H), 8.38 (s, 1H), 8.35 (s, 1H), 7.60 (dd, J = 8.80, 2.40 Hz, 1H), 7.47 (s, 1H), 7.42 (d, J = 2.48 Hz, 1H), 7.35 (d, J = 8.16 Hz, 1H), 4.41 (t, J = 5.0 Hz, 2H), 4. 24 (t, J = 4.72 Hz, 2H), 3.56 (s, 3H), 2.68 (s, 3H), 1.78 (s, 3H)	571		MS (ESI) m/z 617.11 [M+1]+; 1H NMR (400 MHz, MeOD) δ 8.31 (s, 1H), 8.16 (s, 1H), 8.00 (s, 1H), 7.56 (s, 1H),7.51 (d, J = 8.08 Hz, 1H), 7.34 (d, J = 10.84 Hz, 1H), 4.50 (t, J = 4.80 Hz, 2H), 4.38 (t, J = 5.20 Hz, 2H), 2.96 (s, 3H), 2.03 (s, 3H)
568		MS (ESI) m/z 733.16 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.02 (s, 1H), 8.32 (s, 1H), 7.97 (s, 1H), 7.61-7.59 (m, 1H), 7.48 (s, 1H), 7.43 (s, 1H), 7.36 (d, J = 8.8 Hz, 1H), 4.41 (s, 2H), 4.23 (bs, 2H), 3.77 (bs, 2H), 3.55 (s, 3H), 2.69 (s, 3H), 2.22 (s, 6H), 1.75 (s, 3H)	589		MS (ESI) m/z 617.11 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 8.46 (s, 1H), 8.36 (d, J = 5.64 Hz, 1H), 7.60 (dd, J = 8.88, 2.64 Hz, 1H), 7.43-7.39 (m, 2H), 7.36 (d, J = 9.00 Hz, 1H), 4.42 (t, J = 4.52 Hz, 2H), 4.28 (t, J = 4.76 Hz, 2H), 2.69 (s, 3H), 1.94 (s, 3H)
569		MS (ESI) m/z 662.07 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.70 (s, 1H), 8.89 (d, J = 4.76 Hz, 1H), 8.39 (s, 2H), 8.02 (s, 1H), 7.63-7.60 (dd, J = 2.56, 2.44 Hz 1H), 7.56 (d, J = 4.72 Hz, 1H), 7.46 (d, J = 2.44 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.41 (t, J = 4.4 Hz, 2H), 4.24 (t, J = 3.86 Hz, 2H), 3.56 (s, 3H), 1.73 (s, 3H)	590		MS (ESI) m/z 615.23 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.35 (s, 1H), 7.95-7.93 (m, 3H), 7.57 (dd, J = 2.56, 8.92 Hz, 1H), 7.39 (d, J = 2.52 Hz, 1H), 7.33 (d, J = 9.04 Hz, 1H), 4.39 (t, J = 4.48 Hz, 2H), 4.30 (t, J = 4.36 Hz, 2H), 3.69 (s, 3H), 2.10 (s, 3H)

591		MS (ESI) m/z 612.91 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 14.09 (bs, 1H), δ 8.77 (d, J = 4.56 Hz, 1H), 8.37 (s, 1H), 7.97 (s, 1H), 7.59 (d, J = 8.48 Hz, 1H), 7.50 (d, J = 4.56 Hz, 1H), 7.42 (bs, 1H), 7.35 (d, J = 8.84 Hz, 1H), 4.42 (t, J = 4.32 Hz, 2H), 4.26 (t, J =3.20 Hz, 2H), 2.85-2.79 (m, 2H), 1.85 (s, 3H), 0.97 (t, J = 7.24 Hz, 3H)	610		MS (ESI) m/z 670.01 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.22 (s, 1H), 7.93 (s, 1H), 7.59 (dd, J = 8.68, 2.16 Hz, 1H), 7.41-7.34 (m, 3H), 4.40 (t, J = 4.76 Hz, 2H), 4.24 (t, J = 4.68 Hz, 2H), 3.20 (d, J = 7.48 Hz, 2H), 2.69 (s, 3H), 2.57 (d, J = 10.48 Hz, 2H), 2.28 (s, 6H), 1.83 (s, 3H)
595		MS (ESI) m/z 629.10 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.37-8.28 (m, 2H), 7.61 (s, 1H), 7.48-7.43 (m, 1H), 7.31-7.26 (m, 2H), 7.05 (bs, 1H), 4.33 (bs, 2H), 4.24 (bs, 2H), 3.81 (s, 2H), 3.01 (s, 2H), 1.80 (s, 3H)	614		MS (ESI) m/z 617.06 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 8.38 (s, 1H), 8.14 (bs, 2H), 7.74 (t, J = 8.56 Hz, 1H), 7.29 (bs, 1H), 7.20 (d, J = 9.08 Hz, 1H), 4.41 (bs, 1H), 4.36 (bs, 1H), 4.23 (s, 2H), 2.66 (s, 3H), 1.70 (s, 3H)
605		MS (ESI) m/z 615.09 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.34 (s, 1H), 8.16 (s, 1H), 7.52 (d, J = 7.44, 1H), 7.36 (s, 1H), 7.29 (d, J = 9.04 Hz, 1H), 6.54 (s, 1H), 6.30 (s, 1H), 4.88 (s, 2H), 4.38 (s, 2H), 4.31 (s, 2H), 2.32 (s, 3H)	615		MS (ESI) m/z 691.19 [M+1]+; ; 1H NMR (400 MHz, DMSO-d6) δ 8.69 (d, J = 4.72 Hz, 1H), 8.48 (s, 1H), 8.06 (s, 1H), 7.73 (d, J = 8.4 Hz, 1H), 7.66 (d, J = 7.1 Hz, 1H), 7.57 (s, 1H), 7.47 (d, J = 4.64, 1H), 4.78 (s, 2H), 3.95 (s, 2H), 3.37 (d, J = 12.5 Hz, 2H), 2.97 (d, J = 10.68 Hz, 4H), 2.75 (s, 3H), 2.58-2.56 (m, 2H), 2.1 (s, 3H)

616		MS (ESI) m/z 705.23 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.31 (s, 1H), 9.43 (s, 1H), 8.54 (s, 1H), 8.11 (s, 1H), 7.75 (d, J = 8.32 Hz, 1H), 7.69 (dd, J = 8.36, 6.2 Hz, 1H), 7.65 (d, J = 1.96 Hz, 1H), 7.47 (s, 1H), 4.87 (s, 2H), 3.97 (s, 2H), 2.95 (d, J = 10.08 Hz, 4H), 2.80 (s, 3H), 2.66 (s, 3H), 2.62 (s, 4H), 2.17 (s, 3H)	630		MS (ESI) m/z 676.18 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.76 (d, J = 3.7, 1H), 8.69 (s, 1H), 8.31 (s, 1H), 8.05 (s,1H), 7.99 (d, J = 7.8 Hz, 1H), 7.66-7.58 (m, 2H), 7.45 (s, 1H), 7.424 (d, J = 2.56 Hz, 1H), 7.36 (d, J = 8.9, 1H), 4.42 (t, J = 9.2 Hz, 2H), 4.28 (t, J = 9.6 Hz, 2H), 2.73 (s, 3H), 1.87 (s, 3H)
617		MS (ESI) m/z 678.16 [M+1]+; ; 1H NMR (400 MHz, DMSO-d6) δ 8.73 (d, J = 4.76 Hz, 1H), 8.6 (s, 1H), 8.1 (s, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.69 (d, J = 2.0 Hz, 1H), 7.67 (s, 1H), 7.55 (d, J = 4.76 Hz, 1H), 4.88 (s, 2H), 3.97 (s, 2H), 3.56 (s, 4H), 2.58 (s, 4H), 2.13 (s, 3H)	631		MS (ESI) m/z 676.18 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.74 (d, J = 4.7 Hz, 1H), 8.37 (s, 1H), 8.07 (s, 1H), 8.03 (t, J = 7.8 Hz, 1H), 7.68 (d, J = 7.6 Hz, 1H), 7.61 – 7.52 (m, 2H), 7.43 (s, 2H), 7.36 (d, J = 8.9 Hz, 1H), 4.40 (s, 2H), 4.26 (s, 2H), 2.72 (s, 3H), 1.83 (s, 3H)
629		MS (ESI) m/z 676.18 [M+1]+; ; 1H NMR (400 MHz, DMSO-d6) δ 8.78 (d, J = 5.56 Hz, 2H), 8.25 (s, 1H), 8.09 (s, 1H), 7.59 (dd, J = 7.56 Hz, 2.64 Hz, 1H), 7.53 (d, J = 4.88 Hz, 2H), 7.42-7.40 (m, 2H), 7.36 (d, J = 8.92 Hz, 1H), 4.41 (t, J = 4.76 Hz ,2H), 4.28 (t, J = 4.36 Hz, 2H), 2.72 (s, 3H), 1.86 (s, 3H)	632		MS (ESI) m/z 665.30 [M+1]+; 1H-NMR (400 MHz, DMSO-d6), 13.51 (bs, 1H), 8.26 (s ,1H), 8.09 (s, 1H), 7.98 (s, 1H), 7.60 (dd, J = 2.36, 8.88 Hz, 1H), 7.52 (s, 1H), 7.44 (s, 1H),7.42 (d, J = 2.52 Hz, 1H), 7.37 (d, J = 8.88 Hz, 1H), 7.19 (s, 1H), 4.42 (t, J = 5.28 Hz, 2H), 4.28 (t, J = 4.24 Hz, 2H), 2.73 (s, 3H), 1.87 (s, 3H)

633		MS (ESI) m/z 665.23 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 8.35 (s, 1H), 8.19 (d, J = 2.08 Hz, 1H), 8.11 (s, 1H), 7.87 (d, J = 1.52 Hz, 1H), 7.61-7.58 (dd, J = 2.64, 8.88 Hz, 1H), 7.44-7.42 (m, 2H), 7.37 (d, J = 8.88 Hz, 1H), 6.63 (t, J = 2.24 Hz, 1H), 4.41 (t, J = 4.52 Hz, 2H), 4.28 (t, J = 4.12 Hz, 2H), 2.72 (s, 3H), 1.84 (s, 3H)	637		MS (ESI) m/z 725.09 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 8.18 (s,1H), 7.94 (s, 1H), 7.61-7.59 (dd, J = 8.8, 2.4 Hz, 1H), 7.46 (s, 1H), 7.44 (d, J = 2.48 Hz, 1H), 7.36 (d, J = 8.96 Hz, 1H), 4.41 (t, J = 5.2 Hz, 2H), 4.24 (t, J = 5.2 Hz, 2H), 3.94 (s, 2H), 3.40-3.37 (m, 2H), 3.04-2.98 (m, 2H), 2.92 (m, 4H), 2.78 (d, J = 3.52 Hz, 3H), 2.54 (m, 2H), 1.80 (s, 3H), 1.35 (t, J = 7.2 Hz, 3H)
634		MS (ESI) m/z 697.13 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 13.51 (bs, 1H), 9.75 (bs, 1H), 8.23 (s, 1H), 7.92 (s, 1H), 7.61-7.58 (t, J = 6.5 Hz, 1H), 7.42-7.41 (t, J = 6.5 Hz, 2H), 7.37 (d, J = 8.9 Hz, 1H), 4.40 (t, J = 6.2 Hz, 2H), 4.24 (t, J = 6.1 Hz, 2H), 3.83 (m, 2H), 3.49 (m, 2H), 3.24 (m, 2H), 3.03 (m, 2H), 2.28 (s, 3H), 2.71 (s, 3H), 1.82 (s, 3H)	638		MS (ESI) m/z 727.07 [M+1]+; ; 1H NMR (400 MHz, DMSO-d6) δ 12.7 (bs, 1H), 8.09 (s, 1H), 7.98 (s, 1H), 7.59-7.56 (dd, J = 2.8, 9.2 Hz, 1H), 7.40 (d, J = 2.4 Hz, 1H), 7.34 (d, J = 8.8 Hz, 1H), 6.90 (s, 1H), 4.41 (t, J = 6.4 Hz, 2H), 4.28 (t, J = 5.6 Hz, 2H), 4.07 (s, 3H), 3.94 (s, 2H), 3.39 (d, J = 11.2 Hz, 2H), 2.91 (d, J = 11.2 Hz, 4H), 2.78 (d, J = 3.2 Hz, 2H), 2.56 (d, J = 7.6 Hz, 2H), 1.88 (s, 3H)
636		MS (ESI) m/z 642.20 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.87 (bs, 1H), 9.92 (s, 1H), 8.39 (s, 1H), 8.29 (s, 1H), 8.03 (s, 1H), 7.62 (dd, J = 2.40, 8.8 Hz, 1H), 7.57 (s, 1H), 7.42 (d, J = 3.28 Hz, 1H), 7.37 (d, J = 8.92 Hz, 1H), 4.63 (bs, 2H), 4.43 (t, J = 4.84 Hz, 2H), 4.26 (t, J = 4.64 Hz, 2H), 2.96 (s, 6H), 1.76 (s, 3H	640		MS (ESI) m/z 751.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.85 (d, J = 4.9 Hz, 1H), 8.32 (s, 1H), 7.93 (s, 1H), 7.61 (dd, J = 8.9, 2.7 Hz, 1H), 7.53 (d, J = 4.9 Hz, 1H), 7.43 (d, J = 2.6 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 4.41 (t, J = 4.9 Hz, 2H), 4.24 (t, J = 5.0 Hz, 2H), 3.31 (q, J = 10.1 Hz, 2H), 3.07 – 2.58 (m, 6H), 1.75 (s, 3H). Note: piperazine protons were very broad and could not be properly integrated

641	MS (ESI) m/z 642.08 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.74 (d, J = 4.92 Hz, 1H), 8.15 (s, 1H), 7.86 (s, 1H), 7.61 (dd, J = 8.6, 2.4 Hz, 1H), 7.47 (m, 2H), 7.37 (d, J = 9 Hz, 1H), 4.67 (s, 2H), 4.41 (t, J = 5.28 Hz, 2H), 4.25 (t, J = 4.28 Hz, 2H), 2.88 (s, 6H), 2.53 (s, 3H)	644	MS (ESI) m/z 743.07 [M+1]+; ; ; 1H NMR (400 MHz, DMSO-d6) δ 13.2 (bs, 1H), 8.16 (s, 1H), 7.96 (s, 1H), 7.62-7.59 (dd, J = 2.4, 8.8 Hz, 1H), 7.59 (s, 1H), 7.43 (d, J = 2.4 Hz, 1H), 7.37 (d, J = 8.8 Hz, 1H), 4.99 (t, J = 6.0 Hz, 1H), 4.87 (t, J = 6.0 Hz, 1H), 4.42 (t, J = 6.4 Hz, 2H), 4.26 (t, J = 6.8 Hz, 2H), 3.94 (s, 2H), 3.45 (t, J = 6.0 Hz, 2H), 2.93 (m, 4H), 2.78 (s, 3H), 2.50 (m, 2H), 1.76 (s, 3H)
642	MS (ESI) m/z 726.20 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.44 (bs, 1H), 8.27 (s, 1H), 7.95 (s, 1H), 7.59 (dd, J = 8.8, 2.5 Hz, 1H), 7.42-7.41 (m, 2H), 7.35 (d, J = 8.9 Hz, 1H), 4.4 (t, J = 5.9 Hz, 2H), 4.24 (t, J = 5.6 Hz, 2H), 3.83 (s, 2H), 3.47-3.43 (m, 2H), 2.68 (s, 3H), 2.62 (d, J = 10.5 Hz, 2H), 1.89 (d, J = 6.2 Hz, 2H), 1.86 (s, 3H), 1.01 (d, J = 6.2 Hz, 6H)	645	MS (ESI) m/z 729.05 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.04 (bs, 1H), 9.40 (s, 1H), 8.26 (s, 1H), 7.99 (s, 1H), 7.60 (dd, J = 2.28, 8.72 Hz, 1H), 7.53 (bs, 1H), 7.44 (d, J = 2.32 Hz, 1H), 7.36 (d, J = 8.92 Hz, 1H), 5.76-5.65 (d, J = 46.8 Hz, 2H), 4.41 (t, J = 5.16 Hz, 2H), 4.25 (t, J = 5.72 Hz, 2H), 3.94 (s, 2H), 3.40-3.37 (m, 2H), 2.93-2.90 (m, 4H), 2.79 (d, J = 3.32 Hz, 3H), 2.56-2.54 (m, 2H), 1.77 (s, 3H)
643	MS (ESI) m/z 705.27 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.72 (d, J = 4.84 Hz, 1H), 8.05 (s, 1H), 7.75 (d, J = 8.20 Hz, 1H), 7.69 (d, J = 8.48 Hz, 1H), 7.65 (s, 1H), 7.57 (d, J = 4.76 Hz, 1H), 4.88 (s, 2H), 3.86 (s, 2H), 2.50-2.32 (m, 8H, merged with moisture peak in DMSO), 2.17 (s, 3H), 2.10 (s, 3H), 1.23 (s, 3H)	649	MS (ESI) m/z 697.18 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.52 (bs, 2H), 8.22 (s, 1H), 7.59 (s, 1H), 7.61 (dd, J = 2.76, 8.64 Hz , 1H), 7.42 (s, 2H), 7.37 (d, J = 9.0, 1H), 4.42 (t, J = 4.44 Hz, 2H), 4.26 (t, J = 4.96 Hz, 2H), 3.93 (s, 2H), 3.07 (s, 4H), 2.70 (m, 6H), 1.84 (s , 3H)

652		MS (ESI) m/z 667.97 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.29 (s, 1H), 7.93 (s, 1H), 7.61 (dd, J = 2.56 Hz, 8.8 Hz, 1H), 7.41 (s, 2H), 7.37 (d, J = 9.0 Hz, 1H), 4.39 (m, 2H), 4.26 (m, 3H), 3.96 (bs, 2H), 3.55 (bs, 2H), 2.70 (s, 3H), 2.35 (s, 3H), 1.85 (s, 3H)
655		MS (ESI) m/z 715.3 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.84 (d, J = 4.8 Hz, 1H), 8.25 (s, 1H), 7.96 (s, 1H), 7.61 (dd, J = 8.9, 2.7 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.6 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 4.89 (dt, J = 47.3, 4.5 Hz, 2H), 4.41 (t, J = 5.0 Hz, 2H), 4.25 (t, J = 5.0 Hz, 2H), 4.03 – 3.88 (m, 2H), 3.74 – 3.09 (m, 8H), 1.77 (s, 3H)
660		LCMS (ESI) m/z 553.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.14 (d, J = 2.1 Hz, 1H), 8.71 (d, J = 2.1 Hz, 1H), 8.31 (dd, J = 1.8, 0.7 Hz, 1H), 8.23 (t, J = 2.1 Hz, 1H), 7.80 (dd, J = 1.7, 0.8 Hz, 1H), 7.50 – 7.39 (m, 2H), 7.26 (d, J = 8.9 Hz, 1H), 4.43 – 4.31 (m, 4H), 2.11 (s, 3H)
661		LCMS (ESI) m/z 569.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.75 (d, J = 4.3 Hz, 1H), 8.37 – 8.31 (m, 1H), 8.07 (dt, J = 1.7, 0.8 Hz, 1H), 7.98 (s, 1H), 7.64 – 7.47 (m, 3H), 7.29 (d, J = 9.0 Hz, 1H), 7.22 (d, J = 4.2 Hz, 1H), 4.35 (t, J = 5.0 Hz, 2H), 4.21 (t, J = 4.9 Hz, 2H), 1.79 (s, 3H)
662		LCMS (ESI) m/z 553.0 [M+1]+ ; 1H NMR (400 MHz, DMSO-d6) δ 8.71 (dd, J = 5.0, 0.8 Hz, 1H), 8.34 – 8.28 (m, 1H), 8.05 (dd, J = 1.7, 0.8 Hz, 1H), 7.88 (dd, J = 1.8, 0.8 Hz, 1H), 7.57 (dd, J = 5.0, 1.7 Hz, 1H), 7.52 – 7.40 (m, 2H), 7.26 (d, J = 8.9 Hz, 1H), 4.44 – 4.31 (m, 4H), 2.96 (s, 3H), 2.13 (s, 3H).5 (t, J = 4.7 Hz, 2H), 1.69 (s, 3H)
663		LCMS (ESI) m/z 557.0 [M+1]+ 1H NMR (400 MHz, DMSO-d6) δ 8.60 (d, J = 4.7 Hz, 1H), 8.32 (s, 1H), 8.11 (s, 1H), 7.51 (dd, J = 8.9, 2.7 Hz, 1H), 7.33 (d, J = 2.6 Hz, 1H), 7.28 (d, J = 9.0 Hz, 1H), 7.22 (d, J = 4.4 Hz, 1H), 6.32 (d, J = 1.6 Hz, 1H), 4.34 (s, 2H), 4.23 (s, 2H), 1.81 (s, 3H)

664		LCMS (ESI) m/z 615.0 [M+1]+ 1H NMR (400 MHz, DMSO-d6) δ 8.65 (d, J = 1.9 Hz, 1H), 8.35 (d, J = 1.9 Hz, 1H), 8.32 – 8.28 (m, 1H), 8.01 (dd, J = 1.7, 0.8 Hz, 1H), 7.49 – 7.40 (m, 2H), 7.25 (dd, J = 8.6, 0.6 Hz, 1H), 4.36 (dd, J = 11.4, 4.4 Hz, 4H), 3.85 (s, 3H), 2.19 (s, 3H)	668		LCMS (ESI) m/z 613.3 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.33 (d, J = 1.7 Hz, 1H), 7.93 (dt, J = 1.7, 0.8 Hz, 1H), 7.56 (dd, J = 8.9, 2.7 Hz, 1H), 7.42 – 7.29 (m, 2H), 4.39 (t, J = 5.0 Hz, 1H), 4.24 (t, J = 5.0 Hz, 1H), 2.66 (s, 2H), 2.35 (s, 2H), 1.92 (s, 2H)
666		LCMS (ESI) m/z 653.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.88 (d, J = 4.7 Hz, 1H), 8.38 – 8.32 (m, 1H), 8.17 – 8.05 (m, 1H), 7.61 – 7.51 (m, 2H), 7.42 (d, J = 2.6 Hz, 1H), 7.32	670		LCMS (ESI) m/z 670.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 7.57 (dd, J = 8.9, 2.7 Hz, 1H), 7.43 – 7.36 (m, 2H), 7.32 (d, J = 9.0 Hz, 1H), 4.38 (t, J = 4.9 Hz, 2H), 2.67 (s, 4H), 2.32 (s, 3H), 1.87 (s, 3H)
667		LCMS (ESI) m/z 627.3 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.75 (d, J = 5.0 Hz, 1H), 8.35 (dd, J = 1.7, 0.6 Hz, 1H), 7.97 (dt, J = 1.7, 0.8 Hz, 1H), 7.57 (dd, J = 8.9, 2.7 Hz, 1H), 7.49 (d, J = 5.0 Hz, 1H), 7.42 (d, J = 2.6 Hz, 1H), 7.32 (d, J = 9.0 Hz, 1H), 4.37 (t, J = 5.0 Hz, 1H), 4.23 (t, J = 5.1 Hz, 1H), 3.85 (q, J = 6.8 Hz, 0H), 1.83 (s, 2H), 0.99 (d, J = 6.8 Hz, 3H)	672		LCMS (ESI) m/z 625.9 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.33 (d, J = 1.7 Hz, 1H), 8.17 (s, 1H), 7.92 (d, J = 1.7 Hz, 1H), 7.56 (dd, J = 8.9, 2.7 Hz, 1H), 7.44 – 7.38 (m, 2H), 7.32 (d, J = 9.0 Hz, 1H), 4.36 (t, J = 5.1 Hz, 2H), 4.23 t, J = 5.1 Hz, 2H), 1.78 (s, 3H)

675		LCMS (ESI) m/z 690.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.36 (s, 1H), 8.03 (s, 1H), 7.87 (t, J = 7.8 Hz, 1H), 7.56 (dd, J = 8.9, 2.7 Hz, 1H), 7.46 – 7.36 (m, 5H), 7.33 (d, J = 9.0 Hz, 1H), 4.37 (s, 2H), 4.24 (s, 2H), 2.69 (s, 3H), 2.50 (s, 4H), 1.80 (s, 3H)	687		LCMS (ESI) m/z 690.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.34 (s, 1H), 7.85 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.43 (s, 1H), 7.41 (d, J = 2.7 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.86 (t, J = 12.5 Hz, 4H), 4.39 (t, J = 5.0 Hz, 2H), 4.22 (t, J = 5.0 Hz, 2H), 2.72 (s, 3H), 1.79 (s, 3H)
684		LCMS (ESI) m/z 708.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.36 (s, 1H), 8.06 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.56 (dd, J = 9.3, 2.3 Hz, 1H), 7.43 (dd, J = 6.7, 4.0 Hz, 3H), 7.36 (d, J = 9.0 Hz, 1H), 4.41 (bs, 2H), 4.28 (bs, 2H), 2.73 (s, 3H), 2.56 (s, 3H), 1.85 (s, 3H)	705		MS (ESI) m/z 639.0 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ / ppm = 9.81-9.70 (b, 1H), 8.63 (d, J = 4.7 Hz, 1H), 8.09 (s, 1H), 7.72 (d, J = 5.4 Hz, 1H), 7.56 (dd, J = 8.9, 2.6 Hz, 1H), 7.38 (d, J = 2.6 Hz, 1H), 7.37 (d, J = 5.4 Hz, 1H), 7.33 (d, J = 8.9 Hz, 1H), 7.22 (d, J = 4.7 Hz, 1H), 4.38 (t, J = 4.9 Hz, 2H), 4.27 (t, J = 4.9 Hz, 2H), 3.92-3.82 (m, 2H), 3.59-3.50 (m, 2H), 3.30-3.20 (m, 2H), 3.14-3.01 (m, 2H), 2.91 (bs, 3H), 1.90 (s, 3H)
686		LCMS (ESI) m/z 704.0 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.57 (d, J = 5.4 Hz, 1H), 8.27 (s, 1H), 8.08 (s, 1H), 7.57 (dd, J = 8.9, 2.7 Hz, 1H), 7.50 – 7.38 (m, 3H), 7.33 (d, J = 9.0 Hz, 1H), 4.39 (m, 2H), 4.25 (m 2H), 2.70 (s, 3H), 2.61 (s, 3H), 2.00 (s, 3H), 1.81 (s, 3H)	706		MS (ESI) m/z 650.8 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.71 – 8.64 (m, 2H), 8.29 (d, J = 0.6 Hz, 1H), 7.90 (dd, J = 9.2, 3.0 Hz, 1H), 7.78 (d, J = 5.6 Hz, 1H), 7.56 (dd, J = 8.9, 2.7 Hz, 1H), 7.48 (d, J = 5.5 Hz, 1H), 7.41 (d, J = 2.7 Hz, 1H), 7.33 (d, J = 8.9 Hz, 1H), 7.26 (d, J = 4.7 Hz, 1H), 4.43 – 4.35 (m, 2H), 4.34 – 4.15 (m, 1H), 2.19 (d, J = 1.0 Hz, 3H), 1.88 (s, 3H)

708		MS (ESI) m/z 682.0 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.28 (s, 1H), 7.90 (s, 1H), 7.63-7.56 (m, 1H), 7.46-7.38 (m, 2H), 7.35 (d, J = 8.96 Hz, 1H), 4.49-4.32 (m, 2H), 4.31-4.18 (m, 2H), 3.70-3.66 (m, 1H), 3.26-3.22 (m, 2H), 2.69 (s, 3H), 2.32-2.22 (m, 2H), 2.22-2.09 (m, 2H), 2.07 (s, 3H), 1.80 (s, 3H)	
709		MS (ESI) m/z 684.07 [M+1]+; 1H NMR (400 MHz, DMSO-d6) 8.23 (s, 1H), 7.94 (s, 1H), 7.60 (dd, J = 8.80, 2.40 Hz, 1H), 7.44-7.38 (m, 2H), 7.36 (d, J = 8.96 Hz, 1H), 4.40 (t, J = 4.76 Hz, 2H), 4.25 (t, J = 4.24 Hz, 2H), 3.05-3.01 (m, 4H), 2.69 (s, 3H), 2.50-2.30 (m, 6H), 1.91-1.78 (m, 5H)	
711		MS (ESI) m/z 670.05 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.28 (s, 1H), 7.89 (s, 1H), 7.59 (dd, J = 8.80, 2.40, 1H), 7.45-7.40 (m, 2H), 7.35 (d, J = 8.84 Hz, 1H), 4.39 (t, J = 5.40 Hz, 2H),), 4.30-4.22 (m, 2H) 3.72-3.67 (m, 1H), 2.70 (s, 3H), 2.16 (s, 6H), 1.80 (s, 3H), 1.55 (d, J = 6.68 Hz, 3H)	
713		MS (ESI) m/z 710.17 [M+1]+; 1H NMR (400 MHz, DMSO-d6+D2O) δ 9.18 (bs, 1H), 8.20 (s, 1H), 7.97 (s, 1H), 7.61-7.58 (dd, J = 2.4, 8.8 Hz, 1H), 7.43 (s, 1H), 7.37 (d, J = 9.2 Hz, 1H), 4.42 (t, J = 5.6 Hz, 2H), 4.26 (t, J = 3.6 Hz, 2H), 3.43 (bs, 3H), 3.06 (d, J = 6.8 Hz, 2H), 2.92-2.86 (m, 2H), 2.73-2.70 (m, 3H), 2.02 (bs, 1H), 1.83-1.78 (m, 5H), 1.63-1.54 (m, 2H)	
714		MS (ESI) m/z 696.11 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.50 (bs, 1H), 8.19-8.15 (m, 2H), 7.97 (s, 1H), 7.61-7.58 (dd, J = 2.8, 9.2 Hz, 1H), 7.43-7.42 (m, 2H), 7.37 (d, J = 8.8 Hz, 1H), 4.42 (t, J = 4.8 Hz, 2H), 4.26 (t, J = 4.4 Hz, 2H), 3.29 (d, J = 11.2 Hz, 2H), 3.06 (d, J = 11.2 Hz, 2H), 2.83-2.78 (m, 2H), 2.70 (s, 3H), 2.11-2.01 (m, 1H), 1.82 (s, 3H), 1.75 (d, J = 12.4 Hz, 2H), 1.59-1.50 (m, 2H)	
717		MS (ESI) m/z 621.98 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.69 (d, J = 4.76 Hz, 1H), 8.65 (s, 1H), 8.30 (bs, 2H), 7.75 (d, J= 8.32, 1H), 7.69 (m, 2H), 7.54 (d, J=4.72 Hz, 1H), 4.85 (s, 2H), 4.48 (s, 2H), 2.77 (s, 6H)	

719		MS (ESI) m/z 710.06 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.99 (s, 1H), 8.10 (s, 1H), 7.65 (s, 1H), 7.49 (dd, J=8.76, 2.48 Hz, 1H), 7.28-7.24 (m, 3H), 7.13 (d, J = 7.32 Hz, 1H), 4.34 (t, J=5.16 Hz, 2H), 4.22 (t, J=5.12 Hz, 2H), 3.93 (s, 2H), 3.37 (d, J=11.32, 2H,), 3.33-3.29 (m, 2H, merged with moisture peak in DMSO), 2.90-2.88 (m, 4H), 2.78 (s, 3H), 2.67 (s, 3H), 1.72 (s, 3H)
738		MS (ESI) m/z 753.46 [M+1]+; ; 1H-NMR (400 MHz, CD3OD) δ 13.50 (bs, 1H), 8.94 (t, J = 8.44 Hz, 1H), 8.21 (s, 1H), 7.96 (s, 1H), 7.57 (dd, J = 2.25, 8.88 Hz, 1H),7.42 (s, 1H), 7.36 (d, J = 8.80 Hz, 1H), 4.41 (t, J = 4.32 Hz, 2H), 4.25 (t, J = 3.24 Hz, 2H), 3.96 (s, 2H),.3.50 (d, J = 10.48 Hz, 2H), 2.95 (d, J = 11.64 Hz, 2H), 2.82 (d, J = 10.52 Hz, 2H), 2.70 (s, 3H), 2.65 (d, J = 11.68 Hz, 2H). 1.85 (s, 3H), 1.30 (s, 9H)
735		MS (ESI) m/z 690.35 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.67 (d, J = 3.72 Hz, 1H), 8.29 (s, 1H), 8.09 (s, 1H), 7.86 (d, J = 7.76 Hz, 1H), 7.60 (dd, J = 2.52, 8.84 Hz, 1H), 7.50 (d, J = 4.96 Hz, 1H), 7.48 (s, 1H), 7.44 (d, J = 2.6 Hz, 1H), 7.38 (d, J = 8.92 Hz, 1H), 4.43 (t, J = 6.12 Hz, 2H), 4.27 (t, J = 5.32, 2H), 2.73 (s, 3H), 2.24 (s, 3H), 1.84 (s, 3H)
739		MS (ESI) m/z 761.12 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.22 (s, 1H), 7.96 (s, 1H), 7.60 (dd, J = 2.44, 8.88 Hz, 1H), 7.43 (s, 1H), 7.42 (s, 1H), 7.36 (d, J = 8.96 Hz, 1H), 6.58-6.31 (m, 1H), 4.41 (t, J = 4.56 Hz, 2H), 4.25 (t, J = 4.64 Hz, 2H), 3.95 (bs, 2H), 3.60-3.45 (m, 2H), 3.32-3.11 (m, 4H), 2.77-2.72 (m, 4H), 2.70 (s, 3H), 1.83 (s, 3H)
736		MS (ESI) m/z 690.04 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.65 (d, J = 4.0 Hz, 1H), 8.56 (s, 1H), 8.29 (s, 1H), 8.09 (s, 1H), 7.60 (dd, J = 8.8, 2.5 Hz, 1H), 7.56 (d, J = 5 Hz, 1H), 7.46 (s, 1H), 7.45 (d, J = 2.5 Hz, 1H), 7.37 (d, J = 8.9 Hz, 1H), 4.43 (bs, 2H), 4.28-4.26 (m, 2H), 2.73 (s, 3H), 2.11 (s, 3H), 1.84 (s, 3H)	740		MS (ESI) m/z 737.12 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.61 (bs, 1H), 9.01 (bs, 1H), 8.23 (s, 1H), 7.96 (s, 1H), 7.59 (dd, J = 8.88, 2.56 Hz, 1H), 7.42 (s, 2H), 7.37 (d, J = 8.96 Hz, 1H), 4.41 (t, J = 4.16 Hz, 2H), 4.25 (t, J = 4.96 Hz, 2H), 3.93 (s, 2H), 3.43 (s, 2H), 3.32-3.29 (m, 2H), 2.98-2.88 (m, 2H), 2.72 (d, J = 3.60, 3H), 2.69 (s, 3H), 2.18-2.16 (m, 2H), 1.91 (d, J = 8.2 Hz, 2H), 1.84 (s, 3H)

747		MS (ESI) m/z 690.06 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.73 (s, 1H), 8.30 (d, J = 10.6 Hz, 1H), 8.07 (t, J = 9.7 Hz, 2H), 7.66 (bs, 1H), 7.57 (s, 2H), 7.44 (bs, 2H), 7.36-7.29 (m, 1H), 4.39 (bs, 2H), 4.26 (bs, 2H), 3.02 (bs, 2H), 1.77 (d, J = 11.0 Hz, 3H), 1.35 (s, 3H)	754		MS (ESI) m/z 622.96 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 16.04 (s, 1H), 8.18 (s, 1H), 8.02 (s, 1H), 8.01 (s, 1H), 7.71 (d, J = 8.36 Hz, 1H), 7.65 (dd, J = 8.36,1.88 Hz, 1H), 7.58 (d, J = 1.72 Hz, 1H), 4.90 (s, 2H) 3.64 (s, 3H), 2.73 (s, 3H), 2.36 (s, 3H)
751		MS (ESI) m/z 693.99 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.86 (s, 1H), 8.71 (d, J = 4.6 Hz, 1H), 8.33 (s, 1H), 8.13 (s, 1H), 7.72 (t, J = 10.4 Hz, 1H), 7.60 (dd, J = 8.84, 2.28 Hz, 1H), 7.45-7.35 (m, 2H), 7.36 (d, J = 8.9 Hz, 1H), 4.44-4.24 (m, 4H), 2.72 (s, 3H), 1.87 (s, 3H)	774		MS (ESI) m/z 703.98 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.59 (s, 1H), 8.32 (s, 1H), 8.05 (s, 1H), 7.92 (d, J = 7.2 Hz, 1H), 7.60 (dd, J = 2.56, 8.88 Hz, 1H), 7.54 (d, J = 8.04 Hz, 1H), 7.45 (s, 1H), 7.42 (d, J = 2.60 Hz, 1H), 7.36 (d, J = 8.96 Hz, 1H) 4.42 (t, J = 4.64 Hz, 2H), 4.27 (t, J = 4.20 Hz, 2H), 2.90 (q, J = 7.52 Hz, 2H), 2.73 (s, 3H), 1.87 (s, 3H), 1.32 (t, J = 7.60 Hz, 3H)
753		MS (ESI) m/z 629.08 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 16.55 (s, 1H), 8.00- 7.83 (m, 3H), 7.60-7.52 (m, 1H), 7.40- 7.28 (m, 2H), 4.49- 4.23 (m, 4H), 3.70 (s, 3H), 2.69 (s, 3H), 2.16 (s, 3H)	775		MS (ESI) m/z 690.05 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.64 (s, 1H), 8.52 (s, 1H), 8.29 (s, 1H), 8.04 (s, 1H), 7.86 (s, 1H), 7.59 (dd, J = 8.84, 2.52 Hz, 1H), 7.45 (s, 1H), 7.41 (d, J = 2.56 Hz, 1H), 7.36 (d, J = 8.96 Hz , 1H), 4.42 (t, J = 5.76 Hz, 2H), 4.28 (t, J = 4.24 Hz, 2H), 2.73 (s, 3H), 2.43 (s, 3H), 1.87 (s, 3H)

776		MS (ESI) m/z 704.04 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.42 (s, 1H), 8.06 (s, 1H), 7.92 (t, J = 7.80 Hz, 1H), 7.59 (dd, J = 8.80, 2.40 Hz, 1H), 7.50-7.39 (m, 4H), 7.36 (d, J = 8.88 Hz, 1H), 4.40 (s, 2H), 4.27 (s, 2H), 2.80 (q, J = 7.44 Hz, 2H), 2.72 (s, 3H), 1.84 (s, 3H), 1.22 (q, J = 7.44 Hz, 3H)
789		MS (ESI) m/z 670.09 [M+1]+; 1H NMR (400 MHz, DMSO-d6 with D2O) δ 8.24 (s, 1H), 7.97 (s, 1H), 7.56 (dd, J = 8.88, 2.52 Hz, 1H), 7.39-7.37 (m, 2H), 7.31 (d, J = 8.96 Hz, 1H), 4.39-4.34 (m, 2H), 4.22 (bs, 2H), 3.05 (s, 3H), 2.84 (s, 3H), 2.69 (s, 3H), 1.75 (s, 3H)
777		MS (ESI) m/z 693.96 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.85 (dd, J=5.88, 7.96 Hz, 1H), 8.79 (d, J=10.04 Hz, 1H), 8.34 (s, 1H), 8.12 (s, 1H), 7.65-7.58 (m, 2H), 7.45 (s, 1H), 7.43 (d, J=2.56 Hz, 1H), 7.37 (d, J=8.96 Hz, 1H), 4.45-4.26 (m, 4H), 2.72 (s, 3H), 1.87 (s, 3H)
790		MS (ESI) m/z 622.9 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.28 (s, 1H), 7.95 (s, 1H), 7.59 (dd, J=8.84, 2.52 Hz, 1H), 7.42 (s, 1H), 7.41 (d, J=2.56 Hz, 1H), 7.35 (d, J=8.96 Hz, 1H), 5.25 (s, 1H), 4.40 (t, J=4.52 Hz, 2H), 4.25 (t, J=2.44 Hz, 2H), 2.70 (s, 3H), 1.79 (s, 3H)
779		MS (ESI) m/z 679.00 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.37 (s, 1H), 8.02 (s, 1H), 7.87 (d, J= 1.92 Hz, 1H), 7.59 (dd, J = 8.88, 2.62 Hz, 1H), 7.42 (d, J = 3.0 Hz, 2H), 7.35 (d, J = 8.96 Hz, 1H), 6.48 (s, 1H), 4.40 (t, J = 6.04 Hz, 2H), 4.25 (t, J = 5.2 Hz, 2H), 3.93 (s, 3H), 2.70 (s, 3H), 1.82 (s, 3H)
808		MS (ESI) m/z 506.4 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.18 (s, 1H), 7.34 – 7.24 (m, 2H), 6.98 – 6.93 (m, 2H), 4.49 (t, J = 5.2 Hz, 2H), 4.31 (t, J = 5.2 Hz, 2H), 3.85 (t, J = 12.3 Hz, 2H), 3.53 (d, J = 11.8 Hz, 2H), 3.17 (d, J = 12.9 Hz, 2H), 3.05 (d, J = 11.6 Hz, 2H), 2.88 (s, 3H), 2.77 (s, 3H)

832		MS (ESI) m/z = 584.1 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ /ppm = 9.86-9.70 (b, 1H), 8.20 (s, 1H), 7.67 (d, J = 2.6 Hz, 1H), 7.40 (dd, J = 8.9, 2.6 Hz, 1H), 7.17 (d, J = 8.9 Hz, 1H), 4.55 (t, J = 4.5 Hz, 2H), 4.39 (t, J = 4.5 Hz, 2H), 3.84 (bt, J = 12.0 Hz, 2H), 3.53 (bd, J = 12.0 Hz, 2H), 3.17 (d, J = 12.5 Hz, 2H), 3.12-2.97 (m, 2H), 2.92-2.84 (m, 6H)
833		MS (ESI) m/z = 582.1 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ /ppm = 9.84-9.70 (b, 1H), 8.22 (s, 1H), 7.37 (dd, J = 8.8, 2.7, 1H), 7.34-7.24 (m, 5H), 7.23 (d, J = 2.7 Hz, 1H), 7.17 (d, J = 8.8 Hz, 1H), 4.41-4.30 (m, 4H), 3.86 (bt, J = 12.6 Hz, 2H), 3.54 (bd, J = 11.5 Hz, 2H), 3.18 (d, J = 12.5 Hz, 2H), 3.12-2.99 (m, 2H), 2.89 (bs, 3H), 2.23 (s, 3H)
834		MS (ESI) m/z = 683.3 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ /ppm = 9.81-9.69 (b, 1H), 8.84 (d, J = 4.7 Hz, 1H), 8.23 (s, 1H), 7.96 (s, 1H), 7.61 (dd, J = 8.9, 2.7 Hz, 1H), 7.48 (d, J = 4.7 Hz, 1H), 7.43 (d, J = 2.7 Hz, 1H), 7.37 (d, J = 8.9 Hz, 1H), 4.41 (t, J = 5.1 Hz, 2H), 4.25 (t, J = 5.1 Hz, 2H), 3.92-3.82 (m, 2H), 3.57 (bd, J = 11.2 Hz, 2H), 3.26 (bd, J = 13.3 Hz, 2H), 3.15-3.02 (m, 2H), 2.92 (bs, 3H), 1.77 (s, 3H)
835		MS (ESI) m/z = 611.3 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ /ppm = 9.98-9.85 (b, 1H), 8.15 (s, 1H), 7.73-7.64 (bs, 2H), 7.55 (dd, J = 8.9, 2.8 Hz, 1H), 7.46 (d, J = 2.8 Hz, 1H), 7.31 (d, J = 8.9 Hz, 1H), 4.43 (bs, 4H), 3.85 (bt, J = 11.1 Hz, 2H), 3.54 (bd, J = 11.4 Hz, 2H), 3.17 (bd, J = 12.8 Hz, 2H), 3.12-2.99 (m, 2H), 2.89 (s, 3H), 2.62 (s, 6H), 2.37 (s, 3H)
836		MS (ESI) m/z = 653.0 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ /ppm = 9.85-9.74 (b, 1H), 8.06 (s, 1H), 7.70 (d, J = 5.4 Hz, 1H), 7.55 (dd, J = 8.9, 2.6 Hz, 1H), 7.36 (d, J = 2.6 Hz, 1H), 7.32 (d, J = 8.9 Hz, 1H), 7.25 (d, J = 5.4 Hz, 1H), 7.18 (s, 1H), 4.38 (t, J = 4.7 Hz, 2H), 4.28 (t, J = 4.7 Hz, 2H), 3.87 (bt, J = 13 Hz, 2H), 3.56 (bd, J = 11.7 Hz, 2H), 3.25 (bd, J = 13 Hz, 2H), 3.15-3.01 (m, 2H), 2.91 (bs, 3H), 2.62 (s, 3H), 1.96 (s, 3H)
847		LCMS: 694.4.5 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ 8.88 (d, J = 4.8 Hz, 1H), 8.67 (d, J = 2.9 Hz, 1H), 8.29 (s, 1H), 8.13 (s, 1H), 7.89 (dd, J = 9.0, 2.8 Hz, 1H), 7.61 (dd, J = 8.9, 2.7 Hz, 1H), 7.53 (d, J = 4.8 Hz, 1H), 7.44 (d, J = 2.7 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 4.43 (q, J = 4.9 Hz, 2H), 4.28 (q, J = 6.6, 5.9 Hz, 2H), 2.22 (s, 3H), 1.79 (s, 3H)

852		LCMS: 669.6 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ 9.70 (s, 1H), 8.59 (d, J = 4.7 Hz, 1H), 8.05 (s, 1H), 7.68 (d, J = 5.5 Hz, 1H), 7.52 (dd, J = 8.9, 2.7 Hz, 1H), 7.38 – 7.26 (m, 3H), 7.18 (d, J = 4.7 Hz, 1H), 4.35 (t, J = 5.2 Hz, 2H), 4.24 (t, J = 4.9 Hz, 2H), 3.92 (d, J = 12.8 Hz, 2H), 3.76 (t, J = 5.2 Hz, 2H), 3.60 (d, J = 12.0 Hz, 2H), 3.23 (dd, J= 26.4, 8.6 Hz, 4H), 3.09 (s, 3H), 1.86 (s, 3H)	856		LCMS: 720.9 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ 9.81 (d, J = 9.6 Hz, 1H), 8.59 (s, 1H), 8.09 (s, 1H), 7.79 –7.63 (m, 3H), 7.50 (s, 1H), 4.85 (s, 2H), 4.07 – 3.92 (m, 2H), 3.87 – 3.74 (m, 2H), 3.66 (d, J = 11.7 Hz, 2H), 3.29 (d, J = 18.2 Hz, 4H), 3.14 (d, J = 11.5 Hz, 2H), 2.67 (s, 3H), 2.23 (s, 3H)
853		LCMS: 669.6 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ 8.61 (d, J = 4.7 Hz, 1H), 8.08 (s, 1H), 7.70 (d, J = 5.5 Hz, 1H), 7.52 (dd, J = 8.9, 2.7 Hz, 1H), 7.42 – 7.34 (m, 2H), 7.29 (d, J = 9.0 Hz, 1H), 7.19 (d, J = 4.7 Hz, 1H), 4.43 (t, J = 5.4 Hz, 2H), 4.35 (t, J = 5.0 Hz, 2H), 4.23 (t, J = 5.0 Hz, 2H), 3.14 (s, 5H), 3.01 (s, 2H), 2.83 (s, 5H), 1.83 (s, 3H)	859		LCMS: 707.4 [M+H;]+. 1H NMR (400 MHz, DMSO-d6) δ 9.79 (s, 1H), 8.77 (d, J= 4.8 Hz, 1H), 8.59 (s, 1H), 8.11 (s, 1H), 7.76 (d, J= 8.3 Hz, 1H), 7.72 – 7.66 (m, 2H), 7.57 (d, J= 4.8 Hz, 1H), 4.87 (s, 2H), 3.98 (d, J= 12.8 Hz, 2H), 3.80 (t, J= 5.2 Hz, 2H), 3.72 – 3.53 (m, 2H), 3.39 – 3.21 (m, 4H), 3.21 – 3.03 (m, 1H), 2.16 (s, 3H)
855		MS (ESI) m/z 625.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.79 (d, J = 27.2 Hz, 2H), 8.62 (d, J = 4.7 Hz, 1H), 8.08 (s, 1H), 7.72 (d, J = 5.5 Hz, 1H), 7.55 (dd, J = 8.9, 2.7 Hz, 1H), 7.44 – 7.26 (m, 3H), 7.21 (d, J = 4.7 Hz, 1H), 4.38 (t, J = 5.0 Hz, 2H), 4.27 (t, J = 5.0 Hz, 2H), 3.38 (s, 2H), 3.23 (s, 1H), 3.04 (s, 2H), 1.89 (s, 3H)	867		MS (ESI) m/z 732.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.22 (s, 1H), 7.91 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.43 (s, 1H), 7.42 (d, J = 2.7 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.40 (t, J = 4.9 Hz, 2H), 4.24 (t, J = 5.0 Hz, 2H), 3.98 (t, J = 11.9 Hz, 2H), 3.50 (d, J = 13.5 Hz, 2H), 3.34 (d, J = 13.5 Hz, 2H), 3.18 (d, J = 12.0 Hz, 2H), 2.72 (s, 3H), 1.81 (s, 3H)

870		MS (ESI) m/z 650.8 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.71 – 8.64 (m, 2H), 8.29 (d, J = 0.6 Hz, 1H), 7.90 (dd, J = 9.2, 3.0 Hz, 1H), 7.78 (d, J = 5.6 Hz, 1H), 7.56 (dd, J = 8.9, 2.7 Hz, 1H), 7.48 (d, J = 5.5 Hz, 1H), 7.41 (d, J = 2.7 Hz, 1H), 7.33 (d, J = 8.9 Hz, 1H), 7.26 (d, J = 4.7 Hz, 1H), 4.43 – 4.35 (m, 2H), 4.34 – 4.15 (m, 1H), 2.19 (d, J = 1.0 Hz, 3H), 1.88 (s, 3H)
876		LCMS (ESI) m/z 678.8 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.24 (s, 1H), 7.96 (s, 1H), 7.57 (dd, J = 8.9, 2.7 Hz, 1H), 7.43 – 7.36 (m, 2H), 7.33 (d, J = 9.0 Hz, 1H), 4.38 (t, J = 4.9 Hz, 2H), 4.23 (t, J = 4.9 Hz, 2H), 2.68 (s, 3H), 1.76 (s, 3H)
879		LCMS (ESI) m/z 697.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.94 (s, 1H), 8.81 (s, 1H), 7.93 (s, 1H), 7.61 (dd, J = 8.9, 2.7 Hz, 1H), 7.49 – 7.34 (m, 3H), 4.41 (s, 2H), 4.26 (s, 2H), 3.79 (s, 7H), 3.40 (d, J = 12.1 Hz, 2H), 3.18 (d, J = 12.2 Hz, 2H), 3.05 (s, 2H), 2.72 (s, 3H), 2.42 (s, 3H), 1.97 (s, 3H)
887		LCMS (ESI) m/z 682.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 11.8 Hz, 1H), 8.76 (d, J = 4.9 Hz, 1H), 8.41 (d, J = 11.5 Hz, 1H), 7.94 (s, 1H), 7.58 (dd, J= 8.9, 2.7 Hz, 1H), 7.49 (d, J = 4.9 Hz, 1H), 7.39 (d, J = 2.7 Hz, 1H), 7.34 (d, J = 9.0 Hz, 1H), 4.40 (t, J = 5.1 Hz, 2H), 4.22 (t, J = 5.0 Hz, 2H), 3.66 (s, 2H), 3.58 (s, 1H), 3.45 (d, J = 12.3 Hz, 2H), 3.35 (s, 1H), 3.15 – 3.08 (m, 1H), 3.05 (d, J = 12.2 Hz, 1H), 2.75 (d, J = 13.4 Hz, 2H), 2.30 (s, 3H), 1.85 (d, J = 17.3 Hz, 1H), 1.84 (s, 3H
899		MS (ESI) m/z 643.06 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 7.92 (s, 1H), 7.90 (s, 1H), 7.57 (dd, J = 8.80, 2.56 Hz, 1H), 7.31-7.30 (m, 2H), 4.41 (t, J = 4.80 Hz, 2H), 4.33 (t, J= 4.80 Hz, 2H), 3.69 (s, 3H), 2.64 (s, 3H), 2.31(s, 3H), 2.27 (s, 3H)
901		MS (ESI) m/z 690.05 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.71 (s, 1H), 8.65 (d, J = 4.60 Hz, 1H), 8.29 (s, 1H), 8.10 (s, 1H), 7.60 (d, J = 8.88, 2.44 Hz, 1H), 7.48 (bs, 1H), 7.46 (s, 1H), 7.44 (d, J = 2.48 Hz, 1H), 7.36 (d, J = 8.96 Hz, 1H) 4.42 (t, J = 6.20 Hz, 2H), 4.32-4.22 (m, 2H), 2.73 (s, 3H), 2.07 (s, 3H), 1.84 (s, 3H)

902		MS (ESI) m/z 704.06 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.41 (bs, 1H), 8.45 (s, 1H), 8.25 (s, 1H), 8.08 (s, 1H), 7.63-7.57 (m, 2H), 7.46-7.40 (m, 2H), 7.36 (d, J = 8.80 Hz, 1H), 4.45-4.35 (m, 2H), 4.35-4.23 (m, 2H), 2.72 (s, 3H), 2.35 (s, 3H), 2.15 (s, 3H), 1.83 (s, 3H)	905		MS (ESI) m/z 704.03 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.36 (s, 1H), 8.04 (s, 1H), 7.59 (dd, J = 8.84 Hz, 2.60 Hz, 1H), 7.43 (s, 2H), 7.36 (d, J = 8.96 Hz, 1H), 7.30 (s, 1H), 7.25 (s, 1H), 4.40 (s, 2H), 4.27 (s, 2H), 2.72 (s, 3H), 2.50 (s, 3H), 2.39 (s, 3H), 1.82 (s, 3H)
903		MS (ESI) m/z 704.16 [M+1] +; 1H NMR (400 MHz, DMSO-d6) 8.46 (s, 1H), 8.30 (s, 1H), 8.24 (s, 1H), 7.84 (bs, 1H), 7.58-7.49 (m, 1H), 7.37 (s, 1H), 7.29 (d, J = 8.8 Hz, 1H), 7.16 (s, 1H), 4.37 (t, J = 4.68 Hz, 2H), 4.27 (t, J = 4.2 Hz, 2H), 2.64 (s, 3H), 2.31 (s, 3H), 1.95 (s, 3H), 1.85 (s, 3H)	906		MS (ESI) m/z 704.03 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.52 (bs, 1H), 8.37 (s, 1H), 8.11 (s, 1H), 7.72 (d, J = 7.88 Hz, 1H), 7.59 (dd, J = 8.88, 2.4 Hz, 1H), 7.45-7.43 (m, 2H), 7.36-7.31 (m, 2H), 4.43 (t, J = 4.36 Hz, 2H), 4.26 (t, J = 5.88 Hz, 2H), 2.72 (s, 3H), 2.46 (s, 3H), 2.04 (s, 3H), 1.80 (s, 3H)
904		MS (ESI) m/z 704.22 [M+1]+; ; 1H NMR (400 MHz, DMSO-d6) δ 8.38 (s, 1H), 8.04 (s, 1H), 7.73 (d, J= 8.0 Hz, 1H), 7.57 (dd, J = 8.88 Hz, 2.4 Hz, 1H), 7.43 (s, 2H), 7.40 -7.34 (m, 2H), 4.40 (t, J = 4.48 Hz, 2H), 4.22 (t, J = 5.2 Hz, 2H), 2.72 (s, 3H), 2.50 (s, 3H), 2.36 (s, 3H), 1.82 (s, 3H)	907		MS (ESI) m/z 679.00 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.56 (bs, 1H), 8.40 (s, 1H), 7.99 (s, 1H), 7.77 (s, 1H), 7.58 (d, J=7.20 Hz, 1H), 7.42-7.34 (m, 4H), 4.39 (s, 2H), 4.25 (s, 2H), 3.77 (s, 3H), 2.69 (s, 3H), 1.82 (s, 3H)

908		MS (ESI) m/z 670.97 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.44 (s, 1H) 9.15 (d, J = 5.08 Hz, 1H), 8.64 (s, 1H), 8.27 (s, 1H), 7.97 (d, J = 5 Hz, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.70-7.67 (m, 1H), 7.65 (d, J = 0.84 Hz, 1H), 7.49 (s, 1H), 4.89 (s, 2H), 2.64 (s, 3H), 2.22 (s, 3H)	937		MS (ESI) m/z 688.11 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.28 (s, 1H), 8.06 (s, 1H), 7.41-7.35 (m, 2H), 7.25 (dd, J=8.56, 2.84 Hz, 1H), 4.38 (t, J=4.48 Hz, 2H), 4.27 (t, J=4.32 Hz, 2H), 2.72 (s, 3H), 2.63 (s, 6H), 1.90 (s, 3H)
909		MS (ESI) m/z 684.20 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.57 (bs, 1H), 8.23 (s, 1H), 7.93 (s, 1H), 7.59 (dd, J = 2.44, 8.84 Hz, 1H), 7.41 (d, J = 2.76 Hz, 2H), 7.35 (d, J = 8.96 Hz, 1H), 4.40 (t, J = 4.20 Hz, 2H), 4.25 (t, J = 5.88 Hz, 2H), 4.16 (s, 2H), 3.17 (s, 3H), 2.86 (s, 3H), 2.69 (s, 3H), 1.82 (s, 3H)	963		MS (ESI) m/z 705.26 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.54 (bs, 1H), 8.33 (s, 1H), 8.07 (s, 1H), 7.60 (dd, J = 2.48, 8.90 Hz, 1H), 7.55 (s, 1H), 7.43 -7.42 (m, 2H), 7.36 (d, J = 8.92 Hz, 1H), 4.41 (bs, 2H), 4.27 (bs, 2H), 2.72 (s, 3H), 2.65 (s, 1H), 2.56 (s, 1H), 1.84 (s, 3H)
934		MS (ESI) m/z 722.05 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.5 (bs,1H), 8.24 (s, 1H), 8.05 (s, 1H), 7.59 (dd, J = 8.88, 2.4 Hz, 1H), 7.43 -7.40 (m, 4H), 7.36 (d, J = 9.2 Hz,1H), 5.55 (d, J = 44 Hz, 2H), 4.41 (t, J = 5.2 Hz, 2H), 4.27 (t, J = 5.2 Hz, 2H), 2.72 (s, 3H), 2.58 (s, 3H), 1.84 (s, 3H)	964		MS (ESI) m/z 709.07 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.57 (bs, 1H), 9.14 (s, 1H), 8.41 (s, 1H), 8.19 (s, 1H), 7.60 (dd, J = 2.56, 8.92 Hz, 1H), 7.44-7.43 (m, 2H), 7.36 (d, J = 8.96 Hz, 1H), 4.42 (t, J = 5.20 Hz, 2H), 4.27 (t, J = 4.52 Hz, 2H), 2.73 (s, 3H), 2.70 (s, 3H), 1.82 (s, 3H)

965		MS (ESI) m/z 705.10 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.41 (s, 1H), 8.11 (s, 1H), 7.58 (d, J = 8.84 Hz, 1H), 7.46-7.39 (m, 3H), 7.34 (d, J = 8.88 Hz, 1H), 4.39 (t, J = 4.76 Hz, 2H), 4.26 (t, J = 4.44, Hz, 2H), 2.70 (s, 3H), 2.49 (s, merged, 6H), 1.77 (s, 3H)	
966		MS (ESI) m/z 695.07 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.43 (s, 1H) 9.22 (s, 2H), 8.35 (s, 1H), 8.17 (s, 1H), 7.57 (t, J = 6.56 Hz, 1H), 7.42 (d, J = 2.24 Hz, 1H), 7.38 (s, 1H), 7.34 (d, J = 8.88 Hz, 1H), 4.39 (t, J = 2.96 Hz, 2H), 4.27 (t, J = 3.88 Hz, 2H), 2.69 (s, 3H), 1.82 (s, 3H)	
967		MS (ESI) m/z 691.19 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.29 (bs, 1H), 8.16 (bs, 1H), 7.94 (bs, 1H), 7.86-7.83 (m, 1H), 7.59 (d, J = 7.16 Hz, 1H), 7.41-7.28 (m, 3H), 4.41 (bs, 2H), 4.30 (bs, 2H), 2.76 (s, 3H), 2.50 (bs, 3H), 1.86 (bs, 3H)	
968		MS (ESI) m/z 705.13 [M+1]+; 1H NMR (400 MHz, DMSO-d6) 8.63 (s, 1H), 8.37 (s, 1H), 8.14 (s, 1H), 7.60 (dd, J = 8.88, 2.52 Hz, 1H), 7.48-7.43 (m, 2H), 7.36 (d, J = 8.96 Hz, 1H), 4.48-4.35 (m, 2H), 4.30-4.24 (m, 2H), 2.73 (m, 3H), 2.52 (m, 3H), 2.29 (m, 3H), 1.80 (s, 3H)	
969		MS (ESI) m/z 705.12 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.61 (s, 1H), 8.36 (s, 1H), 8.08 (s, 1H), 7.60 (dd, J = 8.80, 2.48 Hz, 1H), 7.45-7.42 (m, 2H), 7.36 (d, J = 8.92, 1H), 4.44-4.38 (m, 2H), 4.31-4.23 (m, 2H), 2.72 (s, 3H), 2.66 (s, 3H), 2.57 (s, 3H), 1.84 (s, 3H)	
991		MS (ESI) m/z 714.06 [M-1]-; 1H NMR (400 MHz, DMSO-d6) δ 8.29 (s, 1H), 7.90 (s, 1H), 7.59 (dd, J = 8.84, 2.40 Hz, 1H), 7.46-7.40 (m, 2H), 7.36 (d, J = 9.00, 1H), 4.39 (t, J = 4.48 Hz, 2H), 4.23 (t, J = 4.08 Hz, 3H), 3.60-3.40 (m, 2H), 3.20-3.02 (m, 2H), 3.01-2.80 (m, 1H), 2.70 (s, 3H), 2.30-2.10 (m, 2H), 2.00-2.82 (m, 2H), 1.81 (s, 3H)	

992		1009	
MS (ESI) m/z 700.13 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.26 (s, 1H), 7.89 (s, 1H), 7.63-7.58 (m, 1H), 7.44-7.39 (m, 2H), 7.36 (d, J = 8.8 Hz, 1H), 4.39 (s, 2H), 4.23 (s, 2H), 3.71-3.50 (m, merged, 2H), 3.31-3.20 (m, 2H), 2.87-.73 (m, 2H), 2.71 (s, 3H), 2.69-2.60 (m. 2H), 1.80 (s, 3H)		MS (ESI) m/z 684.15 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.56 (s, 1H), 8.39 (s, 1H), 7.77 (s, 1H), 7.58 (dd, J = 2.44, 8.84 Hz, 1H), 7.41-7.39 (m, 2H), 7.35 (d, J = 8.96 Hz, 1H), 4.65-4.62 (m, 2H), 4.37 (bs, 2H), 4.32-4.27 (m, 3H), 4.18 (bs, 2H), 3.37 (s, 3H), 2.70 (s, 3H), 1.74 (s, 3H)	
995		1012	
MS (ESI) m/z 744.09 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.20 (bs, 1H), 8.35 (s, 1H), 8.29-8.25 (m, 1H), 8.22 (s, 1H), 8.09-8.06 (m, 1H), 7.57 (d, J = 9.24 Hz, 1H), 7.43-7.33 (m, 3H), 7.07 (t, J = 54.36 Hz, 1H), 4.39 (bs, 2H), 4.27 (bs, 2H), 2.69 (s, 3H), 1.83 (s, 3H)		MS (ESI) m/z 690.14 [M+1]+; ; 1H NMR (400 MHz, DMSO-d6): δ 13.74 (s, 1H), 8.71 (d, J = 5.0 Hz, 2H), 8.26 (s,1H), 8.041 (s, 1H), 7.61 (dd, J = 7.2.24 Hz, J = 2.20 Hz,1H), 7.54 (d, J = 4.64 Hz, 2H), 7.48 (s, 1H), 7.44 (d, J = 2.24 Hz, 1H), 7.38 (d, J = 8.88 Hz, 1H), 4.43 (t, J = 4.52 Hz, 2H), 4.27 (t, J = 4.44 Hz, 2H), 3.06 (m, 2H), 1.80 (s, 3H), 1.39 (t, J = 7.52 Hz, 3H)	
996		1013	
MS (ESI) m/z 642.01 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.33 (s, 1H), 7.89 (s, 1H), 7.59 (dd, J = 2.60, 8.88 Hz, 1H), 7.43 (s, 1H), 7.42 (d, J = 2.64 Hz, 1H), 7.36 (d, J = 8.96 Hz, 1H), 4.39 (t, J = 4.68 Hz, 2H), 4.23 (t, J = 4.64 Hz, 2H), 2.94 (s, 6H), 2.70 (s, 3H), 1.81 (s, 3H)		MS (ESI) m/z 690.14 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.76 (d, J = 4.12 Hz, 1H), 8.69 (s, 1H), 8.26 (s, 1H), 8.04 (s, 1H), 7.98 (d, J = 7.68 Hz, 1H), 7.65-7.59 (m, 2H), 7.49 (s, 1H), 7.44 (d, J = 2.48 Hz, 1H), 7.38 (d, J = 8.96 Hz, 1H), 4.43 (t, J = 4.52 Hz, 2H), 4.27 (t, J = 4.44 Hz, 2H), 3.06 (m, 2H), 1.80 (s, 3H), 1.39 (t, J = 7.52 Hz, 3H)	

1014		MS (ESI) m/z 693.16 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.32 (s, 1H), 8.00 (s, 1H), 7.87 (d, J = 2.56 Hz, 1H), 7.60 (dd, J = 2.56, 8.88 Hz, 1H), 7.46 (s, 1H), 7.44 (d, J = 2.44 Hz, 1H), 7.35 (d, J = 9.00 Hz, 1H), 6.48 (s, 1H), 4.40 (t, J = 4.56 Hz, 2H), 4.24 (t, J = 4.72 Hz, 2H), 3.93 (s, 3H), 3.02 (q, J = 7.36, 2H), 1.76 (s, 3H), 1.35 (t, J = 7.52 Hz, 3H)	1026		MS (ESI) m/z 745.11 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.51 (s, 1H), 9.49 (s, 1H), 8.36 (s, 1H), 8.15 (s, 1H), 7.61 (dd, J = 2.48, 8.8 Hz, 1H), 7.44-7.42 (m, 2H), 7.37 (d, J = 8.8 Hz, 1H), 4.42 (bs, 2H), 4.30 (bs, 2H), 2.72 (s, 3H), 1.89 (s, 3H)
1017		MS (ESI) m/z 722.14 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.72 (bs, 1H), 8.67 (d, J = 2.68 Hz, 1H), 8.22 (s, 1H), 8.08 (s, 1H), 7.90 (d, J = 6.68 Hz, 1H), 7.59 (dd, J = 2.48, 8.92 Hz, 1H), 7.49 (s, 1H), 7.44 (d, J = 2.48 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.41 (t, J = 3.88 Hz, 2H), 4.28 (bs, 2H), 3.04 (q, J = 7.2 Hz, 2H), 2.21 (s, 3H), 1.79 (s, 3H), 1.39 (t, J = 7.2 Hz, 3H)	1027		MS (ESI) m/z 693.14 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.37 (s, 1H), 8.04 (s, 1H), 7.65 (s, 1H), 7.59 (dd, J=8.92 Hz, 1.48 Hz, 1H), 7.44 (s, 2H), 7.36 (s, 1H), 4.41 (s, 2H), 4.25 (s, 2H), 3.86 (s, 3H), 2.71 (s, 3H), 1.86 (s, 3H), 1.79 (s, 3H)
1025		MS (ESI) m/z 727.10 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.54 (bs, 1H), 9.24 (s, 1H), 8.34 (s, 1H), 8.14 (s, 1H), 7.43-7.17 (m, 4H), 4.42 (bs, 2H), 4.28 (bs, 2H), 2.72 (s, 3H), 1.87 (s, 3H)	1028		MS (ESI) m/z 693.16 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.57 (s, 1H), 8.32 (s, 1H), 8.07 (s, 1H), 7.61(dd, J = 2.56 Hz, J = 8.88 Hz, 1H), 7.45-7.43 (m, 2H), 7.37 (d, J = 9.00 Hz, 1H), 6.27 (s, 1H), 4.41 (bs, 3H), 4.27 (bs, 2H), 3.55 (s, 3H), 2.72 (s, 3H), 2.23 (s, 3H), 1.84 (s, 3H)

1029		1032	
MS (ESI) m/z 693.00 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.55 (bs, 1H), 8.34 (s, 1H), 8.01 (s, 1H), 7.59 (dd, J = 8.88, 2.4 Hz, 1H), 7.43- 7.41 (m, 3H), 7.35 (d, J = 8.8 Hz, 1H), 4.40 (t, J = 6.04 Hz, 2H), 4.25 (t, J = 5.2 Hz, 2H), 3.83 (s, 3H), 2.70 (s, 3H), 2.10 (s, 3H), 1.83 (s, 3H)		MS (ESI) m/z 693.10 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.33 (s, 1H), 8.01 (s, 1H), 7.60 (dd, J = 9.92, 3.32 Hz, 1H), 7.45-7.39 (m, 3H), 7.36 (d, J = 8.88 Hz, 1H), 4.46-4.45 (m, 2H), 4.30-4.20 (m, 2H), 3.83 (s, 3H), 2.70 (s, 3H), 2.10 (s, 3H), 1.83 (s, 3H)
1030		1033	
MS (ESI) m/z 693.12 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.55 (bs, 1H), 8.26 (s, 1H), 8.10 (s, 1H), 7.61 (dd, J1=6.48, J2=2.28 Hz 1H), 7.45-7.43 (m, 3H), 7.38 (d, J=8.88 Hz, 1H), 4.42 (bs, 2H), 4.26 (bs, 2H), 3.57 (s, 3H), 2.72 (s, 3H), 1.82 (s, 6H)		MS (ESI) m/z 706.14 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.60 (d, J = 4.4 Hz, 1H), 8.28 (s, 1H), 8.00-7.95 (m, 2H), 7.72 (d, J = 7.72 Hz, 1H), 7.60 (dd, J = 8.88, 2.56 Hz, 1H), 7.46-7.39 (m, 3H), 7.37 (d, J = 8.96 Hz, 1H), 5.45 (s, 2H), 4.42 (t, J = 3.8 Hz, 2H), 4.25 (t, J = 4.3 Hz, 2H), 2.72 (s, 3H), 1.80 (s, 3H)	
1031		1034	
MS (ESI) m/z 693.13 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.56 (bs, 1H), 8.34 (s, 1H), 8.00 (s, 1H), 7.77 (s, 1H), 7.59 (dd, J = 8.84, 2.40 Hz, 1H), 7.43 (s, 2H), 7.36 (d, J = 8.96 Hz, 1H), 4.48-4.36 (m, 2H), 4.35-4.19 (m, 2H), 3.86 (s, 3H), 2.70 (s, 3H), 1.97 (s, 3H), 1.84 (s, 3H)		MS (ESI) m/z 655.18 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.54 (bs, 1H), 8.29 (s, 1H), 7.90 (s, 1H), 7.59 (dd, J = 8.92, 2.32 Hz, 1H), 7.42 (s, 2H), 7.36 (d, J = 8.92 Hz, 1H), 4.77-4.70 (m, 1H), 4.40 (t, J = 6.64 Hz, 2H), 4.23 (t, J = 5.12 Hz, 2H), 2.70 (s, 3H), 1.76 (s, 3H), 0.92-0.75 (m, 4H)	

1035		MS (ESI) m/z 792.25 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.45 (bs, 1H), 8.44 (d, J = 2.52 Hz, 1H), 8.38 (d, J = 3.32 Hz, 1H), 8.34 (s, 1H), 8.11 (s, 1H), 7.60 (dd, J = 2.55, 8.88 Hz, 1H), 7.49-7.42 (m, 4H), 7.35 (d, J = 8.90 Hz, 1H), 4.41 (t, J = 5.24 Hz, 2H), 4.05 (t, J = 4.0 Hz, 2H), 2.72 (s, 3H), 1.77 (s, 3H)	1049		MS (ESI) m/z 639.16 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.27 (s, 1H), 7.90 (s, 1H), 7.59 (dd, J = 8.84, 2.40 Hz, 1H), 7.44-7.39 (m, 2H), 7.35 (d, J = 8.92 Hz, 1H), 4.38 (t, J = 5.56 Hz, 2H), 4.24 (t, J = 6.04 Hz, 2H), 2.69 (s, 3H), 2.30-2.18 (m, 1H) 1.83 (s, 3H), 1.26-1.12 (m, 2 h), 1.00-0.90 (m, 2H)
1036		MS (ESI) m/z 629.11 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.27 (s, 1H), 7.91 (s, 1H), 7.60 (dd, J = 8.92, 2.56 Hz, 1H), 7.43 (s, 1H),, 7.42, (d, J = 2.80 Hz, 1H), 7.36 (d, J = 8.96 Hz, 1H), 4.40 (t, J = 4.72 Hz, 2H), 4.24 (t, J = 4.48 Hz, 2H), 4.13 (s, 3H), 2.71 (s, 3H), 1.78 (s, 3H)	1055		MS (ESI) m/z 684.16 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.55 (s, 1H), 8.40 (s, 1H), 7.77 (s, 1H), 7.59 (dd, J = 2.28 Hz, J = 8.84 Hz, 1H), 7.42 (d, J = 2.40 Hz, 1H), 7.40 (s, 1H), 7.35 (d, J = 8.88, 1H), 5.72 (s, 1H), 4.39-4.30 (m, 6H), 4.18 (t, J = 6.68, 2H), 2.70 (s, 3H), 1.73 (s, 3H), 1.45 (s, 3H)
1046		MS (ESI) m/z 639.16 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.27 (s, 1H), 7.90 (s, 1H), 7.59 (dd, J = 8.84, 2.40 Hz, 1H), 7.44-7.39 (m, 2H), 7.35 (d, J = 8.92 Hz, 1H), 4.38 (t, J = 5.56 Hz, 2H), 4.24 (t, J = 6.04 Hz, 2H), 2.69 (s, 3H), 2.30-2.18 (m, 1H) 1.83 (s, 3H), 1.26-1.12 (m, 2 h), 1.00-0.90 (m, 2H)	1058		MS (ESI) m/z 706.19 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.49 (bs, 1H), 8.27 (s, 1H), 8.05 (s, 1H), 7.56-7.48 (m, 2H), 7.39 (s, 1H), 4.41 (t, J = 5.52 Hz, 2H), 4.27 (t, J = 5.04 Hz), 2.72 (s, 3H), 2.61 (s, 6H), 1.86 (s, 3H)

1059		1074	
MS (ESI) m/z 710.5 [M+1]+; 1H NMR (400 MHz, DMSO-d6) 8.57 (d, J = 1.6 Hz, 1H), 8.27 (s, 1H), 8.10-8.03 (m, 2H), 7.79 (d, J = 8.2 Hz,1H), 7.60 (dd, J = 8.8, 2.6 Hz, 1H), 7.45 (s, 1H), 7.42 (d, J = 2.6 Hz, 1H), 7.36 (d, J = 8.9 Hz, 1H), 4.42 (t, J = 4.24 Hz, 2H), 4.28 (t, J = 5.4 Hz, 2H), 2.73 (s, 3H), 1.87 (s, 3H)		MS (ESI) m/z 697.14 [M+1]+; 1H NMR (400 MHz, DMSO-d6) 8.21(s, 1H), 7.96 (s, 1H), 7.59 (d, J = 8.96 Hz, 1H), 7.43 (s, 1H), 7.41 (s, 1H), 7.36 (d, J = 8.96 Hz, 1H), 5.00 (q, J = 8.40 Hz, 2H), 4.41 (t, J = 5.24 Hz, 2H), 4.25 (t, J = 4.8 Hz, 2H), 2.72 (s, 3H), 1.79 (s, 3H)	
1060		1075	
MS (ESI) m/z 667.06 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.53 (bs, 1H), 8.35 (d, J = 2.68 Hz, 1H), 8.29 (s, 1H), 8.08 (s, 1H), 7.60 (dd, J = 8.84, 2.36 Hz, 1H), 7.46-7.40 (m, 3H), 7.36 (d, J = 8.96 Hz, 1H), 4.50-4.20 (m, 4H), 3.86 (s, 3H), 2.72 (s, 3H), 2.12 (s, 3H), 1.86 (s, 3H)		MS (ESI) m/z 711.15 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.24 (s, 1H), 8.06 (s, 1H), 7.59 (d, J = 8.84 Hz, 1H), 7.43 (d, J = 5.5 Hz, 2H), 7.36 (d, J = 8.9 Hz, 1H), 4.46-3.64 (m, 10H), 2.82 (s, 3H), 2.71 (s, 3H), 1.85 (s, 3H)	
1073		1079	
MS (ESI) m/z 643.20 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.27 (s, 1H), 7.91 (s, 1H), 7.59 (dd, J = 8.84 Hz, 2.56 Hz, 1H), 7.43-7.41 (m, 2H), 7.36 (d, J = 8.96 Hz, 1H), 4.40-4.35 (m, 4H), 4.23 (t, J = 4.16 Hz, 2H), 2.70 (s, 3H), 1.78 (s, 3H), 1.46 (t, J = 6.96 Hz, 3H)		MS (ESI) m/z 767.24 [M+1]+; 1H NMR (400 MHz, DMSO-d6 with D2O) δ 8.00 (d, J = 6.4 Hz, 2H), 7.53 (d, J = 7.2 Hz, 1H), 7.33 (s, 1H), 7.27 (d, J = 8.4 Hz, 1H), 7.19 (s, 1H), 4.33 (bs, 2H), 4.20 (bs, 2H), 2.54 (s, 3H), 2.19 (s, 3H), 1.67 (s, 3H)	

1080		1085	
MS (ESI) m/z 751.17 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.06 (s, 1H), 7.94 (s, 1H), 7.53 (dd, J = 8.76, 2.16 Hz, 1H), 7.40 (d, J = 2.16 Hz, 1H), 7.29 (d, J = 8.92 Hz, 1H), 7.19 (s, 1H), 7.00 (d, J = 6.52 Hz, 1H), 5.76-5.68 (m, 1H), 4.40-4.30 (m, 2H), 4.30-4.15 (m, 2H), 3.70-3.45 (m, 2H), 3.10-2.70 (m, 2H), 2.60 (s, 3H), 2.35-1.90 (m, 7H), 1.69 (s, 3H)		MS (ESI) m/z 711.21 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.19 (s, 1H), 7.91 (s, 1H), 7.61 (dd, J = 8.9 Hz, 2.44 Hz, 1H), 7.47 (s, 1H), 7.43 (d, J = 2.4 Hz, 1H), 7.36 (d, J = 8.9 Hz, 1H), 4.40 (t, J = 5.0 Hz, 2H), 4.24 (t, J = 4.0 Hz, 2H), 3.86 (t, J = 9.2 Hz, 2H), 3.55 (bs, 2H), 3.32 (bs, 2H), 3.10 (bs, 2H), 3.02 (q, J = 15.0 Hz, 2H), 2.89 (s, 3H), 1.79 (s, 3H), 1.36 (t, J = 7.5 Hz, 3H)
1081		1087	
MS (ESI) m/z 805.02 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.67 (d, J = 2.76 Hz, 1H), 8.26 (s, 1H), 8.12 (s, 1H), 7.97 (d, J = 6.76 Hz, 1H), 7.57 (dd, J = 2.56, 8.8 Hz, 1H), 7.36 (t, J = 2.56 Hz, 2H), 7.28 (s, 1H), 4.41-4.21 (m, 6H), 2.82 (bs, 2H), 2.64 (s, 3H), 2.50 (s, 4H), 2.19 (s, 3H), 1.91 (s, 3H), 1.69 (s, 4H)		MS (ESI) m/z 725.29 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 14.50 (bs, 1H), 7.92 (s, 1H), 7.60 (dd, J = 2.52, 9.28 Hz, 1H), 7.47 (s, 1H), 7.43 (d, J = 2.28 Hz, 1H), 7.36 (d, J = 8.88 Hz, 2H), 4.40 (t, J = 5.56 Hz, 2H), 4.24 (t, J = 5.76 Hz, 2H), 3.86 (t, J = 11.28 Hz, 2H), 3.56 (d, J = 11.44 Hz, 2H), 3.21-3.18 (m, 2H), 3.08 (d, J = 10.4 Hz, 2H), 3.01 (q, J = 7.6 Hz, 2H), 2.90 (bs, 3H), 2.37 (s, 3H), 1.90 (s, 3H), 1.36 (t, J = 7.6 Hz, 3H)
1082		1088	
MS (ESI) m/z, 867.35 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.42 (s, 1H), 7.96 (s, 1H), 7.57 (dd, J = 2.52, 8.88 Hz, 1H), 7.36 (d, J = 2.52 Hz, 1H), 7.32 (d, J = 9.0 Hz, 1H), 7.27 (s, 1H), 6.94-6.90 (m, 1H), 4.61-4.56 (m, 1H), 4.37 (bs, 2H), 4.23 (bs, 2H), 3.60 (bs, 2H), 2.95 (bs, 2H), 2.63 (s, 3H), 2.24 (s, 4H), 1.84 (bs, 2H), 1.75 (s, 3H), 1.63 (d, J = 5.36 Hz, 6H), 1.44-1.39 (m, 4H), 1.33-1.20 (m, 4H)		MS (ESI) m/z 708.25 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ13.60 (s, 1H), 10.02 (bs,1H), 8.21 (d, J = 5.4 Hz, 1H), 7.97 (d, J = 5.48 Hz, 1H), 7.62 (d, J = 2.28 Hz, 1H), 7.47 (s, 1H), 7.43 (d, J = 2.24 Hz, 1H), 7.37 (d, J = 8.96 Hz, 1H), 5.95 (s, 1H), 4.42 (bs, 2H), 4.39 (bs, 2H), 4.26 (d, J = 4.55 Hz, 1H), 3.85-3.65 (m, 2H), 3.4-3.33 (m, 1H), 3.04-2.99 (m, 6H), 2.67 (bs, 1H), 1.86 (s, 3H), 1.36 (t, J = 7.52, 3H)

1093		1154	
MS (ESI) m/z 697.18 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.79 (d, J = 4.9 Hz, 1H), 7.95 (s, 1H), 7.61 (dd, J = 2.5, 8.8 Hz, 1H), 7.52 (d, J = 4.8 Hz, 1H), 7.37 (d, J = 2.5 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 4.42 (t, J = 4.8 Hz, 2H), 4.26 (t, J = 4.3 Hz, 2H), 3.90-3.83 (m, 2H), 3.57-3.54 (m, 2H), 3.21-3.18 (m, 2H), 3.10-3.08 (m, 2H), 2.91 (s, 3H), 2.39 (s, 3H), 1.85 (s, 3H)		MS (ESI) m/z 620.27 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.79 (bs, 1H), 8.17 (s, 1H), 7.91 (s, 1H), 7.67-7.62 (m, 3H), 7.51 (bs, 2H), 7.37 (bs, 1H), 5.02 (s, 2H), 3.87-3.45 (m, 4H), 3.21-2.91 (m, 4H), 3.02 (bs, 3H), 2.85 (bs, 3H)	
1151		1156	
MS (ESI) m/z 760.31 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.56 (bs, 1H), 8.89 (d, J = 4.8 Hz, 1H), 8.36 (s, 1H), 7.97 (s, 1H), 7.60 (dd, J = 8.8, 2.4 Hz, 1H), 7.53 (d, J = 4.8 Hz, 1H), 7.45 (d, J = 2.8 Hz, 1H), 7.36 (d, J = 9.2 Hz, 1H), 4.45-4.38 (m, 2H), 4.26-4.19 (m, 2H), 3.80-3.40 (m, 5H), 3.20-2.75 (m, 4H), 2.65-2.50 (s, 2H), 2.27 (s, 3H), 1.68 (s, 3H)		MS (ESI) m/z 765.30 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.26 (bs, 1H), 8.82 (d, J = 4.8 Hz, 1H), 8.28 (s, 1H), 7.93 (s, 1H), 7.59 (d, J = 8.8 Hz, 1H), 7.46 (d, J = 4.4 Hz, 1H), 7.42 (s, 1H), 7.35 (d, J = 10.8 Hz, 1H), 4.39 (bs, 2H), 4.23 (bs, 2H), 3.63 (bs, 2H), 3.31 (bs, 2H), 2.95 (m, 4H), 2.60 (t, J = 7.2 Hz, 4H), 1.71 (s, 3H)	
1153		1158	
MS (ESI) m/z 683.16 [M+1]+; 1H NMR (400 MHz, DMSO-d6) 13.12 (bs, 1H), 8.85 (d, J = 4.8 Hz, 1H), 8.23 (s, 1H), 7.99 (s, 1H), 7.60 (d, J = 9.2, 2.4 Hz, 1H), 7.49 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.4 Hz, 1H), 7.36 (d, J = 9.2 Hz, 1H), 5.00 (q, J = 8.4 Hz, 2H), 4.41 (s, 2H), 4.25 (s, 2H), 1.73 (s, 3H)		MS (ESI) m/z 721.16 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 8.84 (d, J = 4.8 Hz, 1H), 8.41 (s, 1H), 7.83 (s, 1H), 7.60 (dd, J = 2.4, 8.4 Hz, 1H), 7.44 (d, J = 2.4 Hz, 1H), 7.36 (d, J = 8.8 Hz, 1H), 4.71 (s, 2H), 4.63 (s, 2H), 4.40-4.20 (m, 8H), 3.05 (bs, 1H), 1.73 (s, 3H), 0.79-0.77 (m, 4H)	

1159		1192	
	MS (ESI) m/z 709.12 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.4 Hz, 1H), 8.23 (s, 1H), 7.96 (s, 1H), 7.60 (dd, J = 6.4 Hz, 2.4 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.4 Hz, 1H), 7.36 (d, J = 8.8 Hz, 1H), 4.40 (s, 2H), 4.24 (s, 2H), 3.85 (s, 4H), 3.29 (bs, 4H), 3.12 (bs, 1H), 1.76 (s, 3H), 1.01 (s, 2H), 0.85 (s, 2H)		MS (ESI) m/z 717.23 [M+1]+; 1H NMR (400 MHz, DMSO) δ 13.50 (bs, 1H), 8.27 (s, 1H), 8.05 (s, 1H), 7.81 (d, J = 8.0 Hz, 1H), 7.59 (dd, J = 8.0, 4.0 Hz, 1H), 7.43 (s, 2H), 7.36 (d, J = 8.0 Hz, 1H), 6.66 (s, 1H), 6.42 (d, J = 4.0 Hz, 1H), 4.41 (s, 2H), 4.26 (s, 2H), 3.46 (t, J = 8.0 Hz, 2H), 2.83-2.60 (m, 5H), 1.84 (s, 3H)
1178		1197	
	MS (ESI) m/z 715.47 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 8.77 (d, J = 5.2 Hz, 1H), 8.66 (s, 1H), 7.93 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.70-7.66 (m, 2H), 7.56 (d, J = 4.4 Hz, 1H), 4.82 (s, 2H), 4.73-4.41 (m, 8H), 3.05 (bs, 1H), 2.11 (s, 3H), 0.77 (bs, 4H)		MS (ESI) m/z 679.22 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.46 (bs, 1H), 8.23 (s, 1H), 7.94 (s, 1H), 7.59 (d, J = 8.0 Hz, 1H), 7.42 (s, 1H), 7.41 (d, J = 2.4 Hz, 1H), 7.35 (d, J = 8.0 Hz, 1H), 6.46 (t, J = 52.0 Hz, 1H), 4.70-4.60 (m, 2H), 4.41 (s, 2H), 4.24 (s, 2H), 2.71 (s, 3H), 1.79 (s, 3H)
1179		1200	
	MS (ESI) m/z 786.04 [M+1]+. 1H-NMR (400 MHz, DMSO-d6) δ 12.70 (s, 1H), 8.94 (d, J = 4.8 Hz, 1H), 8.31 (s, 1H), 7.97 (s, 1H), 7.63-7.58 (m, 2H), 7.45 (d, J = 2.40 Hz, 1H), 7.37 (d, J = 9.20 Hz, 1H), 4.42 (bs, 2H), 4.22 (bs, 2H), 3.86-3.66 (m, 4H), 3.57 (s, 3H), 3.28-3.122 (m, 5H), 1.67 (s, 3H), 2.01-0.84 (m, 4H)		MS (ESI) m/z 684.22 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 14.29 (bs, 1H), δ 10.03 (bs, 1H), δ 7.98 (s, 1H), δ 7.61 (dd, J = 9.0 Hz, 2.46 Hz, 1H), 7.43 (s, 1H), 7.42 (s, 1H), 7.35 (d, J = 9.2 Hz , 1H), 4.41 (t, J = 5.1 Hz, 2H), 4.28 (t, J = 4.5 Hz, 2H), 3.42 (bs, 2H), 3.32 (bs, 2H), 2.93 (s, 6H), 2.70 (s, 3H), 2.34 (s, 3H), 1.96 (s, 3H)

1206		1213	
MS (ESI) m/z 723.34 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.6 Hz, 1H), 8.19 (s, 1H), 7.90 (s , 1H), 7.58 (dd, J = 2.48, 8.92 Hz, 1H), 7.38 (d, J = 3.16 Hz, 1H), 7.33 (d, J = 8.96 Hz, 1H), 4.39 (t, J = 5.4 Hz, 2H), 4.22 (t, J = 5.2 Hz, 2H), 3.89 (s, 3H), 3.80-3.40 (m, 4H), 3.10-2.90 (m, 4H), 1.69 (s, 3H), 0.47-0.35 (m, 4H)		MS (ESI) m/z 691.29 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.31 (s, 1H), 9.77 (s, 1H), 8.58 (s, 1H), 8.09 (s, 1H), 7.76 -7.64 (m, 3H), 7.50 (s, 1H), 4.84 (s, 2H), 3.93-3.88 (m, 2H), 3.61-3.58 (m, 2H), 3.32-3.29 (m, 2H), 3.12 (bs, 2H), 2.92 (s, 3H), 2.67 (s, 3H), 2.23 (s, 3H)
1207		1214	
MS (ESI) m/z 779.28 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 14.32 (bs, 1H), 7.90 (s, 1H), 7.60 (dd, J = 2.6, 8.9 Hz, 1H), 7.41 (m, 2H), 7.36 (d, J = 8.9 Hz, 1H), 4.40 (s, 2H), 4.26 (s, 2H), 3.66 (m, 2H), 3.20 (m, 2H), 2.97 (m, 2H), 2.70 (s, 3H), 2.66 (m, 1H), 2.49 (s, 3H), 2.44 (s, 3H), 1.97 (s, 3H)		MS (ESI) m/z 700.25 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.83 (bs, 1H), 8.01 (s, 1H), 7.79 (s, 1H), 7.52-7.50 (m, 1H), 7.29-7.20 (m, 4H), 4.34 (bs, 2H), 4.22 (bs, 2H), 3.60-3.38 (m, 2H), 3.25 (bs, 2H), 3.19-2.98 (m, 4H), 2.24 (s, 3H), 1.79 (s, 3H)
1212		1215	
MS (ESI) m/z 677.23 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.11 (bs, 1H), 8.77 (d, J = 4.8 Hz, 1H), 8.59 (s, 1H), 8.11 (s, 1H), 7.76 (d, J = 8.4 Hz, 1H), 7.71-7.67 (m, 2H), 7.56 (d, J = 4.8 Hz, 1H), 4.86 (s, 2H), 3.89-3.86 (m, 2H), 3.59-3.56 (m, 2H), 3.29 (d, J = 11.6 Hz, 2H), 3.11 (bs, 2H), 2.92 (s, 3H), 2.17 (s, 3H)		MS (ESI) m/z 713.31 [M+1]+;1H NMR (400 MHz, DMSO-d6) δ 13.66 (bs, 1H), 9.74 (bs, 1H), 8.22 (s, 1H), 7.92 (s, 1H), 7.60-7.54 (m, 2H), 7.44 (s, 1H), 4.39 (bs, 2H), 4.23 (bs, 2 H), 3.86 (m, 2H), 3.58 (m, 2H), 3.26-2.98 (m, 6H), 2.89 (s, 3H), 1.79 (s, 3H), 1.35 (t, J = 7.6 Hz, 3H)

1218		1223	
MS (ESI) m/z 696.26 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.98 (s, 1H), 8.02 (s, 1H), 7.66 (s, 1H), 7.50 (dd, J = 2.4 Hz, J = 8.8 Hz, 1H), 7.27-7.25 (m, 3H), 7.13 (d, J = 7.6 Hz, 1H), 4.34 (t, J = 4.8 Hz, 2H), 4.22 (t, J = 4.8 Hz, 2H), 3.86 (t, J = 10.8, 2H), 3.55-3.53 (m, 2H), 3.24-3.21 (m, 2H), 3.07 (bs, 2H), 2.89 (s, 3H), 2.68 (s, 3H), 1.7 (s, 3H)		MS (ESI) m/z 655.38 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.89 (bs, 1H), 9.74 (bs, 1H), 8.10 (s, 1H), 7.72 (s, 1H), 7.48-7.44 (m, 2H), 7.36 (d, J = 2.4 Hz, 1H), 7.24 (d, J = 9.2 Hz, 1H), 4.37 (s, 4H), 4.02-4.00 (m, 2H), 3.91-3.75 (m, 2H), 3.54 (d, J = 10.4 Hz, 2H), 3.19 (d, J = 12.0 Hz, 2H), 3.15-2.98 (m, 2H), 2.89 (s, 3H), 2.80 (q, J = 8.0 Hz, 2H), 2.29 (s, 3H), 1.22 (t, J = 7.6 Hz, 3H)	
1221		1224	
MS (ESI) m/z 627.19 [M+1]+ ; 1H NMR (400 MHz, DMSO-d6) δ 13.02 (bs, 1H), 9.72 (bs, 1H), 8.58 (d, J = 4.4 Hz, 1H), 8.15 (s, 1H), 7.90 (s, 1H), 7.54 (d, J = 4.2 Hz, 1H), 7.48 (dd, J = 8.8, 2.5 Hz, 1H), 7.40 (d, J = 2.4 Hz, 1H), 7.25 (d, J = 9.6 Hz, 1H), 4.39 (s, 4H), 3.85 (t, J = 11.3 Hz, 2H), 3.52 (t, J = 11.2 Hz, 2H), 3.21 (d, J = 11.8 Hz, 2H), 3.07 (bs, 2H), 2.89 (s, 3H), 2.24 (s, 3H)		MS (ESI) m/z 656.30 [M+1] +; 1H NMR (400 MHz, DMSO-d6) δ 12.93 (bs, 1H), 8.05 (s, 1H), 7.52 (s, 1H), 7.46 (dd, J = 8.8, 2.4 Hz, 1H), 7.34 (d, J = 2.4 Hz, 1H), 7.23 (d, J = 8.8 Hz, 1H), 6.95 (s, 1H), 4.36 (bs, 4H), 3.91 (s, 3H), 3.75-3.50 (m, 2H), 3.20-2.70 (m, 6H), 2.26 (s, 3H), 2.24 (s, 3H)	
1222		1225	
MS (ESI) m/z 641.28 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.73 (bs, 1H), 8.10 (s, 1H), 7.70 (s, 1H), 7.50-7.40 (m, 2H), 7.35 (d, J = 2.8 Hz, 1H), 7.25 (d, J = 9.2 Hz, 1H), 4.38 (s, 4H), 3.85 (t, J = 22.8 Hz, 2H), 3.54 (d, J = 11.2 Hz, 2H), 3.21 (d, J = 11.6 Hz, 2H), 3.13-2.98 (m, 2H), 2.89 (s, 3H), 2.26 (s, 3H)		MS (ESI) m/z 670.31 [M+1] +; 1H NMR (400 MHz, DMSO-d6) δ 12.39 (bs, 1H), 8.04 (s, 1H), 7.42 (dd, J = 8.0, 4.0 Hz, 1H), 7.28 (d, J = 4.0 Hz, 1H), 7.20 (d, J = 8.0 Hz, 1H), 7.09 (s, 1H), 6.63 (s, 1H), 4.34 (s, 4H), 3.82-3.35 (m, 4H), 2.99 (s, 6H), 2.95-2.69 (m, 4H), 2.24 (s, 3H), 2.22 (s, 3H)	

1226		1238	
MS (ESI) m/z 655.29 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.93 (bs, 1H), 8.09 (s, 1H), 7.46-7.44 (dd, J = 2.0, 8.8 Hz, 1H), 7.21-7.16 (m, 2H), 7.08 (s, 1H), 4.30 (bs, 4H), 3.78 (bs, 2H), 3.14 (m, 4H), 2.91 (bs, 2H), 2.74 (s, 3H), 2.45 (s, 3H), 2.02 (s, 3H), 1.88 (s, 3H)		MS (ESI) m/z 741.31 [M+1]+; 1H NMR (400 MHz, DMSO-d6) 13.98 (bs, 1H), 7.93 (s, 1H), 7.62-7.60 (m, 1H), 7.48 (s, 1H), 7.43 (bs, 1H), 7.37 (d, J = 8.8 Hz, 1H), 4.75 (s, 2H), 4.41 (bs, 2H), 4.25 (bs, 2H), 3.57 (t, J = 12.0 Hz, 2H), 3.44 (bs, 2H), 3.40 (s, 3H), 3.21 (t, J = 10.8 Hz, 2H), 3.10 (bs, 2H), 2.90 (s, 3H), 2.39 (s, 3H), 1.89 (s, 3H)	
1228		1239	
MS (ESI) m/z 707.30 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.87 (d, J = 4 Hz, 1H), 8.19 (s, 1H), 7.68 (s, 1H), 7.60-7.58 (dd, J = 2.4, 8.8 Hz, 1H), 7.45 (t, J = 4 Hz, 2H), 7.37 (d, J = 8.8 Hz, 1H), 4.41 (bs, 2H), 4.23 (bs, 2H), 3.86-2.64 (m, 8H), 2.32 (s, 3H), 1.74 (s, 3H)		MS (ESI) m/z 733.30 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.02 (bs, 1H), 8.83 (d, J = 4.8 Hz, 1H), 8.27 (s, 1H), 7.94 (s, 1H), 7.60 (dd, J = 8.8, 2.8 Hz 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.8 Hz, 1H), 7.36 (d, J = 8.8 Hz, 1H), 6.47-6.19 (m, 1H), 4.40 (s, 2H), 4.24 (s, 2H), 3.70-3.50 (merged, 2H), 3.30-2.80 (m, 8H), 1.75 (s, 3H)	
1237		1241	
MS (ESI) m/z 729.25 [M+1]+; 1H NMR (400 MHz, DMSO-d6) 13.62 (bs, 1H), 7.96 (s, 1H), 7.63-7.60 (dd, J = 2.4, 8.8 Hz, 1H), 7.52 (s, 1H), 7.43 (d, J = 2.4 Hz, 1H), 7.37 (d, J = 8.8 Hz, 1H), 5.79 (d, J = 46.4 Hz, 2H), 4.41 (bs, 2H), 4.26 (bs, 2H), 3.89 (t, J = 12.4 Hz, 2H), 3.56 (t, J = 10.4 Hz, 2H), 3.20 (t, J = 12.8 Hz, 2H), 3.09 (bs, 2H), 2.90 (s, 3H), 2.39 (s, 3H), 1.88 (s, 3H)		MS (ESI) m/z 725.25 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.77 (bs, 1H), 8.83 (d, J = 4.64 Hz, 1H), 8.24 (s, 1H), 7.96 (s, 1H), 7.11 (dd, J = 8.9 Hz, 2.16 Hz, 1H), 7.48 (d, J = 4.6 Hz, 1H), 7.43 (s, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.74 (bs, 4H), 4.59 (bs, 1H), 4.41 (s, 2H), 4.25 (s, 2H), 4.07 (bs, 2H), 3.54 (bs, 2H), 3.30 (bs, 2H), 2.93 (bs, 2H), 1.76 (s, 3H)	

1242		1245	
MS (ESI) m/z 739.32 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.46 (s, 1H), 8.24 (s, 1H), 7.92 (s, 1H), 7.60 (d, J = 8.8 Hz, 1H), 7.42 (d, J = 6 Hz, 2H), 7.36 (d, J = 8.8 Hz, 1H), 4.78-4.73 (m, 4H), 4.59 (bs, 1H), 4.40 (s, 2H), 4.25 (s, 2H), 3.91 (bs, 4H), 3.29 (bs, 2H), 2.92 (bs, 2H), 2.72 (s, 3H), 1.84 (s , 3H)		MS (ESI) m/z 664.29 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.90 (d, J = 4.4 Hz, 1H), 8.41 (s, 1H), 8.10 (s, 1H), 7.60 (dd, J = 8.8, 2.4 Hz, 1H), 7.56 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.4 Hz, 1H), 7.35 (d, J = 8.8 Hz, 1H), 4.43-4.43 (m, 2H), 4.24 (s, 2H), 3.65-3.49 (m, 2H), 2.99-2.89 (m, 4H), 2.74 (s, 2H), 2.24 (s, 3H), 1.69 (s, 3H)	
1243		1246	
MS (ESI) m/z 727.33 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.81 (s, 1H), 8.84 (d, J = 4.8 Hz, 1H), 8.26 (s, 1H), 7.96 (s, 1H), 7.62 (dd, J = 2.4, 9.2 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.4 Hz, 1H), 7.37 (d, J = 8.8 Hz, 1H), 4.42 (t, J = 4.8 Hz, 2H), 4.26 (t, J = 4.8 Hz, 2H), 3.95 (bs, 2H), 3.71 (m, 2H), 3.58 (m, 2H), 3.44 (m, 2H), 3.35 (s, 3H), 3.12 (d, J = 10 Hz, 2H), 3.12 (t, J = 10 Hz, 2H), 1.77 (s, 3H)		MS (ESI) m/z 673.24 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.68 (s, 1H), 8.08 (s, 1H), 7.56 (d, J = 7.84, 1H), 7.45 (s, 1H), 7.37-7.31 (m, 3H), 4.40 (s, 2H), 4.27 (s, 2H), 3.72-3.51 (m, 2H), 2.90 (bs, 4H), 2.25 (s, 5H), 1.83 (s, 3H)	
1244		1247	
MS (ESI) m/z 663.27 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.71 (bs, 1H), 8.73 (d, J = 4.4 Hz, 1H), 8.12 (s, 1H), 7.62 (s, 1H), 7.56 (dd, J = 8.8, 2.4 Hz, 1H), 7.38-7.31 (m, 3H), 4.68 (s, 1H), 4.40 (s, 2H), 4.26 (s, 2H), 3.86 (t, J = 12.0 Hz, 2H), 3.54 (d, J = 11.6 Hz, 2H), 3.22 (d, J = 12.8 Hz, 2H), 3.15-3.00 (m, 2H), 2.91 (s, 3H), 1.82 (s, 3H)		MS (ESI) m/z 673.19 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.77 (d, J = 4.8 Hz, 1H), 8.01 (s, 1H), 7.58 (dd, J = 2.8, 8.8 Hz, 1H), 7.51 (s, 1H), 7.41 (d, J = 4.8 Hz, 1H), 7.37 (d, J = 2.4 Hz, 1H), 7.34 (d, J = 6.8 Hz, 1H), 4.39 (t, J = 4.8 Hz, 2H), 4.24 (t, J = 4.0 Hz, 2H), 3.62 (bs, 2H), 2.81 (bs, 6H), 2.24 (s, 3H), 1.79 (s, 3H)	

1248		1251	
MS (ESI) m/z 653.30 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.54 (s, 1H), 8.06 (s, 1H), 7.52 (s, 1H), 7.31 (t, J = 9.9 Hz, 2H), 7.13 (s, 1H), 7.06 (s, 1H), 4.36 (s, 2H), 4.26 (s, 2H), 3.91-3.42 (m, 2H), 3.22-2.71 (m, 4H), 2.63-2.21 (m, 5H), 2.12 (s, 3H), 1.86 (s, 3H)		MS (ESI) m/z 640.27 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.10 (s, 1H), 8.84 (d, J = 4.5 Hz, 1H), 8.05 (s, 1H), 7.58 (dd, J = 9.0 Hz, 2.5 Hz, 1H), 7.55 (d, J = 4.5 Hz, 1H), 7.47 (d, J = 2.5 Hz, 1H), 7.35 (d, J = 8.9 Hz, 1H), 4.43 (t, J = 4.16 Hz, 2H), 4.27 (t, J = 4.36 Hz, 2H), 3.61 (bs, 4H), 2.96 (bs, 4H), 2.24 (s, 3H), 1.88 (s, 3H)	
1249		1252	
MS (ESI) m/z 653.31 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.73 (bs, 1H), 8.66 (d, J = 4.8 Hz, 1H), 8.05 (s, 1H), 7.55 (dd, J = 8.8, 2.4 Hz, 1H), 7.34-7.31 (m, 2H), 7.24 (d, J = 4.8 Hz, 1H), 7.13 (s, 1H), 4.41-4.34 (m, 2H), 4.30-4.20 (m, 2H), 3.87 (t, J = 11.6 Hz, 2H), 3.56 (d, J = 11.6 Hz, 2H), 3.26 (d, J = 12.0 Hz, 2H), 3.15-3.00 (m, 2H), 2.91 (s, 3H), 2.36 (s, 3H), 1.81 (s, 3H)		MS (ESI) m/z 667.36 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.60 (d, J = 4.7 Hz, 1H),), 8.01 (s, 1H), 7.54-7.51 (dd, J = 8.8, J = 2.5 Hz, 1H), 7.30 (m, 2H), 7.18 (d, J = 4.6 Hz, 1H), 4.37 (t, J = 12.7 Hz, 2H), 4.23 (t, J = 3.4 Hz, 2H), 3.64 (m, 4H), 2.89 (m, 4H), 2.23 (s, 6H), 1.97 (s, 3H), 1.79 (s, 3H)	
1250		1253	
MS (ESI) m/z 640.24 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.74 (bs, 1H), 9.16 (s, 1H), 8.07 (s, 1H), 8.01 (d, J = 5.32 Hz, 1H), 7.62 (dd, J = 8.9, 2.6 Hz, 1H), 7.46 (d, J = 2.6 Hz, 1H) 7.42 (d, J = 5.4 Hz, 1H) 7.36 (d, J = 9.0 Hz, 1H), 4.43 (t, J = 4.9 Hz, 2H), 4.29 (t, J = 4.32 Hz, 2H), 3.87 (t, J = 11.2 Hz, 2H), 3.55 (d, J = 11.6 Hz, 2H), 3.25 (d, 12.36 Hz, 2H), 3.15-3.00 (m, 2H), 2.90 (s, 3H), 1.93 (s, 3H)		MS (ESI) m/z 671.22 [M+1] +; 1H NMR (400 MHz, DMSO-d6) δ 8.01 (s, 1H), 7.78 (d, J = 5.6 Hz, 1H), 7.57 (dd, J = 2.80, 8.8 Hz, 1H), 7.39 (d, J = 2.8 Hz, 1H), 7.37 (d, J = 9.6 Hz, 1H), 7.34-7.31 (m, 2H), 5.59 (d, J = 46.8 Hz, 2H), 4.36 (t, J = 4.4 Hz, 2H), 4.25 (t, J = 4.0 Hz, 2H), 3.61 (bs, 2H), 2.93 (bs, 2H), 2.50 (bs, 2H), 2.25 (bs, 5H), 1.85 (s, 3H)	

1254		1259	
MS (ESI) m/z 664.26 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.8 Hz, 1H), 8.48 (s, 1H), 8.03 (s, 1H), 7.61 (dd, J = 2.4, 11.2 Hz, 1H), 7.50 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.4 Hz, 1H), 7.37 (d, J = 8.8 Hz, 1H), 4.40 (bs, 2H), 4.26 (bs, 2H), 3.57 (m, 2H), 3.02 (m, 4H), 2.60 (m, 2H), 2.24 (s, 3H), 1.76 (s, 3H)		MS (ESI) m/z 666.25 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.38 (d, J = 4.0 Hz 1H), 8.20 (s, 1H), 8.02 (s, 1H), 7.58 (d, J = 6.4 Hz, 1H), 7.42 (d, J = 9.2 Hz, 2H), 7.33 (d, J = 8.8 Hz 1H), 4.39 (s, 2H), 4.23 (s, 2H), 3.67 (s, 2H), 2.32 (s, 6H), 1.68 (s, 3H)
1255		1260	
MS (ESI) m/z 612.23 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.99 (bs, 1H), δ 8.63 (d, J = 4.8 Hz, 1H), δ 8.10 (s, 1H), 7.66 (d, J = 5.6 Hz, 1H), 7.54 (dd, J = 8.7 Hz, 2.5 Hz, 1H), 7.37 (d, J = 2.4 Hz, 1H), 7.33-31 (m, 2H), 7.21 (d, J = 4.4 Hz, 1H), 4.37 (t, J = 5.1 Hz, 2H), 4.27 (t, J = 4.5 Hz, 2H), 3.45-3.43 (m, 2H), 3.32 (bs, 2H), 2.95 (s, 6H), 1.96 (s, 3H)		MS (ESI) m/z 638.08 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.28 (s, 1H), 8.84 (d, J = 4.8 Hz, 1H), 8.47 (bs, 3H), 8.31 (s, 1H), 8.04 (s, 1H), 7.61 (dd, J = 8.8, 2.4 Hz, 1H), 7.49 (d, J = 4.4 Hz, 1H), 7.44 (d, J = 2.8 Hz, 1H), 7.37 (d, J = 9.2 Hz, 1H), 4.41 (bs, 2H), 4.27 (bs, 4H), 1.74 (s, 3H)
1256		1261	
MS (ESI) m/z 653.27 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.63 (d, J = 4.8 Hz, 1H), 8.05 (s, 1H), 7.72 (d, J = 5.6 Hz, 1H), 7.55 (dd, J = 2.4, 8.8 Hz, 1H), 7.42 (d, J = 5.6, Hz, 1H), 7.39 (d, J = 2.4 Hz, 1H), 7.32 (d, J = 8.8 Hz, 1H), 7.22 (d, J = 4.4 Hz, 1H), 4.38 (t, J = 4.4 Hz, 2H), 4.25 (t, J = 5.2 Hz, 2H), 3.85 (s, 2H), 2.47 (m, 4H), 2.27 (m, 4H), 1.83 (s, 3H), 1.23 (s, 3H)		MS (ESI) m/z 713. 27 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.25 (bs, 1H), 9.60 (bs, 1H), 8.84 (d, J = 4.8 Hz , 1H), 8.21 (s, 1H), 7.95 (s, 1H), 7.61 (dd, J = 2.4, 8.8 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.4 Hz, 1H), 7.36 (d, J = 9.2 Hz, 1H), 5.69 (bs, 1H), 4.41 (s, 2H), 4.24 (s, 2H), 3.95-3.89 (m, 3H), 3.63-3.58 (m, 2H), 3.22-3.30 (m, 6H), 2.96-2.89 (m, 4H), 1.75 (s, 3H)

1262		1270	
MS (ESI) m/z 749.29 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.37 (bs, 1H), 8.84 (d, J = 4.8 Hz, 1H), 8.24 (s, 1H), 7.94 (s, 1H), 7.59 (dd, J = 2.4, 8.8 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.4 Hz, 1H), 7.36 (d, J = 9.2 Hz, 1H), 4.40 (s, 2H), 4.23 (s, 2H), 3.96 (m, 2H), 3.48 (m, 4H), 3.24 (m, 1H), 2.96 (s, 3H), 1.72 (s, 3H)		MS (ESI) m/z 691.31 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.11 (bs, 1H), 8.7 (d, J = 4.7 Hz, 1H), 8.62 (s, 1H), 8.26 (s, 1H), 7.76 (d, J = 8.1 Hz, 1H), 7.72-7.66 (m, 2H), 7.25 (d, J = 4.7 Hz, 1H), 5.01-4.45 (m, 2H), 4.20-3.82 (m, 4H), 3.70-3.45 (m, 2H), 2.88 (s, 3H), 2.16 (s, 3H)
1263		1271	
MS (ESI) m/z 682.0 [M+1]+; ; 1H NMR (400 MHz, DMSO-d6) δ 8.28 (s, 1H), 7.90 (s, 1H), 7.63-7.56 (m, 1H), 7.46-7.38 (m, 2H), 7.35 (d, J = 8.96 Hz, 1H), 4.49-4.32 (m, 2H), 4.31-4.18 (m, 2H), 3.70-3.66 (m, 1H), 3.26-3.22 (m, 2H), 2.69 (s, 3H), 2.32-2.22 (m, 2H), 2.22-2.09 (m, 2H), 2.07 (s, 3H), 1.80 (s, 3H)		MS (ESI) m/z 691.28 [M+1]+; ; 1H NMR (400 MHz, DMSO-d6) δ 13.75 (bs, 1H), 9.75 (bs, 1H), 8.74 (d, J = 4.8 Hz, 1H), 8.11 (s, 1H), 7.76-7.69 (m, 2H), 7.65 (s, 1H), 7.58 (d, J = 4.8 Hz, 1H), 4.86 (s, 2H), 3.89 (t, J = 22.4 Hz, 2H), 3.59 (d, J = 11.2 Hz, 2H), 3.30 (d, J = 11.2 Hz, 2H), 3.11 (d, J = 8 Hz, 2H), 2.92 (bs, 3H), 2.64 (s, 3H), 2.22 (s, 3H)
1269		1272	
MS (ESI) m/z 699.27 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.12 (bs, 1H), 8.94 (s, 1H), 8.91 (d, J = 4.8 Hz, 1H), 8.15 (s, 1H), 7.75 (d, J = 9.2 Hz, 1H), 7.57 (d, J = 4.4 Hz, 1H), 7.49 (bs, 2H), 4.18 (t, J = 6.0 Hz, 2H), 3.87 (bs, 2H), 3.54 (d, J = 12.4 Hz, 2H), 3.33 (bs, 2H), 3.22 (d, J = 11.6 Hz, 2H), 3.08 (bs, 2H), 2.90 (s, 3H), 2.52 (s, 3H)		MS (ESI) m/z 711.31 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.8 (d, J = 4.8 Hz, 1H), 8.09 (s, 1H), 7.60 (dd, J = 8.8 Hz, 2.4 Hz, 1H), 7.50 (d, J = 4.8 Hz, 1H), 7.44 (d, J = 2.4 Hz, 1H), 7.35 (d, J = 8.8 Hz 1H), 4.42 (bs, 2H), 4.28 (bs, 2H), 4.08-3.55 (m, 6H), 2.87 (s, 3H), 2.37 (s, 3H), 1.82 (s, 3H)	

1275		1286	
MS (ESI) m/z 724.28 [M+1]+; 1H NMR (400 MHz, DMSO-d6) 13.73 (bs, 1H), 8.17 (s, 1H), 7.96 (s, 1H), 7.62-7.59 (dd, J = 2.8, 9.2 Hz, 1H), 7.47-7.44 (m, 2H), 7.37 (d, J = 8.8 Hz, 1H), 4.41 (bs, 2H), 4.24 (bs, 2H), 3.43-3.40 (m, 2H), 3.23-2.86 (m, 6H), 2.73 (s, 3H), 2.02 (bs, 1H), 1.79 (bs, 5H), 1.64-1.55 (m, 2H), 1.37 (t, J = 7.6 Hz, 3H)		MS (ESI) m/z 714.39 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.23 (bs, 1H), 8.14 (s, 1H), 7.52 (dd, J = 8.8 Hz, 2.5 Hz, 1H), 7.27-7.25 (m, 2H), 7.23-7.21 (m, 2H), 4.34-4.33 (m, 2H), 4.27-4.25 (m, 2H), 3.87 (t, J = 12.3 Hz, 2H), 3.55-3.53 (m, 2H), 3.18-3.15 (m, 2H), 3.08-3.06 (m, 2H), 2.89 (s, 3H), 2.04 (s, 3H), 1.83 (s, 3H)	
1276		1287	
MS (ESI) m/z 710.27 [M+1]+; ; 1H NMR (400 MHz, DMSO-d6) δ 13.70 (bs, 1H), 8.45 (bs, 1H), 8.17 (s, 1H), 7.96 (s, 1H), 7.61-7.59 (dd, J = 6.8, 8.8 Hz, 1H), 7.46-7.43 (m, 2H), 7.37 (d, J = 8.8 Hz, 1H), 4.41 (bs, 2H), 4.24 (bs, 2H), 3.30 (m, 2H), 3.06-2.98 (m, 4H), 2.84 (m, 2H), 2.08 (bs, 1H), 1.79 (s, 3H), 1.75 (d, J = 13.6 Hz, 2H), 1.60 (t, J = 10.0 Hz, 2H), 1.37 (t, J = 7.6 Hz, 3H)		MS (ESI) m/z 704.27 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.8 Hz, 1H), 8.20 (s, 1H), 7.98 (s, 1H), 7.60 (dd, J = 8.8 Hz, 2.4 Hz, 1H), 7.49 (d, J = 4.4 Hz, 1H), 7.42-7.36 (m, 2H), 4.41 (bs, 6H), 4.24 (s, 2H), 3.31 (d, J = 6.4 Hz, 2H), 3.21 (d, J = 4.8 Hz, 2H), 1.81 (s, 3H)	
1283		1288	
MS (ESI) m/z 682.22 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 14.06 (bs, 1H), 8.79 (d, J = 5.2 Hz, 1H), 7.97 (d, J = 5.2 Hz, 1H), 7.61 (dd, J = 2.8, 9.2 Hz, 1H), 7.52 (d, J = 4.8 Hz, 1H), 7.9 (d, J = 2.4 Hz, 1H), 7.38 (d, J = 9.2 Hz, 1H), 4.42 (bs, 2H), 4.27 (bs, 2H), 4.20 (d, J = 6.0 Hz, 2H), 4.02 (d, J = 8.0 Hz, 2H), 3.95 (bs, 1H), 3.38 (d, J = 5.6 Hz, 2H), 2.85 (d, J = 4.8 Hz, 3H), 2.33 (s, 3H), 1.88 (s, 3H)		MS (ESI) m/z 706.37 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.4 Hz 1H), 8.21 (s, 1H), 7.98 (s, 1H) 7.59 (dd, J = 8.9, 2.6 Hz, 1H), 7.49 (d, J = 4.8 Hz 1H), 7.42 (d, J = 2.8 Hz, 1H), 7.36 (d, J = 8.8 Hz, 1H), 6.18 - 6.46 (m, 1H), 4.41 (t, J = 6.02 Hz, 2H), 4.25 (t, J = 8.0 Hz, 2H), 3.39 (s, 4H), 3.09 (s, 2H), 2.73 (s, 3H), 1.77 (s, 3H)	

1289		1293	
MS (ESI) m/z 620.27 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.79 (bs, 1H), 8.17 (s, 1H), 7.91 (s, 1H), 7.67-7.62 (m, 3H), 7.51 (bs, 2H), 7.37 (bs, 1H), 5.02 (s, 2H), 3.87-3.45 (m, 4H), 3.21-2.91 (m, 4H), 3.02 (bs, 3H), 2.85 (bs, 3H)		MS (ESI) m/z 765.30 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.26 (bs, 1H), 8.82 (d, J = 4.8 Hz, 1H), 8.28 (s, 1H), 7.93 (s, 1H), 7.59 (d, J = 8.8 Hz, 1H), 7.46 (d, J = 4.4 Hz, 1H), 7.42 (s, 1H), 7.35 (d, J = 10.8 Hz, 1H), 4.39 (bs, 2H), 4.23 (bs, 2H), 3.63 (bs, 2H), 3.31 (bs, 2H), 2.95 (m, 4H), 2.60 (t, J = 7.2 Hz, 4H), 1.71 (s, 3H)	
1291		1298	
MS (ESI) m/z 709.12 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.4 Hz, 1H), 8.23 (s, 1H), 7.96 (s, 1H), 7.60 (dd, J = 6.4 Hz, 2.4 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.4 Hz, 1H), 7.36 (d, J = 8.8 Hz, 1H), 4.40 (s, 2H), 4.24 (s, 2H), 3.85 (s, 4H), 3.29 (bs, 4H), 3.12 (bs, 1H), 1.76 (s, 3H), 1.01 (s, 2H), 0.85 (s, 2H)		MS (ESI) m/z 650.26 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.06 (bs, 1H), 8.75 (d, J = 4.8 Hz, 1H), 8.57 (s, 1H), 8.14 (s, 1H), 7.77 (d, J = 8.0 Hz, 1H), 7.70-7.66 (m, 2H), 7.55 (d, J = 4.8 Hz, 1H), 4.88 (s, 2H), 3.38-3.23 (m, 4H), 3.18-3.08 (m, 2H), 2.78 (s, 6H), 2.16 (s, 3H)	
1292		1372	
MS (ESI) m/z 759.38 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.30 (bs, 1H), 8.83 (d, J = 4.8 Hz, 1H), 8.25 (s, 1H), 7.96 (s, 1H), 7.60 (dd, J = 6.4, 9.2 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.4 Hz, 1H), 7.36 (d, J = 8.8 Hz, 1H), 4.40 (s, 2H), 4.24 (s, 2H), 3.85-3.52 (m, 5H), 3.02 (m, 8H), 1.75 (m, 3H)		MS (ESI) m/z 606.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.63 (dd, J = 5.0, 0.8 Hz, 1H), 8.38 (d, J = 1.7 Hz, 1H), 8.26 (dd, J = 1.7, 0.8 Hz, 1H), 8.03 (dd, J = 1.7, 0.8 Hz, 1H), 7.70 (dd, J = 5.0, 1.8 Hz, 1H), 7.57 – 7.39 (m, 2H), 7.27 (d, J = 8.9 Hz, 1H), 4.40 (s, 4H), 3.39 (s, 3H), 2.23 (s, 3H)	

1374		1377	
MS (ESI) m/z 628.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.36 (d, J = 1.7 Hz, 1H), 8.25 (s, 3H), 7.99 (d, J = 1.7 Hz, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.45 (s, 1H), 7.39 – 7.34 (m, 2H), 4.41 (d, J = 5.1 Hz, 2H), 4.27 (t, J = 5.1 Hz, 2H), 3.41 (d, J = 6.0 Hz, 2H), 3.28 (t, J = 6.5 Hz, 2H), 1.83 (s, 3H)		MS (ESI) m/z 746.4 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.31 (s, 1H), 8.16 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.45 – 7.34 (m, 3H), 5.49 (d, J = 22.9 Hz, 2H), 4.58 (t, J = 13.1 Hz, 2H), 4.42 (s, 2H), 4.29 (s, 2H), 3.82 (s, 2H), 2.72 (s, 3H), 1.84 (s, 3H)	
1375		1380	
MS (ESI) m/z 624.0 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 11.41 (s, 1H), 8.83 (d, J = 4.7 Hz, 1H), 8.34 (d, J = 1.6 Hz, 1H), 7.95 (s, 1H), 7.81 (d, J = 1.6 Hz, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.45 – 7.39 (m, 2H), 7.35 (d, J = 9.0 Hz, 1H), 6.92 (s, 1H), 4.40 (d, J = 5.0 Hz, 2H), 4.25 (t, J = 4.9 Hz, 2H), 1.74 (s, 3H)		MS (ESI) m/z 690.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.60 – 8.48 (m, 1H), 8.37 (s, 1H), 8.12 (s, 1H), 7.86 (d, J = 7.8 Hz, 1H), 7.60 (dd, J = 8.9, 2.8 Hz, 1H), 7.52 – 7.42 (m, 3H), 7.36 (d, J = 9.0 Hz, 1H), 4.50 – 4.34 (m, 2H), 4.27 (d, J = 5.4 Hz, 2H), 2.72 (s, 3H), 2.10 (s, 3H), 1.81 (s, 3H)	
1376		1381	
MS (ESI) m/z 714.3 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.27 (s, 1H), 7.95 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.46 – 7.40 (m, 2H), 7.36 (d, J = 9.0 Hz, 1H), 4.40 (d, J = 5.0 Hz, 2H), 4.25 (s, 2H), 3.91 (s, 2H), 2.70 (s, 5H), 2.58 (s, 2H), 1.83 (s, 3H)		MS (ESI) m/z 694.0 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.87 (s, 1H), 8.76 – 8.65 (m, 1H), 8.34 (s, 1H), 8.14 (s, 1H), 7.73 (t, J = 5.5 Hz, 1H), 7.60 (dd, J = 8.9, 2.6 Hz, 1H), 7.49 – 7.40 (m, 2H), 7.37 (d, J = 9.0 Hz, 1H), 4.50 – 4.18 (m, 4H), 2.72 (s, 3H), 1.87 (s, 3H)	

1383		1389	
MS (ESI) m/z 708.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.42 (s, 1H), 8.28 (s, 1H), 8.05 (s, 1H), 7.98 – 7.90 (m, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.47 – 7.40 (m, 2H), 7.37 (d, J = 9.0 Hz, 1H), 4.42 (t, J = 5.0 Hz, 2H), 4.29 (d, J = 4.9 Hz, 2H), 2.73 (s, 3H), 2.58 (d, J = 2.9 Hz, 3H), 1.88 (s, 3H)		MS (ESI) m/z 706.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 10.03 (s, 1H), 9.47 (s, 1H), 9.18 (s, 1H), 8.23 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.49 (s, 1H), 7.41 (d, J = 9.0 Hz, 1H), 7.30 (d, J = 2.7 Hz, 1H), 7.19 (s, 1H), 4.53 (t, J = 5.2 Hz, 2H), 4.15 (t, J = 5.2 Hz, 2H), 2.67 (d, J = 0.7 Hz, 3H), 2.33 (s, 3H), 2.29 (s, 3H)
1384		1391	
MS (ESI) m/z 728.0 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.72 (d, J = 9.9 Hz, 1H), 8.31 (s, 1H), 8.13 (s, 1H), 8.03 (d, J = 9.1 Hz, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.45 (s, 1H), 7.43 (d, J = 2.7 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.53 – 4.20 (m, 4H), 2.72 (s, 3H), 1.88 (s, 3H)		MS (ESI) m/z 711.0 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.13 (s, 1H), 7.93 (s, 1H), 7.58 (dd, J = 8.9, 2.7 Hz, 1H), 7.39 – 7.31 (m, 2H), 7.28 (s, 1H), 4.40 (s, 2H), 4.26 (s, 2H), 3.87 (s, 5H), 3.57 (d, J = 11.7 Hz, 2H), 3.27 (d, J = 12.9 Hz, 2H), 3.09 (d, J = 10.7 Hz, 2H), 2.91 (d, J = 4.2 Hz, 3H), 2.66 (s, 3H), 1.83 (s, 3H)
1388		1392	
MS (ESI) m/z 708.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.63 – 8.59 (m, 1H), 8.33 (s, 1H), 8.11 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.50 (d, J = 10.7 Hz, 1H), 7.45 (s, 1H), 7.43 (d, J = 2.7 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.53 – 4.02 (m, 4H), 2.72 (s, 3H), 2.62 (s, 3H), 1.85 (s, 3H)		MS (ESI) m/z 740.9 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.79 (s, 1H), 7.93 (s, 1H), 7.61 (dd, J = 8.9, 2.7 Hz, 1H), 7.44 (s, 1H), 7.41 (d, J = 2.7 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 5.35 (s, 1H), 4.41 (t, J = 5.0 Hz, 2H), 4.26 (t, J = 5.0 Hz, 2H), 3.97 (t, J = 12.1 Hz, 2H), 3.79 (t, J = 5.2 Hz, 2H), 3.64 (d, J = 11.8 Hz, 2H), 3.15 (dd, J = 29.0, 12.1 Hz, 4H), 2.71 (s, 3H), 2.43 (s, 3H), 1.97 (s, 3H)	

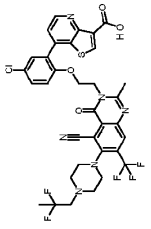
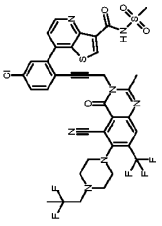
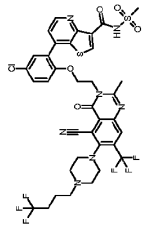
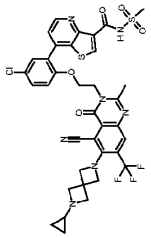
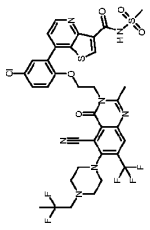
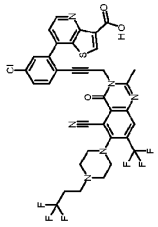
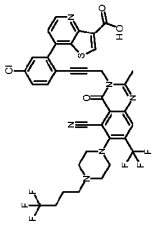
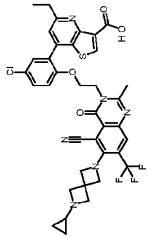
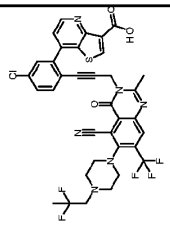
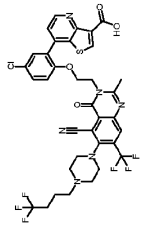
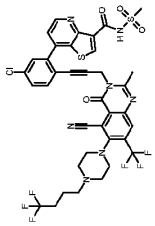
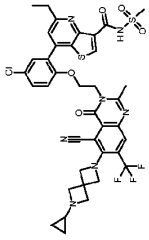
1393		1417	
[01858] MS (ESI) m/z 741.0 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.59 (s, 2H), 7.93 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.43 (s, 1H), 7.41 (d, J = 2.7 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.42 (t, J = 5.6 Hz, 4H), 4.26 (t, J = 5.0 Hz, 2H), 3.16 (s, 4H), 3.00 (s, 2H), 2.82 (s, 4H), 2.70 (s, 3H), 2.40 (s, 3H), 1.92 (s, 3H)		MS (ESI) m/z 708.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 10.05 (s, 1H), 8.04 – 7.95 (m, 1H), 7.61 (dd, J = 8.9, 2.7 Hz, 1H), 7.45 (s, 1H), 7.41 (d, J = 2.7 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 6.54 (s, 1H), 5.91 (s, 1H), 4.42 (t, J = 5.1 Hz, 2H), 4.34 – 4.21 (m, 2H), 4.13 (d, J = 17.4 Hz, 1H), 3.84 (d, J = 16.9 Hz, 1H), 3.70 – 3.57 (m, 1H), 3.40 – 3.27 (m, 1H), 3.02 – 2.89 (m, 3H), 2.71 (s, 3H), 2.64 (s, 1H), 2.41 (s, 3H), 1.98 (s, 3H)
1394		1420	
MS (ESI) m/z 696.4 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.77 (s, 1H), 9.59 (s, 1H), 8.15 (d, J = 5.8 Hz, 1H), 7.94 (d, J = 2.2 Hz, 1H), 7.61 (dd, J = 8.9, 2.7 Hz, 1H), 7.47 (s, 1H), 7.44 (d, J = 2.6 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 4.42 (t, J = 5.0 Hz, 2H), 4.35 – 4.18 (m, 3H), 4.01 (dt, J = 22.5, 10.9 Hz, 2H), 3.11 (d, J = 8.1 Hz, 1H), 3.01 (q, J = 7.5 Hz, 2H), 2.86 (dd, J = 11.5, 5.1 Hz, 2H), 1.81 (s, 3H), 1.36 (t, J = 7.5 Hz, 3H)		MS (ESI) m/z 723.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.37 (s, 1H), 7.78 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.42 – 7.40 (m, 2H), 7.36 (d, J = 8.9 Hz, 1H), 4.70 (s, 2H), 4.61 (s, 2H), 4.49 – 4.39 (m, 2H), 4.38 (t, J = 5.0 Hz, 2H), 4.27 – 4.17 (m, 4H), 2.82 (d, J = 5.2 Hz, 3H), 2.70 (s, 3H), 1.92 (s, 3H)
1416		1570	
MS (ESI) m/z 711.0 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.75 (s, 1H), 7.93 (s, 1H), 7.61 (dd, J = 8.9, 2.7 Hz, 1H), 7.44 (s, 1H), 7.41 (d, J = 2.7 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 4.40 (t, J = 4.9 Hz, 2H), 4.26 (t, J = 5.0 Hz, 2H), 3.86 (t, J = 12.3 Hz, 2H), 3.56 (d, J = 11.4 Hz, 3H), 3.20 (d, J = 12.6 Hz, 2H), 3.09 (q, J = 11.2 Hz, 2H), 2.95 – 2.87 (m, 3H), 2.71 (s, 3H), 2.42 (s, 3H), 1.96 (s, 3H)		MS (ESI) m/z 715.47 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 8.77 (d, J = 5.2 Hz, 1H), 8.66 (s, 1H), 7.93 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.70-7.66 (m, 2H), 7.56 (d, J = 4.4 Hz, 1H), 4.82 (s, 2H), 4.73-4.41 (m, 8H), 3.05 (bs, 1H), 2.11 (s, 3H), 0.77 (bs, 4H)

1612		1615	
MS (ESI) m/z 775.53 [M+1]+; 1H NMR (400 MHz, DMSO-d6 with D2O) δ 8.75 (d, J = 4.68 Hz 1H), 8.10 (d, J = 9.44 Hz, 1H), 8.03 (s, 1H), 7.53 (dd, J = 2.56, 8.92 Hz, 1H), 7.34 (d, J = 2.60 Hz, 1H), 7.31 (d, J = 4.68 Hz, 1H), 7.27 (d, J = 9.0 Hz, 1H), 4.35 (bs, 2H), 4.25-4.20 (m, 6H), 3.55 (bs, 2H), 2.93 (bs, 2H), 2.50 (bs, 2H), 2.20 (s, 5H), 1.58 (s, 3H), 1.27 (t, J = 7.04 Hz, 6H)		MS (ESI) m/z 745.50 [M+1]+; 1H NMR (400 MHz, DMSO-d6 with D2O) δ 8.63 (d, J = 4.80 Hz, 1H), 8.12 (s, 1H), 7.98 (d, J = 8.80 Hz, 1H), 7.49 (dd, J = 2.40, 8.80 Hz, 1H), 7.32 (d, J = 2.40 Hz, 1H), 7.23 (d, J = 9.20 Hz, 1H), 7.14 (d, J = 4.4 Hz, 1H), 4.31 (s, 2H), 4.20 (s, 2H), 3.49 (bs, 3H), 2.84 (bs, 4H), 1.75 (bs, 2H), 1.70 (s, 3H), 0.44 (d, J = 6.00 Hz, 2H), 0.38 (bs, 2H)	
1613		1619	
MS (ESI) m/z 719.52 [M+1]+ ; 1H NMR (400 MHz, DMSO-d6 with D2O) δ 8.60 (d, J = 4.00 Hz 1H), 8.14 (s, 1H), 7.97 (d, J = 8.80 Hz, 1H), 7.49 (dd, J = 2.40, 8.80 Hz, 1H), 7.34 (d, J = 2.00 Hz, 1H), 7.24 (d, J = 9.20 Hz, 1H), 7.13 (d, J = 4.80 Hz, 1H), 4.32 (bs, 2H), 4.21 (bs, 2H), 3.67 (bs, 2H), 3.11 (bs, 4H), 2.76 (bs, 2H), 2.59 (s, 3H), 1.74 (s, 3H)		MS (ESI) m/z 642.01[M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.33 (s, 1H), 7.89 (s, 1H), 7.59 (dd, J = 2.60, 8.88 Hz, 1H), 7.43 (s, 1H), 7.42 (d, J = 2.64 Hz, 1H), 7.36 (d, J = 8.96 Hz, 1H), 4.39 (t, J = 4.68 Hz, 2H), 4.23 (t, J = 4.64 Hz, 2H), 2.94 (s, 6H), 2.70 (s, 3H), 1.81 (s, 3H)	
1614		1899	
MS (ESI) m/z 801.60 [M+1]+; 1H NMR (400 MHz, DMSO-d6 with D2O) δ 8.75 (d, J = 4.80 Hz, 1H), 8.09 (d, J = 9.60 Hz, 1H), 8.03 (s, 1H), 7.53 (dd, J = 2.40, 8.80 Hz, 1H), 7.33-7.30 (m, 2H), 7.26 (d, J = 8.80 Hz, 1H), 4.34 (s, 2H), 4.23-4.19 (m, 6H), 3.50 (bs, 2H), 2.79 (bs, 5H), 1.67 (bs, 2H), 1.58 (s, 3H), 1.27 (t, J = 6.80 Hz, 6H), 0.43 (bs, 2H), 0 .35 (bs, 2H)		MS (ESI) m/z 571 [M+1]; 1H NMR (400 MHz, DMSO-d6) δ 8.79 (s, 1H), 8.43 (d, J=16.6 Hz, 2H), 8.11 (s, 1H), 7.79 (bs, 1H), 7.60 (s, 1H), 7.46 (m, 2H), 7.35 (m, 1H), 4.40 (s, 2H), 4.20 (s, 2H), 3.89 (s, 1H)	

1900	MS (ESI) m/z 599.1 [M+1]	1903	MS (ESI) m/z 603.21 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.84 (d, J = 4.8 Hz, 1H), 8.38 (bs, 1H), 8.28 (s, 1H), 8.01 (bs, 1H), 7.63 (d, J = 8.4 Hz, 1H), 7.54 (d, J = 11.4 Hz, 1H), 7.49 (d, J = 4.8 Hz, 1H), 4.43 (t, J = 4.4 Hz, 2H), 4.25 (t, J = 4.4 Hz, 2H), 1.73 (s, 3H)
1901	MS (ESI) m/z 579.15 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.75(d, J =4.48 Hz, 1H), 8.59 (s, 1H), 8.41 (s, 1H), 8.14 (s, 1H), 7.76 (d, J=8.8 Hz, 1H), 7.69 (d, J=6.04 Hz, 2H), 7.56 (d, J=4.48 Hz, 1H), 4.88(s, 2H), 2.10 (s, 3H)	1904	MS (ESI) m/z 619.07 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.86 (d, J = 4.4 Hz, 1H), 8.24 (s, 1H), 8.08 (s, 1H), 7.60 (dd, J = 8.8, 2.6 Hz, 1H), 7.51 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.6 Hz, 1H), 7.36 (d, J = 8.8 Hz, 1H), 4.41 (t, J = 4.7 Hz, 2H), 4.25 (t, J = 4.7 Hz, 2H), 1.69 (s, 3H)
1902	MS (ESI) m/z 627.8 [M+1]+	1905	MS (ESI) m/z 633.04 [M+1]+

1906		1909	MS (ESI) m/z 708.1 [M+1]+
1907	MS (ESI) m/z 656.15 [M+1]	1910	MS (ESI) m/z 690.3 [M+1]+
1908	MS (ESI) m/z 724.6 [M+1]+	1911	MS (ESI) m/z 722.0 [M+1]+

1912	MS (ESI) m/z 773.3 [M+1]+	1915	1918
1913	MS (ESI) m/z 850.3 [M+1]+	1916	1919
1914		1917	1920

1921	1924	1927	1930
			
1922	1925	1928	1931
			
1923	1926	1929	1932
			

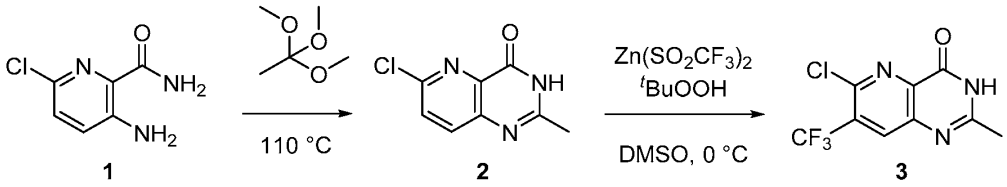
1933	2015	2019	MS (ESI) m/z 624.0 [M+1]+
1934	2016	2028	MS (ESI) m/z 747.2 [M+1]+
1994	2018	2036	MS (ESI) m/z 615.1 [M+1]+
2037	MS (ESI) m/z 626.05 [M+1]+		

Example 3. General Methods for Synthesizing Other Compounds

[0405] Compounds in Table 3 can be synthesized using methods described in Example 3. Many of the reactions described in Examples 1 and 2 were also used to synthesize compounds in Table 3.

Example 3A. Methods of synthesizing the left-hand side

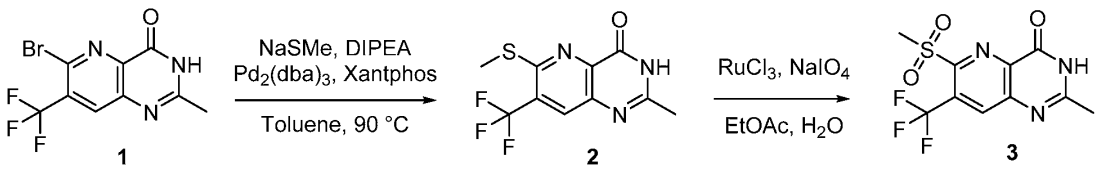
Example 3A.1



[0406] 3-amino-6-chloropicolinamide (1, 3.00 g, 16.6 mmol) is dissolved in 1,1,1-triethoxyethane (45 mL, 16.6 mmol) in a flame dried round bottom flask equipped with a stir bar. The reaction mixture heated to 110 °C for 90 min then cooled to 10 °C and diluted with cold ether. The solids are filtered and washed several times with cold ether. Drying the solids *in vacuo* afforded 6-chloro-2-methylpyrido[3,2-d]pyrimidin-4(3H)-one (2).

[0407] 6-chloro-2-methylpyrido[3,2-d]pyrimidin-4(3H)-one (2, 1.00 g, 5.1 mmol) is dissolved in DMSO (30 mL) in a round bottomed flask equipped with a stir bar. The reaction mixture is stirred at 10 °C while bis(trifluoromethylsulfonyl)zinc (4.23 g, 12.8 mmol) is added in 1 portion. *tert*-Butyl hydroperoxide (3.53 mL, 19.2 mmol) is then added dropwise via addition funnel. After 5 min the reaction mixture is warmed to room temperature and after an additional 5 min it is warmed to 50 °C for 6.5 h. The reaction mixture is cooled to room temperature and then the reaction mixture is diluted with saturated sodium bicarbonate and ethyl acetate. The layers are separated and the aqueous phase extracted with ethyl acetate three times. The combined organic material is washed with brine and dried over magnesium sulfate. The solids are filtered and solvent removed *in vacuo* to afford 6-chloro-2-methyl-7-(trifluoromethyl)pyrido[3,2-d]pyrimidin-4(3H)-one (**3**).

Example 3A.2

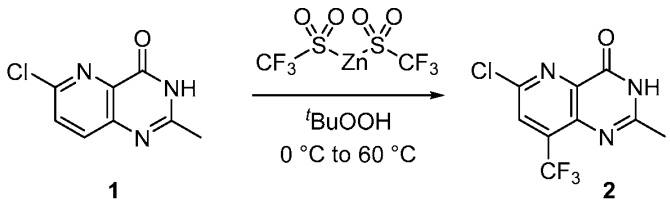


[0408] A solution of 6-bromo-2-methyl-7-(trifluoromethyl)pyrido[3,2-d]pyrimidin-4(3*H*)-one (**1**, 0.3 g, 0.977 mmol), sodium thiomethoxide (0.102 g, 1.46 mmol), *N*,*N*-diisopropylethylamine

(0.378 g, 2.93 mmol), and Xantphos (0.056 g, 0.097 mmol) in toluene (3 mL) is degassed for 10 min using argon. Then, tris(dibenzylideneacetone)dipalladium(0) (0.042 g, 0.048 mmol) is added and the mixture is degassed again with argon for 5 min. The reaction mixture is stirred at 90 °C for 2 h. After this time, the reaction mixture is diluted with water and extracted with ethyl acetate. The organic layer is dried over anhydrous sodium sulfate, filtered, and concentrated to dryness under reduced pressure to obtain the crude product. This is purified by flash column chromatography using silica gel (100-200 mesh) and 60-80 % ethyl acetate in hexanes as eluent to afford 2-methyl-6-(methylthio)-7-(trifluoromethyl)pyrido[3,2-d]pyrimidin-4(3*H*)-one (**2**).

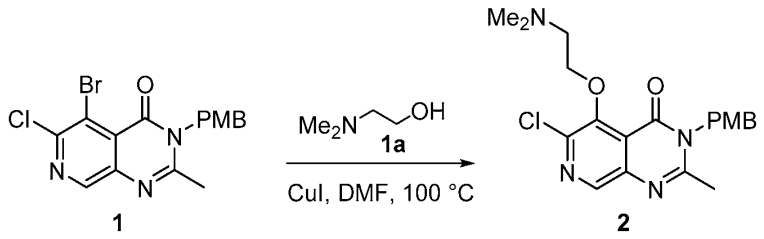
[0409] To a solution of 2-methyl-6-(methylthio)-7-(trifluoromethyl)pyrido[3,2-d]pyrimidin-4(3*H*)-one (**2**, 0.2 g, 0.727 mmol) in ethyl acetate (4.0 mL) and water (1.0 mL) is added ruthenium(III) chloride (0.007 g, 0.0363 mmol) followed by sodium periodate (0.929 g, 4.36 mmol). The reaction mixture is stirred at room temperature for 30 min. After this time, the reaction mixture is filtered and the filtrate is concentrated under reduced pressure to obtain the crude product. This is purified by pentane wash to afford 2-methyl-6-(methylsulfonyl)-7-(trifluoromethyl)pyrido[3,2-d]pyrimidin-4(3*H*)-one (**3**).

Example 3A.3



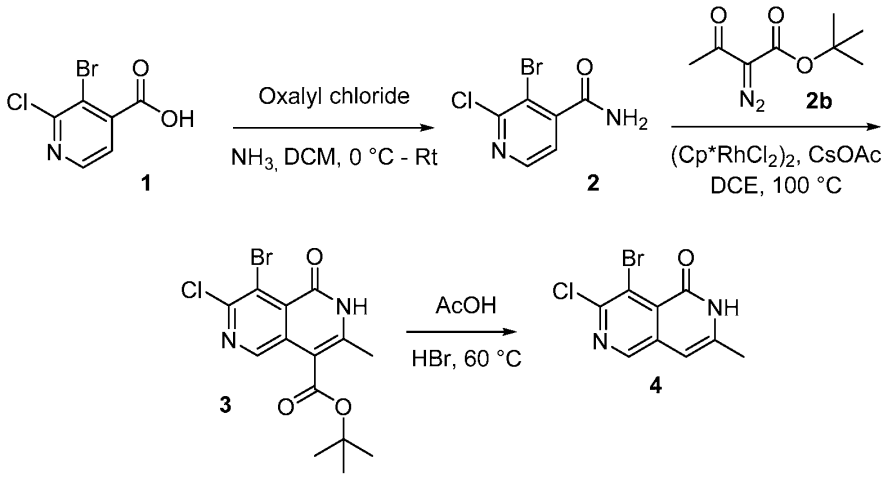
[0410] 6-chloro-2-methylpyrido[3,2-d]pyrimidin-4(3H)-one (1, 1.00 g, 5.1 mmol) is dissolved in dimethyl sulfoxide (30 mL) in a round bottomed flask equipped with a stir bar. The reaction mixture is stirred at 10 °C while bis(trifluoromethylsulfonyl)zinc (4.23 g, 12.8 mmol) is added in 1 portion. *tert*-Butyl hydroperoxide (3.53 mL, 19.2 mmol) is then added dropwise via addition funnel. After 5 min the reaction mixture is warmed to room temperature and after an additional 5 min it is warmed to 50 °C for 6.5 h. The reaction mixture is cooled to room temperature and then diluted with saturated aqueous sodium bicarbonate and ethyl acetate. The layers are separated and the aqueous phase extracted with ethyl acetate three times. The combined organic material is washed with brine and dried over magnesium sulfate. The solids are filtered and solvent removed *in vacuo* to afford a mixture of 6-chloro-2-methyl-8-(trifluoromethyl)pyrido[3,2-d]pyrimidin-4(3H)-one (2).

Example 3A.4



[0411] 5-bromo-6-chloro-3-(4-methoxybenzyl)-2-methylpyrido[3,4-d]pyrimidin-4(3H)-one (**1**, 50 mg, 0.13 mmol) and copper(I) iodide (26.5 mg, 0.139 mmol) are combined in a sealable vessel with a stirbar and suspended in 1 mL 2-(dimethylamino)ethan-1-ol (**1a**). The resulting mixture is sparged with argon for 3 min and then sealed, vigorously stirred, and heated at 100 °C. After 10 min LCMS shows complete consumption of the starting material. The mixture is cooled to room temperature and concentrated. The residue is taken up in MeCN/DMSO and purified by prep-HPLC (MeCN/water+0.1 %TFA) to afford 6-chloro-5-(2-(dimethylamino)ethoxy)-3-(4-methoxybenzyl)-2-methylpyrido[3,4-d]pyrimidin-4(3H)-one (**2**).

Example 3A.5

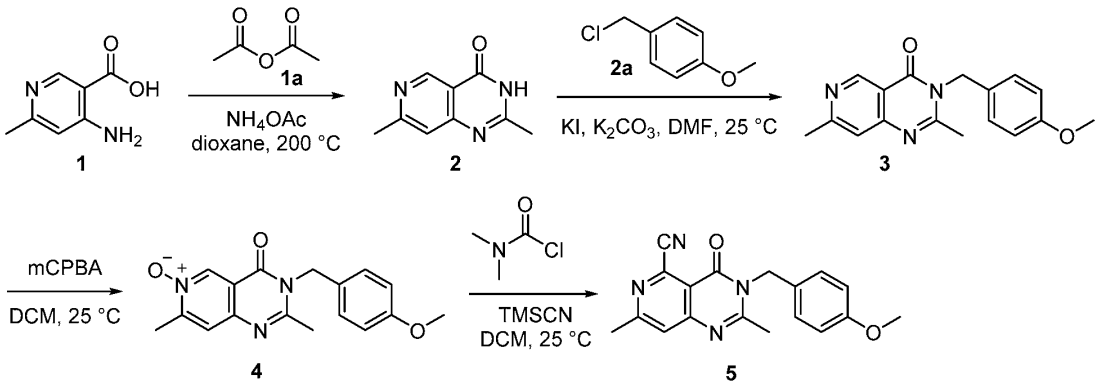


[0412] To a solution of 3-bromo-2-chloroisonicotinic acid (1, 3.0 g, 12.76 mmol) in dichloromethane (20 mL) is added *N,N*-dimethylformamide (0.09 mL, 1.27 mmol) at 0 °C followed by oxalyl chloride (1.7 mL, 19.14 mmol). Then the reaction mixture is stirred at -25 °C for 2 h. After completion, the reaction mixture is evaporated to dryness under reduced pressure. Crude reaction mixture is diluted with dichloromethane (10 mL) and poured into ice cold aqueous ammonia in a drop wise manner. Precipitated solid is filtered through sintered funnel and dried under vaccum to afford 3-bromo-2-chloroisonicotinamide (2).

[0413] To a solution of 3-bromo-2-chloroisonicotinamide (**2**, 2.5 g, 10.68 mmol), pentamethylcyclopentadienylrhodium(III) chloride dimer (0.33 g, 0.53 mmol) and cesium acetate (1.02 g, 5.34 mmol) in 1,2-dichloroethane (25 mL) is added *tert*-butyl 2-diazo-3-oxobutanoate (**2b**, 2.96 g, 16.00 mmol) to the reaction mixture at room temperature under nitrogen atmosphere. Reaction mixture is heated to 100 °C for 16 h. After completion, the reaction mixture is cooled to room temperature, concentrated to dryness under reduced pressure followed by washing with ether and pentane to afford *tert*-butyl 8-bromo-7-chloro-3-methyl-1-oxo-1,2-dihydro-2,6-naphthyridine-4-carboxylate (**3**).

[0414] To *tert*-butyl 8-bromo-7-chloro-3-methyl-1-oxo-1,2-dihydro-2,6-naphthyridine-4-carboxylate (**3**, 3.0 g, 8.00 mmol) 30 % hydrobromic acid in acetic acid (30 mL) is added and the reaction mixture is stirred at 80 °C for 16 h. After completion, the reaction is quenched with ice cold water and extracted with ethyl acetate. The organic layer is washed with cold water, dried over anhydrous sodium sulfate, filtered and concentrated to dryness under reduced pressure to afford crude 8-bromo-7-chloro-3-methyl-2,6-naphthyridin-1(2H)-one (**4**).

Example 3A.6



[0415] 4-Amino-6-methylnicotinic acid (1, 700 mg, 4.6 mmol) and ammonium acetate (1.58 g, 20.6 mmol) are dissolved in 1,4-dioxane (8 mL) and acetic anhydride (1a, 1.74 mL, 18.4 mmol) in an oven-dried microwave vial equipped with a stir bar. The reaction mixture is stirred at 200 °C in a microwave reactor for 24 h. Solvent is removed *in vacuo*. Ethyl acetate is added and the precipitate is filtered and washed once with ethyl acetate. Solids are dried under vacuum to afford 2,7-dimethylpyrido[4,3-d]pyrimidin-4(3H)-one (2).

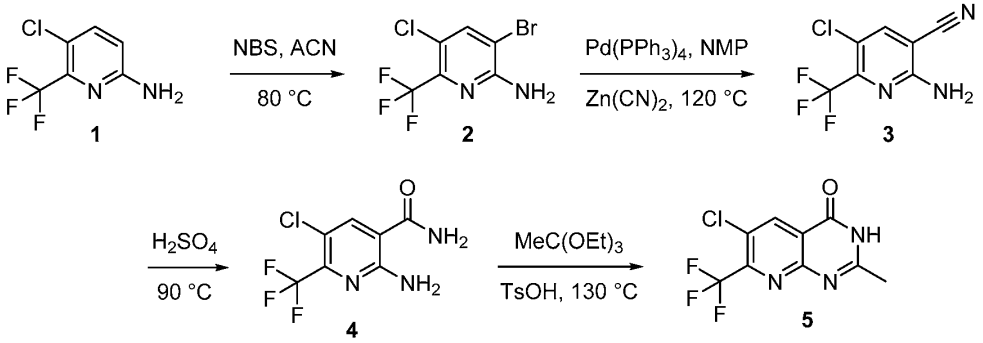
[0416] 2,7-Dimethylpyrido[4,3-d]pyrimidin-4(3H)-one (2, 92 mg, 0.50 mmol) and 1-(chloromethyl)-4-methoxybenzene (2a, 0.08 mL, 0.60 mmol) are dissolved in *N,N* dimethylformamide (2.5 mL) in an oven-dried screw capped vial equipped with a stir bar. The reaction mixture is stirred at room temperature while potassium carbonate (137.9 mg, 1 mmol)

and potassium iodide (16.5 mg, 0.10 mmol) are added sequentially. After 20 h the reaction mixture is diluted with ethyl acetate and then washed with a 50:50 water:brine solution and then twice more with 100 % brine. The organic material is then dried over magnesium sulfate, filtered and solvent removed *in vacuo*. Purification via silica gel chromatography (25-100 % ethyl acetate in hexanes) afforded the 3-(4-methoxybenzyl)-2,7-dimethylpyrido[4,3-d]pyrimidin-4(3H)-one (3).

[0417] 3-(4-Methoxybenzyl)-2,7-dimethylpyrido[4,3-d]pyrimidin-4(3H)-one (3, 109 mg, 0.37 mmol) is dissolved in dichloromethane (2 mL) in an oven-dried screw capped vial equipped with a stir bar. The reaction mixture is stirred at 0 °C while is 3-chlorobenzenecarboperoxoic acid (84 mg, 0.49 mmol) added slowly. After 5 min the reaction mixture is warmed to room temperature. After 3 h the reaction mixture is diluted with saturated aqueous sodium bicarbonate and dichloromethane. The layers are separated and the aqueous phase extracted with dichloromethane once. The combined organic material is washed with brine and dried over magnesium sulfate. The solids are filtered and solvent removed *in vacuo* to afford3-(4-methoxybenzyl)-2,7-dimethyl-4-oxo-3,4-dihydropyrido[4,3-d]pyrimidine 6-oxide (4).

[0418] 3-(4-Methoxybenzyl)-2,7-dimethyl-4-oxo-3,4-dihydropyrido[4,3-d]pyrimidine 6-oxide (4, 25 mg, 0.06 mmol) is dissolved in dichloromethane (1 mL) in an oven-dried screw capped vial equipped with a stir bar. The reaction mixture is stirred at 25 °C and then trimethylsilyl cyanide (0.04 mL, 0.32 mmol) and *N,N*-dimethylcarbamoyl chloride (0.03 mL, 0.32 mmol) are added sequentially. After 45 min the reaction mixture is warmed to 45 °C. After 14 h the reaction mixture is cooled to room temperature and solvent is removed *in vacuo*. Purification via silica gel chromatography (25-80 % ethyl acetate in dichloromethane) afforded 3-(4-methoxybenzyl)-2,7-dimethyl-4-oxo-3,4-dihydropyrido[4,3-d]pyrimidine-5-carbonitrile (5).

Example 3A.7



[0419] A solution of 5-chloro-6-(trifluoromethyl)pyridin-2-amine (**1**, 100 mg, 0.51 mmol) and *N*- Bromosuccinimide (91 mg, 0.51 mmol) in MeCN (4 mL) heated at 80 °C for 1 hr. After this

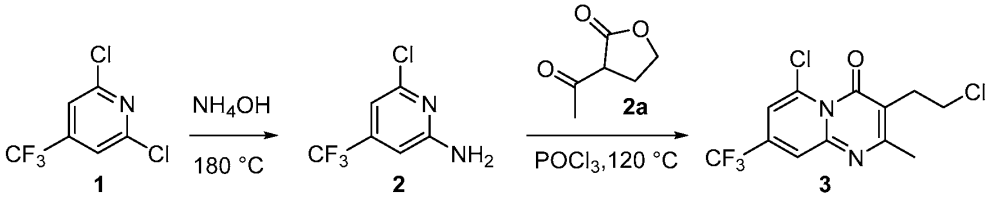
time, the reaction mixture is concentrated, diluted with water and extracted with ethyl acetate. The combined organic layer is washed with water and brine solution, dried over sodium sulfate and concentrated. The crude material then directly loaded on an Isco loading column. Purified by column chromatography using 5 to 40 % ethyl acetate in hexane as eluent and product eluted around 20 % ethylacetate/hexane. The desired fractions are concentrated under reduced pressure to afford 3-bromo-5-chloro-6-(trifluoromethyl)pyridin-2-amine (**2**).

[0420] A solution of 3-bromo-5-chloro-6-(trifluoromethyl)pyridin-2-amine (**2**, 50 mg, 0.18 mmol) and dicyanozinc (24 mg, 0.19 mmol) in NMP (3 mL) is purged with argon-gas for 5-min, then Pd(PPh3)4 (21 mg, 0.018 mmol) is added. The mixture is heated at 120 °C for 30 min in microwave. After completion, the reaction mixture is directly loaded on the silica column. Purified by column chromatography using 0 to 20 % methanol in dichloromethane as eluent and product eluted around 10 % methanol/dicholomethane. The desired fractions are concentrated under reduced pressure to afford 2-amino-5-chloro-6-(trifluoromethyl)nicotinonitrile (**3**).

[0421] 2-amino-5-chloro-6-(trifluoromethyl)nicotinonitrile (**3**, 550 mg, 2.5 mmol) is dissolved in concentrated sulfuric acid (1 mL) in a round bottom flask, and the mixture is stirred at 90 °C for 15 min. After this time, the reaction stopped and the mixture is cooled to room temperature. The reaction mixture is poured into ice-water and adjusted to pH 8 with saturated sodium hydrogen carbonate solution. The precipitate is collected by filtration and washed with cold water and dried in high vacuum to afford 2-amino-5-chloro-6-(trifluoromethyl)nicotinamide (**4**).

[0422] A solution of 2-amino-5-chloro-6-(trifluoromethyl)nicotinamide (**4**, 65 mg, 0.27 mmol), 1,1,1-triethoxyethane (0.13 mL, 1.09 mmol) and ethanol (2 mL) in a vial is heated to 120 °C in oil bath for 3 h. After this time, the reaction mixture is diluted with 50 % DMSO/MeOH, filtered and the crude is purified by HPLC (C18, prep column, 5-35 % MeCN/water + 0.1 % TFA) to afford 6-chloro-2-methyl-7-(trifluoromethyl)pyrido[2,3-d]pyrimidin-4(3H)-one (**5**).

Example 3A.8

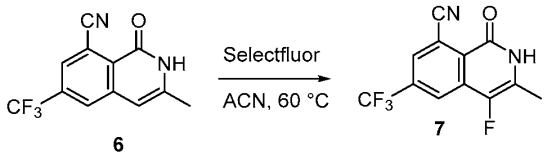


[0423] A solution of 2,6-dichloro-4-(trifluoromethyl)pyridine (1, 10.0 g, 4.6 mmol), ammonium hydroxide (50 mL) is heated at 180 °C for 4 h. After completion, the reaction

mixture is filtered, washed with water & dried to afford 6-chloro-4-(trifluoromethyl)pyridin-2-amine (2).

[0424] To a mixture of 6-chloro-4-(trifluoromethyl)pyridin-2-amine (2, 2.2 g, 1.0 mmol) in phosphorous oxychloride (5 mL), 3-acetyldihydrofuran-2(3H)-one (2a, 0.256 g, 2.0 mmol) is added at room temperature followed by heating and stirring at 20 °C for 1.5 h. After completion, the reaction mixture is poured into crushed ice & extracted with ethyl acetate. Organic layer is dried over anhydrous sodium sulfate and concentrated to dryness under reduced pressure to afford 6-chloro-3-(2-chloroethyl)-2-methyl-8-(trifluoromethyl)-4H-pyrido[1,2-a]pyrimidin-4-one (3).

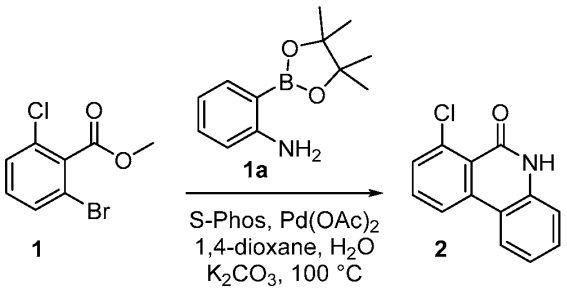
Example 3A.9



6 7

[0425] To a solution of 3-methyl-1-oxo-6-(trifluoromethyl)-1,2-dihydroisoquinoline-8-carbonitrile (6, 0.2 g, 0.793 mmol) in acetonitrile (2 mL), 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate) or selectfluor (0.42 g, 1.190 mmol) and catalytic amount of acetic acid are added and the reaction mixture is stirred at 60 ° C for 8 h. After completion, the reaction mixture is quenched with water and extracted with ethyl acetate. The organic layer is washed with brine solution, dried over anhydrous sodium sulphate, filtered and concentrated under reduced pressure. The crude is purified by column chromatography using silica gel (100-200 mesh) and 0-40 % ethyl acetate in hexane as eluent. The desired fractions are concentrated under reduced pressure to afford 4-fluoro-3-methyl-1-oxo-6-(trifluoromethyl)-1,2-dihydroisoquinoline-8-carbonitrile (7).

Example 3A.10

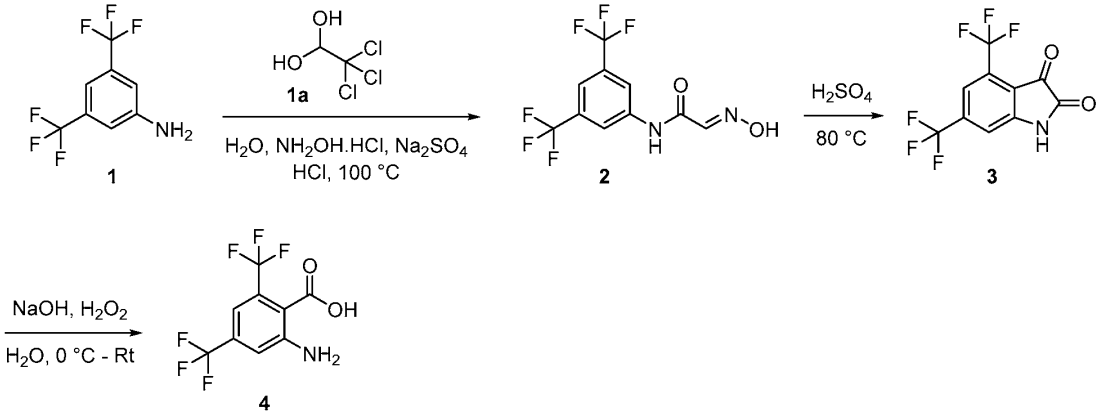


1 2

[0426] A bottle of 1,4-dioxane is sparged with argon gas for 10 min. Methyl 2-bromo-6-chlorobenzoate (1, 257.7 mg, 1.0 mmol), SPhos (37.0 mg, 0.09 mmol), palladium(II) acetate (6.7

mg, 0.03 mmol), potassium carbonate (276.9 mg, 2.0 mmol) and 2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (1a, 257.7 mg, 1.0 mmol) are dissolved in 1,4-dioxane (2 mL) and water (0.20 mL) in an oven-dried screw cap vial equipped with a stir bar. The vial is sealed and the reaction mixture sparged with argon gas for 5 min. The reaction mixture is stirred vigorously at 100 °C for 13 h. The reaction mixture is then cooled to room temperature and diluted with water (20 mL). The solids are filtered to afford a thick yellow semisolid that is taken up in dichloromethane (20 mL) and filtered again. The white solids that remained are collected and dried, affording 7-chlorophenanthridin-6(5H)-one (2).

Example 3A.11



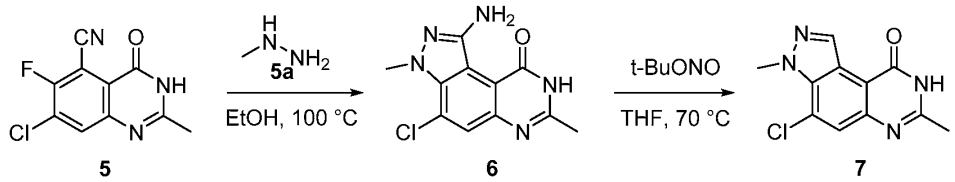
[0427] To a stirred solution of 3,5-bis(trifluoromethyl)aniline (1, 10 g, 43.64 mmol) and 402f (1a, 8.66 g, 52.37 mmol) in water (90 mL) is added hydroxyl amine hydrochloride (10.91 g, 157.11 mmol), followed by sodium sulphate (13.63 g, 96.01 mmol) at room temperature and the mixture is stirred at same temperature for 10 min. Concentrated hydrochloric acid (10.0 mL) is added slowly. The reaction mixture is heated to reflux for 16 h and allowed to cool to room temperature. The solid precipitate formed is filtered and washed with diethyl ether and dried under vacuum to afford (E)-*N*-(3,5-bis(trifluoromethyl)phenyl)-2-(hydroxyimino)acetamide (2).

[0428] A solution of (E)-*N*-(3,5-bis(trifluoromethyl)phenyl)-2-(hydroxyimino)acetamide (2, 8.0 g, 26.65 mmol) in concentrated sulfuric acid (60.0 mL) is heated to 85 °C and stirred for 4 h. After completion, the reaction is quenched with ice cold water. Solid is obtained, filtered, washed with water and dry under vacuum to afford 4, 6-bis (trifluoromethyl) indoline-2, 3-dione (3).

[0429] To a stirred solution of 4, 6-bis (trifluoromethyl) indoline-2, 3-dione (3, 6.5 g, 22.96 mmol) in 1 N sodium hydroxide solution (120.0 mL) is added hydrogen peroxide solution (30 % in water, 9.10 mL, 80.36 mmol) drop wise at 0 °C. The reaction is allowed to warm up to room

temperature and stirred for 4 h. After completion, the reaction mixture is quenched with 1 N hydrochloric acid and extracted with ethyl acetate. The organic layer is washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated to dryness under reduced pressure to afford 2-amino-4,6-bis(trifluoromethyl)benzoic acid (4).

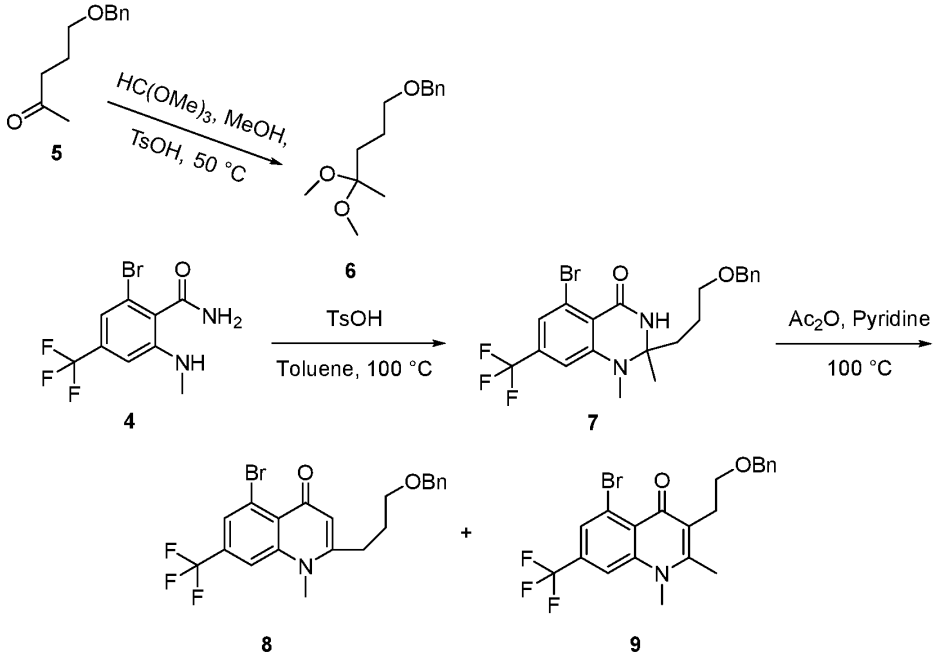
Example 3A.12



[0430] To a solution of 7-chloro-6-fluoro-2-methyl-4-oxo-3,4-dihydroquinazoline-5-carbonitrile (**5**, 0.280 g, 1.17 mmol) in ethanol (3 mL), methylhydrazine (**7**, 0.33 mL, 5.85 mmol) is added. This mixture is heated at 100 °C for 16 h. The reaction mixture is cooled and the resulting precipitate is collected by filtration and dried to afford 1-amino-4-chloro-3,7-dimethyl-3,8-dihydro-9*H*-pyrazolo[4,3-f]quinazolin-9-one (**6**).

[0431] To a solution of 1-amino-4-chloro-3,7-dimethyl-3,8-dihydro-9*H*-pyrazolo[4,3-f]quinazolin-9-one (**6**, 0.100 g, 0.37 mmol) in tetrahydrofuran (2 mL), *tert*-butyl nitrite (0.14 mL, 1.1 mmol) is added. This mixture is heated at 70 °C for 16 h. The reaction mixture is cooled, diluted with water, and extracted with 10 % methanol in dichloromethane. The organic layer is dried over anhydrous sodium sulfate, filtered, and concentrated. The crude product is purified by silica gel (100-200 mesh) column chromatography using 0-70 % ethyl acetate in hexanes as eluent to afford 4-chloro-3,7-dimethyl-3,8-dihydro-9*H*-pyrazolo[4,3-f]quinazolin-9-one (**7**).

Example 3A.13



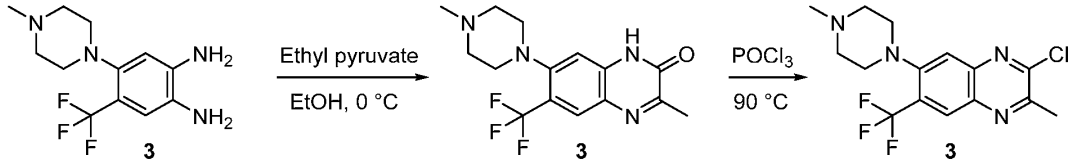
[0432] *p*-Toluenesulfonic acid monohydrate (74.7 mg, 0.39 mmol) is added to a stirred solution of 5-benzyloxypentan-2-one (5, 3.02 g, 15.7 mmol) in methanol (15 mL) and trimethyl orthoformate (3.44 mL, 31.4 mmol) at room temperature under a reflux condenser under argon. The resulting reaction mixture is heated at 50 °C under a reflux condenser under argon for 1.5 h. After cooling to room temperature, sodium methoxide (25 wt. % in methanol) (0.18 mL, 0.78 mmol) is added and then most of the solvent is removed on a rotary evaporator. The residue is partitioned between ethyl acetate and brine with a little 0.1 N NaOH in it. The organics are washed with brine, dried over magnesium sulfate, filtered, concentrated on a rotary evaporator, and dried under high vacuum to afford crude (((4,4-dimethoxypentyl)oxy)methyl)benzene (6).

[0433] 2-Bromo-6-(methylamino)-4-(trifluoromethyl)benzamide (4, 1.11 g, 3.7 mmol), (((4,4-dimethoxypentyl)oxy)methyl)benzene (6, 1.33 g, 5.6 mmol), *p*-toluenesulfonic acid monohydrate (35.5 mg, 0.19 mmol) and toluene (20 mL) are combined in a 100 mL round bottom flask with a stirbar, stirred vigorously, and heated at 100 °C under argon for 40 min. Most of the volatiles are removed on a rotary evaporator. The residue is purified via silica gel chromatography (10-80 % ethyl acetate in hexanes) to afford 2-(3-(benzyloxy)propyl)-5-bromo-1,2-dimethyl-7-(trifluoromethyl)-2,3-dihydroquinazolin-4(1H)-one (7).

[0434] 2-(3-(benzyloxy)propyl)-5-bromo-1,2-dimethyl-7-(trifluoromethyl)-2,3-dihydroquinazolin-4(1H)-one (7, 1.64 g, 3.48 mmol), acetic anhydride (11.1 mL, 118 mmol),

and pyridine (1.12 mL, 13.9 mmol) are combined in a sealable vessel with a stirbar, sealed, stirred, and heated at 110 °C with a block heater for 16 h. Most of the volatiles are removed on a rotary evaporator. The residue is taken up in ethyl acetate and purified via silica gel chromatography (30-90 % ethyl acetate in hexanes) to afford 2-(3-(benzyloxy)propyl)-5-bromo-1-methyl-7-(trifluoromethyl)quinolin-4(1H)-one (8) and 3-(2-(benzyloxy)ethyl)-5-bromo-1,2-dimethyl-7-(trifluoromethyl)quinolin-4(1H)-one (9).

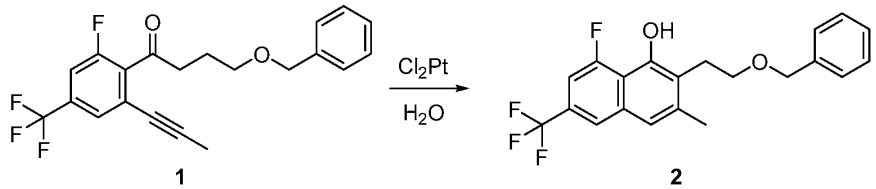
Example 3A.14



[0435] To a solution of 4-(4-methylpiperazin-1-yl)-5-(trifluoromethyl)benzene-1,2-diamine (3, 12.0 g, 43.7 mmol) in ethanol (120 mL) at 0 °C is added ethyl pyruvate (10.0 g, 87.5 mmol) and the treaction mixture is stirred for 3 h at room temperature. After completion, the reaction mixture is cooled to 0 °C, filtered and washed with diethyl ether which is dried under reduced pressure to afford 3-methyl-7-(4-methylpiperazin-1-yl)-6-(trifluoromethyl)quinoxalin-2(1H)-one (4).

[0436] To a solution of 3-methyl-7-(4-methylpiperazin-1-yl)-6-(trifluoromethyl)quinoxalin-2(1H)-one (4, 4.3 g, 13.1 mmol) is added phosphoryl chloride (43 mL) at room temperature. Then the reaction mixture is stirred for 6 h at 90 °C. After completion, the reaction mixtureis quenched with icec-cold water, ad*J* usted the pH 8 with 1N aqueous hydrochloric acid solution and extracted with ethyl acetate, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure to get the crude mass. The crude compound is purified by Combi flash (12g, Redi Sep column) using 4% methanol in dichloromethane as eluent. The desired fractions are concentrated under reduced pressure to afford 2-chloro-3-methyl-7-(4-methylpiperazin-1-yl)-6-(trifluoromethyl)quinoxaline (5).

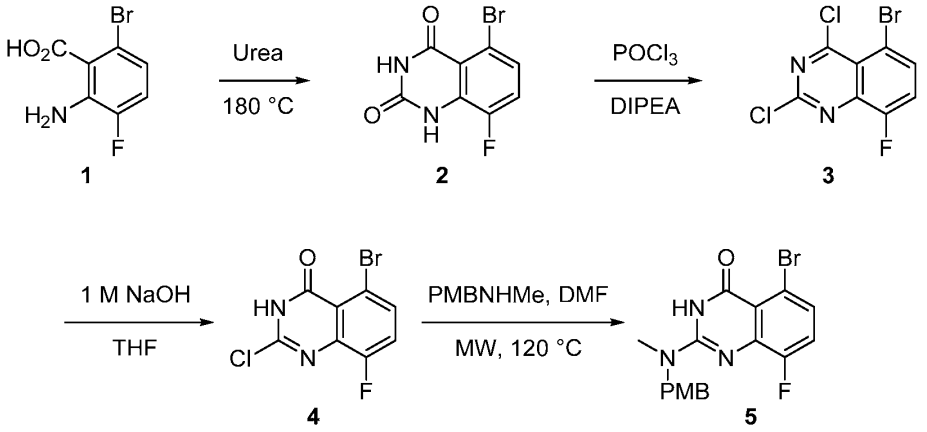
Example 3A.15



[0437] To 4-benzyloxy-1-[2-fluoro-6-prop-1-ynyl-4-(trifluoromethyl)phenyl]butan-1-one (**1**, 50.mg, 0.13200 mmol) in 1,4-Dioxane (1 mL) and water (0.01mL, 0.79000 mmol) is added

dichloroplatinum (3.52mg, 0.01320 mmol) and CO (29.6mg, 1.06 mmol) is bubbled through the reaction mixture for 5 mins. The mixture is stirred at 25 °C for 30 min followed by heating to 100 for 12hr to afford 2-(2-(benzyloxy)ethyl)-8-fluoro-3-methyl-6-(trifluoromethyl)naphthalen-1-ol (**2**) after workup.

Example 3A.16



[0438] A mixture of 2-amino-6-bromo-3-fluorobenzoic acid (2.00 g, 8.55 mmol) and urea (4.00 g, 66.60 mmol) is heated at 180 °C for 3 h, then cooled to 80 °C. Water (7-10 mL) is added. The reaction is stirred at reflux for 10 m. The resulting mixture is cooled to room temperature and filtered. The dark brown solid is washed with water and ethyl ether, and dried under vacuum to afford 5-bromo-8-fluoroquinazoline-2,4(1*H*,3*H*)-dione (2).

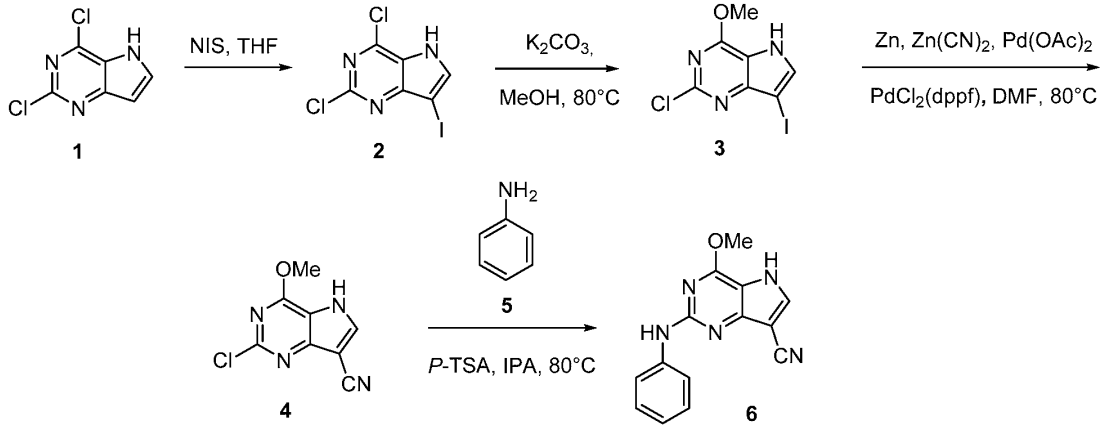
[0439] To a solution of 5-bromo-8-fluoroquinazoline-2,4(1*H*,3*H*)-dione (2, 445 mg, 1.72 mmol) in phosphorus oxychloride (6.2 mL) is added *N*,*N*-diisopropylethylamine (1.20 mL, 6.89 mmol) dropwise. The reaction is stirred at 120 °C overnight. The resulting mixture is cooled to room temperature and azeptroped with toluene. The crude is diluted with ethyl acetate and washed with water. The combined organics are dried over sodium sulfate, decanted and concentrated. The crude is purified via column chromatography (silica, ethyl acetate/hexanes = 0-10 %) to afford 5-bromo-2,4-dichloro-8-fluoroquinazoline (3).

[0440] To a solution of 5-bromo-2,4-dichloro-8-fluoroquinazoline (3, 395 mg, 1.33 mmol) in tetrahydrofuran (2 mL) is added 1 M sodium hydroxide solution (6.70 mL, 6.70 mmol). The reaction is stirred at room temperature for 1 h 45 min. The resulting mixture is acidified to ~pH 4 with acetic acid. The precipitate is filtered, washed with ethyl ether and dried under vacuum to afford 5-bromo-2-chloro-8-fluoroquinazolin-4(3*H*)-one (4).

[0441] To a solution of 5-bromo-2-chloro-8-fluoroquinazolin-4(3*H*)-one (4, 100 mg, 0.36 mmol) in *N*,*N*-dimethylformamide (2 mL) is added 1-(4-methoxyphenyl)-*N*-methylmethanamine (68

uL, 0.45 mmol). The reaction is microwaved at 120 °C for 10 m. The resulting mixture is cooled to room temperature and sit for 90 min. The precipitate is filtered and washed with ethyl ether. The filtrate is concentrated and triturated with ethyl acetate. The combined solids are dried under vacuum to afford 5-bromo-8-fluoro-2-((4-methoxybenzyl)(methyl)amino)quinazolin-4(3*H*)-one (5).

Example 3A.17



[0442] To a solution of 2,4-dichloro-5*H*-pyrrolo[3,2-*d*]pyrimidine (1, 25.0 g, 132.9 mmol) in tetrahydrofuran (250 mL), *N*-iodosuccinimide (35.89 g, 159.5 mmol) is added portion wise over a period of 10 min and the reaction mixture is allowed to stir at room temperature for 30 h. After completion, the reaction mixture is quenched with water and extracted with ethyl acetate. The organic layer is washed with water, separated, dried over anhydrous sodium sulphate and concentrated under reduced pressure to afford 2,4-dichloro-7-iodo-5*H*-pyrrolo[3,2-*d*]pyrimidine (2).

[0443] To a solution of 2,4-dichloro-7-iodo-5*H*-pyrrolo[3,2-*d*]pyrimidine (2, 30.0 g, 95.5 mmol) in methanol (600 mL), potassium carbonate (39.62 g, 286.7 mmol) is added portion wise over a period of 10 min and the reaction mixture is allowed to stir at 80 °C for 24 h. After completion, the reaction mixture is concentrated, diluted with water and extracted with ethyl acetate. The organic layer is washed with water, separated, dried over anhydrous sodium sulphate and concentrated under reduced pressure to get crude. The crude is triturated with diethyl ether to afford 2-chloro-7-iodo-4-methoxy-5*H*-pyrrolo[3,2-*d*]pyrimidine (3).

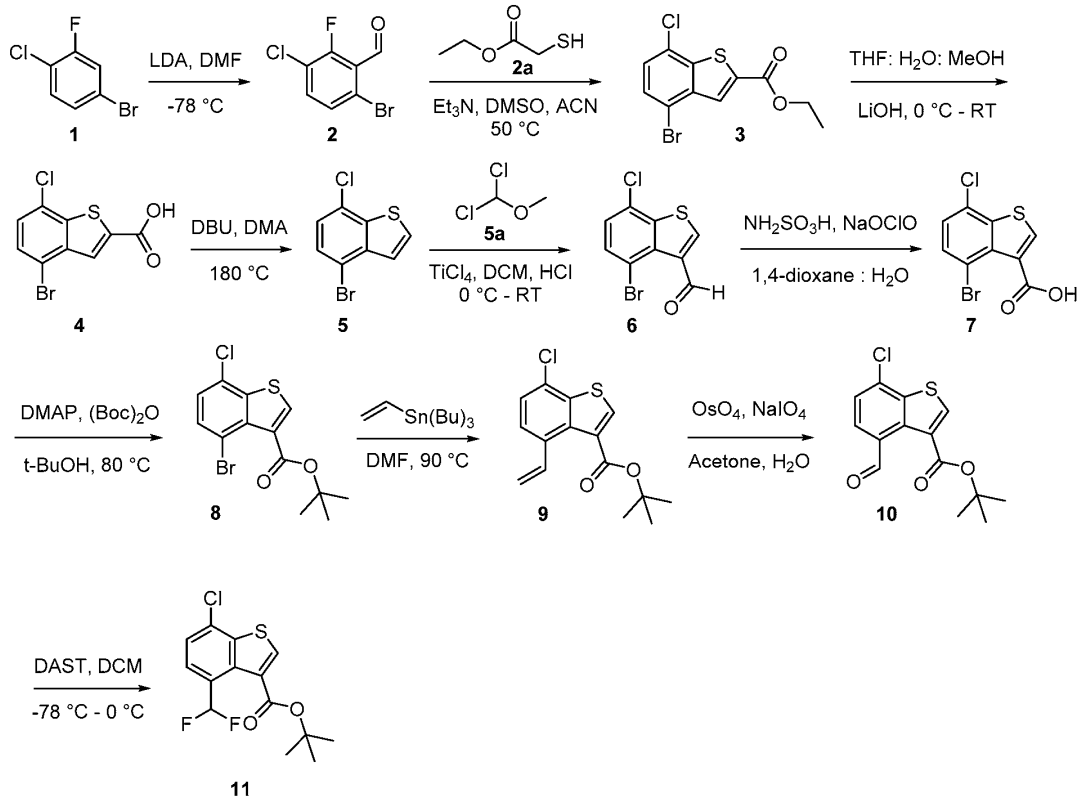
[0444] To a solution of 2-chloro-7-iodo-4-methoxy-5*H*-pyrrolo[3,2-*d*]pyrimidine (3, 24.0 g, 77.54 mmol) in *N,N*-dimethylformamide (240 mL), zinc cyanide (9.11 g, 77.54 mmol), zinc acetate (14.22 g, 77.54 mmol) and zinc dust (2.02 g, 31.01 mmol) are added at room temperature. The reaction mixture is degassed with argon for 15 min. [1,1'-

Bis(diphenylphosphino)ferrocene]palladium(II) (5.67 g, 7.75 mmol) and palladium acetate (0.87 g, 3.87 mmol) are added and mixture is heated at 80 °C for 1 h. After completion, the reaction mass is diluted with ethyl acetate and washed with cold water. The organic layer is separated, dried over anhydrous sodium sulphate, filtered and concentrated to get crude. The crude is purified by column chromatography over silica gel (100-200 mesh) using 0-50 % ethyl acetate in hexanes as eluent. The desired fractions are concentrated *in vacuo* to afford 2-chloro-4-methoxy-5*H*-pyrrolo[3,2-*d*]pyrimidine-7-carbonitrile (4).

[0445] To a solution of 2-chloro-4-methoxy-5*H*-pyrrolo[3,2-*d*]pyrimidine-7-carbonitrile (4, 10.0 g, 47.9 mmol) in isopropanol (100 mL), aniline (5, 43.76 mL, 479.3 mmol) and *p*-toluene sulfonic acid monohydrate (10.93 g, 57.48 mmol) are added. The reaction mixture is allowed to stir at 80 °C for 16 h. After completion, the reaction mixture is quenched with water and extracted with ethyl acetate. The organic layer is washed with water, brine, dried over anhydrous sodium sulphate and concentrated under reduced pressure to get crude. The crude is triturated with n-pentane, diethyl ether and dried under high vacuo to afford 4-methoxy-2-(phenylamino)-5*H*-pyrrolo[3,2-*d*]pyrimidine-7-carbonitrile (6).

Example 3B. Methods of synthesizing the right-hand side

Example 3B.1



[0446] A solution of 4-bromo-1-chloro-2-fluorobenzene (1, 20.0 g, 95.69 mmol) in tetrahydrofuran (200 mL) is cooled at -78 °C, then lithium di-isopropyl amide (2 M in tetrahydrofuran) (57.2 mL, 114.83 mmol) is added dropwise to the mixture and reaction mixture is stirred at -78 °C for 1 h. Then, *N,N*-dimethylformamide (20.0 mL) is added drop wise for 15 min at -78 °C and reaction mixture is stirred for 30 min. After completion reaction mixture is quenched with ammonium chloride solution, diluted with water, and extracted with diethyl ether. The organic layer is dried over anhydrous sodium sulphate, filtered and concentrated to get crude compound. Crude compound obtained is washed with pentane to afford 6-bromo-3-chloro-2-fluorobenzaldehyde (2).

[0447] To a solution of 6-bromo-3-chloro-2-fluorobenzaldehyde (2, 18.0 g, 75.94 mmol), in acetonitrile (180.0 mL) and dimethylsulphoxide (48.0 mL), triethyl amine (31.96 mL, 227.84 mmol) is added at 0 °C followed by ethyl 2-mercaptoacetate (2a, 18.2 g, 151.89 mmol) and continued stirring at 50 °C for 4 h. After completion, reaction mixture is diluted with water and extracted with ethyl acetate, washed with 1 N hydrochloric acid, water and brine solution. Organic layer is dried over sodium sulfate and concentrated to dryness under reduced pressure. Triturated with ethanol, filtered and dried to afford ethyl 4-bromo-7-chlorobenzo[b]thiophene-2-carboxylate (3).

[0448] To a solution of ethyl ethyl 4-bromo-7-chlorobenzo[b]thiophene-2-carboxylate (3, 18.0 g, 56.42 mmol) and in tetrahydrofuran: water: methanol (90.0 mL: 45 mL: 45 mL), lithium hydroxide (13.54 g, 564.26 mmol) is added, and the reaction mixture is continued stirring for 2 h. After completion, reaction mixture is poured on chilled 1 N aqueous hydrochloric acid, and extracted with ethyl acetate, washed with water and brine solution. Organic layer is dried over anhydrous sodium sulfate and concentrated to dryness under reduced pressure. Triturated with ether, filtered and dried to afford 4-bromo-7-chlorobenzo[b]thiophene-2-carboxylic acid (4).

[0449] To a solution of 4-bromo-7-chlorobenzo[b]thiophene-2-carboxylic acid (4, 15.0 g, 51.90 mmol), in *N,N*-dimethyl acetamide (150.0 mL), 1, 8-diazabicyclo (5.4.0) undec-7-ene (39.55 g, 259.51 mmol) is added and mixture is heated at 180 °C for 4 h. After completion, reaction mixture is cooled to room temperature diluted with water and acidified by 1 N hydrochloric acid and extracted with ethyl acetate, washed with, water and brine solution. Organic layer is dried over anhydrous sodium sulfate and concentrated to dryness under reduced pressure to afford 4-bromo-7-chlorobenzo[b]thiophene (5).

[0450] To a solution of 4-bromo-7-chlorobenzo[b]thiophene (5, 4.00 g, 16.19 mmol) in dichloromethane (100.0 mL), dichloro(methoxy)methane (5a, 4.59 g, 24.29 mmol) is added at 0

°C followed by titanium tetrachloride (2.79 g, 24.29 mmol) at same temperature and the reaction mixture is continued stirring for 16 h at room temperature. After completion, reaction mixture is quenched with 1 N aqueous hydrochloric acid and continued stirring for 2 h, diluted with water and extracted with dichloromethane, washed with water and brine solution. Organic layer is dried over anhydrous sodium sulfate and concentrated to dryness under reduced pressure. The crude product is purified by flash chromatography using silica (100-200 mesh) using 0-10 % ethyl acetate in hexanes as eluent. The desired fractions are concentrated under reduced pressure to afford 4-bromo-7-chlorobenzo[b]thiophene-3-carbaldehyde (6).

[0451] To a solution of 4-bromo-7-chlorobenzo[b]thiophene-3-carbaldehyde (6, 2.50 g, 9.12 mmol) in 1,4-dioxane (24.0 mL) and water (8.0 mL), (3:1 ratio) is added sodium chlorite (1.24 g, 13.68 mmol), followed by sulfamic acid (5.30 g, 54.74 mmol) at room temperature and the mixture is continued stirring for 16 h. After completion, reaction mixture is concentrated under reduced pressure; residue is acidified to pH-2 by 2 N hydrochloric acid and extracted with ethyl acetate, washed with water and brine solution. Organic layer is dried over anhydrous sodium sulfate and concentrated to dryness under reduced pressure. The residue is triturated with n-pentane, filtered and dried to afford 4-bromo-7-chlorobenzo[b]thiophene-3-carboxylic acid (7).

[0452] To a solution of 4-bromo-7-chlorobenzo[b]thiophene-3-carboxylic acid (7, 1.40 g, 4.81 mmol) in t-butanol (15.0 mL), di-*tert*-butyl dicarbonate (2.0 g, 9.62 mmol) followed by dimethylaminopyridine (0.586 g, 4.81 mmol) is added at room temperature. The solution is heated at 90 °C and continued stirring for 16 h. After completion, reaction mixture is concentrated under reduced pressure; diluted with water and extracted with ethyl acetate, washed with water and brine solution. Organic layer is dried over sodium sulfate and concentrated to dryness under reduced pressure. The crude is purified by flash chromatography using silica (100-200 mesh) by eluting with gradient of 5-10 % ethyl acetate in hexanes. The desired fractions are concentrated under reduced pressure to afford *tert*-butyl 4-bromo-7-chlorobenzo[b]thiophene-3-carboxylate (8).

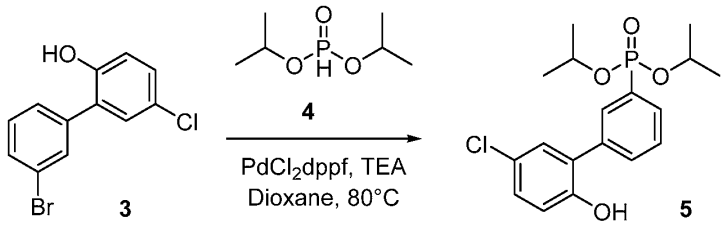
[0453] A solution of *tert*-butyl 4-bromo-7-chlorobenzo[b]thiophene-3-carboxylate (8, 1.10 g, 3.17 mmol) and tributyl(vinyl)stannane (1.20 g, 3.80 mmol) in *N,N*-dimethylformamide (11 mL) is degassed using argon for 15 min. Bis(triphenylphosphine)palladium dichloride (0.222 g, 0.3170 mmol) is added to the reaction mixture and heated at 90 °C for 2 h. The reaction mixture is cooled to room temperature, diluted with ethyl acetate and water. The organic layer is separated, washed with brine, dried over anhydrous sodium sulphate, filtered and concentrated under reduced pressure to get the crude. The crude is purified by column chromatography using

silica (100-200 mesh) and 2.0-5.0 % ethyl acetate in hexanes as eluent. The desired fractions are concentrated under reduced pressure to afford *tert*-butyl 7-chloro-4-vinylbenzo[b]thiophene-3-carboxylate (9).

[0454] A solution of *tert*-butyl 7-chloro-4-vinylbenzo[b]thiophene-3-carboxylate (9, 0.6 g, (2.04 mmol) in acetone (10 mL) and water (2 mL) is cooled to 0 °C and osmium tetraoxide (4 % solution in water)(1.3 mL, 0.2040 mmol) followed by sodium periodate (1.3 g, 6.12 mmol) is added. The mixture is stirred at room temperature for 1 h. After completion, the reaction mixture is filtered and filtrate is concentrated under reduced pressure to get the crude product. The crude is purified by pentane wash to afford *tert*-butyl 7-chloro-4-formylbenzo[b]thiophene-3-carboxylate (10).

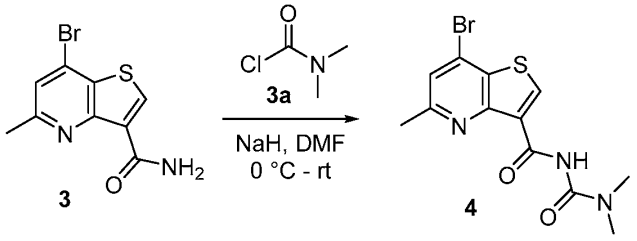
To a stirred solution of *tert*-butyl 7-chloro-4-formylbenzo[b]thiophene-3-carboxylate (10, 0.550 g, 1.85 mmol) in dichloromethane (10 mL), diethylaminosulfur trifluoride (0.503 g, 2.77 mmol) is added at 0 °C. The reaction is allowed to warm at room temperature and stirred for 4 h. After completion, reaction mixture is concentrated under reduced pressure to get crude. The crude is purified by column chromatography using silica (100-200 mesh) and 5.0-10.0 % ethyl acetate in hexanes as eluent. The desired fractions are concentrated under reduced pressure to afford *tert*-butyl 7-chloro-4-(difluoromethyl)benzo[b]thiophene-3-carboxylate (11).

Example 3B.2



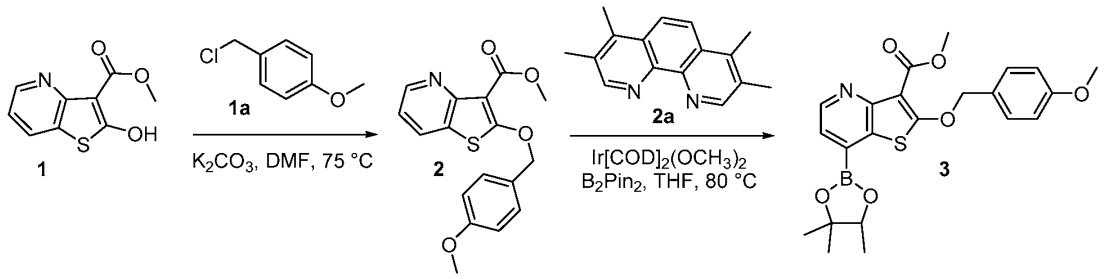
[0455] A solution of 3'-bromo-5-chloro-[1,1'-biphenyl]-2-ol (3, 0.5 g, 1.7 mmol), diisopropyl phosphonate (4, 0.585 g, 3.5 mmol), and triethyl amine (0.533 g, 5.2 mmol) in isopropyl alcohol is degassed with argon for 10 min followed by the addition of bis(diphenylphosphino) ferrocene-palladium(II)dichloride.dichloromethane complex The reaction mixture is stirred at 100 °C for 16 h. After completion, the volatiles are removed under reduced pressure. Crude is purified by flash column chromatography using 30 % ethyl acetate hexanes to afford diisopropyl (5'-chloro-2'-hydroxy-[1,1'-biphenyl]-3-yl)phosphonate (5).

Example 3B.3



[0456] To a solution of 7-bromo-5-methylthieno[3,2-b]pyridine-3-carboxamide (3, 1.50 g, 5.55 mmol) in *N,N*-dimethylformamide (20 mL), sodium hydride is added at 0 °C and stirred for 10 min. Then, dimethylcarbamic chloride (3a, 0.71 g, 6.66 mmol) is added and the mixture is stirred at room temperature for 2 h. After completion, the reaction mixture is diluted with ethyl acetate, washed with cold water and brine, dried over anhydrous sodium sulphate, filtered and concentrated. The crude product is triturated with diethyl ether and pentane and dried to afford 7-bromo-*N*-(dimethylcarbamoyl)-5-methylthieno[3,2-b]pyridine-3-carboxamide (4).

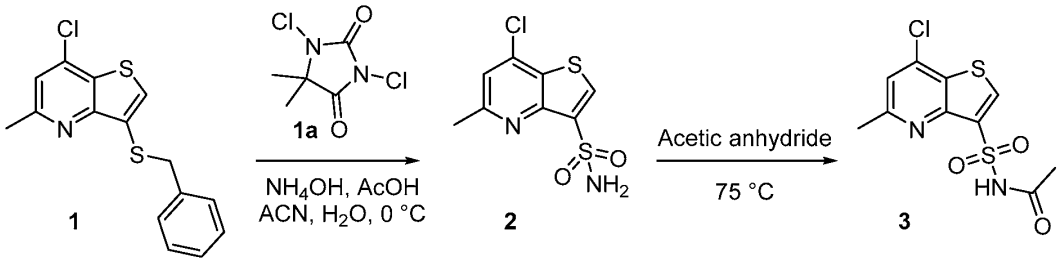
Example 3B.4



[0457] Methyl 2-hydroxythieno[3,2-b]pyridine-3-carboxylate (1, 748 mg, 3.6 mmol) is dissolved in *N,N*-dimethylformamide (20 mL) in an oven dried screw cap vial equipped with a stir bar. Potassium carbonate (210 mg, 1.52 mmol) is added, followed by the dropwise addition of 1-(chloromethyl)-4-methoxybenzene (1a, 0.42 mL, 4.2 mmol). The vial is sealed and heated to 75 °C. After 22 h additional 4-methoxybenzyl chloride (0.42 mL, 4.2 mmol) and potassium carbonate (946.2 mg, 6.8 mmol) are added and the reaction mixture continued to stir at 75 °C. After 3 h the reaction mixture is cooled to room temperature and diluted with ethyl acetate and water. The layers are separated and the aqueous phase is extracted with ethyl acetate twice. The combined organic material is washed with brine, dried over magnesium sulfate, filtered, and solvent removed *in vacuo* to afford a dark brown oil. Purification via silica gel chromatography, eluting with hexanes and ethyl acetate afforded methyl 2-((4-methoxybenzyl)oxy)thieno[3,2-b]pyridine-3-carboxylate (2).

[0458] A bottle of tetrahydrofuran is sparged with argon gas for 1 h. An oven dried microwave vial equipped with a stir bar is charged with bis(pinacolato)diboron (308.4 mg, 1.21 mmol), methyl 2-((4-methoxybenzyl)oxy)thieno[3,2-b]pyridine-3-carboxylate (2, 381 mg, 1.16 mmol), 3,4,7,8-tetramethyl-1,10-phenanthroline (2a, 21.8 mg, 0.093 mmol), and (1Z,5Z)-cycloocta-1,5-diene; methoxyiridium (30.6 mg, 0.046 mmol). Tetrahydrofuran (2.3 mL) is added, the vial is sealed and placed under an atmosphere of argon before being stirred in an oil bath at 80 °C. After 16 h the reaction mixture is cooled to room temperature and solvent removed *in vacuo*. The crude residue is used without further purification for the subsequent reaction. Methyl 2-((4-methoxybenzyl)oxy)-7-(4,4,5-trimethyl-1,3,2-dioxaborolan-2-yl)thieno[3,2-b]pyridine-3-carboxylate (3).

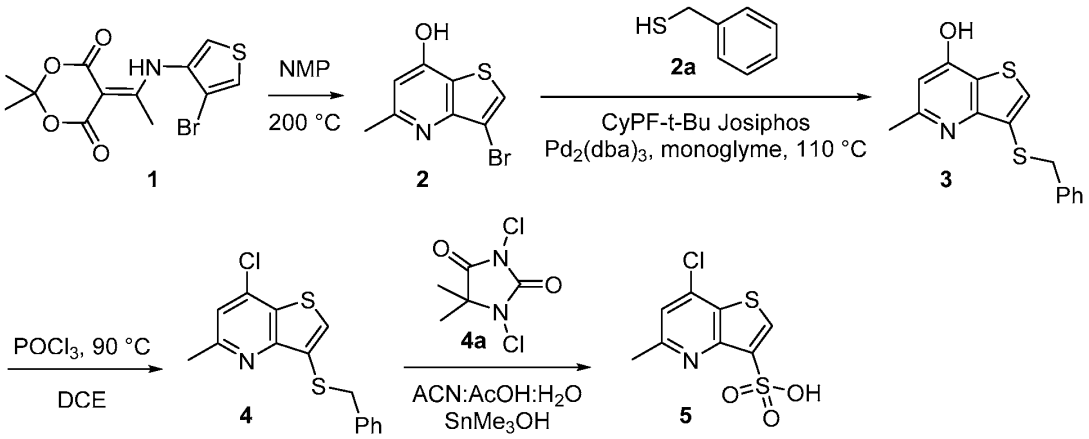
Example 3B.5



[0459] To a solution of 3-(benzylthio)-7-chloro-5-methylthieno[3,2-b]pyridine (1, 0.7 g, 2.3 mmol) in a mixture of acetonitrile, acetic acid and water (40:2:1) (10.0 mL) at 0 °C. 1,3-Dichloro-5,5-dimethylimidazolidine-2,4-dione (1a, 0.9 g, 4.60 mmol) at 0 °C and the mixture is stirred for 1 h. Ammonium hydroxide (35 % in water, 6.0 mL) is added is added to the reaction mixture at 0 °C and stirring is continued for 2 h. After completion, the reaction mixture is diluted with water and extracted with ethyl acetate. The organic layer is washed with water and saturated brine, dried over anhydrous sodium sulfate, filtered and concentrated. The crude product is washed with n-pentanes to afford 7-chloro-5-methylthieno[3,2-b]pyridine-3-sulfonamide (2).

[0460] To a solution of methyl 7-chloro-5-methylthieno[3,2-b]pyridine-3-sulfonamide (2, 0.50 g, 1.9 mmol) in acetic anhydride (6.0 mL) is added zinc chloride (0.08 g, 0.57 mmol) at room temperature and the mixture is heated and stirred for 16 h at 75 °C. After completion, the reaction mixture is diluted with water and extracted with ethyl acetate. The organic layer is washed with water, saturated brine, dried over anhydrous sodium sulfate, filtered and concentrated. The crude product is purified by washing with diethyl ether and n-pentanes to afford *N*-((7-chloro-5-methylthieno[3,2-b]pyridin-3-yl)sulfonyl)acetamide (3).

Example 3B.6



[0461] A solution of 5-(1-((4-bromothiophen-3-yl)amino)ethylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (1, 0.250 g, 0.722 mmol) in *N*-methyl pyrrolidone (2 mL) is heated in microwave at 200 °C for 30 min. After completion, the reaction mixture is diluted with dichloromethane and then silica gel is added. The solvent is then evaporated and the free flow silica gel is then loaded on the Isco column and purified via silica gel chromatography eluting with methanol/ethylacetate. The desired fractions are concentrated under reduced pressure to afford 3-bromo-5-methylthieno[3,2-b]pyridin-7-ol (2).

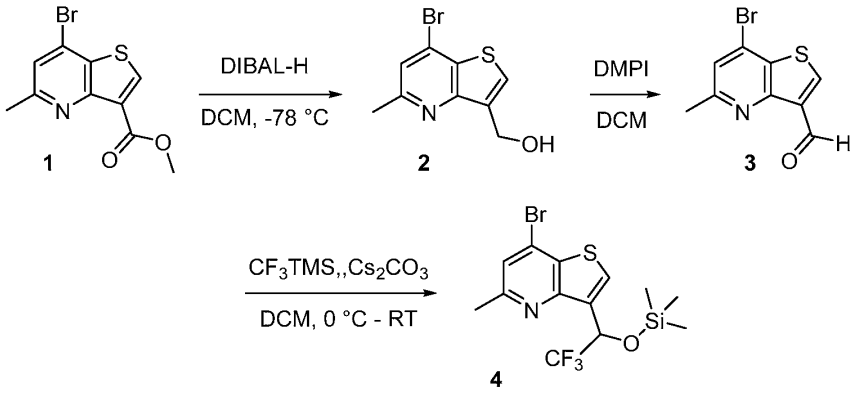
[0462] To a solution of 3-bromo-5-methylthieno[3,2-b]pyridin-7-ol (2, 177 mg, 0.725 mmol), phenylmethanethiol (2a, 0.361 g, 2.91 mmol) and *N,N*-diisopropylethylamine (0.379 mL, 2.15 mmol) in monoglyme (4 mL) is added premixed solution of tris(dibenzylideneacetone)dipalladium(0) (132 mg, 0.145 mmol) and (*R*)-1-[(*S*P)-2-(dicyclohexylphosphino)ferrocenyl]ethyldi-*tert*-butylphosphine (80 mg, 0.145 mmol) in monoglyme (1 mL) at room temperature. The reaction mixture is purged with argon gas for 5 min, and the mixture is heated at 110 °C for 15 h. After completion, the reaction mixture is diluted with dichloromethane and then silica gel is added. The solvent is then evaporated and the free flow silica gel is then loaded on the Isco column and purified via silica gel chromatography eluting with Ethylacetate/hexanes. The desired fractions are concentrated under reduced pressure to afford 3-(benzylthio)-5-methylthieno[3,2-b]pyridin-7-ol (3).

[0463] To a solution of 3-(benzylthio)-5-methylthieno[3,2-b]pyridin-7-ol (3, 0.100 g, 0.347 mmol) in 1,2-dichloroethane (3.0 mL), phosphoryl trichloride (0.1 mL, 1.04 mmol) and catalytic amount of *N,N*-dimethylformamide (0.050 mL) are added at room temperature. The reaction mixture is heated at 90 °C for 2 h. After completion, the reaction mixture is diluted with dichloromethane and then silica gel is added. The solvent is then evaporated and the free flow

silica gel is then loaded on the Isco column and purified via silica gel chromatography eluting with methanol/dichloromethane to afford 3-(benzylthio)-7-chloro-5-methylthieno[3,2-b]pyridine (4).

[0464] A solution of 3-(benzylthio)-7-chloro-5-methylthieno[3,2-b]pyridine (4, 50 mg, 0.163 mmol) and 1,3-dichloro-5,5-dimethyl-imidazolidine-2,4-dione (4a, 64 mg, 0.329 mmol) in mixture of acetonitrile (3 mL)/water (2 mL)/ acetic acid (0.4 mL) is stirred at room temperature for 1 h. To this mixture is then added hydroxyl(trimethylstannane) (295 mg, 1.63 mmol) and then stirred for 15 h at 50 °C. The reaction mixture is then concentrated to afford crude 7-chloro-5-methylthieno[3,2-b]pyridine-3-sulfonic acid (5).

Example 3B.7

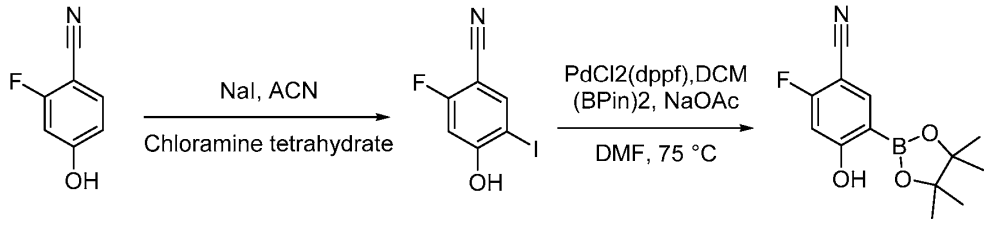


[0465] To a solution of methyl 7-bromo-5-methylthieno[3,2-b]pyridine-3-carboxylate (**1**, 3.00 g, 10.4 mmol) in dichloromethane (30.0 mL) at -78 °C, diisobutylaluminium hydride (10.40 mL, 15.7 mmol) is added. The reaction mixture is stirred this temperature for 3 h. After this time, the reaction mixture is diluted with water and extracted with dichloromethane. The organic layer is washed with water and then brine, dried over anhydrous sodium sulfate, and concentrated to dryness under reduced pressure to afford (7-bromo-5-methylthieno[3,2-b]pyridin-3-yl)methanol (**2**).

[0466] To a solution of (7-bromo-5-methylthieno[3,2-b]pyridin-3-yl)methanol (**2**, 1.70 g, 3.87 mmol) in dichloromethane (20.0 mL) at 0 °C, 1,1,1-tris(acetyloxy)-1,1-dihyro-1,2-benziodoxol-3-(1H)-one (3.28 g, 7.75 mmol) is added. The reaction mixture is stirred at room temperature for 3 h. After this time, the reaction mixture is filtered with Celite and washed with dichloromethane. The filtrate is concentrated to dryness under reduced pressure to obtain the crude product. This is purified by silica gel (100-200 mesh) column chromatography using 30-50 % ethyl acetate in hexanes as eluent. The desired fractions are concentrated under reduced pressure to afford 7-bromo-5-methylthieno[3,2-b]pyridine-3-carbaldehyde (**3**).

[0467] To a solution of 7-bromo-5-methylthieno[3,2-b]pyridine-3-carbaldehyde (**3**, 0.50 g, 1.95 mmol) in dichloromethane (5.0 mL) at 0 °C, trifluoromethyltrimethylsilane (0.416 g, 2.92 mmol) and cesium carbonate (3.17 g 9.75 mmol) is added. The reaction mixture is stirred at room temperature for 1 h. Then, the reaction mixture is diluted with water and extracted with dichloromethane. The organic layer is washed with water and then brine solution, dried over anhydrous sodium sulfate, and concentrated to dryness under reduced pressure to afford 7-bromo-5-methyl-3-(2,2,2-trifluoro-1-((trimethylsilyl)oxy)ethyl)thieno[3,2-b]pyridine (**4**).

Example 3B.8

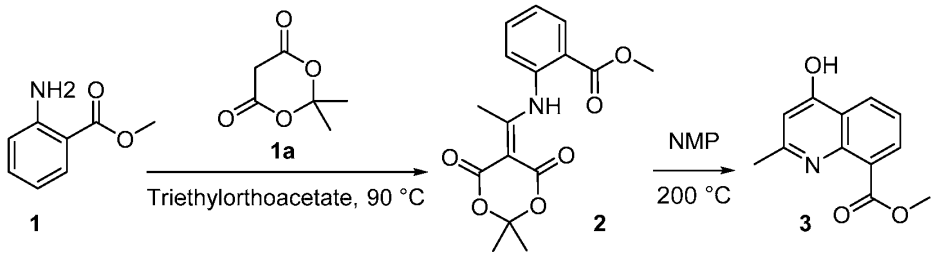


1 **2** **3**

[0468] To a stirred solution of 2-fluoro-4-hydroxybenzonitrile (1, 20 g, 145.0 mmol) in acetonitrile (80 mL) are added sodium iodide (24 g, 160.0 mmol) and chloramine tetrahydrate (45 g, 160.0 mmol) and stirred at room temperature for 16 h. The reaction mixture is diluted with water and extracted with ethyl acetate. The organic layer is washed with water and saturated brine, dried over anhydrous sodium sulphate, filtered and concentrated. The crude product is purified by column chromatography using silica gel (100-200 mesh) and 10 % ethyl acetate in hexanes as eluent. The desired fractions are concentrated under reduced pressure to afford 2-fluoro-4-hydroxy-5-iodobenzonitrile (2).

[0469] To a solution of 2-fluoro-4-hydroxy-5-iodobenzonitrile (2, 7.0 g, 26.6 mmol) in 1,4-dioxane (70 mL), sodium acetate (4.36 g, 53.23 mmol) and bis pinacolato diboron (20.26 g , 79.8 mmol) are added at room temperature and the mixture is degassed with argon for 10 min. [1,1'-Bis(diphenylphosphino)ferrocene]dichloropalladium dichloromethane complex (1.9 g, 2.66 mmol), is added to the reaction mixture and degassed for another 15 min. The reaction mixture is heated at 75 °C for 16 h. After completion, the reaction mass is diluted with water and extracted with ethyl acetate. The organic layer is washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated to dryness under reduced pressure. The crude product is purified by Combiflash (12 g, RediSep column) using 20 % ethyl acetate in hexanes as eluent. The desired fractions are concentrated under reduced pressure to afford 2-fluoro-4-hydroxy-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile (3).

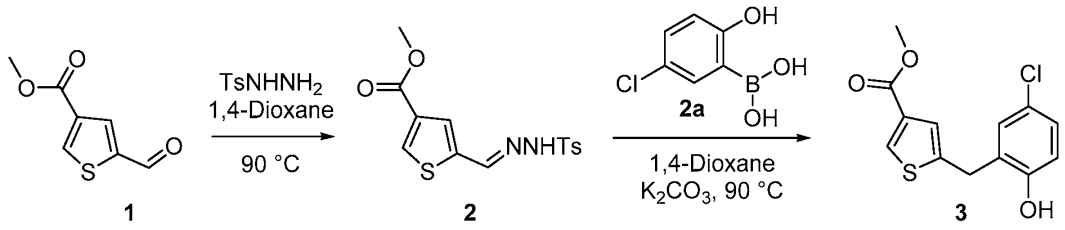
Example 3B.9



[0470] A solution of 2,2-dimethyl-1,3-dioxane-4,6-dione (1a, 1.048 g, 7.27 mmol) and 1,1,1-triethoxyethane (10.0 mL) is stirred and heated at 90 °C for 2 h in a closed vessel. Methyl 2-aminobenzoate (1, 1 g, 6.62 mmol) is added portion wise at 90 °C under argon atmosphere and continued heating at 90 °C for 6 h. After completion, the reaction mass is cooled to room temperature, added water and extracted with ethyl acetate. The organic layer is dried over anhydrous sodium sulfate, filtered and concentrated under vacuo to get crude. The crude methyl 2-((1-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)ethyl)amino)benzoate (2).

[0471] A solution of methyl 2-((1-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)ethyl)amino)benzoate (2, 0.900 g, 2.82 mmol) in *N*-methyl pyrrolidone (1 mL) is heated in microwave at 200 °C for 30 min. After completion, the reaction mixture is diluted with dichloromethane and then silica gel is added. The solvent is then evaporated and the free flow silica gel is then loaded on the Isco column and purified via silica gel chromatography eluting with methanol/ethylacetate. The desired fractions are concentrated under reduced pressure to afford methyl 4-hydroxy-2-methylquinoline-8-carboxylate (3).

Example 3B.10

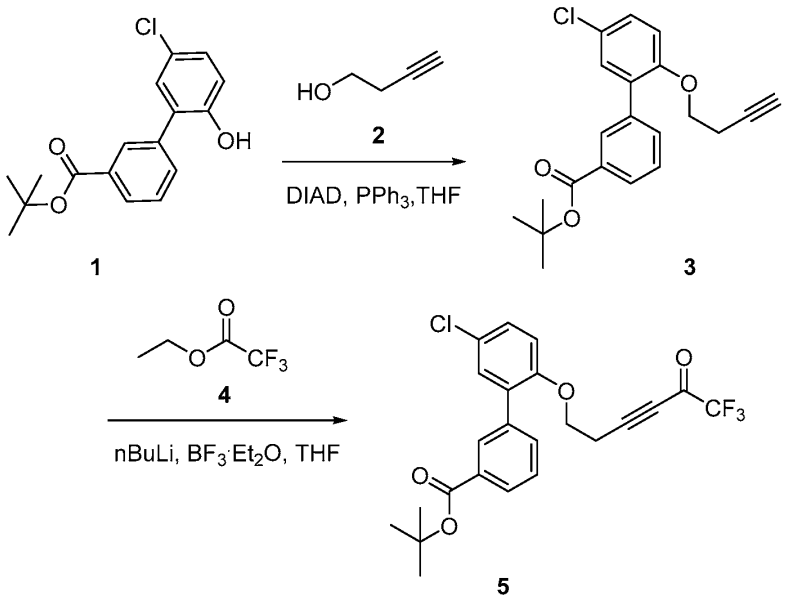


[0472] A solution of methyl 5-formylthiophene-3-carboxylate (**1**, 2.00 g, 11.7 mmol) and 4-methylbenzenesulfonohydrazide (2.19 g, 11.7 mmol) in 1,4-dioxane (20 mL) is heated at 90 °C for 16 h. The reaction mixture is cooled at room temperature, concentrated under reduced pressure to get the crude. The crude is washed with diethyl ether and dried under vacuum to afford methyl (Z)-5-((2-tosylhydrazineylidene)methyl)thiophene-3-carboxylate (**2**).

[0473] To a solution of methyl (Z)-5-((2-tosylhydrazineylidene)methyl)thiophene-3-carboxylate (**2**, 0.50 g, 1.47 mmol), (5-chloro-2-hydroxyphenyl)boronic acid (**2a**, 0.307 g, 1.77 mmol) and

potassium carbonate (0.40 g, 2.94 mmol) in 1,4-dioxane:water (4:1, 5 mL) is added and reaction mixture is stirred at 90 °C for 16 h. After completion, the reaction mixture is diluted with water and extracted with ethyl acetate. The organic layer is dried over anhydrous sodium sulfate, filtered and concentrated to dryness under reduced pressure to get crude. The crude is purified by flash column chromatography using silica (100-200 mesh) and 10-20 % ethyl acetate in hexanes as eluent to afford methyl 5-(5-chloro-2-hydroxybenzyl)thiophene-3-carboxylate (**3**).

Example 3B.11



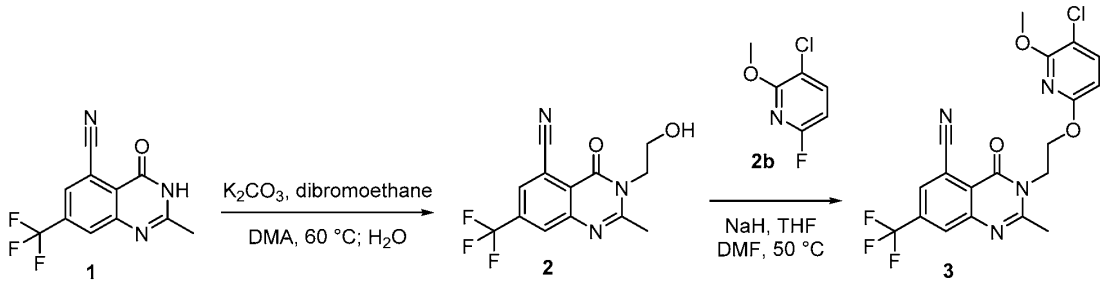
[0474] To a cooled solution of *tert*-butyl 5'-chloro-2'-hydroxy-[1,1'-biphenyl]-3-carboxylate (1, 2.65 g, 8.7 mmol), but-3-yn-1-ol (2, 0.66 mL, 8.7 mmol) and triphenylphosphine (2.28 g, 8.7 mmol) in tetrahydrofuran (14 mL) at 5 °C is added diisopropyl azodicarboxylate (1.71 mL, 8.7 mmol) via syringe over ca. 2 min. This is warmed to room temperature after 15 min and stirred for an additional 18 h. The solvent is removed *in vacuo* and residue purified via automated flash chromatography, eluting with hexanes and ethyl acetate to afford *tert*-butyl 2'-(but-3-yn-1-yloxy)-5'-chloro-[1,1'-biphenyl]-3-carboxylate (3).

[0475] A flame-dried round bottom flask is charged with ethyl 2,2,2-trifluoroacetate (4, 0.26 mL, 2.18 mmol) and tetrahydrofuran (13 mL). It is cooled to -78 °C and boron trifluoride diethyl etherate (0.29 mL, 2.32 mmol) is added dropwise. After 50 min *tert*-butyl 2'-(but-3-yn-1-yloxy)-5'-chloro-[1,1'-biphenyl]-3-carboxylate (3, 460 mg, 1.29 mmol) is added slowly followed by slow addition of *n*-butyllithium solution (2.5 M in hexanes, 0.62 mL, 1.55 mmol). After 1 h the reaction is quenched at -78 °C with the slow addition of saturated aqueous ammonium chloride solution. The solution is warmed to room temperature and ethyl acetate is added. The layers are

separated, and the aqueous phase is extracted with ethyl acetate twice. The combined organic material is washed with brine, dried over magnesium sulfate, filtered, and concentrated. Purification via automated flash chromatography, eluting with hexanes and ethyl acetate, afforded *tert*-butyl 5'-chloro-2'-((6,6,6-trifluoro-5-oxohex-3-yn-1-yl)oxy)-[1,1'-biphenyl]-3-carboxylate (5)

Example 3C. General Coupling methods

Example 3C.1



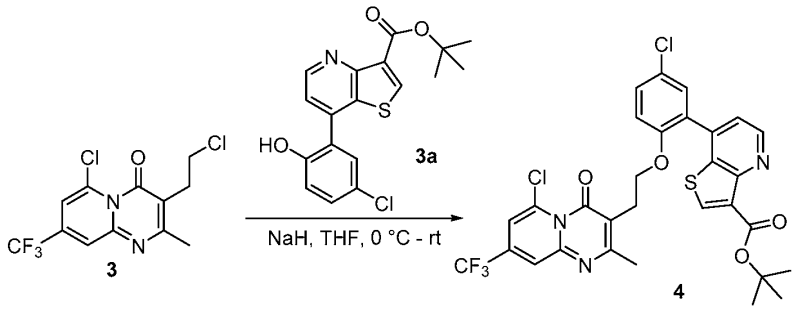
[0476] Sodium methoxide (25 wt. % in methanol) (3.16 mL, 13.8 mmol) is added to a stirred solution of 3-chloro-2,6-difluoro-pyridine (2a, 2.01 g, 13.4 mmol) in Methanol (5 mL) at 0 °C. The cold bath is removed and the resulting cloudy mixture is stirred at room temperature under argon for 35 min. The reaction mixture is poured into water (100 mL). Solids are collected by vacuum filtration, washed thoroughly with water, and air dried using vacuum suction for 30 min. The solids are dried under high vacuum to afford 3-chloro-6-fluoro-2-methoxypyridine (2b).

[0477] Potassium carbonate (1.82 g, 13.2 mmol) is added to a stirred solution of 2-methyl-4-oxo-7-(trifluoromethyl)-3,4-dihydroquinazoline-5-carbonitrile (1, 835 mg, 3.30 mmol) and 1,2-dibromoethane (2.84 mL, 33.0 mmol) in DMA (15 mL) at room temperature under argon. The resulting mixture is heated at 60 °C under argon for 3 h. Water (0.59 mL, 33.0 mmol) is added. The resulting mixture is heated at 60 °C under argon for 1 h 15 min. After cooling to room temperature the reaction mixture is partitioned between ethyl acetate and water. The organics are washed three times with brine, dried over magnesium sulfate, filtered, concentrated on a rotary evaporator, and purified via silica gel chromatography (20-90 % ethyl acetate in hexanes) to afford 3-(2-hydroxyethyl)-2-methyl-4-oxo-7-(trifluoromethyl)-3,4-dihydroquinazoline-5-carbonitrile (2).

[0478] 3-(2-Hydroxyethyl)-2-methyl-4-oxo-7-(trifluoromethyl)-3,4-dihydroquinazoline-5-carbonitrile (2, 390 mg, 1.31 mmol) is dissolved in DMF (4 mL) with stirring under argon. THF (6 mL) is added and the resulting solution is cooled to -78 °C. Sodium hydride (34.6 mg, 1.44 mmol) is added and the resulting cloudy mixture is stirred at -78 °C under argon for 10 min. 3-

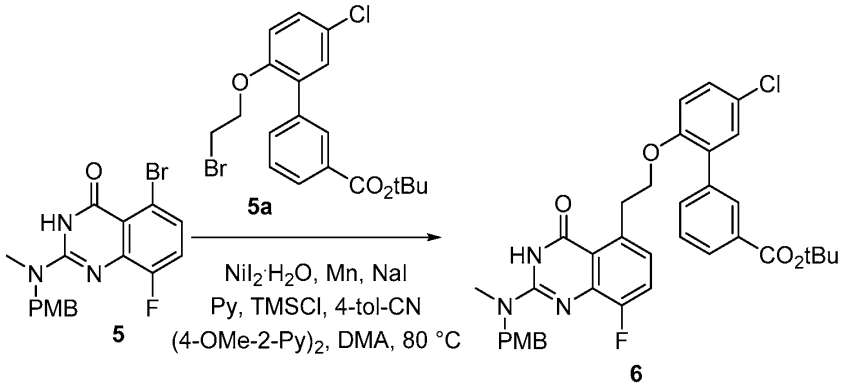
Chloro-6-fluoro-2-methoxypyridine (2b, 254 mg, 1.57 mmol) is added and the cold bath is removed. The resulting mixture is stirred at room temperature under argon for 20 min and then heated at 50 °C under a reflux condenser under argon for 2.5 h. After cooling to room temperature the resulting mixture is partitioned between ethyl acetate and a mixture of brine and saturated aqueous ammonium chloride. The organics are washed twice more with brine, concentrated on a rotary evaporator with silica gel, and purified via silica gel chromatography (0-100 % ethyl acetate in hexanes) to afford impure 3-(2-((5-chloro-6-methoxypyridin-2-yl)oxy)ethyl)-2-methyl-4-oxo-7-(trifluoromethyl)-3,4-dihydroquinazoline-5-carbonitrile (3).

Example 3C.2



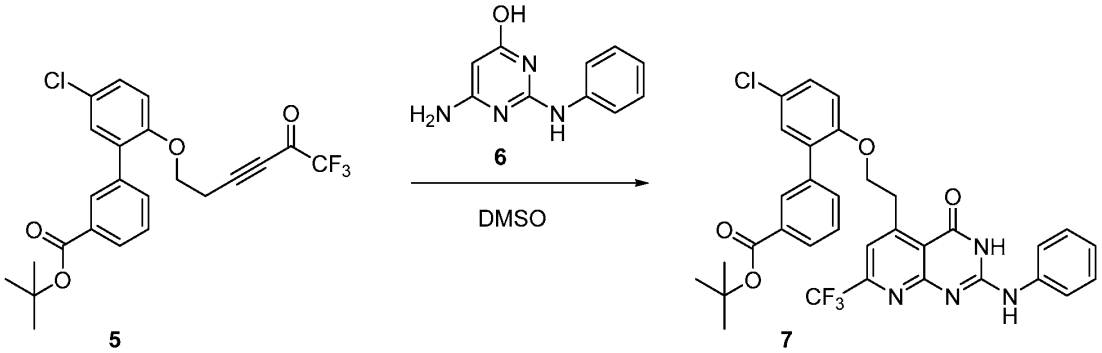
[0479] To a solution of *tert*-butyl 7-(5-chloro-2-hydroxyphenyl)thieno[3,2-b]pyridine-3-carboxylate (3a, 2.0 g, 5.5 mmol) in tetrahydrofuran (15 mL), sodium hydride (0.276 g, 6.9 mmol) is added at 0 °C and the mixture is stirred for 0.5 h. 6-Chloro-3-(2-chloroethyl)-2-methyl-8-(trifluoromethyl)-4H-pyrido[1,2-a]pyrimidin-4-one (3, 1.5 g, 4.6 mmol) in tetrahydrofuran is added to the reaction mixture and stirred for 16 h. After completion, the reaction mixture is poured into crushed ice and extracted with ethyl acetate. Organic layer is dried over anhydrous sodium sulfate and concentrated to dryness under reduced pressure. The crude compound obtained is purified through column chromatography using 0-50 % ethyl acetate in hexanes as eluent; the fractions containing desired product is distilled off under reduced pressure to afford *tert*-butyl 7-(5-chloro-2-(2-(6-chloro-2-methyl-4-oxo-8-(trifluoromethyl)-4H-pyrido[1,2-a]pyrimidin-3-yl)ethoxy)phenyl)thieno[3,2-b]pyridine-3-carboxylate (4).

Example 3C.3



[0480] To a mixture of 5-bromo-8-fluoro-2-((4-methoxybenzyl)(methyl)amino)quinazolin-4(3*H*)-one (5, 95 mg, 0.23 mmol), *tert*-butyl 2'-(2-bromoethoxy)-5'-chloro-[1,1'-biphenyl]-3-carboxylate (5a, 99 mg, 0.24 mmol), nickel(II) iodide hydrate (30 mg, 0.08 mmol), sodium iodide (17 mg, 0.12 mmol), p-tolunitrile (11 mg, 0.09 mmol), 4,4'-dimethoxy-2,2'-bipyridine (20 mg, 0.09 mmol) in freshly sparged *N,N*-dimethylacetamide (1.2 mL) are added chlorotrimethylsilane (1 drop), pyridine (1 drop) and manganese (25 mg, 0.46 mmol). The reaction is stirred at 80 °C overnight. The resulting mixture is cooled to room temperature and filtered through a pad of Celite. The filtrate is extracted with ethyl acetate and water. The combined organics are dried over sodium sulfate, decanted and concentrated. The crude is purified via column chromatography (silica, ethyl acetate/hexanes = 0-40 %) to afford 5'-chloro-2'-(2-(8-fluoro-2-((4-methoxybenzyl)(methyl)amino)-4-oxo-3,4-dihydroquinazolin-5-yl)ethoxy)-[1,1'-biphenyl]-3-carboxylic acid (6).

Example 3C.4

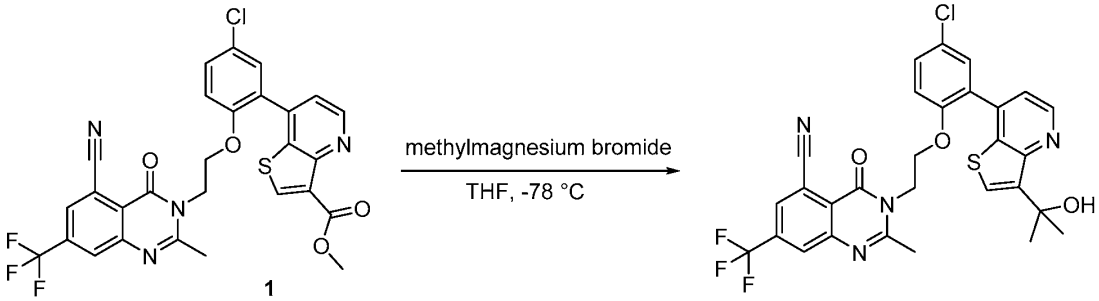


[0481] 6-Amino-2-(phenylamino)pyrimidin-4-ol (6, 114 mg, 0.45 mmol) is dissolved in dimethylsulfoxide (1.1 mL) and *tert*-butyl 5'-chloro-2'-((6,6,6-trifluoro-5-oxohex-3-yn-1-yl)oxy)-[1,1'-biphenyl]-3-carboxylate (5, 203 mg, 0.45 mmol) is added in 1 portion. The neon

solution is stirred at room temperature for 19 h. The reaction mixture is diluted with water and filtered. The solid is dried in a vacuum oven for 2 h to afford *tert*-butyl 5'-chloro-2'-(2-(4-oxo-2-(phenylamino)-7-(trifle.oromethyl)-3,4-dihydropyrido[2,3-*d*]pyrimidin-5-yl)ethoxy)-[1,1'-biphenyl]-3-carboxylate (7)

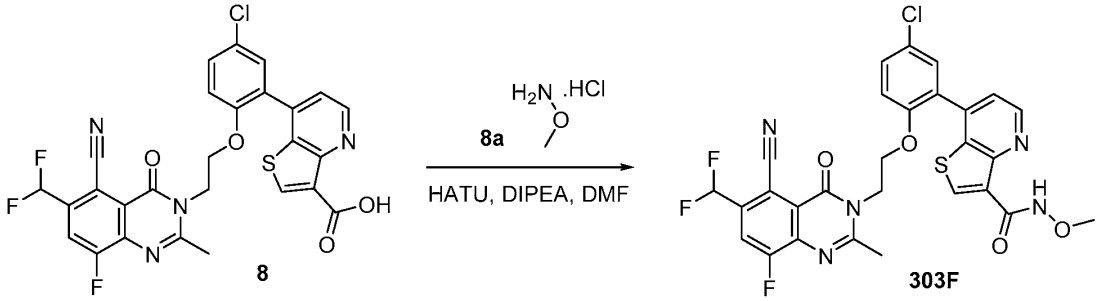
Example 3D. Post Coupling modification methods

Example 3D.1



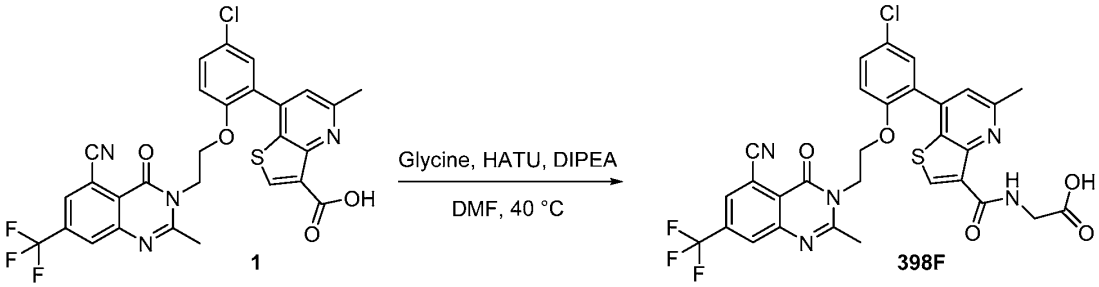
[0482] Methylmagnesium bromide (3 M in diethyl ether) (0.051 mL, 0.152 mmol) is added to a stirred solution of methyl 7-(5-chloro-2-(2-(5-cyano-2-methyl-4-oxo-7-(trifluoromethyl)quinazolin-3(4H)-yl)ethoxy)phenyl)thieno[3,2-b]pyridine-3-carboxylate (1, 30.3 mg, 0.051 mmol) in THF (2.5 mL) at -78 °C under argon. The reaction mixture quickly became dark yellow colored. After 20 min the reaction mixture is quenched with saturated aqueous ammonium chloride (0.5 mL), diluted with water (0.5 mL), and partitioned between ethyl acetate and brine. The organics are dried over magnesium sulfate, filtered, concentrated on a rotary evaporator, and dried under high vacuum at 40 °C for 45 min to afford an orange residue. This is dissolved in THF (2.5 mL) with stirring and cooled to -78 °C under argon. Methylmagnesium bromide (3 M in diethyl ether) (0.051 mL, 0.152 mmol) is added and the reaction mixture is stirred at -78 °C under argon for 20 min. The reaction mixture is quenched with saturated aqueous ammonium chloride (0.5 mL), diluted with water (0.5 mL), and partitioned between ethyl acetate and brine. The organics are dried over magnesium sulfate, filtered, concentrated on a rotary evaporator, and purified via preparatory HPLC (15-57 % acetonitrile in water with 0.1 % TFA). Fractions containing desired product are combined and neutralized with saturated aqueous sodium bicarbonate. The acetonitrile is removed on a rotary evaporator. The residual aqueous phase is extracted three times with dichloromethane. The combined organics are dried over sodium sulfate, filtered, and concentrated on a rotary evaporator. The residue is taken up in acetonitrile and water and lyophilized to dryness to afford 3-(2-(4-chloro-2-(3-(2-hydroxypropan-2-yl)thieno[3,2-b]pyridin-7-yl)phenoxy)ethyl)-2-methyl-4-oxo-7-(trifluoromethyl)-3,4-dihydroquinazoline-5-carbonitrile (Cpd. No. 352F).

Example 3D.2



[0483] To a solution 7-(5-chloro-2-(2-(5-cyano-6-(difluoromethyl)-8-fluoro-2-methyl-4-oxoquinazolin-3(4H)-yl)ethoxy)phenyl)thieno[3,2-b]pyridine-3-carboxylic acid (8, 0.10 g, 0.171 mmol) in *N,N*-dimethylformamide (2.0 mL), 1-[bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxide hexafluorophosphate (0.098 g, 0.256 mmol) is added and mixture is stirred at room temperature for 15 min. The reaction mixture is cooled to 0 °C, *N,N*-diisopropylethylamine (0.12 mL, 0.684 mmol) and O-methylhydroxylamine hydrochloride (8a, 0.017 g, 0.205 mmol) are added and the mixture is stirred at room temperature for 1.5 h. After completion, the reaction mixture is diluted with ethyl acetate and washed with cold water and brine solution, dried over anhydrous sodium sulphate and concentrated under reduced pressure. The crude is purified by prep-HPLC to afford 7-(5-chloro-2-(2-(5-cyano-6-(difluoromethyl)-8-fluoro-2-methyl-4-oxoquinazolin-3(4H)-yl)ethoxy)phenyl)-*N*-methoxythieno[3,2-b]pyridine-3-carboxamide (Cpd. No. 303F).

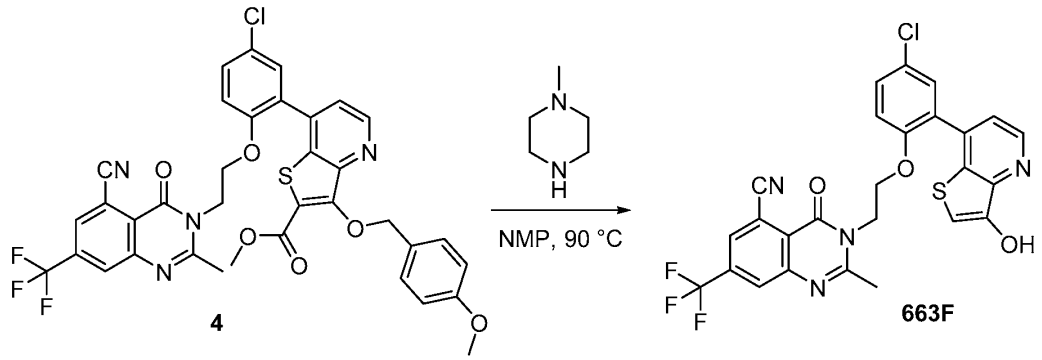
Example 3D.3



[0484] *N,N*-diisopropylethylamine (0.028 mL, 0.163 mmol) is added to a stirred mixture of 7-(5-chloro-2-(2-(5-cyano-2-methyl-4-oxo-7-(trifluoromethyl)quinazolin-3(4H)-yl)ethoxy)phenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylic acid (1, 32.5 mg, 0.054 mmol) and HATU (22.7 mg, 0.060 mmol) in DMF (0.3 mL) at room temperature under argon. All solids dissolved within 5 min and then shortly thereafter a lot of solids precipitated. After 20 min glycine (6.1 mg, 0.081 mmol) is added followed by more DMF (0.2 mL). The resulting mixture is sealed and stirred vigorously at room temperature for 20 min. More glycine (18.0 mg, 0.240 mmol) is added. The

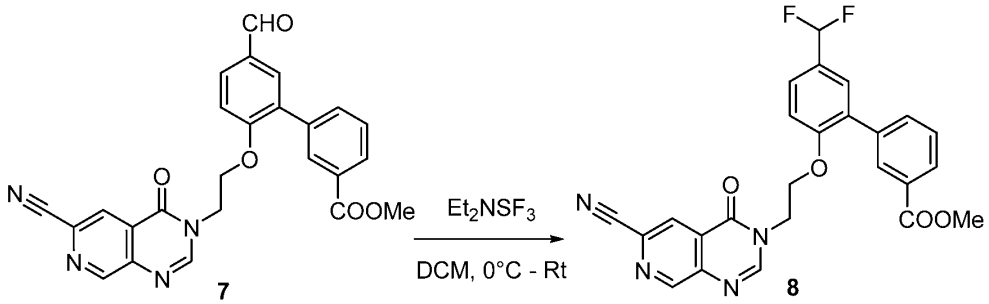
resulting mixture is sealed, stirred vigorously, and heated at 40 °C with a heating block for 14 h. The reaction mixture is diluted with methanol, filtered, and purified via preparatory HPLC (20-70 % acetonitrile in water with 0.1 % TFA). Fractions containing the desired product are combined and lyophilized to dryness to afford (7-(5-chloro-2-(2-(5-cyano-2-methyl-4-oxo-7-(trifluoromethyl)quinazolin-3(4H)-yl)ethoxy)phenyl)-5-methylthieno[3,2-b]pyridine-3-carbonyl)glycine (Cpd. No. 398F).

Example 3D.4



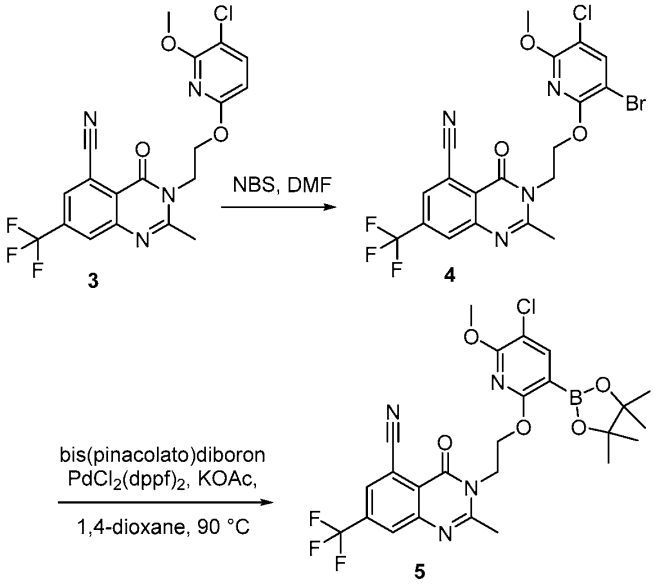
[0485] 1-Methylpiperazine (0.05 mL, 0.73 mmol) and methyl 7-(5-chloro-2-(2-(5-cyano-2-methyl-4-oxo-7-(trifluoromethyl)quinazolin-3(4H)-yl)ethoxy)phenyl)-3-((4-methoxybenzyl)oxy)thieno[3,2-b]pyridine-2-carboxylate (4, 82 mg, 0.11 mmol) are dissolved in *N*-methyl pyrrolidinone (1.8 mL) in a screw capped vial equipped with a stir bar. The vial is sealed and heated in a heating block at 145 °C for 4.5 h. The reaction mixture is cooled to room temperature. The reaction mixture is diluted with ethyl acetate and filtered through Celite and volatile solvent removed *in vacuo*. The residual material is diluted with dimethylsulfoxide and purified via RP-HPLC to afford 3-(2-(4-chloro-2-(3-hydroxythieno[3,2-b]pyridin-7-yl)phenoxy)ethyl)-2-methyl-4-oxo-7-(trifluoromethyl)-3,4-dihydroquinazoline-5-carbonitrile (Cpd. No. 663F).

Example 3D.5



[0486] To a solution of methyl 2'-(2-(6-cyano-4-oxopyrido[3,4-*d*]pyrimidin-3(4*H*)-yl)ethoxy)-5'-formyl-[1,1'-biphenyl]-3-carboxylate (7, 0.10 g, 0.22 mmol) in dichloromethane (8 mL), diethylaminosulfur trifluoride (0.052 g, 0.33 mmol) is added at 0 °C. The reaction mixture is stirred at room temperature for 16 h. After completion, the reaction mixture is quenched with 10 % aqueous sodium hydroxide solution at 0 °C to pH~ 7 and extracted with dichloromethane (50 mL). The organic layer is washed with water (50 mL), brine (20 mL), dried over anhydrous sodium sulfate and concentrated under reduced pressure to get crude. The crude is purified by combiflash column (4 g, Redisep) using 10-50 % ethyl acetate in hexanes to afford methyl 2'-(2-(6-cyano-4-oxopyrido[3,4-*d*]pyrimidin-3(4*H*)-yl)ethoxy)-5'-(difluoromethyl)-[1,1'-biphenyl]-3-carboxylate (8).

Example 3D.6

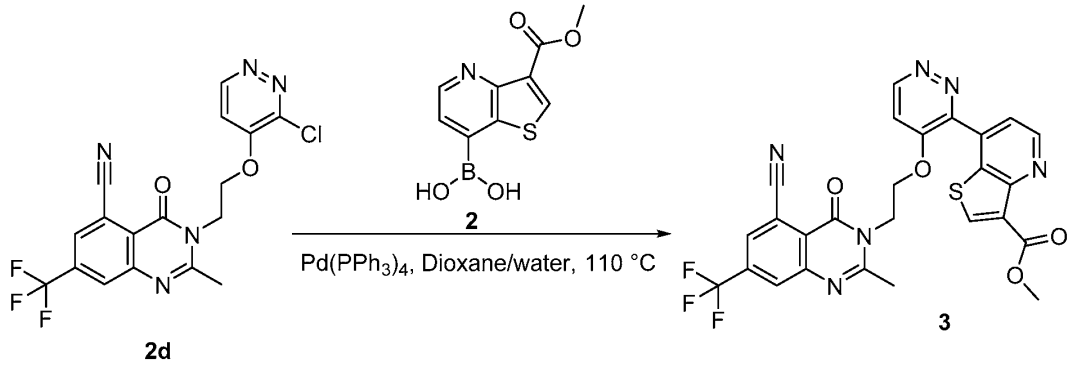


3 **4** **5**

[0487] *N*-bromosuccinimide (39.2 mg, 0.22 mmol) is added to a stirred solution of 3-(2-((5-chloro-6-methoxypyridin-2-yl)oxy)ethyl)-2-methyl-4-oxo-7-(trifluoromethyl)-3,4-dihydroquinazoline-5-carbonitrile (3, 92 mg, 0.21 mmol) in DMF (1 mL) at room temperature. The resulting clear yellow reaction mixture is capped and stirred at room temperature for 3.5 h. More *N*-bromosuccinimide (19.0 mg, 0.11 mmol) is added and the reaction mixture is capped and stirred at room temperature for 2 h. The reaction mixture is diluted with ethyl acetate and washed three times with brine. The organics are dried over magnesium sulfate, filtered, concentrated on a rotary evaporator, and purified via silica gel chromatography (0-100 % ethyl acetate in hexanes) to afford 3-(2-((3-bromo-5-chloro-6-methoxypyridin-2-yl)oxy)ethyl)-2-methyl-4-oxo-7-(trifluoromethyl)-3,4-dihydroquinazoline-5-carbonitrile (4).

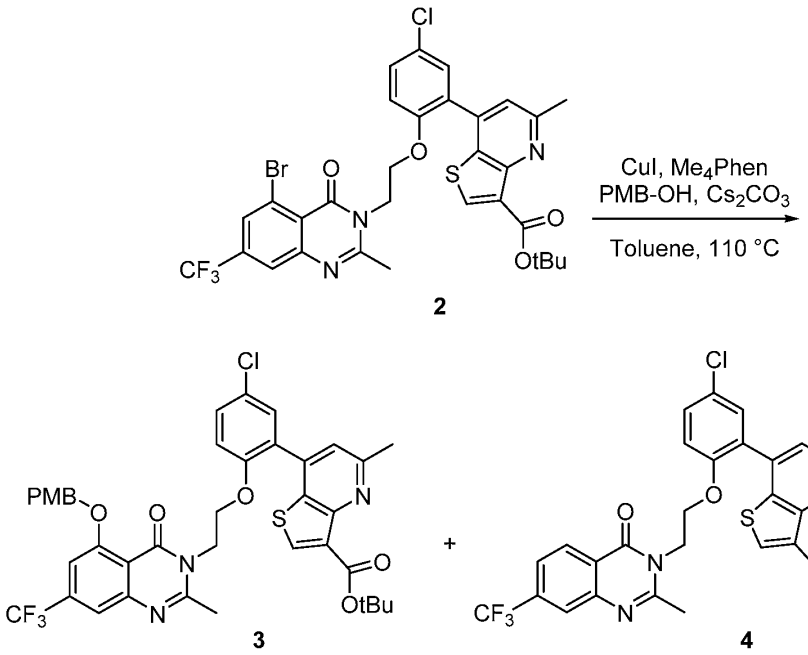
[0488] 3-(2-((3-Bromo-5-chloro-6-methoxypyridin-2-yl)oxy)ethyl)-2-methyl-4-oxo-7-(trifluoromethyl)-3,4-dihydroquinazoline-5-carbonitrile (4, 76.3 mg, 0.147 mmol), potassium acetate (43.4 mg, 0.44 mmol), bis(pinacolato)diboron (44.9 mg, 0.177 mmol), $PdCl_2(dppf).CH_2Cl_2$ (12 mg, 0.015 mmol), and 1,4-dioxane (0.5 mL) are combined in a 1 dram vial with a stirbar and sparged with argon gas for 1 min. The resulting mixture is sealed, stirred vigorously, and heated at 90 °C with a heating block for 3 h. The reaction mixture is loaded directly onto a silica gel loading column and purified via silica gel chromatography (0-80 % ethyl acetate in hexanes) to afford impure 3-(2-((5-chloro-6-methoxy-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridin-2-yl)oxy)ethyl)-2-methyl-4-oxo-7-(trifluoromethyl)-3,4-dihydroquinazoline-5-carbonitrile (5)

Example 3D.7



[0489] To a solution of 3-(2-((3-chloropyridazin-4-yl)oxy)ethyl)-2-methyl-4-oxo-7-(trifluoromethyl)-3,4-dihydroquinazoline-5-carbonitrile (2d, 20.0 mg, 0.049 mmol), methyl (3-(methoxycarbonyl)thieno[3,2-b]pyridin-7-yl)boronic acid (2, 15.58 mg, 0.049 mmol), Potassium Carbonate (0.15 mL, 0.150 mmol) in 1,4-dioxane (1.5 mL) is added tetrakis(triphenylphosphine)palladium(0) (5.64 mg, 0.0049 mmol) at room temperature and the mixture is degassed by bubbling argon through it for 5 min. The reaction mixture is heated to 90 °C for 16 h. After completion of the reaction, the reaction is diluted with water and extracted with ethyl acetate. The organic layer is washed with water and saturated brine solution, dried over anhydrous sodium sulphate, filtered, and concentrated to dryness under reduced pressure. The crude product is purified by Combiflash (12 g, RediSep column) using 1-5 % methanol in dichloromethane as eluent to afford methyl 7-(4-(2-(5-cyano-2-methyl-4-oxo-7-(trifluoromethyl)quinazolin-3(4H)-yl)ethoxy)pyridazin-3-yl)thieno[3,2-b]pyridine-3-carboxylate (3).

Example 3D.8

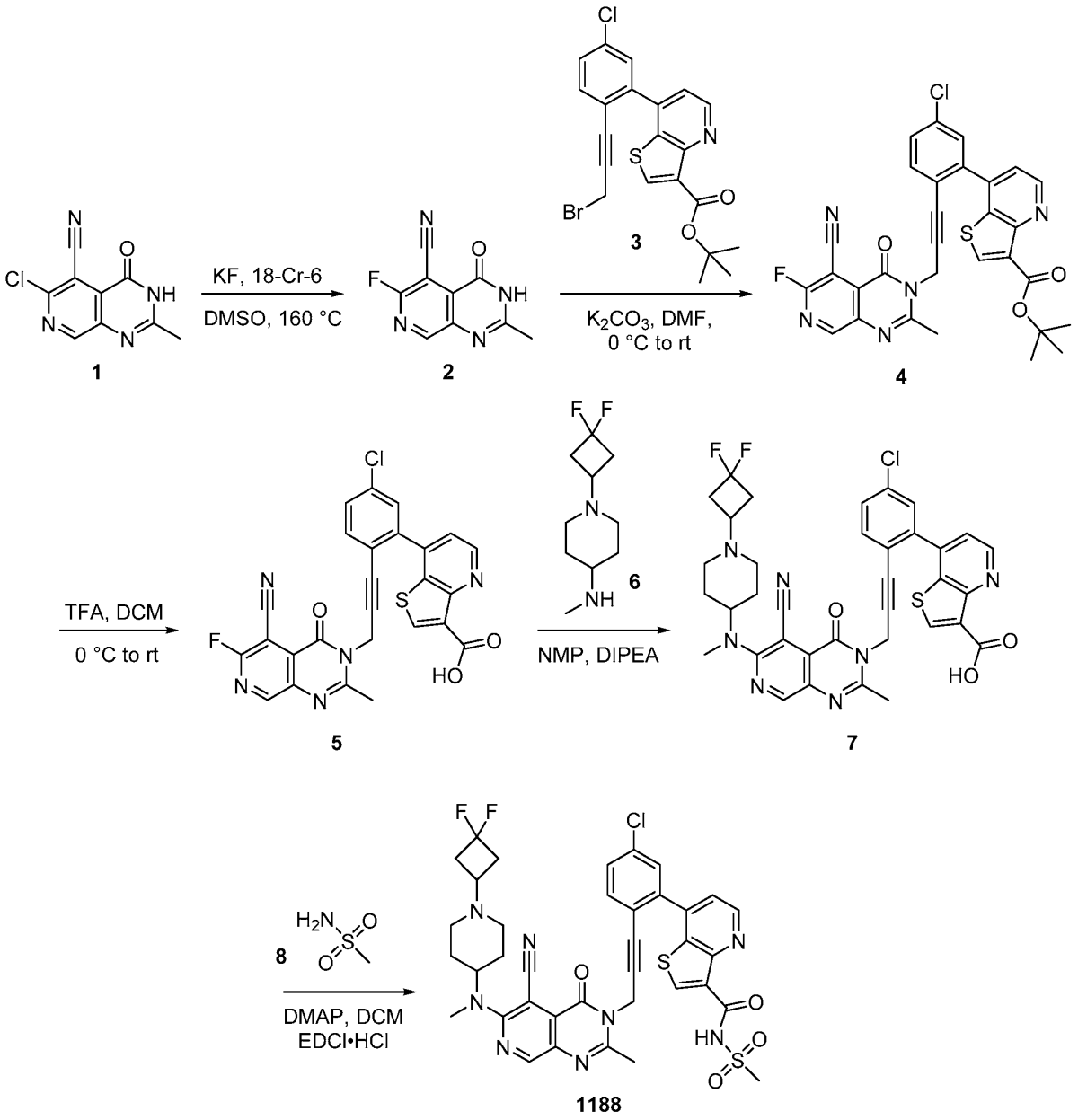


[0490] A flame-dried vial is charged with *tert*-butyl 7-(2-(2-(5-bromo-2-methyl-4-oxo-7-(trifluoromethyl)quinazolin-3(4H)-yl)ethoxy)-5-chlorophenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (2, 106 mg, 0.150 mmol), 3,4,7,8-tetramethyl-1,10-phenanthroline (10.8 mg, 0.0457 mmol), copper(I) iodide (6.2 mg, 0.033 mmol), and cesium carbonate (94 mg, 0.290 mmol). The vial is evacuated and backfilled with argon twice. Toluene (1.4 mL) and (4-methoxyphenyl)methanol (29 uL, 33 mg, 0.24 mmol) are added, and the mixture is degassed for 5 min, then stirred at 110 °C. After 4 h, the mixture is allowed to cool down to room temperature and stir an additional 14 h, then diluted with EtOAc, then washed with water. The aq. phase is extracted (3 x EtOAc), and the combined organic phases are dried (Na_2SO_4), filtered, and concentrated. Purification by column chromatography (SiO_2, 0-50 % EtOAc/hexane) provided 61 mg of a ca. 1:1 mixture of products *tert*-butyl 7-(5-chloro-2-(2-(5-((4-methoxybenzyl)oxy)-2-methyl-4-oxo-7-(trifluoromethyl)quinazolin-3(4H)-yl)ethoxy)phenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (3) and *tert*-butyl 7-(5-chloro-2-(2-(2-methyl-4-oxo-7-(trifluoromethyl)quinazolin-3(4H)-yl)ethoxy)phenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (4).

[0491] Compounds made using one or more of the general methods described above are shown in Table 3. Where provided, characterization data is to the right of the compounds.

Example 4. Specific Examples

Example 4A. Synthesis of Compound 1188, 7-(5-chloro-2-(3-(5-cyano-6-((1-(3,3-difluorocyclobutyl)piperidin-4-yl)(methyl)amino)-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)prop-1-yn-1-yl)phenyl)-N-(methylsulfonyl)thieno[3,2-b]pyridine-3-carboxamide



[0492] A solution of 6-chloro-2-methyl-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidine-5-carbonitrile (**1**, 10.0 g, 45.45 mmol) in Dimethyl sulfoxide (200 mL) was purged with argon gas for 10 minutes. 18-crown-6 ether (17.99 g, 68.18 mmol), and Pottasium fluoride (13.2 g, 227.25

mmol) were added to reaction mixture and purging continued for 5 minutes. Reaction mixture was then stirred in preheated oil bath at 160 °C for 2 h. Reaction mixture cooled down, poured on to ice cold water and extracted with ethyl acetate. Ethyl acetate layer was washed with brine solution, dried over anhydrous sodium sulphate and concentrated under reduced pressure to get crude product. The crude product obtained was triturated with diethyl ether and dried to get pure 6-fluoro-2-methyl-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidine-5-carbonitrile (**2**) as light brown solid. Yield: 7.3 g, 78 %; MS (ESI) m/z 205.14 [M+1] +.

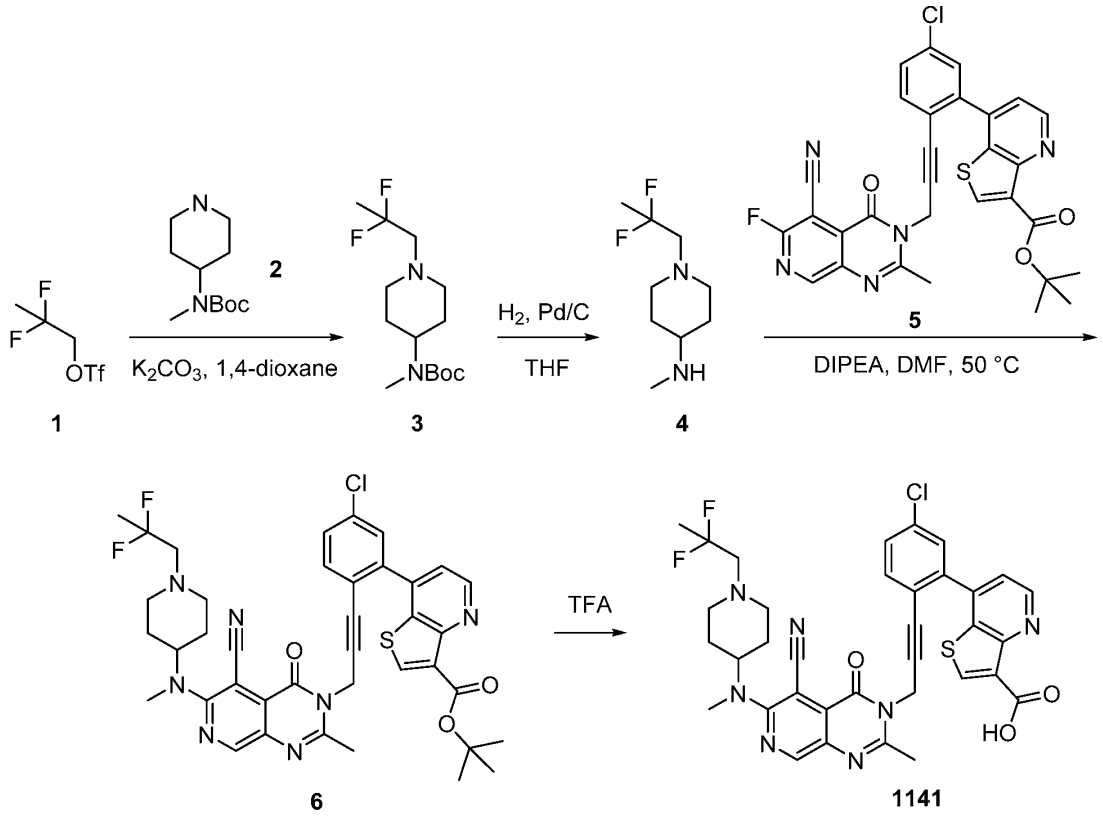
[0493] To a solution of 6-fluoro-2-methyl-4-oxo-3,4-dihydropyrido[3,4-d]pyrimidine-5-carbonitrile (**2**, 3.70 g, 18.13 mmol) and Potassium carbonate (4.96 g, 36.27 mmol) in N,N-Dimethylformamide (74.0 mL), tert-butyl 7-(2-(3-bromoprop-1-yn-1-yl)-5-chlorophenyl)thieno[3,2-b]pyridine-3-carboxylate (**3**, 5.85 g, 12.69 mmol) was added at 0 °C and reaction mixture was allowed to come at room temperature over a period of 1h. After completion, the reaction mixture was poured onto ice cold water. Solid precipitated out was filtered, and dried to get crude product. The crude product was purified by column chromatography using silica gel (100-200 mesh) and 80 to 90 % Ethyl acetate in hexanes as eluents. The desired fractions were concentrated under reduced pressure to get solid. Solid obtained was triturated with methanol and dried to afford tert-butyl 7-(5-chloro-2-(3-(5-cyano-6-fluoro-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)prop-1-yn-1-yl)phenyl)thieno[3,2-b]pyridine-3-carboxylate (**4**) as pale yellow solid. Yield: 4.25 g, 40%; MS (ESI) m/z 586.32 [M+1] +. 1H NMR (400 MHz, DMSO-d6) δ 8.94 (s, 1H), 8.68 (d, J = 4.80 Hz, 1H), 8.51 (s, 1H), 7.74 (d, J = 8.40 Hz, 1H), 7.67-7.63(m, 3H), 7.40 (d, J = 4.80 Hz, 1H), 4.88 (s, 2H), 2.18 (s, 3H), 1.59 (s, 9H).

[0494] To a solution of tert-butyl 7-(5-chloro-2-(3-(5-cyano-6-fluoro-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)prop-1-yn-1-yl)phenyl)thieno[3,2-b]pyridine-3-carboxylate (**4**, 0.13 g, 0.22 mmol) in dichloromethane (1.0 mL), 2,2,2-trifluoroacetic acid (1.0 mL) was added at 0 °C, and reaction mixture was stirred at room temperature for 6 h. After completion, reaction mixture concentrated under reduced pressure to get solid. The solid obtained was triturated with diethyl ether and dried to 7-(5-chloro-2-(3-(5-cyano-6-fluoro-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)prop-1-yn-1-yl)phenyl)thieno[3,2-b]pyridine-3-carboxylic acid (**5**) as off white solid. Yield: 0.090 g, 81%; MS (ESI) m/z 530.12 [M+1]+. 1H-NMR (400 MHz, DMSO-d6) δ 8.92 (s, 1H), 8.75 (d, J = 5.44 Hz, 1H), 8.59 (s, 1H), 7.76 (d, J = 8.44 Hz, 1H), 7.69-7.68 (m, 2H), 7.52 (d, J = 4.36 Hz, 1H), 4.87 (s, 2H), 2.13 (s, 3H).

[0495] To a solution of 7-(5-chloro-2-(3-(5-cyano-6-fluoro-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)prop-1-yn-1-yl)phenyl)thieno[3,2-b]pyridine-3-carboxylic acid (**5**, 0.10 g, 0.189 mmol) and 1-(3,3-difluorocyclobutyl)-N-methylpiperidin-4-amine (**6**, 0.077 g, 0.37 mmol) in N-methyl-2-pyrrolidone (1.5 mL) was added N,N-diisopropylethylamine (0.064 mL, 0.37 mmol). The reaction mixture was stirred at room temperature for 72 h. After completion, reaction mixture was directly purified by preparative HPLC to afford 7-(5-chloro-2-(3-(5-cyano-6-((1-(3,3-difluorocyclobutyl)piperidin-4-yl)(methyl)amino)-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)prop-1-yn-1-yl)phenyl)thieno[3,2-b]pyridine-3-carboxylic acid (**7**) as a yellow solid. Yield: 0.050 g, 44 %; MS (ESI) m/z, 714.50 [M+1] +; 1H-NMR (400 MHz, DMSO-d6) δ 9.80 (bs, 1H), 8.76 (s, 1H), 8.75 (s, 1H), 8.65 (s, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.70-7.67 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 4.83 (s, 2H), 4.56 (bs, 1H), 3.56 (bs, 4H), 3.11 (bs, 1H), 3.06 (s, 3H), 3.05 (bs, 4H), 2.13 (bs, 4H), 2.11 (s, 3H).

[0496] To a solution of 7-(5-chloro-2-(3-(5-cyano-6-((1-(3,3-difluorocyclobutyl)piperidin-4-yl)(methyl)amino)-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)prop-1-yn-1-yl)phenyl)thieno[3,2-b]pyridine-3-carboxylic acid (**7**, 1.70 g, 2.377 mmol) and methanesulfonamide (**8**, 0.564 g, 5.94 mmol) in dichloromethane (17.0 mL) were added 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (0.737 g, 4.754 mmol) and 4-(dimethylamino) pyridine (0.725 g, 5.94 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 14 h. After completion, the reaction mixture was diluted with water and extracted with dichloromethane. The organic layer was dried over anhydrous sodium sulphate, filtered and concentrated to get crude compound. The crude compound was purified by preparative HPLC to afford 7-(5-chloro-2-(3-(5-cyano-6-((1-(3,3-difluorocyclobutyl)piperidin-4-yl)(methyl)amino)-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)prop-1-yn-1-yl)phenyl)-N-(methylsulfonyl)thieno[3,2-b]pyridine-3-carboxamide (Cpd. No. **1188**) as a yellow solid. Yield: 1.20 g, 63%; MS (ESI) m/z 791.62 $[M+1]^+$; ^{1}H-NMR (400 MHz, DMSO-d$_6$) δ 12.47 (s, 1H), 8.81-8.78 (m, 3H), 7.77 (d, *J* = 8.40 Hz, 1H), 7.71-7.67 (m, 2H), 7.62 (d, *J* = 4.80 Hz, 1H), 4.83 (s, 2H), 4.59 (bs, 1H), 3.74-3.54 (m, 6H), 3.08 (s, 3H), 2.98-2.88 (m, 6H), 2.11-2.05 (m, 4H), 2.00 (s, 3H).

Example 4B. Synthesis of Compound 1141, 7-(5-chloro-2-(3-(5-cyano-6-((1-(2,2-difluoropropyl)piperidin-4-yl)(methyl)amino)-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)prop-1-yn-1-yl)phenyl)thieno[3,2-b]pyridine-3-carboxylic acid



[0497] Benzyl methyl(piperidin-4-yl)carbamate (**2**, 0.990 g, 3.99 mmol), 2,2-difluoropropyl trifluoromethanesulfonate (**1**, 1.09 g, 4.78 mmol), potassium carbonate (1.10 g, 7.97 mmol), and 1,4-dioxane (15 mL) were combined in a 100 mL round bottom flask with a stirbar under argon. The resulting mixture was stirred vigorously at room temperature under argon for 17 h. The reaction mixture was filtered through Celite and the filter cake was washed thoroughly with ethyl acetate. The filtrate was concentrated on a rotary evaporator. The residue was taken up in dichloromethane and purified via silica gel chromatography (5-60 % ethyl acetate in hexanes) to afford benzyl (1-(2,2-difluoropropyl)piperidin-4-yl)(methyl)carbamate (**3**) as a colorless oil. Yield: 958 mg, 74 %; MS (ESI) m/z 327.3 [M+1]+; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 – 7.27 (m, 5H), 5.14 (s, 2H), 4.12 – 3.81 (m, 1H), 2.99 (d, *J* = 11.2 Hz, 2H), 2.82 (s, 3H), 2.66 (t, *J* = 13.7 Hz, 2H), 2.32 (bs, 2H), 1.86 – 1.68 (m, 2H), 1.70 – 1.50 (m, 5H).

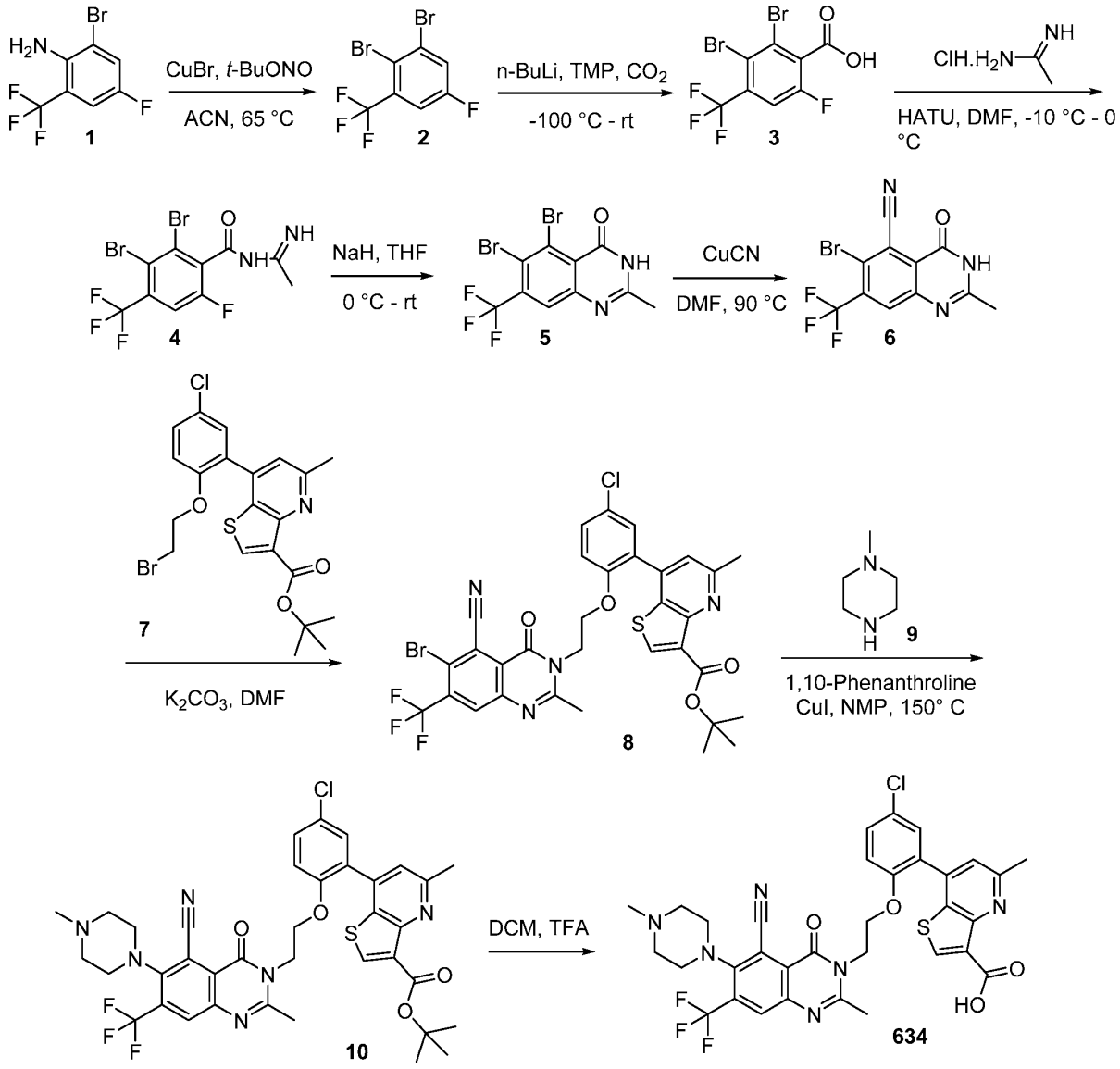
[0498] Benzyl (1-(2,2-difluoropropyl)piperidin-4-yl)(methyl)carbamate (**3**, 255 mg, 0.781 mmol) was dissolved with stirring in THF (15 mL) in a 100 mL round bottom flask. A

combination vacuum/argon/hydrogen manifold was attached and the atmosphere in the flask was removed and replaced with argon twice. 10 % palladium on carbon (41.6 mg, 0.039 mmol) was added and the atmosphere in the flask was removed and replaced with hydrogen twice. The resulting mixture was stirred vigorously under hydrogen at room temperature for 45 min. The reaction mixture was filtered through Celite and the filter cake washed thoroughly with diethyl ether. The filtrate was concentrated on a rotary evaporator at room temperature to afford 1-(2,2-difluoropropyl)-N-methylpiperidin-4-amine (**4**) as a colorless oil with some black carbon impurities. Yield: 150 mg, quantitative yield; MS (ESI) m/z 193.2 [M+1]+; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 2.94 – 2.86 (m, 2H), 2.65 (t, *J* = 13.6 Hz, 2H), 2.42 (s, 3H), 2.38 – 2.21 (m, 3H), 1.88 – 1.79 (m, 2H), 1.62 (t, *J* = 18.7 Hz, 3H), 1.42 – 1.30 (m, 2H); ^{19}F NMR (377 MHz, Chloroform-*d*) δ -91.92 (qt, *J* = 19.0, 13.6 Hz, 2F).

[0499] A mixture of *tert*-butyl 7-(5-chloro-2-(3-(5-cyano-6-fluoro-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)prop-1-yn-1-yl)phenyl)thieno[3,2-b]pyridine-3-carboxylate (**5**, 100 mg, 0.17 mmol), 1-(2,2-difluoropropyl)-*N*-methylpiperidin-4-amine (**4**, 98 mg, 0.51 mmol) and *N,N*-diisopropylethylamine (0.3 mL, 1.71 mmol) in *N,N*-dimethylformamide (2 mL) was stirred at 50 °C over the weekend. The resulting mixture was concentrated and purified via column chromatography (silica, ethyl acetate/dichloromethane = 0-40 %) to afford *tert*-butyl 7-(5-chloro-2-(3-(5-cyano-6-((1-(2,2-difluoropropyl)piperidin-4-yl)(methyl)amino)-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)prop-1-yn-1-yl)phenyl)thieno[3,2-b]pyridine-3-carboxylate (**6**) as a yellow solid. Yield: 98 mg, 76 %; MS (ESI) *m/z* 758.2 $[M+1]^+$.

[0500] *tert*-Butyl 7-(5-chloro-2-(3-(5-cyano-6-((1-(2,2-difluoropropyl)piperidin-4-yl)(methyl)amino)-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)prop-1-yn-1-yl)phenyl)thieno[3,2-b]pyridine-3-carboxylate (**6**, 97 mg, 0.13 mmol) was dissolved in trifluoroacetic acid (3 mL). The reaction was stirred at room temperature for 5 h. The resulting mixture was concentrated. The crude was purified via reversed-phase HPLC (C18, acetonitrile/water = 15-45 %) to afford 7-(5-chloro-2-(3-(5-cyano-6-((1-(2,2-difluoropropyl)piperidin-4-yl)(methyl)amino)-2-methyl-4-oxopyrido[3,4-d]pyrimidin-3(4H)-yl)prop-1-yn-1-yl)phenyl)thieno[3,2-b]pyridine-3-carboxylic acid (**1141**) as a yellow solid. Yield: 68 mg, 75 %; MS (ESI) *m/z* 702.2 $[M+1]^+$; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.76 (d, *J* = 4.8 Hz, 1H), 8.74 (s, 1H), 8.65 (s, 1H), 7.78 – 7.74 (m, 1H), 7.71 – 7.67 (m, 2H), 7.55 (d, *J* = 4.8 Hz, 1H), 4.83 (s, 2H), 3.11 (s, 3H), 2.09 (s, 3H), 1.78 (t, *J* = 19.5 Hz, 3H).

Example 4C. Synthesis of Compound 634, 7-(5-chloro-2-(2-(5-cyano-2-methyl-6-(4-methylpiperazin-1-yl)-4-oxo-7-(trifluoromethyl)quinazolin-3(4H)-yl)ethoxy)phenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylic acid



[0501] A suspension of copper(I) bromide (89.8 g, 620.1 mmol) and *tert*-butyl nitrite (63.8 mL, 620.1 mmol) in acetonitrile (2500 mL) was heated at 65 °C for 15 min. A solution of 2-bromo-4-fluoro-6-(trifluoromethyl)aniline (**1**, 100 g, 387.6 momol) in acetonitrile was added and heated the reaction mixture at 65 °C for 1 h. After completion, the reaction mass was quenched with water and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulphate, filtered and concentrated under reduced pressure to get the crude material. The crude

compound was purified by column chromatography using 0-5 % ethyl acetate in hexanes over silica gel (100-200 mesh) to afford 1,2-dibromo-5-fluoro-3-(trifluoromethyl)benzene (**2**) as off white solid. Yield: 70.0 g, 55 %; no ionization in LCMS; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (dd, *J*= 7.32, 2.84, 1H), 7.43 (dd, *J*= 8.24, 2.80, 1H).

[0502] To a solution of 2,2,6,6-tetramethylpiperidine (7.09 mL, 43.61 mmol) in dry tetrahydrofuran (100 mL) was added *n*-butyllithium (1.2 M, 27.25 mL, 32.71 mmol) drop wise at -78 °C under argon atmosphere. The reaction mixture was warmed to 0 °C and stirred for 30 min It was again cooled to -78 °C and a solution of 1,2-dibromo-5-fluoro-3-(trifluoromethyl)benzene (**2**, 10.0 g, 31.15 mol) in dry tetrahydrofuran (70 mL) was added at -100 °C and the reaction mixture was stirred for 45 min at -100 °C. Carbon dioxide gas was bubbled through the reaction mass at this temperature for 15 min and it was gradually warmed to room temperature in 2 h. After completion, the reaction mixture was quenched with water and washed with diethyl ether. The aqueous layer was acidified to pH ~3-2 with 6 N aqueous hydrogen chloride, extracted with ethyl acetate, washed the organic layer, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure to afford 2,3-dibromo-6-fluoro-4-(trifluoromethyl)benzoic acid (**3**) as brown solid. Yield: 10.0 g, crude, 87 %; MS (ESI) m/z 362.9 $[M-1]^-$.

[0503] To a solution of 2,3-dibromo-6-fluoro-4-(trifluoromethyl)benzoic acid (**3**, 27.0 g, 75.8 mmol) and acetamidine hydrochloride (4, 9.31 g, 98.5 mmol) in *N,N*-dimethylformamide (180 mL), O-(7-azabenzotriazol-1-yl)-*N,N*,N',N'-tetramethyluronium hexafluorophosphate (36.5 g, 98.5 mmol) and *N,N*-diisopropylethyl amine (32.25 mL, 221.9 mmol) were added at-10 °C and stirred for 3 h at 0 °C. After completion, the reaction mass was quenched with ice-water and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulfate and concentrated to dryness under reduced pressure. The residue was washed with pentanes to afford 2,3-dibromo-6-fluoro-*N*-(1-iminoethyl)-4-(trifluoromethyl)benzamide (**4**) as a brown gum. Yield: 30 g (crude); MS (ESI)) m/z 404.8 $[M+1]^+$.

[0504] To a solution of 2,3-dibromo-6-fluoro-*N*-(1-iminoethyl)-4-(trifluoromethyl)benzamide (**4**, 30.0 g, 74.4 mmol) in tetrahydrofuran (250 mL), sodium hydride (60 %) (5.9 g, 148.8 mmol) was added at 0 °C, warmed to room temperature and continued to stir at room temperature for 16 h. After completion, the reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulfate and concentrated to dryness under reduced pressure. The residue was washed with diethyl ether to afford 5,6-dibromo-2-methyl-7-(trifluoromethyl)quinazolin-4(3H)-one (**5**) as white solid. Yield: 9.95 g, 35 %; MS (ESI) m/z 383.01 $[M-1]^-$.

[0505] To a stirred solution of 5,6-dibromo-2-methyl-7-(trifluoromethyl)quinazolin-4(*3H*)-one (**5**, 6.0 g, 15.62 mmol) in dimethylformamide (90 mL), copper(I) cyanide (1.53 g, 17.18 mmol) was added at room temperature and the reaction mixture was heated and stirred at 90 °C for 2 h. After completion, the reaction mass was cooled to room temperature, diluted with ethyl acetate and washed with water and 1 N aqueous hydrogen chloride. The organic layer was separated, dried over sodium sulphate and concentrated under reduced pressure. The crude compound was purified by Combi flash (40g, Redi Sep column) using 70 % ethyl acetate in hexanes as eluent. The desired fractions were concentrated under reduced pressure to afford 6-bromo-2-methyl-4-oxo-7-(trifluoromethyl)-3,4-dihydroquinazoline-5-carbonitrile (**6**) as yellow solid. Yield: 3.2 g, 62.7 %; MS (ESI) m/z 330.06 $[M-1]^-$.

[0506] To a stirred solution of 6-bromo-2-methyl-4-oxo-7-(trifluoromethyl)-3,4-dihydroquinazoline-5-carbonitrile (**6**, 2.0 g, 6.0 mmol) in *N,N*-dimethylformamide (25.0 mL) was added potassium carbonate (2.48 g, 18.0 mmol) at room temperature and the mixture was stirred for 20 min. Then *tert*-butyl 7-(2-(2-bromoethoxy)-5-chlorophenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (**7**, 2.91 g, 6.0 mmol) was added to the reaction mixture at room temperature and stirring was continued for 16 h. After completion, the reaction mixture was diluted with water and extracted with ethyl acetate. The organic layer was washed with water and saturated brine, dried over anhydrous sodium sulphate, filtered and concentrated. The crude product was purified by column chromatography using silica gel (100-200 mesh) and 70 % ethyl acetate in hexanes as eluent. The desired fractions were concentrated under reduced pressure to afford *tert*-butyl 7-(2-(2-(6-bromo-5-cyano-2-methyl-4-oxo-7-(trifluoromethyl)quinazolin-3(4H)-yl)ethoxy)-5-chlorophenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (**8**) as a white solid. Yield: 1.7 g, 70 %; MS (ESI) m/z 731.14 $[M-1]^-$.

[0507] To a solution of *tert*-butyl 7-(2-(2-(6-bromo-5-cyano-2-methyl-4-oxo-7-(trifluoromethyl)quinazolin-3(4H)-yl)ethoxy)-5-chlorophenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (**8**, 0.20 g, 0.273 mmol) in *N*-Methyl-2-pyrrolidone (5.0 mL) was added 1-methylpiperazine (**9**, 0.06 mL, 0.546 mmol) and the reaction mixture was degassed by argon for 10 min. Then copper(I) iodide (0.005 g, 0.027 mmol) and 1,10-phenanthroline (0.009 g, 0.054 mmol) was added and reaction mixture was heated at 150 °C for 6 h. After completion reaction mixture was diluted with water, and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulphate, filtered and concentrated to get crude compound. Crude compound obtained was purified by column chromatography using silica gel (100-200 mesh) and 3-4 % methanol in dichloromethane to afford *tert*-butyl 7-(5-chloro-2-(2-(5-cyano-2-methyl-

6-(4-methylpiperazin-1-yl)-4-oxo-7-(trifluoromethyl)quinazolin-3(4H)-yl)ethoxy)phenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (**10**) as white solid. Yield: 0.08 g, 39 %;MS (ESI) m/z, 751.23 $[M-1]^-$.

[0508] To a solution *tert*-butyl 7-(5-chloro-2-(2-(5-cyano-2-methyl-6-(4-methylpiperazin-1-yl)-4-oxo-7-(trifluoromethyl)quinazolin-3(4H)-yl)ethoxy)phenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylate (**10**, 0.10 g, 0.132 mmol) in dichloromethane (1.5 mL), 2,2,2-trifluoroacetic acid (0.5 mL) was added at 0 °C, and reaction mixture was stirred for 12 h at room temperature. After completion, reaction mixture concentrated under reduced pressure to get the crude compound. The crude compound was purified by preparative HPLC to afford 7-(5-chloro-2-(2-(5-cyano-2-methyl-6-(4-methylpiperazin-1-yl)-4-oxo-7-(trifluoromethyl)quinazolin-3(4H)-yl)ethoxy)phenyl)-5-methylthieno[3,2-b]pyridine-3-carboxylic acid (**634**) as white solid. Yield: 0.020g, 21 %; MS (ESI) m/z 697.13 $[M+1]^+$. ^{1}H-NMR (400 MHz, DMSO-d_6) δ 13.51 (bs, 1H), 9.75 (bs, 1H), 8.23 (s, 1H), 7.92 (s, 1H), 7.61-7.58 (t, *J* = 6.5 Hz, 1H), 7.42-7.41 (t, *J*= 6.5 Hz, 2H), 7.37 (d, *J* = 8.92 Hz, 1H), 4.40 (t, *J* = 6.16 Hz, 2H), 4.24 (t, *J* = 6.12, 2H), 3.83 (m, 2H), 3.49 (m, 2H), 3.24 (m, 2H), 3.03 (m, 2H), 2.28 (s, 3H), 2.71 (s, 3H), 1.82 (s, 3H)

Table 3. Other Compounds

Compound	Characterization	Compound	
1		MS (ESI) m/z 436.26 [M+1]+; UPLC: 99.88 %; 1H NMR (400 MHz, DMSO-d6) δ 12.94 (s, 1H), 8.95 (s, 1H), 8.59 (d, J = 5.2 Hz, 1H), 7.89-7.86 (m, 2H), 7.82 (s, 1H), 7.50 (d, J = 7.6 Hz, 1H), 7.43-7.38 (m, 2H), 7.27 (d, J = 2.6 Hz, 1H), 7.19 (d, J = 8.92 Hz, 1H), 4.34 (s, 4H), 2.23 (s, 3H)	4		MS (ESI) m/z 439.2 [M+1]+; UPLC: 96.95 %; 1H NMR (400 MHz, DMSO-d6) δ 13.07 (bs, 1H), 8.00 (s, 1H), 7.95 (s, 1H), 7.87 (d, J = 7.8 Hz, 1H), 7.80-7.75 (m, 1H), 7.60 (d, J = 7.8 Hz, 1H), 7.45 (s, 1H), 7.43-7.38 (m, 2H), 7.35 (d, J = 2.6 Hz, 1H), 7.29-7.24 (m, 1H), 7.20 (d, J = 8.8 Hz, 1H), 4.29 (dd, J = 14.0, 4.44 Hz, 4H)
2		MS (ESI) m/z 437.16 [M+1]+; UPLC: 97.10 %; 1H NMR (400 MHz, DMSO-d6) δ 12.97 (s, 1H), 7.99 (s, 1H), 7.93 (s, 1H), 7.87 (d, J = 7.7 Hz, 1H), 7.77-7.75 (m, 1H), 7.71-7.68 (m, 2H), 7.57 (d, J = 7.7 Hz, 1H), 7.41-7.38 (m, 2H), 7.34 (d, J = 3.7 Hz, 1H), 7.20 (d, J = 8.8 Hz, 1H), 4.32 (s, 4H)	5		MS (ESI) m/z 421.21 [M+1]+; UPLC: 97.35 %; 1H NMR (400 MHz, DMSO-d6) δ 13.05 (s, 1H), 9.01 (s, 1H), 8.62 (d, J = 5.3 Hz, 1H), 7.97-7.96 (m, 2H), 7.90 (d, J = 7.8 Hz, 1H), 7.60 (d, J = 7.8 Hz, 1H), 7.45-7.39 (m, 2H), 7.34 (d, J = 2.6 Hz, 1H), 7.27 (d, J = 7.4 Hz, 1H), 7.20 (d, J = 8.92 Hz, 1H), 6.50 (d, J = 7.32 Hz, 1H), 4.32-4.30 (m, 4H)
3		MS (ESI) m/z 439.25 [M+1]+; UPLC: 99.82 %; 1H NMR (400 MHz, DMSO-d6) δ 12.85 (bs, 1H), 8.17-8.14 (m, 1H), 8.03 (s, 1H), 7.93 (s, 1H), 7.88 (d, J = 7.8 Hz, 1H), 7.58 (d, J = 7.6 Hz, 1H), 7.42-7.36 (m, 4H), 7.34 (d, J = 2.5 Hz, 1H), 7.20 (d, J = 7.7 Hz, 1H), 4.32-4.30 (m, 4H)	6		MS (ESI) m/z 421.21 [M+1]+; UPLC: 97.08 %; 1H NMR (400 MHz, DMSO-d6) δ 13.04 (s, 1H), 9.31 (s, 1H), 8.69 (d, J = 4.72 Hz, 1H), 7.95 (s, 1H), 7.89 (d, J = 7.56 Hz, 1H), 7.61-7.57 (m, 1H), 7.42-7.38 (m, 2H), 7.34 (s, 1H), 7.20 (d, J = 8.76 Hz, 1H), 6.40 (d, J = 7.2 Hz, 1H), 4.31 (s, 4H)

7		MS (ESI) m/z 421.18 [M+1]+; UPLC: 99.14 %; 1H NMR (400 MHz, DMSO-d6) δ 13.03 (s, 1H), 8.76 (s, 1H), 8.07 (d, J = 8.04 Hz, 1H), 7.98 (s, 1H), 7.91 (d, J = 7.8 Hz, 1H), 7.69-7.66 (m, 1H), 7.62 (d, J = 7.76 Hz, 1H), 7.44 (t, J = 7.72 Hz, 1H), 7.40-7.34 (m, 2H), 7.23-7.19 (m, 2H), 6.37 (d, J = 7.2 Hz, 1H), 4.32 (s, 4H)	
8		MS (ESI) m/z 583.31 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.46 (bs, 1H), 8.84 (d, J = 4.4 Hz, 1H), 8.47 (s, 1H), 7.85 (s, 1H), 7.71-7.22 (m, 6H), 4.39-4.37 (m, 2H), 4.23-4.20 (m, 2H), 1.73 (s, 3H)	
9		MS (ESI) m/z 420.37 [M+1]+; UPLC: 99.10 %; 1H NMR (400 MHz, DMSO-d6) δ 13.07 (s, 1H), 8.18 (d, J = 8.04 Hz, 1H), 8.00 (s, 1H), 7.92 (d, J =7.7 Hz, 1H), 7.68 (t, J = 7.0 Hz, 1H), 7.63-7.58 (m, 2H), 7.50-7.42 (m, 2H), 7.40-7.34 (m, 2H), 7.20 (d, J = 8.7 Hz, 1H), 7.13 (d, J = 7.3 Hz, 1H), 6.37 (d, J = 7.36 Hz, 1H), 4.31-4.27 (m, 4H).	
10			MS (ESI) m/z 421.21 [M+1]+; UPLC: 99.17 %; 1H NMR (400 MHz, DMSO-d6) δ 8.89-8.87 (m, 1H), 8.48 (dd, J = 8.0, 1.5 Hz, 1H), 7.99 (s, 1H), 7.90 (d, J = 7.7 Hz, 1H), 7.55 (d, J = 7.7 Hz, 1H), 7.49-7.33 (m, 5H), 7.19 (d, J = 8.7 Hz, 1H), 6.43 (d, J = 7.56 Hz, 1H), 4.30 (s, 4H)
11			MS (ESI) m/z 421.21 [M+1]+; UPLC: 98.51 %; 1H NMR (400 MHz, DMSO-d6) δ 12.98 (bs, 1H), 8.11 (dd, J = 8.0, 1.2 Hz, 1H), 8.10 (s, 1H), 7.94 (s, 1H), 7.89 (d, J = 7.6 Hz, 1H), 7.83-7.78 (m, 1H), 7.63 (d, J = 8.0 Hz, 1H), 7.54-7.50 (m, 2H), 7.41-7.37 (m, 2H), 7.35 (d, J = 2.6 Hz, 1H), 7.20 (d, J = 8.8 Hz, 1H), 4.32 (s, 4H)
12			MS (ESI) m/z 422.22 [M+1]+; UPLC: 97.46 %; 1H NMR (400 MHz, DMSO-d6) δ 13.02 (bs, 1H), 8.94 (d, J = 2.72 Hz, 1H), 8.49 (dd, J = 7.84, 1.6 Hz, 1H), 8.25 (s, 1H), 7.96 (s, 1H), 7.87 (d, J = 7.68 Hz, 1H), 7.60-7.53 (m, 2H), 7.48-7.34 (m, 3H), 7.20 (d, J = 8.72 Hz, 1H), 4.33 (s, 4H)

13		MS (ESI) m/z 422.18 [M+1]+; UPLC: 98.27 %; 1H NMR (400 MHz, DMSO-d6) δ 12.94 (bs, 1H), 9.26 (s, 1H), 8.82 (d, J = 5.6 Hz, 1H), 8.19 (s, 1H), 7.92 (s, 1H), 7.86 (d, J = 7.7 Hz, 1H), 7.59-7.54 (m, 2H), 7.41-7.37 (m, 2H), 7.33 (d, J = 2.6 Hz, 1H), 7.20 (d, J = 8.8 Hz, 1H), 4.33 (s, 4H)
14		MS (ESI) m/z 422.24 [M+1]+; UPLC: 93.73 %; 1H NMR (400 MHz, DMSO-d6) δ 9.39 (s, 1H), 9.30 (s, 1H), 7.94 (s, 1H), 7.87 (d, J = 7.9 Hz, 1H), 7.66 (d, J = 7.6 Hz, 1H), 7.58 (d, J = 7.4 Hz, 1H), 7.44-7.38 (m, 2H), 7.32 (s, 1H), 7.20 (d, J = 8.8 Hz, 1H), 6.38 (d, J = 7.5 Hz, 1H), 4.32 (s, 4H)
15		MS (ESI) m/z 422.18 [M+1]+; UPLC: 96.38 %; 1H NMR (400 MHz, DMSO-d6) δ 13.03 (bs, 1H), 9.43 (d, J = 5.4 Hz, 1H), 8.19 (d, J = 5.0 Hz, 1H), 7.95 (s, 1H), 7.88 (d, J = 6.6 Hz, 1H), 7.60 (d, J = 7.7 Hz, 1H), 7.50 (d, J = 7.6 Hz, 1H), 7.45-7.33 (m, 3H), 7.20 (d, J = 8.8 Hz, 1H), 6.76 (d, J = 7.4 Hz, 1H), 4.34-4.31 (m, 4H)
16		MS (ESI) m/z 642.21 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.86 (d, J = 4.7 Hz, 1H), 8.11 (s, 1H), 8.07 (s, 1H), 7.63 (dd, J = 8.8, 2.3 Hz, 1H), 7.51 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.5 Hz, 1H), 7.39 (d, J = 9.1 Hz, 1H), 4.67 (bs, 2H), 4.45 (t, J = 5.2 Hz 2H), 4.29 (t, J = 3.9 Hz 2H), 2.93 (s, 6H), 1.78 (s, 3H)
17		MS (ESI) m/z 423.23 [M+1]+; UPLC: 92.07 %; 1H NMR (400 MHz, DMSO-d6) δ 9.43 (s, 1H). 9.39 (s, 1H), 8.58 (s, 1H), 7.86 (s, 1H), 7.85 (d, J = 7.7 Hz, 1H), 7.58 (d, J = 7.7 Hz, 1H), 7.41-7.37 (m, 2H), 7.33 (d, J = 2.6 Hz, 1H), 7.20 (d, J = 8.8 Hz, 1H), 4.31 (s, 4H)
18		MS (ESI) m/z 423.23 [M+1]+; UPLC: 99.81 %; 1H NMR (400 MHz, DMSO-d6) δ 13.07 (bs, 1H), 9.48 (d, J = 5.0 Hz, 1H), 8.33 (s, 1H), 8.23 (d, J =5.1 Hz, 1H), 7.93 (s, 1H), 7.86 (d, J = 7.8 Hz, 1H), 7.62 (d, J = 6.2 Hz, 1H), 7.44-7.34 (m, 3H), 7.20 (d, J = 8.8 Hz, 1H), 4.33 (s, 4H)

19		22	
MS (ESI) m/z 423.23 [M+1]+; UPLC: 96.78 %; 1H NMR (400 MHz, DMSO-d6) δ 8.99 (d, J = 2.0 Hz, 1H), 8.85 (d, J = 2.0 Hz, 1H), 8.32 (s, 1H), 7.95 (s, 1H), 7.86 (d, J = 7.8 Hz, 1H), 7.58 (d, J = 7.7 Hz, 1H), 7.40-7.36 (m, 2H), 7.34 (d, J = 2.7 Hz, 1H), 7.20 (d, J = 8.8 Hz, 1H), 4.36-4.35 (m, 4H)		MS (ESI) m/z 585.30 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.80 (d, J = 4.8 Hz, 1H), 8.44 (s, 1H), 8.04 (d, J = 9.72 Hz, 1H), 7.61-7.59 (dd, J = 2.56 Hz, J = 2.64 Hz, 1H), 7.50-7.36 (m, 4H), 4.42 (t, J = 4.56 Hz, 2H), 4.28 (t, J = 4.64 Hz, 2H), 1.87 (s, 3H)
20		23	
MS (ESI) m/z 422.22 [M+1]+; UPLC: 97.46 %; 1H NMR (400 MHz, DMSO-d6) δ 12.98 (bs, 1H), 8.74 (d, J = 8.0 Hz, 1H), 8.36 (s, 1H), 7.98 (d, J = 8.1 Hz, 1H), 7.94 (s, 1H), 7.84 (d, J = 7.8 Hz, 1H), 7.62 (d, J = 7.7 Hz, 1H), 7.42-7.38 (m, 2H), 7.35 (d, J = 2.6 Hz, 1H), 7.20 (d, J = 8.8 Hz, 1H), 4.35 (s, 4H)		MS (ESI) m/z 438.28 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.10 (s, 1H), 8.53 (s, 1H), 8.29 (s, 1H), 7.93 (s, 1H), 7.89 (d, J = 7.6 Hz , 1H), 7.83 (dd, J = 2.12, 8.44 Hz, 1H), 7.77 (d, J = 1.96 Hz, 1H), 7.56 (d, J = 7.72 Hz, 1H), 7.43 (t, J = 15.5 Hz, 1H), 7.33 (d, J = 8.64 Hz, 1H), 4.44 (d, J = 4.84 Hz, 2H), 4.40 (d, J = 4.68 Hz, 2H)
21		24	
MS (ESI) m/z 422.18 [M+1]+; UPLC: 98.77 %; 1H NMR (400 MHz, DMSO-d6) δ 12.96 (bs, 1H), 8.79 (dd, J = 4.1, 1.1 Hz, 1H), 8.06-8.04 (m, 2H), 7.93 (s, 1H), 7.88 (d, J = 7.7 Hz, 1H), 7.81-7.78 (m, 1H), 7.60-7.58 (m, 1H), 7.42-7.38 (m, 2H), 7.34 (d, J = 2.6 Hz, 1H), 7.21 (d, J = 8.8 Hz, 1H), 4.34 (s, 4H)		MS (ESI) m/z 485.37 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.74 (s, 1H), 9.11 (s, 1H), 8.56 (s, 1H), 8.01 (s, 1H), 7.74-7.77 (m, 1H), 7.32-7.40 (m, 3H), 7.13-7.16 (m, 2H), 4.29 (s, 4H), 1.55 (s, 3H)

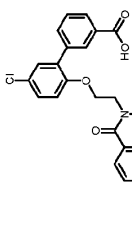
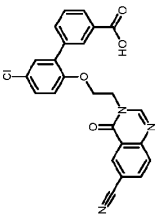
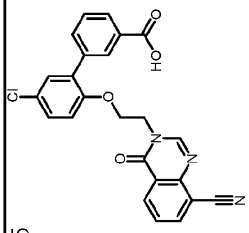
25		28	
MS (ESI) m/z 457.23 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.05 (s, 1H), 9.19 (s, 1H), 8.86 (s, 1H), 8.62 (s, 1H), 8.34 (s, 1H), 7.99-8.07 (m, 2H), 7.72 (s, 1H), 7.58-7.63 (m, 2H), 7.04 (s, 1H), 5.48 (s, 2H)		MS (ESI) m/z 496.36 [M+1]+ UPLC: 99.32 %; 1H NMR (400 MHz, DMSO-d6) δ 12.97 (s, 1H), 8.17-8.15 (m, 2H), 8.04 (d, J=8.56 Hz, 1H), 7.90-7.89 (m, 1H), 7.84-7.82 (m, 1H), 7.61-7.58 (m, 1H), 7.52-7.25 (m, 4H), 7.21 (d, J=8.88 Hz, 1H), 4.35 (s, 4H)	
26		29	
MS (ESI) m/z 530.0 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.01 (s, 1H), 8.88 (s, 1H), 8.02 (s, 1H), 7.58-7.90 (m, 2H), 7.64 (s, 2H), 7.54 (s, 4H), 7.30-7.36 (m, 4H), 7.16 (s, 1H), 4.26 (s, 4H)		MS (ESI) m/z 448.31 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.09 (s, 1H), 8.63(d, J = 4.47Hz, 1H), 8.53 (s, 1H), 8.31 (s, 1H), 7.99 (s, 1H), 7.63 (d, J = 3.64 Hz, 1H), 7.49-7.45 (m, 2H), 7.25 (d, J = 8.68 Hz, 1H), 4.38 (m, 4H)	
27		30	
MS (ESI) m/z 471.32 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.06 (s, 1H), 8.38 (s, 1H), 8.20 (s, 1H), 8.039 (d, J =8.56 1H), 7.87-7.86 (m, 1H), 7.82-7.81 (m, 1H), 7.62-7.58 (m, 1H), 7.43 - 7.39 (m, 2H), 7.33 (d, J = 2.64 Hz, 1H), 7.21 (d, J = 8.84 Hz, 1H), 4.35 (s, 4H)		MS (ESI) m/z 504.39 [M+1]+. UPLC: 99.59 %; 1H NMR (400 MHz, DMSO-d6) δ 8.96 (s, 1H), 8.81(d, J = 4.88 Hz, 1H), 8.55 (s, 1H), 8.45 (s, 1H), 7.91 (s, 1H), 7.61-7.59 (dd, J = 2.60, 8.88 Hz, 1H), 7.49-7.46 (m, 2H), 7.35 (d, J = 8.96 Hz, 1H), 4.40-4.38 (t, J = 5.00 Hz, 2H), 4.25-4.23 (t, J = 4.84 Hz, 2H)	

31		MS (ESI) m/z 457.36 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.92 (s, 1H), 8.92 (s, 1H), 8.42 (s, 1H), 7.86 (s, 1H), 7.81 (d, J = 11.08 Hz, 1H), 7.57 (d, J = 7.8 Hz, 1H), 7.42-7.37 (m, 2H), 7.30 (d, J = 2.72 Hz, 1H), 7.21 (d, J = 8.88 Hz, 1H), 4.61 (t, J = 5.12 Hz, 2H), 4.42 (t, J = 10.08 Hz, 2H), 2.11-2.05 (m, 1H), 1.03-0.99 (m, 2H), 0.77-0.72 (m, 2H).	37		MS (ESI) m/z 510.40 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.95 (s, 1H), 8.13 (d, J = 8.0 Hz, 1H), 8.06 (d, J = 7.6 Hz, 1H), 7.83-7.84 (m, 2H), 7.36-7.72 (m, 4H), 7.27-7.28 (m, 1H), 7.21 (d, J = 8.8 Hz, 1H), 4.35 (s, 4H), 2.22 (s, 3H)
32		MS (ESI) m/z 515.33 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.03 (s, 1H), 9.13 (s, 1H), 8.32 (s, 1H), 8.23 (s, 1H), 7.92 (s, 1H), 7.86 (t, J = 5.76 Hz, 2H), 7.61 (d, J = 7.72 Hz, 1H), 7.43-7.39 (m, 2H), 7.34 (d, J = 2.44 Hz, 1H), 7.2 (d, J = 8.84 Hz, 1H), 4.35 (m, 4H), 2.59 (s, 3H)	40		MS (ESI) m/z 603.21 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.84 (d, J = 4.8 Hz, 1H), 8.38 (bs, 1H), 8.28 (s, 1H), 8.01 (bs, 1H), 7.63 (d, J = 8.4 Hz, 1H), 7.54 (d, J = 11.4 Hz, 1H), 7.49 (d, J = 4.8 Hz, 1H), 4.43 (t, J = 4.4 Hz, 2H), 4.25 (t, J = 4.4 Hz, 2H), 1.73 (s, 3H)
33		MS (ESI) m/z 511.34 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.66 (s, 1H), 7.84 (d, J = 7.6 Hz, 2H), 7.74-7.47 (t, J = 5.6 Hz, 1H), 7.43-7.36 (m, 3H), 7.25 (d, J = 2.4 Hz, 1H), 7.17 (d, J = 8.8 Hz, 1H), 4.37 (d, J = 4.4 Hz ,2H), 4.33 (d, J = 3.6 Hz, 2H), 2.89 (s, 3H)	41		MS (ESI) m/z 441.24 [M-1]-; 1H NMR (400 MHz, DMSO-d6) δ 13.06 (s, 1H), 9.1 (s, 1H), 8.6 (s, 1H), 8.57 (s, 1H), 7.84 (d, J = 5.6 Hz , 1H), 7.75 (s, 1H), 7.69 (d, J = 8.3 Hz, 1H), 7.50 -7.44 (m, 3H), 7.36 (d, J = 1.76 Hz, 1H), 6.46 -6.39 (m, 1H), 6.27 (d, J = 16.09 Hz, 1H), 4.73 (d, J = 5.12 Hz, 2H)

42		MS (ESI) m/z 445.39 [M+1]+ UPLC: 99.76 %; 1H NMR (400 MHz, DMSO-d6) δ 13.01 (s, 1H), 9.12(s, 1H), 8.51 (s, 1H), 8.47 (s, 1H), 7.69 (s, 1H), 7.64-7.62 (m, 1H), 7.48 (d, J=7.72 Hz, 1H), 7.41-7.34 (m, 3H), 7.19 (s, 1H), 3.90-3.87 (m, 2H), 2.55-2.50 (m, 2H), 1.80-1.74 (m, 2H)	47		MS (ESI) m/z 558.95 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.36 (s, 1H), 8.85 (d, J = 4.68 Hz, 1H), 8.57 (d, J = 1.16 Hz, 1H), 8.23 (d, J = 1.23 Hz, 1H), 8.17 (s, 1H), 7.61-7.58 (dd, J = 2.72 Hz, J = 2.68 Hz, 1H), 7.49 (d, J = 4.72 Hz, 1H), 7.40 (d, J = 2.72 Hz, 1H), 7.36 (d, J = 8.96 Hz, 1H), 4.40 (t, J = 4.40 Hz, J = 4.76 Hz, 2H), 4.18 (t, J = 4.44 Hz, J = 4.28 Hz, 2H), 1.48 (d, J = 3.52 Hz, 3H)
43		MS (ESI) m/z 457.36 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.08 (b, 1H), 9.14(s, 1H), 8.56 (d, J = 4.52 Hz, 2H), 7.92 (d, J = 7.44 Hz, 1H), 7.88 (s, 1H), 7.62-7.54 (m, 2H), 7.34 (dd, J = 8.44 Hz, 1H), 7.23 (d, J = 2.2 Hz, 1H), 7.03 (d, J = 8.48 Hz, 1H), 4.02-3.97 (m, 1H), 3.79-3.74 (m, 1H), 1.94 (q, J = 6.68 Hz, 1H), 1.61 (q, J = 6.76 Hz, 1H), 1.07 (t, J = 7.04 Hz, 2H)	52		MS (ESI) m/z 454.33 [M+1]+. 1H NMR (400 MHz, DMSO-d6) δ 9.12 (s, 1H), 8.69 (s, 1H), 8.56 (s, 1H), 8.20 (d, J = 2.64 Hz, 1H), 8.06 (s, 1H), 7.51 (dd, J = 8.88 Hz, 1H), 7.37 (d, J = 9 Hz, 1H), 4.68 (t, J = 5.52 Hz, 2H), 4.54 (t, J = 5.48 Hz, 2H)
46		MS (ESI) m/z 638.09 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.16 (s, 1H), 8.82 (d, J = 4.84 Hz, 1H), 8.57 (s, 1H), 8.21 (s, 1H), 8.13 (s, 1H), 7.62-7.59 (dd, J = 2.48 Hz, J = 2.44 Hz, 1H), 7.53 (d, J = 4.8 Hz, 1H), 7.40-7.30 (m, 2H), 4.51-4.46 (m, 4H)	53		MS (ESI) m/z 453.31 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.99 (b, 1H), 9.09(s, 1H), 8.60 (s, 1H), 8.53 (s, 1H), 7.83 (d, J = 2.52 Hz, 1H), 7.62 (d, J = 4.04 Hz, 1H), 7.55 (d, J = 4 Hz, 1H), 7.42-7.40 (m, 1H), 7.31 (d, J = 8.96 Hz, 1H), 4.61 (t, J = 5.36 Hz, 2H), 4.58 (t, J = 5.28 Hz, 2H)

54		MS (ESI) m/z 454.36 [M+1]+. 1H NMR (400 MHz, DMSO-d6) δ 9.13 (s, 1H), 8.63 (s, 1H), 8.57 (s, 1H), 8.25 (bs, 1H), 7.79 (s, 1H), 7.38 (dd, J = 8.72 Hz, 1H), 7.24 (d, J = 8.8 Hz, 1H), 4.50 (t, J = 2.96 Hz, 4H).	
55		MS (ESI) m/z 534.37 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.94 (s, 1H), 8.11 (d, J = 8.56 Hz, 1H), 7.96 (d, J = 8.52 Hz, 1H), 7.82 (d, J = 7.68 Hz, 1H), 7.48-7.21 (m, 4H), 7.15 (d, J = 9.48 Hz, 2H), 4.30 (s, 4H), 3.75 (s, 1H), 1.98 (s, 3H)	
56		MS (ESI) m/z 510.73 [M+1]+; UPLC: 99.83 %; 1H NMR (400 MHz, DMSO-d6) δ 12.91 (s, 1H), 8.61(d, J = 4.56 Hz, 1H), 8.14 (d, J = 8.60 Hz, 1H), 7.98 (d, J = 8.44 Hz, 2H), 7.59-7.58 (m, 1H), 7.51-7.23 (m, 4H), 4.39 (s, 4H), 2.22 (s, 3H)	
57		MS (ESI) m/z 535.17 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.41 (s, 1H), 8.13(d, J = 8.72 Hz, 1H), 7.99 (d, J = 8.6 Hz, 1H), 7.49-7.19 (m, 5H), 4.32 (s, 4H), 4.06 (s, 1H), 2.08 (s, 3H)	
62		MS (ESI) m/z 508.04 [M-1]- UPLC: 98.04 %; 1H NMR (400 MHz, DMSO-d6) δ 12.92 (s, 1H), 8.13(d, J = 8.64 Hz, 1H), 7.97 (d, J = 8.56 Hz, 1H), 7.86 (d, J = 7.84 Hz, 1H), 7.83 (s, 1H), 7.53-7.20 (m, 6H), 4.35 (s, 4H), 2.20 (s, 3H)	
63		MS (ESI) m/z 535.26 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.57 (s, 1H), 7.84-7.79 (m, 2H), 7.61-7.36 (m, 4H), 7.24 (s, 1H), 7.18 (d, J = 8.88 Hz, 1H), 4.34 (s, 4H), 2.17 (s, 3H)	

64		MS (ESI) m/z 560.18 [M+1]+. 1H NMR (400 MHz, DMSO-d6) δ 12.93 (bs, 1H), 8.12 (s, 1H), 7.85-7.83(m, 2H), 7.63-7.19 (m, 7H), 4.35 (s, 4H), 2.21 (s, 3H)	
66		MS (ESI) m/z 445.13 [M-1]-; UPLC: 93.91 %; 1H NMR (400 MHz, DMSO-d6) δ 12.94 (s, 1H), 9.09 (s, 1H), 8.52 (s, 1H), 8.26 (s, 1H), 7.85-7.83 (m, 2H), 7.58 (d, J = 7.84 Hz, 1H), 7.44-7.39 (m, 2H), 7.32 (d, J = 2.60 Hz, 1H), 7.20 (d, J = 8.88 Hz, 1H) 4.35 (s, 4H)	
67		MS (ESI) m/z 423.16 [M+1]+; UPLC: 97.88 %; 1H NMR (400 MHz, DMSO-d6) δ 12.98 (bs, 1H), 8.02 (s, 1H), 7.92-7.91 (m, 3H), 7.56-7.55 (m, 1H), 7.44 (t, J = 8.0 Hz, 1H), 7.39 (dd, J = 8.8, 2.8 Hz, 1H), 7.33 (d, J = 2.4 Hz, 1H), 7.2 (d, J = 8.8 Hz, 1H), 4.32-4.29 (m, 4H), 3.69 (s, 3H)	
68		MS (ESI) m/z 424.24 [M+1]+; UPLC: 97.94 %; 1H NMR (400 MHz, DMSO-d6) δ 12.98 (bs, 1H), 7.95-7.91 (m, 2H), 7.78 (s, 1H), 7.58-7.55 (m, 1H), 7.44 (t, J = 7.6 Hz, 1H), 7.38 (dd, J = 8.8, 2.4 Hz, 1H), 7.34 (d, J = 2.4 Hz, 1H), 7.19 (d, J = 8.8 Hz, 1H), 7.09 (d, J = 3.2 Hz, 1H), 6.43 (d, J = 3.2 Hz, 1H), 4.27 (s, 4H), 3.66 (s, 3H)	
69		MS (ESI) m/z 424.27 [M+1]+; UPLC: 98.50 %; 1H NMR (400 MHz, DMSO-d6) δ 8.00 (s, 1H), 7.89 (d, J = 7.6 Hz, 1H), 7.78 (s, 1H), 7.51 (d, J = 7.6 Hz, 1H), 7.42-7.34 (m, 4H), 7.18 (d, J = 8.8 Hz, 1H), 6.28 (d, J = 2.8 Hz, 1H), 4.28 (s, 4H), 3.97 (s, 3H)	
70		MS (ESI) m/z 450.27 [M+1]+; UPLC: 96.87 %; 1H NMR (400 MHz, DMSO-d6) δ 12.98 (bs, 1H), 8.97 (s, 1H), 8.60 (d, J = 5.2 Hz, 1H), 7.89-7.87 (m, 3H), 7.54-7.52 (m, 1H), 7.43-7.37 (m, 2H), 7.28 (d, J = 2.8 Hz, 1H), 7.18 (d, J = 8.8 Hz, 1H), 4.37-4.24 (m, 4H), 2.60-2.49 (m, 2H), 0.97 (t, J = 7.2 Hz, 3H)	

71		MS (ESI) m/z 450.27 [M+1]+; UPLC: 96.87 %; 1H NMR (400 MHz, DMSO-d6) δ 12.98 (bs, 1H), 8.97 (s, 1H), 8.60 (d, J = 5.2 Hz, 1H), 7.89-7.87 (m, 3H), 7.54-7.52 (m, 1H), 7.43-7.37 (m, 2H), 7.28 (d, J = 2.8 Hz, 1H), 7.18 (d, J = 8.8 Hz, 1H), 4.37-4.24 (m, 4H), 2.60-2.49 (m, 2H), 0.97 (t, J = 7.2 Hz, 3H)	74		MS (ESI) m/z 446.22 [M+1]+; UPLC: 97.68 %; 1H NMR (400 MHz, DMSO-d6) δ 12.95 (bs, 1H), 8.21 (d, J = 8.2 Hz, 1H), 8.15 (s, 1H), 8.09 (s, 1H), 7.89-7.84 (m, 3H), 7.57 (d, J = 7.7 Hz, 1H), 7.41-7.38 (m, 2H), 7.33 (d, J = 2.5 Hz, 1H), 7.20 (d, J = 8.8 Hz, 1H), 4.39-4.32 (m, 4H)
72		MS (ESI) m/z 435.22 [M+1]+; UPLC: 95.85 %; 1H NMR (400 MHz, DMSO-d6) δ 12.98 (bs, 1H), 8.05 (d, J = 8.0 Hz, 1H), 7.91-7.89 (m, 2H), 7.78 (t, J = 7.2 Hz, 1H), 7.56 (d, J = 8.0 Hz, 1H), 7.52-7.37 (m, 4H), 7.29 (d, J = 2.4 Hz, 1H), 7.19 (d, J = 8.8 Hz, 1H), 4.33 (s, 4H), 2.22 (s, 3H)	75		MS (ESI) m/z 446.25 [M+1]+; UPLC: 97.45 %; 1H NMR (400 MHz, DMSO-d6) δ 12.96 (s, 1H), 8.36-8.31 (m, 2H), 8.24 (s, 1H), 7.90 (s, 1H), 7.83 (d, J = 7.8 Hz, 1H), 7.65 (t, J = 7.8 Hz, 1H), 7.55 (d, J = 7.8 Hz, 1H), 7.41-7.33 (m, 3H), 7.21 (d, J = 8.8 Hz, 1H), 4.34 (s, 4H)
73		LCMS Purity: 96.35 %, MS: m/z 444.18 [M-1]-; 1H NMR (DMSO-d6, 400 mHz) δ 12.96 (bs, 1H), 8.09 (s, 1H), 8.02 (m, 1H), 7.92 (m, 3H), 7.85 (d, J = 7.8 Hz, 1H), 7.60 (d, J = 7.8 Hz, 1H), 7.41-7.39 (m, 2H), 7.33 (d, J = 2.7 Hz, 1H), 7.21 (d, J = 8.8 Hz, 1H), 4.33 (m, 4H)	76		MS (ESI) m/z 439.21 [M+1]+; UPLC: 99.71 %; 1H NMR (400 MHz, DMSO-d6) δ 8.08 (s, 1H), 7.94-7.85 (m, 3H), 7.70-7.68 (m, 1H), 7.58 (d, J = 7.86 Hz, 1H), 7.53-7.48 (m, 1H), 7.40-7.29 (m, 3H), 7.20 (d, J = 8.8 Hz, 1H), 4.33 (s, 4H)

77	MS (ESI) m/z 457.25 [M+1]+; UPLC: 95.49 %; 1H NMR (400 MHz, DMSO-d6) δ 12.95 (bs, 1H), 8.07-7.96 (m, 2H), 7.89-7.85 (m, 2H), 7.72-7.67 (m, 1H), 7.57 (d, J = 7.8 Hz, 1H), 7.43-7.38 (m, 2H), 7.32 (d, J = 2.6 Hz, 1H), 7.20 (d, J = 8.8 Hz, 1H), 4.33-4.30 (m, 4H)	80	MS (ESI) m/z 453.20 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.13 (s, 1H), 8.56 (s, 2H), 7.87 (s, 1H), 7.72 (s, 1H), 7.51 (d, J = 2.56 Hz, 1H), 7.31 (dd, J = 8.8 Hz, 2.56 Hz, 1H), 7.15 (d, J = 8.92 Hz, 1H), 4.45 (t, J = 4.76 Hz, 2H), 4.41 (t, J = 4.72 Hz, 2H)
78	MS (ESI) m/z 457.21 [M+1]+; UPLC: 95.45 %; 1H NMR (400 MHz, DMSO-d6) δ 12.96 (bs, 1H), 8.01 (s, 1H), 7.92 (s, 1H), 7.87 (d, J = 7.8 Hz, 1H), 7.60 (d, J = 7.8 Hz, 1H), 7.44-7.33 (m, 4H), 7.28-7.25 (m, 1H), 7.20 (d, J = 9.6 Hz, 1H), 4.31-4.25 (m, 4H)	81	MS (ESI) m/z 454.29 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.17 (bs, 1H), 9.14 (s, 1H), 8.75 (s, 1H), 8.59 (s, 1H), 8.20 (bs, 2H), 7.51 (d, J = 8.00 Hz, 1H), 7.35 (d, J = 8.96 Hz, 1H), 4.66 (bs, 2H), 4.55 (bs, 2H)
79	MS (ESI) m/z 437.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.13 (s, 1H), 8.74 (s, 1H), 8.60 (s, 1H), 7.69 (d, J = 2.6 Hz, 1H), 7.40 (dd, J = 8.84 Hz, 2.64 Hz, 1H), 7.24 (d, J = 8.96 Hz, 1H), 7.15 (bs, 1H), 7.03(d, J = 3.32 Hz, 1H), 4.53 (s, 4H)	82	MS (ESI) m/z 450.29 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.23 (bs, 1H), 9.13 (s, 1H), 8.67 (s, 1H), 8.57 (s, 1H), 7.49 (d, J = 2.44 Hz, 1H), 7.41 (bs, 1H), 7.17-7.14 (m, 1H), 7.09 (d, J = 8.2 Hz, 1H), 7.04 (bs, 1H), 4.49 (t, J = 4.32 Hz, 2H), 4.46 (t, J = 4.56 Hz, 2H), 3.84 (s, 3H)

83		MS (ESI) m/z 453.31 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.74 (s, 1H), 9.12 (s, 1H), 8.63 (s, 1H), 8.56 (s, 1H), 8.09 (bs, 1H), 7.77 (d, J = 2.68 Hz, 2H), 7.36 (dd, J = 8.8 Hz, 2.4 Hz, 1H), 7.25 (d, J = 8.8 Hz, 1H), 4.55 (t, J = 4.8 Hz, 2H), 4.48 (t, J = 5.2 Hz, 2H)
84		MS (ESI) m/z 451.30 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.60 (bs, 1H), 9.09 (s, 1H), 8.52 (s, 1H), 8.25 (s, 1H), 7.52 (dd, J = 8.76 Hz, 2.6 Hz, 1H), 7.34 (d, J = 2.64 Hz, 1H), 7.24 (d, J = 8.92 Hz, 1H), 6.52 (s, 1H), 4.36 (s, 4H), 3.56 (s, 3H)
85		MS (ESI) m/z 449.36 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.09 (s, 1H), 8.98 (bs, 2H), 8.54 (s, 1H), 8.43 (bs, 1H), 7.67 (bs, 1H), 7.51 (d, J = 8.8 Hz, 1H), 7.26 (d, J = 7.84 Hz, 1H), 4.44 (s, 4H)
86		MS (ESI) m/z 483.24 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.27 (s, 1H), 9.10 (s, 1H), 8.52 (s, 1H), 8.22 (s, 1H), 7.64 (t, J = 8.32 Hz, 1H),7.46 (dd, J = 8.8 Hz, 2.56 Hz, 1H), 7.31 (d, J = 2.52 Hz, 1H), 7.21-7.18 (m, 2H), 4.32(s, 4H)
87		MS (ESI) m/z 478.30 [M+1]+;1H NMR (400 MHz, DMSO-d6) δ 9.08 (s, 1H), 9.08 (s, 1H), 8.51 (s, 1H), 8.37 (s, 1H), 7.57 (s, 1H), 7.45 (dd, J = 8.76 Hz, 2.6 Hz, 1H), 7.38 (d, J = 2.72 Hz, 1H), 7.23 (d, J = 8.88 Hz, 1H), 6.87 (bs, 1H), 4.38 (bs, 4H), 3.88 (s, 3H)
88		MS (ESI) m/z 478.30 [M+1]+; 1H NMR (400 mHz, DMSO-d6) δ 13.10 (s, 1H), 9.06 (s, 1H), 8.57 (s, 1H), 8.53 (s, 1H), 8.47 (s, 1H), 8.11-8.08 (m, 1H), 7.73 (d, J = 2.68 Hz, 1H), 7.37 (dd, J = 8.76 Hz, 2.68Hz, 1H), 7.21 (d, J = 8.88 Hz, 1H), 4.44 (s, 4H), 2.95 (d, J = 4.24 Hz, 3H)

89		MS (ESI) m/z 483.24 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.31 (s, 1H), 9.08 (s, 1H), 8.51 (s, 1H), 8.22 (s, 1H), 7.81-7.77 (m, 1H), 7.51-7.48 (m, 2H), 7.35 (d, J = 2.6 Hz, 1H), 7.23 (d, J = 8.92 Hz, 1H), 4.36-4.33 (m, 4H)	
90		MS (ESI) m/z 479.35 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.12 (s, 1H), 8.58 (s, 1H), 8.56 (s, 1H), 8.41 (bs, 1H), 7.63 (bs, 1H), 7.41 (dd, J = 8.8 Hz, 2.4 Hz, 1H), 7.21 (d, J = 9.2 Hz, 1H), 4.47-4.43 (m, 4H), 3.90 (s, 3H)	
91		MS (ESI) m/z 483.22 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.83 (bs, 1H), 9.11(s, 1H), 8.54 (s, 1H), 8.23 (s, 1H), 7.46-7.43 (m, 1H), 7.35 (bs, 1H), 7.28 (d, J = 2.56 Hz, 1H), 7.20 (d, J = 8.96 Hz, 1H), 7.07 (t, J = 9.12 Hz, 1H), 4.32 (s, 4H)	
92		MS (ESI) m/z 487.31 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.41 (bs, 1H), 9.07 (s, 1H), 8.47 (s, 1H), 7.96 (s, 1H), 7.65 (dd, J = 8.12 Hz, 1.72 Hz, 1H), 7.43-7.40 (m, 2H), 7.19-7.17 (m, 2H), 6.79 (d, J = 8.2 Hz, 1H), 4.26 (s, 4H), 1.44-1.38 (m, 1H), 0.70-0.47 (m, 4H)	
93		MS (ESI) m/z 472.23 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.50 (bs, 1H), 9.05 (s, 1H), 8.49 (s, 1H), 8.20 (s, 1H), 8.16 (s, 1H), 8.07 (t, J = 1.48 Hz, 1H), 8.01 (t, J = 1.48 Hz, 1H), 7.45 (dd, J = 8.8 Hz, 2.68 Hz, 1H), 7.41 (d, J = 2.6 Hz, 1H), 7.24 (d, J = 8.8 Hz, 1H), 4.38-4.33 (m, 4H)	
94		MS (ESI) m/z 472.37 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.87 (bs, 1H), 9.10 (s, 1H), 8.54 (s, 1H), 8.31 (bs, 1H), 7.98 (bs, 1H), 7.72 (bs, 1H), 7.62 (bs, 1H), 7.45 (dd, J = 8.4, 2.0 Hz, 1H), 7.39 (d, J = 2.4 Hz, 1H), 7.22 (d, J = 8.8 Hz, 1H), 4.35 (s, 4H)	

95		MS (ESI) m/z 493.24 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.04 (bs, 1H), 9.04 (s, 1H), 8.47 (s, 1H), 8.24 (s, 1H), 7.56 (bs, 2H), 7.41 (dd, J = 8.8 Hz, 2.52 Hz, 1H), 7.34-7.32 (m, 2H), 7.22 (d, J = 8.84 Hz, 1H), 4.37-4.33 (m, 4H), 2.45 (s, 3H)	
96		MS (ESI) m/z 491.20 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.97 b(s, 1H), 9.09 (s, 1H), 8.52 (s, 1H), 8.31 (s, 1H), 7.36 (dd, J = 8.72, 2.56 Hz, 1H), 7.24 (d, J = 2.64 Hz, 1H), 7.17 (d, J = 8.88 Hz, 1H), 7.13 (d, J = 1.64 Hz, 1H), 7.01 (d, J = 1.64 Hz, 1H), 6.16 (s, 2H), 4.35 (s, 4H)	
97		MS (ESI) m/z 495.31 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.08 (s, 1H), 8.50 (s, 1H), 8.13 (s, 1H), 7.41-7.35 (m, 2H), 7.14-7.12 (m, 2H), 6.78 (d, J = 12.88 Hz, 1H), 4.27 (t, J = 4.2 Hz, 2H), 4.25 (t, J = 4.08 Hz, 2H), 3.62 (s, 3H)	
98		MS (ESI) m/z 495.31 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.56 (bs, 1H), 9.07 (d, J = 0.68 Hz, 1H), 8.91 (s, 1H), 8.53 (s, 1H), 8.48 (s, 1H), 7.74 (d, J = 2.8 Hz, 1H), 7.49 (dd, J = 8.92 Hz, 2.72 Hz, 1H), 7.28 (d, J = 9.0 Hz, 1H), 4.48-4.44 (m, 4H), 2.41 (s, 3H)	
99		MS (ESI) m/z 498.33 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.78 (bs, 1H), 8.83 (s, 1H), 8.73 (d, J = 7.84 Hz, 1H), 8.33 (s, 2H), 8.19 (s, 1H), 8.07 (d, J = 7.8 Hz, 1H), 7.85-7.81 (m, 1H), 7.76-7.72 (m, 2H), 7.52 (dd, J = 8.76, 2.64 Hz, 1H), 7.32 (d, J = 8.92 Hz, 1H), 4.49 (t, J = 4.92 Hz, 2H), 4.37 (t, J = 4.88 Hz, 2H)	
100		MS (ESI) m/z 498.33 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.15 (d, J = 3.12 Hz, 1H), 8.78 (s, 1H), 8.65 (d, J = 7.24 Hz, 1H), 8.47 (d, J = 1.76 Hz, 1H), 8.30 (bs, 2H), 8.15 (s, 1H), 7.89-7.86 (m, 1H), 7.52-7.49 (m, 2H), 7.30 (d, J = 8.8 Hz, 1H), 4.42 (t, J = 4.88 Hz, 2H), 4.32 (t, J = 4.72 Hz, 2H).	

101		MS (ESI) *m/z* 501.29 $[M+1]^+$; ^{1}H NMR (400 mHz, DMSO-*d*6) δ 9.11 (s, 1H), 8.53 (s, 1H), 8.34 (s, 1H), 7.46 (dd, *J* = 8.88, 2.6 Hz, 1H), 7.36 (t, *J* = 6.8 Hz, 1H), 7.27 (d, *J* = 2.68 Hz, 1H), 7.20 (d, *J* = 8.92 Hz, 2H), 4.34 (s, 4H)	
102		MS (ESI) m/z 501.29 $[M+1]^+$; 1H NMR (400 mHz, DMSO-d6) δ 12.88 (s, 1H), 8.87 (s, 1H), 8.50 (s, 1H), 8.31 (s, 1H), 8.21 (s, 1H), 7.69 (s, 1H), 7.64 (s, 1H), 7.43-7.40 (m, 1H), 7.34 (d, J = 2.16 Hz, 1H), 7.25 (d, J = 8.76 Hz, 1H), 4.40 (t, J = 4.68 Hz, 2H), 4.31 (t, J = 4.52 Hz, 2H), 4.23 (s, 3H)	
103		MS (ESI) m/z 504.35 $[M+1]^+$; 1H NMR (400 MHz, DMSO-d6) δ 13.58 (s, 1H), 11.07 (s, 1H), 9.03 (d, J = 0.68 Hz, 1H), 8.44 (s, 1H), 8.36 (d, J = 8.68 Hz, 1H), 8.32 (s, 1H), 7.84 (d, J = 2.2 Hz, 1H), 7.50 (dd, J = 8.64, 2.12 Hz, 1H), 7.38 (dd, J = 8.88, 2.72 Hz, 1H), 7.27 (d, J = 2.6 Hz, 1H), 7.20 (d, J = 8.84 Hz, 1H), 4.35 (s, 4H), 2.19 (s, 3H)	
104		MS (ESI) m/z 489.37 $[M+1]^+$; 1H NMR (400 MHz, DMSO-d6) δ 12.61 (bs, 1H), 9.09 (s, 1H), 8.52 (s, 1H), 8.37 (s, 1H), 7.48 (bs, 1H), 7.37 (bs, 1H), 7.33 (dd, J = 8.80, 2.60 Hz, 1H), 7.23 (d, J = 2.60 Hz, 1H), 7.15 (d, J = 8.80 Hz, 1H), 4.66 (t, J = 8.72 Hz, 2H), 4.35 (bs, 4H), 3.22 (t, J = 8.68 Hz, 2H)	
105		MS (ESI) m/z 503.38 $[M+1]^+$; 1H NMR (400 mHz, DMSO-d6) δ 9.03 (s, 1H), 8.49 (s, 1H), 8.26 (bs, 1H), 7.85 (s, 1H), 7.74 (bs, 1H), 7.53 (s, 1H), 7.38 (d, J = 8.6 Hz, 1H), 7.31 (d, J = 2.4 Hz, 1H), 7.19 (d, J = 9.16 Hz, 1H), 4.33 (s, 4H), 1.27 (s, 9H)	
106		MS (ESI) m/z 491.31 $[M+1]^+$; 1H NMR (400 MHz, DMSO-d6) δ 9.06 (s, 1H), 8.51 (s, 1H), 8.30 (s, 1H), 7.73 (bs, 1H), 7.68 (bs, 1H), 7.39-7.36 (m, 2H), 7.29 (d, J = 2.6 Hz, 1H), 7.18 (d, J = 8.88 Hz, 1H), 4.64 (t, J = 5.12 Hz, 1H), 4.34 (s, 4H), 3.62 (t, J = 5.92 Hz, 2H), 2.76 (t, J = 6.64 Hz, 2H)	

107		MS (ESI) m/z 507.29 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.79 (s, 1H), 9.05 (s, 1H), 8.50 (s, 1H), 8.28 (s, 1H), 7.38-7.35 (m, 1H),7.31 (d, J = 2.6 Hz, 1H), 7.18-7.16 (m, 2H), 7.10 (d, J = 1.8 Hz, 1H), 4.34 (bs, 4H), 3.80 (s, 3H)), 3.76 (s , 3H)	110		MS (ESI) m/z 514.40 [M+1]+; 1H NMR (400 MHz, DMSO-d6) 13.11 (bs, 1H), 9.03 (s, 1H), 8.48 (s, 1H), 8.17 (s, 1H), 7.97 (t, J = 1.68 Hz, 1H), 7.82 (t, J = 1.36 Hz, 1H), 7.71 (t, J = 1.60 Hz, 2H), 7.43 (dd, J = 8.88, 2.76 Hz, 1H), 7.23 (d, J = 8.92 Hz, 1H), 4.36-4.32 (m, 4H), 1.72 (s, 6H)
108		MS (ESI) m/z 511.18 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.06 (s, 1H), 8.52(s, 1H), 8.36 (s, 1H), 7.57 (d, J = 2.12 Hz, 1H), 7.54 (bs, 1H), 7.38 (dd J = 8.88 Hz, 2.72 Hz, 1H), 7.33 (d, J = 2.60 Hz, 2H), 7.18(d, J = 8.8 Hz, 1H), 4.36 (s, 4H), 3.89 (s, 3H)	111		MS (ESI) m/z 513.32 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.20 (bs, 1H), 9.08 (d, J = 0.6 Hz, 1H), 8.54 (d, J = 0.64 Hz, 1H), 8.30 (s, 1H), 7.78 (d, J = 2.24 Hz, 1H), 7.59 (dd, J = 8.44, 2.28 Hz, 1H), 7.41-7.38 (m, 1H), 7.34 (d, J = 2.6 Hz, 1H), 7.21-7.19 (m, 2H), 7.18 (t, J = 67.48 Hz, 1H), 4.35 (s, 4H).
109		MS (ESI) m/z 498.25 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.98 (bs, 1H), 9.05 (s, 1H), 8.71 (s, 1H), 8.51 (s, 1H), 8.40 (s, 1H), 8.28 (s, 1H), 7.77 (t, J = 54.52 Hz, 1H), 7.49-7.45 (m, 2H), 7.23 (d, J = 8.76 Hz, 1H), 4.38 (s, 4H).	112		MS (ESI) m/z 525.31 [M+1]+; 1H NMR (400 mHz, DMSO-d6) δ 13.50 (s, 1H), 9.02 (s, 1H), 8.47 (s, 1H), 8.30 (t, J = 1.6 Hz, 1H), 8.18 (s, 1H), 8.13 (s, 2H), 7.50-7.48 (m, 1H), 7.46 (s, 1H), 7.26 (d, J = 8.8 Hz, 1H), 4.39-4.38 (m, 2H), 4.33-4.32 (m, 2H), 3.32 (s, 3H)

113		MS (ESI) m/z 531.29 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.10 (s, 1H), 8.57 (s, 1H), 8.54 (bs, 1H), 7.74 (bs, 1H), 7.37-7.32 (m, 2H), 7.30 (d, J = 2.52 Hz, 1H), 7.16 (d, J = 8.88 Hz, 1H), 7.09 (d, J = 8.04 Hz, 1H), 4.39 (t, J = 4.76 Hz, 2H), 4.34 (t, J = 4.68 Hz, 2H)	116		MS (ESI) m/z 487.39 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.10 (s, 1H), 8.54 (s, 1H), 8.11 (s, 1H), 7.68 (bs, 1H), 7.51 (dd, J = 8.8, 2.4 Hz, 1H), 7.31 (d, J = 2.8 Hz, 1H), 7.22 (d, J = 8.8 Hz, 1H), 4.33 (s, 4H), 2.50 (s, 3H)
114		MS (ESI) m/z 492.36 [M+1]+;1H NMR (400 MHz, DMSO-d6) δ 12.58 (bs, 1H), 9.07 (s, 1H), 8.55 (s, 1H), 8.35 (s, 1H), 7.32 (d, J = 7.16 Hz, 1H), 7.22 (s, 1H), 7.12 (d, J = 8.88 Hz, 1H), 6.92 (s, 1H), 6.87 (s, 1H), 5.10 (bs, 2H), 4.38 (bs, 2H), 4.30 (bs, 2H), 3.76 (s, 3H)	117		MS (ESI) m/z 487.31 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.27 (bs, 1H), 11.92 (s, 1H), 8.91 (s, 1H), 8.40 (bs, 1H), 8.37 (s, 1H), 7.99 (s, 1H), 7.74 (d, J = 2.64 Hz, 1H), 7.68 (t, J = 2.84 Hz, 1H), 7.42 (dd, J = 8.88, 2.8 Hz, 1H), 7.26 (d, J = 8.76 Hz, 1H), 6.84 (t, J = 1.96 Hz, 1H), 4.47 (t, J = 4.72 Hz, 2H), 4.38 (t, J = 4.64 Hz, 2H)
115		MS (ESI) m/z 462.35 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.11 (s, 1H), 8.56 (s, 1H), 8.19 (d, J = 3.72 Hz, 1H), 8.12 (s, 1H), 7.41 (dd, J = 8.8, 2.8 Hz, 1H), 7.23 (bs, 1H), 7.16-7.14 (m, 2H), 4.28 (bs, 4H), 2.03 (s, 3H)	118		MS (ESI) m/z 498.41 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.97 (s, 1H), 8.56 (d, J = 8.56 Hz, 1H), 8.40 (s, 1H), 8.02 (d, J = 5.72 Hz, 1H), 7.70 (t, J = 7.08 Hz, 1H), 7.62-7.60 (m, 2H), 7.54 (dd, J = 8.76, 2.64 Hz, 1H), 7.29-7.26 (m, 2H), 7.18 (d, J = 5.64 Hz, 1H), 4.33-4.23 (m, 2H), 4.17-4.09 (m, 2H)

119		MS (ESI) m/z 601.13 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.92 (bs, 1H), 8.83 (d, J = 4.64 Hz, 1H), 8.38 (s, 1H), 7.87 (s, 1H), 7.59 (dd, J = 8.76, 2.24 Hz, 1H), 7.51 (t, J = 52.0 Hz, 1H), 7.49 (d, J = 4.68 Hz, 1H), 7.43 (d, J = 2.28 Hz, 1H), 7.35 (d, J = 8.96 Hz, 1H), 4.39 (t, J = 5.56 Hz, 2H), 4.23 (t, J = 4.92 Hz, 2H), 1.73 (s, 3H)
123		MS (ESI) m/z 599.53 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.77 (d, J = 4.92 Hz, 1H), 8.08 (d, J = 9.72 Hz, 1H), 7.60(dd, J = 8.88, 2.64 Hz, 1H), 7.53 (d, J = 4.96 Hz, 1H), 7.41 (d, J = 2.56 Hz,1H), 7.38 (t, J = 64.56 Hz, 1H), 7.35 (d, J = 1.72 Hz, 1H), 4.44 (t, J = 5.40 Hz, 2H), 4.23 (t, J = 4.84 Hz, 2H), 2.49 (s, 3H), 1.96 (s, 3H)
124		UPLC: MS (ESI) m/z 443.28 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.10 (s, 1H), 8.51(s, 1H), 8.41(s, 1H), 7.94 (s, 1H), 7.73 (d, J = 7.52 Hz, 1H), 7.41 (d, J = 7.68 Hz, 1H), 7.25 (t, J = 7.52 Hz, 1H), 7.06 (d, J = 8.76 Hz, 1H), 6.88-6.85(dd, J = 2.84 Hz, J = 2.72 Hz, 1H), 6.82 (d, J = 2.92 Hz, 1H), 4.34 (t, J = 4.6 Hz, J = 4.88 Hz 2H), 4.23 (d, J = 4.48 Hz), 3.72 (s, 3H)
125		UPLC: MS (ESI) m/z 429.28 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.20 (bs, 1H), 9.10 (s, 1H), 8.51 (s, 1H), 8.37 (s, 1H), 7.87 (s, 1H), 7.69 (d, J = 7.68 Hz, 1H), 7.42 (d, J = 7.76 Hz, 1H), 7.25 (t, J = 7.64 Hz, 1H), 6.96 (d, J = 8.68 Hz, 1H), 6.71-6.68 (dd, J = 2.96 Hz, J=2.92 Hz, 1H), 6.65 (d, J=2.8 Hz, 1H), 4.30 (t, J = 4.8 Hz, 2H), 4.17 (t, J = 4.88 Hz, 2H)
126		MS (ESI) m/z 463.36 [M+1]+; UPLC: 99.75 %; 1H NMR (400 MHz, DMSO-d6) δ 13.01 (s, 1H), 9.10 (s, 1H), 8.53 (s, 1H), 8.29 (s, 1H), 7.89 (s, 1H), 7.86 (d, J =7.76 Hz, 1H), 7.58 (t, J = 8.20 Hz, 2H), 7.48 (s, 1H), 7.44 (t, J = 7.68 Hz, 1H) 7.30 (d, J = 8.60 Hz, 1H), 7.14-6.86 (m, 1H), 4.42-4.38 (m, 4H)
127		MS (ESI) m/z 471.32 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.94 (bs, 1H), 9.10 (s, 1H), 8.51 (s, 1H), 7.99 (s, 1H), 7.78 (dd, J = 7.56, 11.2 Hz, 1H), 7.43-7.34 (m, 3H), 7.17-7.15 (m, 2H), 4.28 (s, 4H), 3.80 (s, 1H)

128		MS (ESI) m/z 471.29 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 16.5 (bs, 1H), 8.92 (s, 1H), 8.47(s, 1H), 8.23 (s, 1H), 7.97 (d, J = 1.48 Hz, 2H),7.55-7.51 (m, 2H), 7.43 (dd, J = 2.56 Hz, J = 2.68 Hz 1H), 7.39 (d, J = 2.6 Hz, 1H), 7.23 (d, J = 8.76 Hz, 1H), 4.36 (s, 4H)	
129		MS (ESI) m/z 461.21 [M+1]+. UPLC: 99.41 %; 1H NMR (400 MHz, DMSO-d6) δ 12.88 (s, 1H), 9.02 (s, 1H), 8.45 (s, 1H), 8.40 (s, 1H), 7.75 (s, 1H), 7.57 (d, J =7.76 Hz, 1H), 7.44-7.38 (m, 2H), 7.29 (d, J = 2.60 Hz, 1H), 7.23 (d, J = 8.88 Hz, 1H) 7.16 (t, J = 7.72 Hz, 1H), 5.14-5.09 (m, 1H), 4.53-4.49 (m, 1H), 4.42-4.37 (m, 1H), 1.43 (d, J = 6.96 Hz, 3H)	
130		MS (ESI) m/z 439.10 [M-1]-; 1H NMR (400 MHz, DMSO-d6) δ 12.83 (bs,1H), 9.17 (s, 1H), 8.56 (d, J = 8.44 Hz, 2H), 7.96 (s, 1H), 7.71-7.68 (m, 2H), 7.62 (d, J = 8.36 Hz, 1H), 7.53 (d, J = 2.04 Hz, 1H), 7.51-7.58 (dd, J = 2.08 Hz, J= 2.20 Hz, 1H), 7.37 (t, J = 7.68 Hz, 1H), 4.91 (s, 2H)	
131		MS (ESI) m/z 479.32 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.03 (bs, 1H), 10.82 (s, 1H), 8.79 (s, 1H), 8.62 (s, 1H), 7.98 (s, 1H), 7.95 (s, 1H),7.87 (d, J = 7.76 Hz, 1H), 7.58 (d, J = 7.56 Hz, 1H), 7.42-7.38 (m, 2H), 7.34 (d, J = 2.76 Hz, 1H), 7.19 (d, J = 8.92 Hz, 1H), 4.32 (s, 4H), 2.13 (s, 3H)	
132		MS (ESI) m/z 479.35 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.01 (s, 1H), 8.90 (d, J = 4.8 Hz, 1H), 8.49 (s, 1H), 8.17 (s, 1H), 7.92 (s, 1H), 7.86 (d, J= 7.6 Hz, 1H), 7.61 (d, J = 8.0 Hz, 1H), 7.43-7.38 (m, 2H), 7.34 (d, J = 2.4 Hz, 1H), 7.21 (d, J = 8.8 Hz, 1H), 4.35 (s, 4H), 2.93 (s, 3H)	
133		MS (ESI) m/z 514 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.9 (s, 1H), 8.29(d, J = 8.72 Hz, 1H), 8.19 (s, 1H), 8.07 (d, J = 8.64 Hz, 1H), 7.88 (s, 1H), 7.83 (d, J = 7.76 Hz ,1H), 7.60 (d, J = 7.76 Hz ,1H), 7.38-7.42 (m, J = 8.32 Hz, 2H), 7.33 (d, J = 2.68 Hz, 1H), 7.22 (d, J = 8.8 Hz,1H), 4.3 (s, 4H)	

134		MS (ESI) m/z 462 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.9 (b, 1H), 9.04(s, 1H), 8.63 (d, J = 4.96 Hz, 1H), 8.48 (s, 1H), 7.915 (s, 1H), 7.56 (dd, J = 1.52 Hz, J = 4.96Hz ,1H), 7.484 (dd, J = 1.68, 8.92 Hz, 1H), 7.40 (d, J = 2.6 Hz, 1H), 7.24 (d, J = 8.92 Hz, 1H), 4.385 (s, 4H), 2.278 (s, 3H)	137		MS (ESI) m/z 493.44 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.96 (s,1H), 8.92 (s, 1H), 8.08 (s, 1H), 8.04 (d, J = 4.32 Hz, 1H), 7.93 (s, 1H),7.89 (s, 1H), 7.86 (s, 1H), 7.56 (d, J = 6.88 Hz, 1H), 7.40-7.36 (m, 2H), 7.33 (d, J = 2.56 Hz, 1H), 7.20 (d, J = 8.84 Hz, 1H), 4.328 (s, 4H), 3.75 (s, 2H), 2.59 (d, J = 4.6 Hz, 3H)
135		UPLC: MS (ESI) m/z 518.43 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.86 (s, 1H), 8.84 (d, J = 4.8 Hz, 1H), 8.43 (s, 1H), 8.36 (s, 1H), 7.60-7.57 (dd, J = 2.6 Hz, J = 2.6 Hz, 1H), 7.47 (d, J = 4.76 Hz, 1H), 7.43 (d, J = 2.6 Hz, 1H), 7.33(d, J = 8.96 Hz, 1H), 4.38 (t, J = 4.8 Hz, 2H), 4.25 (t, J = 4.76, 5.0 Hz, 2H), 1.81 (s, 3H)	138		MS (ESI) m/z 436.10 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.97 (s,1H), 8.89 (s, 1H), 8.04 (s, 1H), 7.90 (s, 1H), 7.86 (d, J = 7.72 Hz, 1H), 7.76 (s, 1H),7.57 (d, J = 1.28 Hz, 1H), 7.409-7.37 (m, 2H), 7.333-7.326 (m, 2H), 7.20 (d, J = 8.88 Hz, 1H), 4.34 (s, 4H), 2.607 (s, 3H).
136		MS (ESI) m/z 488.32 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.96 (bs, 1H), 8.93 (s, 1H), 8.67 (s, 1H), 8.32 (s, 1H), 8.06 (s, 1H), 7.928-7.86 (m, 3H), 7.61 (d, J = 7.2 Hz, 1H), 7.45-7.39 (m, 2H), 7.341 (s, 1H), 7.21 (d, J = 8.4 Hz, 1H), 6.62 (s, 1H), 4.35 (s, 4H)	139		MS (ESI) m/z 496.35 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.927 (bs, 1H), 8.187 (s, 1H), 8.158 (s, 1H), 8.079 (s, 1H), 7.91 (s, 1H), 7.83 (d, J = 7.8 Hz, 1H), 7.599 (d, J = 7.96 Hz, 1H), 7.419-7.08 (m, 5H), 4.349 (s, 4H)

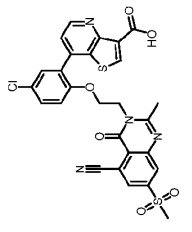
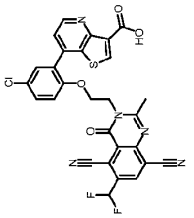
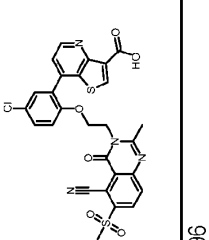
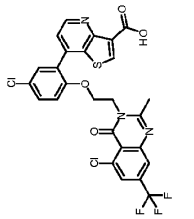
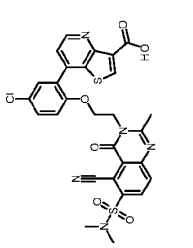
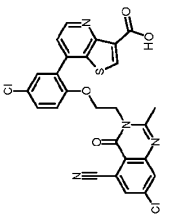
141	MS (ESI) m/z 494.34 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.931 (bs, 1H), 8.061(d, J = 8.88 Hz, 1H), 7.875-7.82 (m, 3H), 7.517 (d, J = 7.4 Hz, 1H), 7.425-7.386 (m, 2H), 7.276 (d, J = 2.28 Hz, 1H), 7.205 (d, J = 8.8 Hz, 1H), 4.343 (s, 4H), 2.173 (s, 3H)	144	MS (ESI) m/z 662.39 [M+1]+; 1H NMR (400 MHz, DMSO-d6):δ 12.63 (s, 1H), 8.86 (d, J = 4.8 Hz, 1H), 8.54 (s, 1H), 8.06 (d, J = 9.8 Hz, 1H), 7.63-7.60 (dd, J = 2.5, 2.6 Hz, 1H), 7.55 (d, J = 4.8 Hz, 1H), 7.42-7.36 (m, 3H), 4.44 (t, J = 6.1 Hz, 2H), 4.28 (t, J = 5.8 Hz, 2H), 3.53 (s, 3H), 1.90 (s, 3H)
142	MS (ESI) m/z 528.44 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.9 (s, 1H), 8.28(d, J = 7.92 Hz, 1H), 8.08 (d, J = 7.84 Hz, 1H), 7.92 (s, 1H), 7.85 (d, J = 7.76 Hz, 1H), 7.53 (d, J = 7.76 Hz ,1H), 7.33-7.41 (m, 2H), 7.28 (d, J = 4.4 Hz, 1H), 7.21 (d, J = 8.8 Hz, 1H), 4.3 (s, 4H), 2.24 (s, 3H)	148	MS (ESI) m/z 540.47 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.10 (bs, 1H), 8.15-8.13 (m, 1H), 8.07-8.00 (m, 2H), 7.70 (d, J = 1.3 Hz, 1H), 7.63-7.58 (m, 2H), 7.44-7.42 (dd, J = 2.6, 8.7 Hz, 1H), 7.39 (d, J = 2.6 Hz, 1H), 7.2 (d, J= 8.9 Hz, 1H), 7.08-6.82 (t, J = 51.9 Hz, 1H), 4.43 (t, J = 6.1 Hz, 2H), 4.34 (t, J = 5.5 Hz, 2H)
143	MS (ESI) m/z 553.44 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.77 (s, 1H), 8.42 (s, 1H), 8.12 (d, J = 6.84 Hz, 1H), 7.99 (t, J = 6.8 Hz, 1H), 7.89 (d, J = 7.28 Hz, 1H), 7.72 (d, J = 4.16 Hz, 1H), 7.47-7.44 (m, 2H), 7.37(d, J = 8.08 Hz, 1H), 6.59 (t, J = 51.6 Hz, 1 H), 4.41(s, 2H), 4.34 (s, 2H)	153	MS (ESI) m/z 510.40 [M+1] +; 1H NMR (400 MHz, DMSO-d6) δ 12.94 (bs, 1H), 8.12 (s, 1H), 8.00 (s, 1H), 7.89-7.84 (m, 2H), 7.53 (d, J = 7.6 Hz, 1H), 7.41-7.20 (m, 5H), 4.35 (m, 4H), 2.20 (s, 3H)

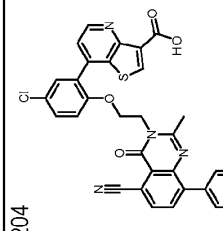
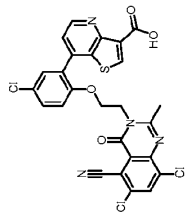
154		MS (ESI) m/z 528.08 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.37 (s, 1H), 7.87 (d, J = 7.72 Hz, 1H), 7.81 (s, 1H), 7.54 (d, J = 7.88 Hz, 1H), 7.45 (m, 2H), 7.27 (d, J = 4 Hz, 1H), 7.27 (d, J = 8 Hz, 1H),4.39 (m, 4H), 2.21(s, 3H)	
160		MS (ESI) m/z 567.16 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.76 Hz, 1H), 8.40 (s, 1H), 8.12 (d, J = 8.6 Hz, 1H), 7.82 (d, J = 8.52 Hz, 1H), 7.59 (dd, J = 2.4, 8.92 Hz, 1H), 7.50-7.23 (m, 4H), 4.42-4.23 (m, 4H), 1.79 (s, 3H)	
161		MS (ESI) m/z 497.87 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.64 (d, J = 4.92 Hz, 1H), 8.20 (s, 1H), 8.163 (d, J = 8.6, 1H), 8.0474 (t, J = 8.4 Hz 2H), 7.67 (dd, J = 1.4, 6.4 Hz, 1H), 7.65 (m, 4H), 4.39(m, 4H)	
163		MS (ESI) m/z 521.15 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.40 (b, 1H), 8.49(d, J = 4.84 Hz, 1H), 8.14 (d, J = 6.28 Hz, 1H), 8.07-8.02 (m, 2H), 7.49 (m, 1H), 7.43 (d, J = 4.88 Hz, 1H), 7.28 (d, J = 2.2 Hz, 1H), 7.23 (d, J = 8.92 Hz, 1H), 6.71 (t, J = 52.2 Hz, 1H) 4.38-4.33 (m, 4H), 4.19 (s, 1H)	
165		MS (ESI) m/z 520.17 [M+1]+. 1H NMR (400 MHz, DMSO-d6) δ 12.91 (bs, 1H), 8.12(d, J = 6.68 Hz, 1H), 8.04-7.98 (m, 2H), 7.78-7.76 (m, 1H), 7.42-7.37 (m, 3H), 7.20-7.07 (m, 2H), 6.68-6.42 (t, J = 52.32 Hz, 1H), 4.36-4.30 (m, 4H), 3.90 (s, 1H)	
166		MS (ESI) m/z 497.15 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.59 (s, 1H), 8.15 (d, J = 5.56 Hz, 1H), 8.07-7.99 (m, 3H), 7.645 (s, 1H), 7.51-7.46 (m, 2H), 7.23 (d, J = 8.92 Hz, 1H), 7.04-6.78 (m, 2H), 4.44-4.38 (m, 4H)	

167		MS (ESI) m/z 478.15 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.912 (bs, 1H), 8.028 (d, J = 8.84 Hz, 1H), 7.879 (d, J = 7.72 Hz, 2H), 7.813 (s, 1H), 7.696 (d, J = 9.36 Hz, 1H), 7.52 (d, J = 7.48 Hz, 1H), 7.449-7.394 (m, 2H), 7.283 (s, 1H), 7.2079 (d, J = 8.8 Hz, 1H), 4.334 (m, 4H), 2.163 (s, 3H)	172		MS (ESI) m/z 486.2 [M+1]+. 1H NMR (300 MHz, DMSO-d6) δ 13.00 (bs, 1H), 11.10 (bs, 1H), 8.04 (s, 1H), 7.93 (d, J = 7.5 Hz, 1H), 7.63 (d, J = 7.8 Hz, 1H), 7.51-7.46 (m, 1H), 7.38-7.34 (m, 2H), 7.18 (d, J = 8.4 Hz, 2H), 6.75-6.68 (m, 1H), 6.43 (bs, 1H), 4.24-4.20 (m, 2H), 3.49-3.46 (m, 2H), 2.84 (d, J = 4.8 Hz, 3H)
170		MS (ESI) m/z 421.2 [M+1]+; 1H NMR (500 MHz, DMSO-d6) δ 13.01 (bs, 1H), 12.21 (bs, 1H), 8.13 (s, 1H), 8.03 (s, 1H), 7.94 (d, J = 7.5 Hz, 1H), 7.62-7.61 (m, 1H), 7.55-7.50 (m, 3H), 7.35-7.34 (m, 2H), 7.20-7.17 (m, 2H), 4.27 (t, J = 6.5 Hz, 2H), 3.62 (t, J = 6.5 Hz, 2H)	173		MS (ESI) m/z 563.4 [M+1]+; 1H NMR (300 MHz, DMSO-d6) δ 12.16 (bs, 1H), 10.34 (bs, 1H), 8.13 (s, 1H), 7.31 (s, 1H), 7.21 (s, 1H), 7.19 (d, J = 7.5 Hz, 1H), 6.87 (d, J = 7.5 Hz, 2H), 6.76-6.75 (m, 1H), 6.68-6.54 (m, 5H), 6.37 (d, J = 8.1 Hz, 1H), 6.29-6.24 (m, 1H), 3.48 (t, J = 6.6 Hz, 2H), 2.74 (t, J = 6.3 Hz, 2H)
171		MS (ESI) m/z 468.2 [M+1]+; 1H NMR (300 MHz, DMSO-d6) δ 8.03 (s, 1H), 7.93 (d, J = 7.5 Hz, 1H), 7.64 (d, J = 7.5 Hz, 1H), 7.54-7.49 (m, 1H), 7.37-7.34 (m, 2H), 7.27-7.16 (m, 2H), 6.78-6.73 (m, 1H), 4.20 (t, J = 6.5 Hz, 2H), 3.47 (t, J = 6.5 Hz, 2H), 2.87 (d, J = 3.3 Hz, 3H)	174		MS (ESI) m/z 555.31 [M+1]+; UPLC: 97.62 %; 1H NMR (400 MHz, DMSO-d6) δ 13.00 (bs, 1H), 10.97 (bs, 1H), 9.04 (s, 1H), 8.01 (s, 1H), 7.92 (d, J = 7.76 Hz, 1H), 7.82 (d, J = 7.92 Hz, 2H), 7.60 (d, J = 7.60 Hz, 1H), 7.45 (t, J = 7.68 Hz, 1H), 7.39-7.33 (m, 4H), 7.18 (d, J = 8.84 Hz, 1H), 7.12-7.07 (m, 1H), 6.86 (d, J = 10.32 Hz, 1H), 4.30 (t, J = 5.96 Hz, 2H), 3.59 (t, J = 5.84 Hz, 2H

175		MS (ESI) m/z 583.21 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 10.68 (bs, 1H), 8.90 (s, 1H), 8.79 (d, J = 4.96 Hz, 1H), 8.57 (s, 1H), 7.66 (d, J = 7.72 Hz, 2H), 7.57-7.60 (dd, J = 2.68 Hz, J = 2.56 Hz, 1H), 7.52 (d, J = 2.56 Hz, 1H), 7.43 (s, 1H), 7.37-7.32 (m, 4H), 7.01-7.07 (m 1H), 4.51 (d, J = 4.72 Hz, 2H), 4.23 (t, J = 4.56 Hz, 2H)	
176		MS (ESI) m/z 513.32 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.0 (bs, 1H), 11.02 (bs, 1H), 8.91 (s, 1H), 8.38 (s, 1H), 8.02 (s, 1H), 7.93 (d, J = 7.6 Hz, 1H), 7.74 (d, J = 7.16 Hz, 2H), 7.60 (d, J = 7.44 Hz, 1H), 7.50 (t, J =7.56 Hz, 1H), 7.38-7.34 (m, 4H), 7.19 (d, J = 8.80 Hz, 1H), 7.07 (t, J = 7.32 Hz, 1H), 6.88 (s, 1H), 4.30 (t, J = 6.0 Hz, 2H), 3.56 (d, J = 5.72 Hz, 2H)	
177		MS (ESI m/z 544.12 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.99 (s, 1H), 11.73(s, 1H), 8.07 (s, 1H), 7.999-7.995 (t, J = 1.64 Hz, 1H), 7.94-7.91 (td, J = 9.08, J = 1.36 Hz, 1H), 7.56-7.53 (td, J = 7.80, J = 1.64 Hz, 1H), 7.47-7.44 (t, J = 7.68 Hz, 1H), 7.39-7.34 (m, 3H), 7.16 (d, J = 8.88 Hz, 1H), 4.33-4.24 (m, 4H), 3.56-3.53 (t, J = 6.0, 2H)	
178		LCMS (ESI) m/z 581.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.94 (bs, 1H), 11.10 (bs, 1H), 8.91 (s, 1H), 8.06 (s, 1H), 7.90 (d, J = 6.0 Hz, 1H), 7.71 (d, J = 5.7 Hz, 2H), 7.63 (d, J = 8.0 Hz, 1H), 7.45 (t, J = 6.0 Hz, 1H), 7.41-7.34 (m, 5H) 7.26 (s, 1H), 7.19 (d. J = 6.8 Hz, 1H), 7.11 (t, J = 6.0 Hz, 1H), 4.35 (m, 2H), 3.68 (m, 2 H)	
179		MS (ESI) m/z 538.4 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.99 (b, 1H), 11.20 (s, 1H), 9.09 (s, 1H), 8.11 (s, 1H), 8.00-8.01 (m, 1H), 7.94-7.91 (m, 1H), 7.84 (d, J = 8 Hz, 2H), 7.58-7.55 (m, 1H), 7.48 (t, J = 8 Hz, 1H), 7.40-7.34 (m, 4H), 7.18 (d, J = 9 Hz, 1H), 7.13-7.09 (m, 1H), 4.31 (t, J = 6 Hz, 2H), 3.57 (t, J = 6 Hz, 2H)	
180		MS (ESI) m/z 598.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.8 Hz, 1H), 8.51 (s, 1H), 8.27 – 8.26 (m, 1H), 8.16 (dd, J = 1.5, 0.6 Hz, 1H), 7.56 (dd, J = 8.9, 2.7 Hz, 1H), 7.49 (d, J = 4.8 Hz, 1H), 7.41 (d, J = 2.7 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 4.23 (t, J = 6.1 Hz, 2H), 3.62 (s, 3H), 2.89 (t, J = 6.1 Hz, 2H), 1.85 (s, 3H)	

188		191	
MS (ESI) m/z 603.15 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.80-8.74 (m, 1H), 8.44-8.42 (m, 1H), 8.22 (d, J = 8.8, 1H), 8.02 (d, J = 8.8 HZ, 1H), 7.65-7.58 (m, 1H), 7.55-7.28 (m, 4H), 6.73-6.42 (m, 1H), 4.42(s, 2H), 4.34 (s, 2H)		MS (ESI) m/z 550.33 [M-1]-; 1H NMR (400 MHz, DMSO-d6) δ 13.07 (s, 1H), 8.10 (d, J = 7.56 Hz, 1H), 8.005 (t, J = 8.38 Hz, 2H), 7.93 (t, J = 4.28 Hz, 2H), 7.55-7.52 (m, 1H), 7.49 (d, J = 5.6 Hz, 1H), 7.34 (t, J = 3.96 Hz, 1H), 7.30 (d, J = 5.52, 1H), 7.27 (s, 1H), 6.44 (t, J = 5.2 Hz, 1H), 4.35 (t, J = 5.52 Hz, 2H), 4.28 (t, J = 4.42 Hz, 2H)	
189		192	
MS (ESI) m/z 553.14 [M+1]+; UPLC: 98.14 %; 1H NMR (400 MHz, DMSO-d6) δ 13.149 (s, 1H), 8.54 (d, J = 5.48, 1H), 8.21 (d, J = 5.2 Hz, 1H), 8.174 (s, 1H), 8.13 (d, J = 7.32 Hz, 1H), 7.96-8.00 (t, J = 7.64 Hz, 1H), 7.91 (d, J = 8.12 Hz, 1H), 7.59-7.56 (dd, J = 2.6, 8.84 Hz, 1H), 7.36-7.33 (m, 2H), 6.63-6.37 (t, J = 52.08 Hz, 1H), 4.40 (d, J = 4.68, 2H), 4.32 (d, J = 4.68, 2H)		MS (ESI) m/z 542.2 [M-1]-; 1H NMR (400 MHz, DMSO-d6) δ 8.60 (s, 1H), 8.16-8.14 (m, 1H), 8.09-8.03 (m, 2H), 7.76 (s, 1H), 7.39-7.36 (dd, J = 2.60, 2.64 Hz, 1H), 7.13 (d, J = 8.84 Hz, 1H), 7.06 (d, J = 2.6 Hz, 1H), 6.91 (s, 1H), 4.72-4.64 (m, 2H), 4.39 (s, 2H), 4.29 (s, 2H)	
190		193	
MS (ESI) m/z 553.14 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.61 (m, 1H), 9.29 (s, 1H), 8.11-8.07 (t, J = 7.48 Hz, 2H), 8.04-8.00 (t, J = 7.52 Hz, 1H), 7.93 (d, J = 8.2 Hz, 1H), 7.60-7.55 (m, 2H), 7.41 (d, J = 2.52 Hz, 1H), 7.54 (d, J = 8.96 Hz, 1H), 6.68-6.43 (t, J = 51.88 Hz, 1H), 4.40 (d, J = 4.76, 2H), 4.33 (d, J = 4.64, 2H)		MS (ESI) m/z 542.2 [M-1]-; 1H NMR (400 MHz, DMSO-d6) δ 8.60 (s, 1H), 8.16-8.14 (m, 1H), 8.09-8.03 (m, 2H), 7.76 (s, 1H), 7.39-7.36 (dd, J = 2.60, 2.64 Hz, 1H), 7.13 (d, J = 8.84 Hz, 1H), 7.06 (d, J = 2.6 Hz, 1H), 6.91 (s, 1H), 4.72-4.64 (m, 2H), 4.39 (s, 2H), 4.29 (s, 2H)	

194		MS (ESI) m/z 595.18 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.5 Hz, 1H), 8.39 (s, 1H), 8.31 (s, 1H), 8.12 (s, 1H), 7.59 (d, J = 8.8 Hz, 1H), 7.48 (d, J = 4.7 Hz, 1H), 7.43 (s, 1H), 7.35 (d, J = 9.1 Hz, 1H), 4.41 (t, J = 4.0 Hz, 2H), 4.24 (t, J = 5.5 Hz, 2H), 1.74 (s, 3H)	197		MS (ESI) m/z 592.22 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.81 (d, J = 4.76 Hz, 1H), 8.67 (s, 1H), 8.55 (s, 1H), 7.61 (dd, J = 2.44, 8.96 Hz, 1H), 7.51-7.24 (m, 4H), 4.43 (s, 2H), 4.31 (s, 2H), 1.98 (s, 3H)
195		MS (ESI) m/z 595.27 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.7 Hz, 1H), 8.417 (s, 1H), 8.35 (d, J = 8.72 Hz, 1H), 7.87 (d, J = 8.76, 1H), 7.60 (dd, J = 8.8 Hz 2.44 Hz, 1H), 7.48 (d, J = 4.68 Hz, 1H), 7.43 (d, J = 2.44 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.405 (d, J = 4.1 Hz, 2H), 4.269 (s, 2H), 3.539 (s, 3H), 1.83 (s, 3H)	198		MS (ESI) m/z 592.01 [M-1]-; 1H NMR (400 MHz, DMSO-d6) δ 8.85 (d, J = 4.84 Hz, 1H), 8.39 (s, 1H), 7.78 (s, 1H), 7.66 (s, 1H), 7.61-7.58 (dd, J = 2.52 Hz, 6.36 Hz, 1H), 7.53 (d, J = 4.80 Hz, 1H), 7.44 (d, J = 2.56 Hz, 1H), 7.354 (d, J = 9.00 Hz, 1H), 4.38-4.36 (m, 2H), 4.20-4.18 (m, 2H), 1.74 (s, 3H)
196		MS (ESI) m/z 624.18 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.84 (d, J = 4.8 Hz, 1H), 8.43 (s, 1H), 8.26 (d, J = 8.76 Hz, 1H), 7.82 (d, J = 8.76, 1H), 7.60 (dd, J = 8.8 Hz, 2.64 Hz, 1H), 7.52 (d, J = 4.8 Hz, 1H), 7.46 (d, J = 2.6 Hz, 1H), 7.36 (d, J = 8.96 Hz, 1H), 4.41(t, J = 4.48 Hz, 2H), 4.25 (t, J = 4.68 Hz , 2H), 2.85 (s, 6H). 1.76 (s, 3H)	200		MS (ESI) m/z 551.26 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.76 Hz, 1H), 8.38 (s, 1H), 8.11 (s, 1H), 7.73 (d, J = 1.6 Hz, 1H), 7.59 (dd, J = 8.8, 2.3 Hz, 1H), 7.49 (d, J = 4.7 Hz, 1H), 7.43 (d, J = 2.3 Hz, 1H), 7.35 (d, J = 9.0 Hz, 1H), 4.39 (t, J = 4.4 Hz, 2H), 4.22 (t, J = 5.7 Hz, 2H), 1.74 (s, 3H)

204		MS (ESI) m/z 595.21 [M+1]+; UPLC: 99.31 %; 1H NMR (400 MHz, DMSO-d6) δ 9.25 (s, 1H), 9.10(s, 2H), 8.75 (d, J = 4.8 Hz, 1H), 8.55 (s, 1H), 8.10-8.03 (q, 2H), 7.61-7.58 (dd, J = 2.6 Hz, 2.6 Hz 1H),7.49 (d, J = 4.76 Hz, 1H), 7.44 (d, J = 8.12, 1H), 7.38 (d, J = 8.92 Hz, 1H), 4.46 (t, J = 4.84 Hz, 2H), 4.28 (t, J = 6.44 Hz, 2H), 1.93 (s, 3H)	209		MS (ESI) m/z 585.06 [M+1]+; UPLC: 99.28 %; 1H NMR (400 MHz, DMSO-d6) δ 13.20 (s, 1H), 8.80 (d, J = 4.72 Hz, 1H), 8.54(s, 1H), 8.39 (s,1H), 7.60-7.58 (dd, J =2.32, 2.24 Hz, 1H), 7.45-7.42 (dd, J = 4.76, 2.64 Hz, 2H), 7.36 (d, J =8.92 Hz, 1H), 4.38 (s, 2H), 4.23 (s, 2H), 1.86 (s, 3H).
207		MS (ESI) m/z 585.08 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.31 (bs, 1H), 8.83 (d, J = 4.7 Hz, 1H), 8.36 (s, 1H), 7.92 (s, 1H), 7.59 (dd, J = 8.8, 2.5 Hz, 1H), 7.47 (d, J = 4.7 Hz, 1H), 7.42 (d, J = 2.5 Hz, 1H), 7.35 (d, J = 8.8 Hz, 1H), 4.39 (t, J = 5.6 Hz, 2H), 4.23 (t, J = 4.8 Hz, 2H), 1.72 (s, 3H)	211		MS (ESI) m/z 541.16 [M+1]+; UPLC: 99.9 %; 1H NMR (400 MHz, DMSO-d6) δ 8.81 (d, J = 4.80 Hz, 1H), 8.65 (s, 1H), 8.05 (d, J = 7.76 1H), 7.89 (d, J = 7.72, 1H), 7.60 (d, J = 2.4 Hz, 1H), 7.46 (d, J = 2.44 Hz, 2H), 7.36 (d, J = 9 Hz, 1H), 4.75 (s, 1H), 4.40 (s, 2H), 4.26 (s, 2H), 1.93 (s, 3H)
208		MS (ESI) m/z 594.02 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.33 (bs, 1H), 8.83 (d, J = 4.6 Hz, 1H), 8.44 (s, 1H), 7.61-7.57 (m, 2H), 7.47-7.42 (m, 2H), 7.33 (d, J = 8.5 Hz, 1H), 4.35 (bs, 2H), 4.17 (bs, 2H), 1.71 (s, 3H)	212		MS (ESI) m/z 542.12 [M+1]+; UPLC: 99.61 %; 1H NMR (400 MHz, DMSO-d6) δ 13.34 (bs, 1H), 8.83 (d, J = 4.56 Hz, 1H), 8.47(s, 1H), 8.32 (s, 1H), 8.15 (s,1H), 7.60-7.57 (dd, J = 3.52,1.72 Hz,1H), 7.46 (d, J = 4.60 Hz, 1H), 7.42 (d, J = 2.32 Hz, 1H), 7.34 (d, J = 8.96 Hz, 1H), 4.41-4.39 (t, J = 5.28 Hz, 2H), 4.25-4.22 (t, J = 5.04 Hz, 2H), 1.77 (s, 3H)

213		MS (ESI) m/z 541.16 [M+1]+; UPLC: 99.87 %; 1H NMR (400 MHz, DMSO-d6) δ 13.34 (bs, 1H), 8.83 (d, J = 4.84 Hz, 1H), 8.38 (s, 1H), 8.02 (s, 1H), 7.74 (s,1H), 7.60-7.57 (dd, J = 8.84, 2.36 Hz, 1H), 7.47-7.43 (dd, J = 11.20, 4.8 Hz, 2H), 7.34 (d, J = 8.92 Hz, 1H), 4.71 (s, 1H), 4.38 (s, 2H), 4.21 (s, 2H), 1.72 (s, 3H)	218		MS (ESI) m/z 618.02 [M+1]+. 1H NMR (400 MHz, DMSO-d6) δ 13.2 (s, 1H), 8.85-8.84 (d, J = 4.0 Hz, 1H), 8.47 (s, 1H), 8.21 (s, 1H), 8.01 (s, 1H), 7.59-7.58 (d, J=4.0 Hz, 1H), 7.51-7.50 (d, J = 4.0 Hz, 1H), 7.39-7.38 (m, 2H), 4.46-4. (bs, 2H), 4.31 (bs, 2H), 1.76 (s, 3H)
216		MS (ESI) m/z 644.23 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83-8.79 (m, 3H), 8.29 (s, 1H), 8.22 (s, 1H), 7.93 (s, 1H), 7.84 (d, J = 5.68 Hz, 2H), 7.59 (dd, J = 2.56, J=8.84 Hz, 1H), 7.51 (d, J = 4.8 Hz, 1H), 7.44 (d, J=2.60 Hz, 1H), 7.34 (d, J=8.96 Hz, 1H) 4.38 (t, J = 5.76 Hz, 2H), 4.22 (t, J = 4.60 Hz, 2H), 1.69 (s, 3H)	219		MS (ESI) m/z 628.23 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.65 (bs, 1H), 8.83 (d, J = 4.76 Hz, 1H), 8.31 (s, 1H), 8.03 (d, J = 3.84 Hz, 2H), 7.60-7.57 (dd, J = 2.4 Hz 6.36 Hz, 1H), 7.48 (d, J = 4.72 Hz, 1H), 7.43 (d, J = 2.44 Hz, 1H), 7.35 (d, J = 8.96 Hz, 1H), 4.38-4.35 (m, 2H), 4.25-4.22 (m, 2H), 1.77 (s, 3H)
217		MS (ESI) m/z 581.08 [M+1]+. 1H NMR (400 MHz, DMSO-d6) δ 13.39 (bs, 1H), 8.84 (d, J = 4.4 Hz, 1H), 8.26 (s, 1H), 8.13 (s, 1H), 7.81 (s, 1H), 7.59 (dd, J = 8.8, 2.4 Hz, 1H), 7.49 (d, J = 7.2 Hz, 1H), 7.43 (d, J = 2.4 Hz, 1H), 7.35 (d, J = 8.8 Hz, 1H), 4.40 (t, J = 5.9 Hz, 2H), 4.23 (t, J = 4.8 Hz, 2H), 2.14 (t, J = 19.6 Hz, 3H), 1.72 (s, 3H)	220		MS (ESI) m/z 610.05 [M+1]+. 1H NMR (400 MHz, DMSO-d6) δ 13.2 (s, 1H), 8.83-8.82 (d, J = 4, 1H), 8.20 (s, 1H), 7.93-7.87 (m, 2H), 7.60-7.57 (m, 1H), 7.46-7.42 (m, 2H), 7.35-7.33 (d, J = 8 Hz, 1H), 4.36-4.38 (t, J = 4 Hz, 2H), 4.25-4.24 (t, J = 4 Hz, 2H), 1.78 (s, 3H)

221		MS (ESI) m/z 592.03 [M+1]+. 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J=4.8 Hz, 1H), 8.41 (s, 1H), 7.81 (s, 1H), 7.60-7.57 (dd, J=8.0, 2.52 Hz, 1H), 7.49 (d, J=4.7 Hz, 1H), 7.44 (d, J=2.52 Hz, 1H), 7.37-7.33 (m, 2H), 5.90 (s, 1H), 4.36-4.34 (t, J=7.52 Hz, 2H), 4.18-4.15 (t, J=7.96 Hz, 2H), 1.7 (s, 3H)	224		MS (ESI) m/z 599.14 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.3 (s, 1H), 8.83 (d, J = 4 Hz, 1H), 8.66 (s, 1H), 8.36 (s, 1H), 8.32 (s, 1H), 7.60-7.58 (d, J = 8.0 Hz, 1H), 7.46 (d, J = 4.0 Hz, 1H), 7.40 (s, 1H), 7.35 (d, J = 12 Hz, 1H), 4.42-4.40 (t, J = 4.0 Hz, 2H), 4.28-4.26 (t, J = 5.6 Hz, 2H), 1.82 (s, 3H)
222		MS (ESI) m/z 607.03 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.84 Hz, 1H), 8.39 (s, 1H), 7.60-7.57 (m, 1H), 7.49 (d, J = 4.84 Hz, 1H), 7.43 (d, J = 2.6 Hz, 1H), 7.39 (s, 1H), 7.35 (s, 1H), 7.25 (s, 1H), 4.35-4.34 (t, J = 4.72 Hz, 2H),4.20-4.18 (t, J = 4.32 Hz, 2H), 2.46 (s, 3H), 1.75(s, 3H)	228		MS (ESI) m/z 540.16 [M-1]-; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.8 Hz, 1H), 8.35 (t, J = 4.18 Hz, 2H), 7.78 (d, J = 8.6 Hz, 1H), 7.61-7.58 (dd, J = 2.56, 2.56 Hz, 1H), 7.49 (d, J = 4.72 Hz, 1H), 7.42 (d, J = 2.56 Hz, 1H), 7.36 (d, J = 8.96 Hz, 1H), 4.40 (d, J = 4.64 Hz, 2H), 4.26 (d, J = 4.32 Hz, 2H), 1.79 (s, 3H)
223		MS (ESI) m/z 638.04 [M+1]. 1H NMR (400 MHz, DMSO-d6) δ 13.2 (s, 1H), 8.83 (s, 1H), 8.32 (s, 1H), 8.23 (s, 1H), 8.09 (s, 1H), 7.59-7.57 (d, J = 8 Hz, 1H), 7.43 (d, J = 12 Hz, 2H), 7.34 (d, J=8 Hz, 1H), 4.43-4.41 (t, J=4.0 Hz, 2H), 4.31-4.29(t, J=4.0 Hz, 2H), 3.61(s, 3H), 1.93 (s, 3H)	229		MS (ESI) m/z 595.18 [M+1]+; UPLC: 99.8 %; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.80 Hz, 1H), 8.76 (s, 1H), 8.37 (d, J = 7.92, 1H), 8.10 (d, J = 7.88, 1H), 7.59 (dd, J = 2.04, 3.76 Hz, 1H), 7.44-7.47 (m, 2H), 7.37 (d, J = 8.92 Hz, 1H), 4.34 (s, 2H), 4.29 (s, 2H), 3.62 (s, 3H), 2.061 (s, 3H)

230	MS (ESI) m/z 585.05 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.19 (bs, 1H), 8.83 (d, J = 4.8 Hz, 1H), 8.40 (s, 1H), 7.64-7.54 (m, 2H), 7.48-7.28 (m, 4H), 4.40 (t, J = 5.7 Hz, 2H), 4.24 (t, J = 5.2 Hz, 2H), 1.76 (s, 3H)	233	MS (ESI) m/z 556.20 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.10 (s,1H), 8.49 (s, 1H), 8.40 (s, 1H), 7.87 (s, 1H), 7.83 (s, 1H), 7.55 (d, J = 7.6 Hz, 1H), 7.44-7.39 (m, 2H), 7.28 (d, J = 2.4 Hz, 1H), 7.20 (d, J=8.84, 1H), 5.13 (d, J = 45.76 Hz, 2H), 4.33-4.31 (m, 4H), 3.46 (s, 3H)
231	MS (ESI) m/z 503.25 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.57 (s, 1H), 8.54 (s, 1H), 7.88 (d, J = 7.24 Hz, 1H), 7.81 (s, 1H), 7.48 (d, J = 7.16 Hz, 1H), 7.39 (m, 2H), 7.26 (s, 1H), 5.08 (d, J = 45.84 Hz, 2H), 4.31 (s, 4H)	234	MS (ESI) m/z 541.29 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.76 Hz, 1H), 8.36 (d, J = 3.88 Hz, 2H), 8.19 (d, J = 1.08 Hz, 1H), 7.5996-7.5708 (m, 1H), 7.45 (d, J = 4.76 Hz, 1H), 7.41 (d, J = 2.6 Hz, 1H), 7.35 (d, J = 8.96 Hz, 1H), 6.02 (s, 1H), 4.39 (d, J = 4.76 Hz, 2H), 4.2060 (s, 2H), 1.63 (s, 3H)
232	MS (ESI) m/z 527.16 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.96 (s, 1H), 8.58 (d, J = 0.68, 1H), 8.46 (s, 1H), 7.88 (d, J = 7.56 Hz, 1H), 7.47 (t, J = 7.72, 1H), 7.41-7.38 (m, 2H), 7.16 (d, J = 8.92, 1H), 7.13 (d, J = 2.52 ,1H), 5.02 (d, J = 46.24 Hz, 2H), 4.28 (s, 4H), 3.73(s, 1H)	235	MS (ESI) m/z 594.36 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.3202 (bs, 1H), 8.84 (d, J = 4.76 Hz, 1H), 8.34 (s, 1H), 8.31 (d, J = 1.4 Hz, 1H), 8.22 (d, J = 1.36 Hz, 1H), 7.6002-7.5717 (m, 1H), 7.46 (d, J = 4.76 Hz, 1H), 7.44 (d, J = 2.52 Hz, 1H), 7.36 (d, J = 8.96 Hz, 1H), 6.18 (s, 1H), 4.4153 (t, J = 5.32 Hz, 2H), 4.2160 (t, J = 5.4 Hz, 2H), 3.4635 (s, 3H), 1.6167 (s, 3H)

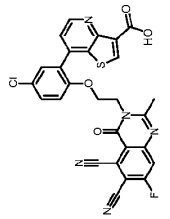
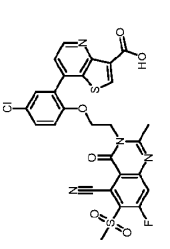
236		MS (ESI) m/z 583.31 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.4 (bs, 1H), 8.82 (d, J = 4.8 Hz, 1H), 8.40 (s, 1H), 7.86 (d, J = 9.2 Hz, 1H), 7.77 (d, J = 9.2 Hz, 1H), 7.69-7.32 (m, 5H), 4.40-4.38 (m, 2H), 4.24-4.21 (m, 2H), 1.74 (s, 3H)	
237		MS (ESI) m/z 624.32 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.87 (s, 1H), 8.85 (d, J = 4.48 Hz, 1H), 8.34 (d, J = 7.72 Hz, 1H), 8.03 (d, J = 7.92, 1H), 7.59 (d, J = 8.8 Hz , 1H), 7.51 (d, J = 1.96 Hz, 1H), 7.48 (d, J = 4.56 Hz, 1H), 7.35 (d, J = 9 Hz, 1H), 4.41(t, J = 4 Hz, 2H), 4.29 (t, J = 4.28 Hz , 2H), 2.84 (s, 6H). 1.99 (s, 3H)	239		MS (ESI) m/z 576.04 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) 8.82 (d, J = 4.8, 1H), 8.75 (s, 1H), 8.55 (s, 1H), 7.61 (dd, J = 2.48 Hz, 8.8 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.44 (d, J = 2.36 Hz, 1H), 7.38 (d, J = 8.92, 1H), 4.42 (t, J = 4.64 Hz, 2H), 4.29 (t, J = 4.32 Hz, 2H), 1.95 (s, 3H)
238		MS (ESI) m/z 610.19 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.85 (m, 2H), 8.30 (d, J = 7.76Hz, 1H), 8.03 (d, J = 7.72 Hz, 1H), 7.58 (d, J = 8.8Hz, 1H), 7.52 (d, J = 1.76 Hz , 1H), 7.45 (d, J = 4.44 Hz, 1H), 7.35 (d, J = 8.84 Hz, 1H), 4.41(t, J = 4.6 Hz, 2H), 4.29 (t, J = 4.96 Hz , 2H), 2.54 (d, J = 5.92 Hz, 3H). 2.11 (s, 3H)	240		MS (ESI) m/z 560.21 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.24 (bs, 1H), 8.80 (d, J = 4.60 Hz, 1H), 8.68 (d, J = 8.84 Hz, 1H), 8.51 (s, 1H), 7.59 (dd, J = 6.64 Hz, 2.8 Hz, 1H), 7.45 (d, J = 4.76 Hz, 1H), 7.43 (d, J = 2.28 Hz, 1H), 7.37 (d, J = 8.84 Hz, 1H), 4.42 (t, J = 4.96 Hz, 2H), 4.28 (t, J = 5.04 Hz, 2H), 1.95 (s, 3H)
		241		MS (ESI) m/z 553.18 [M+1]+; 1H NMR (400 MHz, DMSO-d6) 8.83 (d, J = 4.76 Hz, 1H), 8.47 (s, 1H), 8.09 (t, J = 9.48 Hz, 1H), 7.60 (dd, J = 2.16, 8.8 Hz, 1H), 7.51 (d, J = 4.64 Hz, 1H), 7.41 (d, J = 2.16 Hz, 1H), 7.37 (d, J = 8.92 Hz, 1H), 4.42 (bs, 2H). 4.26 (bs, 2H), 1.84 (s, 3H)

242		MS (ESI) m/z 569.11 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.84 (d, J = 4.68 Hz, 1H), 8.36 (s, 1H), 7.91 (d, J = 6.84 Hz, 1H), 7.60 (dd, J = 2.28 Hz, 8.84 Hz, 1H), 7.48 (d, J = 4.68 Hz, 1H), 7.42 (d, J = 2.32 Hz, 1H), 7.35 (d, J = 8.96 Hz, 1H), 4.39 (t, J = 5.64 Hz, 2H), 4.22 (t, J = 5.64 Hz, 2H), 1.73 (s, 3H)
243		MS (ESI) m/z 581.08 [M+1]+. 1H NMR (400 MHz, DMSO-d6) δ 12.35 (bs, 1H), 8.84 (d, J = 4.8 Hz, 1H), 8.40 (s, 1H), 7.65 (d, J = 9.6 Hz, 1H), 7.60 (dd, J = 8.8, 2.4 Hz, 1H), 7.49 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.8 Hz, 1H), 7.36 (d, J = 8.8 Hz, 1H), 4.40-4.38 (m, 2H), 4.24-4.22 (m, 2H), 1.75 (s, 3H)
244		MS (ESI) m/z 551.16 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.76 Hz, 1H), 8.39 (s, 1H), 8.06 (d, J = 8.88,1H), 7.68 (d, J = 8.8, 1H), 7.58-7.61 (m, 1H), 7.50 (d, J = 4.56 Hz, 1H), 7.43 (d, J = 2.52 Hz, 1H), 7.39 (d,J = 9.0 Hz, 1H), 4.40 (s, 2H), 4.23 (s, 2H), 1.74 (s, 3H)
245		MS (ESI) m/z 535.14 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.33 (bs, 1H), 8.83 (d, J = 4.8 Hz, 1H), 8.4 (s, 1H), 7.93 (t, J = 9.0 Hz, 1H), 7.76 (dd, J = 9.0, 5.0 Hz, 1H), 7.59 (dd, J = 8.8, 2.5 Hz, 1H), 7.51 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.5 Hz, 1H), 7.36 (d, J = 8.9 Hz, 1H), 4.4 (t, J = 4.8 Hz, 2H), 4.23 (t, J = 4.7 Hz, 2H), 1.73 (s, 3H)
247		MS (ESI) m/z 658.02 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.85 (d, J = 4.84 Hz, 1H), 8.42 (s, 1H), 7.88 (s, 1H), 7.60 (dd, J = 2.4, 8.88 Hz, 1H), 7.52 (d, J = 4.8 Hz, 1H), 7.45 (d, J = 2.4 Hz, 1H), 7.36 (d, J = 9.2 Hz, 1H), 4.41 (t, J = 4.72 Hz, 2H), 4.23 (t, J = 4.44 Hz, 2H), 2.96 (s, 6H), 1.71 (s, 3H)
248		MS (ESI) m/z 636.23 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.84 (d, J = 4.76 Hz, 1H), 8.43 (s, 1H), 8.26 (d, J = 8.72 Hz, 1H), 7.84 (d, J = 8.72 Hz, 1H), 7.61 (dd, J = 8.92, 2.6 Hz, 1H), 7.51 (d, J = 4.76 Hz, 1H), 7.46 (d, J = 2.6 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 4.41 (t, J = 5.6 Hz, 2H), 4.25 (t, J = 5.52 Hz, 2H), 3.96 (t, J = 7.52 Hz, 4H), 2.19-2.11 (m, 2H), 1.76 (s, 3H)

249		MS (ESI) m/z 650.15 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.8 Hz, 1H), 8.40 (s, 1H), 8.28 (d, J = 8.72 Hz, 1H), 7.82 (d, J = 8.76 Hz, 1H), 7.60 (dd, J = 8.92, 2.56 Hz, 1H), 7.50 (d, J = 4.76 Hz, 1H), 7.45 (d, J = 2.6 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.40 (t, J = 5.24 Hz, 2H), 4.25 (t, J = 1.96 Hz, 2H),3.36 (t, J = 6.48 Hz, 4H), 1.83 (t, J = 6.52, 4H), 1.75 (s, 3H)
250		MS (ESI) m/z 652.16 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.84 (d, J = 4.84 Hz, 1H), 8.43 (s, 1H), 8.31 (d, J = 8.76 Hz, 1H), 7.81 (d, J =8.8, Hz, 1H), 7.61 (dd, J = 2.72, 8.92 Hz, 1H), 7.52 (d, J = 4.84 Hz, 1H), 7.46 (d, J = 2.72 Hz, 1H), 7.36 (d, J = 9.04 Hz, 1H), 4.41 (t, J = 4.56 Hz, 2H), 4.24 (t, J = 4.5 Hz, 2H), 3.41(d, J = 7.04 Hz, 4H), 1.74 (s, 3H), 1.10 (t, J = 7.04 Hz, 6H)
251		MS (ESI) m/z 663.32 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.84 (d, J = 4.76 Hz, 1H), 8.41 (s, 1H), 8.26 (d, J = 8.76 Hz, 1H), 7.82 (d, J = 8.72 Hz, 1H),7.60 (dd, J = 8.8, 2.52 Hz, 1H),7.50 (d, J = 4.76 Hz, 1H),7.46 (d, J = 2.45 Hz, 1H),7.36 (d, J = 8.96 Hz, 1H), 4.40 (bs, 2H), 4.23 (bs, 2H), 3.20 (d, J = 5.2 Hz,4H), 1.75 (s, 3H), 1.55 (s, 4H), 1.46 (d, J = 3.64 Hz, 2H)
252		MS (ESI) m/z 686.21 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.8 Hz, 1H), 8.72 (t, J = 6.1, 1H), 8.4 (s, 1H) 8.20 (d, J = 8.7, 1H), 7.73 (d, J = 8.7 Hz, 1H), 7.60 (dd, J = 2.1, 8.92 Hz, 1H), 7.46 (m, 2H), 7.37 (d, J = 9 Hz, 1H), 7.1 (m, 4H), 7.07 (t, J = 7.1 Hz, 1H), 4.39 (d, J = 4.56, 2H), 4.24 (m, 4H), 1.72 (s, 3H)
253		MS (ESI) m/z 714.20 [M+1]+; 1H NMR (400 MHz, DMSO-d6) 8.84 (d, J = 4.8 Hz, 1H), 8.41 (s, 1H), 8.33 (d, J = 8.76 Hz, 1H), 7.80 (d, J = 8.76 Hz, 1H), 7.62 (dd, J = 2.68, 8.90 Hz, 1H), 7.51 (d, J = 4.80 Hz, 1H), 7.44 (d, J = 2.60 Hz, 1H), 7.38 (d, J = 9.00 Hz, 1H),7.35-7.28 (m, 4H), 7.15-7.20 (m, 1H), 4.59 (s, 2H), 4.40 (t, J = 4.64 Hz, 2H), 4.25 (t, J = 4.36 Hz, 2H), 3.30 (q, J = 6.92 Hz, 2H), 1.75 (s, 3H), 0.91 (t, J = 7.12 Hz, 3H).
254		MS (ESI) m/z 517.17 [M+1]+; UPLC: 98.39 %; 1H NMR (400 MHz, DMSO-d6) δ 13.42 (s, 1H), 8.82 (d, J= 4.72 Hz, 1H), 8.37(s, 1H), 7.95 (d, J = 6.52 Hz, 1H), 7.91-7.87 (t, 1H), 7.70 (d, J = 8.16, Hz 1H), 7.60-7.57 (dd, J = 2.48 Hz, 1H), 7.47 (d, J = 4.76 Hz, 1H), 7.43 (d, J = 2.52 Hz, 1H), 7.35 (d, J = 8.96 Hz, 1H), 4.41-4.22 (m, 4H), 1.77 (s, 3H)

256		MS (ESI) m/z 581.07 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.22 (bs, 1H), 8.83 (s, 1H), 8.80 (d, J = 4.8 Hz, 1H), 8.10 (s, 1H), 7.87 (d, J = 8.4 Hz, 1H), 7.62 (dd, J = 8.4, 2.0 Hz, 1H), 7.52 (d, J = 2.0 Hz, 1H), 7.43 (d, J = 4.8 Hz, 1H), 6.48-6.41 (m, 1H), 5.97 (d, J = 16.0 Hz, 1H), 4.70 (d, J = 4.4 Hz, 2H), 2.36 (s, 3H)
257		MS (ESI) m/z 579.06 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.76 (d, J = 4.7 Hz, 1H), 8.62 (s, 1H), 8.09 (s, 1H), 7.76 (d, J = 8.4 Hz, 1H), 7.69 (d, J = 2.0 Hz, 1H), 7.67 (s, 1H), 7.55 (d, J = 4.8 Hz, 1H), 4.85 (s, 2H), 2.09 (s, 3H)
258		MS (ESI) m/z 536.11 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.74 (d, J = 4.7 Hz, 1H), 8.6 (s, 1H), 8.51 (d, J = 1.4 Hz, 1H), 8.32 (d, J = 1.4 Hz, 1H), 7.76 (d, J = 9.1 Hz, 1H), 7.68 (m, 2H), 7.53 (d, J = 4.7 Hz, 1H), 4.86 (s, 2H), 2.13 (s, 3H).
262		MS (ESI) m/z 601.02 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.53 (bs, 1H), 8.86 (d, J = 4.8 Hz, 1H), 8.46 (s, 1H), 8.06 (d, J = 4.6 Hz, 2H), 7.60 (dd, J = 8.8, 2.6 Hz, 1H), 7.52 (d, J = 4.7 Hz, 1H), 7.40 (d, J = 2.5 Hz, 1H), 7.36 (d, J = 8.9 Hz, 1H), 4.41 (m, 2H), 4.19 (m, 2H), 1.46 (d, J = 3.3 Hz, 3H)
263		MS (ESI) m/z 608.02 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.21 (bs, 1H), 8.87 (d, J = 4.7 Hz, 1H), 8.56 (s, 1H), 8.11 (s, 1H), 8.01 (s, 1H), 7.61 (dd, J = 8.8, 2.8 Hz, 1H), 7.52 (d, J = 4.8 Hz, 1H), 7.39-7.37 (m, 2H), 4.45 (m, 2H), 4.33 (m, 2H), 1.92 (s, 3H)
264		MS (ESI) m/z 601.15 [M+1]+. 1H NMR (400 MHz, DMSO-d6) δ 8.84 (d, J = 4.8 Hz, 1H), 8.33 (d, J = 1.6 Hz, 1H), 8.30 (s, 1H), 7.96 (d, J = 1.2 Hz 1H), 7.60 (dd, J = 8.8, 2.4 Hz, 1H), 7.50 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.4 Hz, 1H), 7.35 (d, J = 8.8 Hz, 1H), 4.40 (t, J = 4.8 Hz, 2H), 4.24 (t, J = 4.8 Hz, 2H), 1.73 (s, 3H)

268		MS (ESI) m/z 652.05 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.81 (d, J = 4.80 Hz, 1H), 8.50 (s, 1H), 8.24 (s, 1H), 8.08 (s, 1H), 7.60 (dd, J = 2.60, 2.64 Hz, 1H), 7.52 (d, J = 4.76 Hz, 1H), 7.42-7.38 (m, 2H), 4.47 (bs, 2H), 4.39 (bs, 2H), 1.89 (s, 3H)	271 MS (ESI) m/z 605.04 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.30 (bs, 1H), 8.84 (d, J = 4.68 Hz, 1H), 8.36 (s, 1H), 8.35 (d, J = 1.38 Hz, 1H), 7.98 (s, 1H), 7.58 (dd, J = 2.60, 2.60 Hz, 1H), 7.47 (d, J = 4.72 Hz, 1H), 7.43 (d, J = 2.60 Hz, 1H), 7.33 (d, J = 8.96 Hz, 1H), 4.33 (t, J = 4.79 Hz, 2H), 4.20 (t, J = 4.94 Hz, 2H), 1.75 (s, 3H)
269		MS (ESI) m/z 634.05 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.21 (bs, 1H), 8.77 (d, J = 4.84 Hz, 1H), 8.43 (s, 1H), 8.41 (s, 1H), 8.36 (s, 1H), 7.60-7.58 (m, 1H), 7.48 (d, J = 4.72 Hz, 1H), 7.44-7.17 (m, 3H), 4.45 (t, J = 4.47 Hz, 2H), 4.35 (t, J = 4.35 Hz, 2H), 1.99 (s, 3H)	273 MS (ESI) m/z 558.95 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.86-8.85 (d, J = 4.8 Hz, 1H), 8.57 (d, J = 1.2 Hz, 1H), 8.23 (d, J = 1.2 Hz, 1H), 8.17 (s, 1H), 7.61-7.58 (dd, J = 2.8, 8.8 Hz, 1H), 7.50-7.49 (d, J = 4.8 Hz, 1H), 7.40 (d, J = 2.8 Hz, 1H), 7.37-7.35 (d, J = 8.8 Hz, 1H), 4.40 (d, J = 4.4 Hz, 2H), 4.18 (t, J 4.4 Hz, 2H), 1.49 (d, J = 3.6 Hz, 3H)
270		MS (ESI) m/z 629.04 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.21 (bs, 1H), 8.80 (d, J = 4.80 Hz, 1H), 8.54 (s, 1H), 8.33 (s, 1H), 7.94 (s, 1H), 7.62-7.59 (m, 1H), 7.50 (d, J = 4.76 Hz, 1H), 7.42-7.38 (m, 2H), 4.47 (t, J =4.47 Hz, 2H), 4.36 (t, J = 4.36 Hz, 2H), 1.85 (s, 3H)	274 MS (ESI) m/z 611.97 [M+1]+. 1H NMR (400 MHz, DMSO-d6) δ 8.87 (d, J = 4.7 Hz, 1H), 8.47 (s, 1H), 8.23 (s, 1H), 8.12 (s, 1H), 7.59 (d, J = 9.3 Hz, 1H), 7.52 (d, J = 4.5 Hz, 1H), 7.41 (s, 1H), 7.37 (d, J = 8.9 Hz, 1H), 4.42 (t, J = 5.2 Hz, 2H), 4.19 (t, J = 5.2 Hz, 2H), 3.52 (s, 3H), 1.46 (s, 3H)

276		MS (ESI) m/z 559.95 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.81 (bs, 1H), 8.85 (d, J = 4.76 Hz, 1H), 8.39 (s, 1H), 7.69 (d, J = 9.60 Hz, 1H), 7.60 (dd, J = 8.84, 2.48 Hz, 1H), 7.50 (d, J = 4.76 Hz, 1H), 7.42 (d, J = 2.56 Hz, 1H), 7.36 (d, J = 8.96 Hz, 1H), 4.40 (t, 4.40 Hz, 2H), 4.25 (t, J = 4.80, 2H), 1.80 (s, 3H)	279		MS (ESI) m/z 613.19 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.85 (d, J = 4.72 Hz, 1H), 8.43 (s, 1H), 7.64 (d, J = 11.36 Hz, 1H), 7.60 (dd, J = 8.88, 2.56 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.6 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.40 (t, J = 5.0 Hz, 2H), 4.24 (t, J = 4.64, 2H), 3.58 (s, 3H), 1.78 (s, 3H)
277		MS (ESI) m/z 629.53 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.35 (bs, 1H), 8.84 (d, J = 4.8 Hz, 1H), 8.32 (s, 1H), 8.21 (s, 1H), 7.60 (dd, J = 8.8, 2.4 Hz, 1H), 7.49 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.8 Hz, 1H), 7.37 (d, J = 8.8 Hz, 1H), 4.42 (t, J = 4.4 Hz, 2H), 4.25 (t, J = 5.2 Hz, 2H), 1.71 (s, 3H)	280		MS (ESI) m/z 642.15 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.86 (d, J = 4.84 Hz, 1H), 8.31 (s, 1H), 8.05 (d, J = 6.32 Hz, 1H), 7.59 (dd, J = 8.88, 2.56 Hz, 1H), 7.51 (d, J = 4.84 Hz, 1H), 7.45 (d, J = 2.56 Hz, 1H), 7.35 (d, J = 9.0 Hz, 1H), 4.40 (t, J = 4.60 Hz, 2H), 4.22 (t, J = 4.32 Hz, 2H), 2.94 (s, 6H), 1.62 (s, 3H)
278		MS (ESI) m/z 613.09 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.21 (bs, 1H), 8.84 (d, J = 3.28 Hz, 1H), 8.26 (s, 1H), 8.07 (d, J = 5.96 Hz, 1H), 7.59 (d, J = 7.96 Hz, 1H), 7.47 (bs, 1H), 7.41 (s, 1H), 7.36 (d, J = 8.68 Hz, 1H), 4.42 (s, 2H), 4.24 (s, 2H), 3.58 (s, 3H), 1.72 (s, 3H)	281		MS (ESI) m/z 641.95 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.85 (d, J = 4.76 Hz, 1H), 8.40 (s, 1H), 7.64 (d, J = 11.52 Hz, 1H), 7.60 (dd, J = 2.60, 8.96 Hz, 1H), 7.48 (d, J = 4.76 Hz, 1H), 7.44 (d, J = 2.64 Hz, 1H), 7.36 (d, J = 8.92 Hz, 1H), 4.39 (t, J = 4.4 Hz, 2H), 4.22 (t, J = 4.36, 2H), 2.92 (s, 6H), 1.77 (s, 3H)

282		MS (ESI) m/z 700.01 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.84 (d, J = 4.84 Hz, 1H), 8.41 (s, 1H), 8.32 (d, J = 8.76 Hz, 1H), 7.81 (d, J = 8.76, Hz, 1H), 7.61 (dd, J = 2.60, 8.92 Hz, 1H), 7.50 (d, J = 4.80 Hz, 1H), 7.46 (d, J = 2.68 Hz, 1H), 7.36 (d, J = 9.04 Hz, 1H), 4.41 (bs, 2H), 4.24 (bs, 2H), 3.41(m, 4H), 2.14 -2.07 (m, 4H), 1.76 (s, 3H)	288		MS (ESI) m/z 642.18 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.84 (d, J = 4.56 Hz, 1H), 8.45 (s, 1H), 8.11 (d, J = 5.2 Hz, 1H), 7.61 (d, J = 7 Hz, 1H), 7.52 (d, J = 4.52 Hz, 1H), 7.45 (d, J = 2.12 Hz, 1H), 7.37 (d, J= 8.68 Hz, 1H), 4.42 (t, J = 4.6 Hz, 2H), 4.27 (t, J = 6.32 Hz, 2H), 2.89 (s, 6H), 1.83 (s, 3H)
283		MS (ESI) m/z 700.22 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.85 (d, J = 4.84 Hz, 1H), 8.41 (s, 1H), 8.34 (d, J = 8.8 Hz, 1H), 7.82 (d, J= 8.8, Hz, 1H), 7.61 (dd, J = 2.72, 8.92 Hz, 1H), 7.505 (d, J = 4.84 Hz, 1H), 7.46 (d, J = 2.72 Hz, 1H), 7.36 (m, 6H), 4.48 (s, 2H), 4.41 (t, J = 4.56 Hz, 2H), 4.24 (t, J = 4.56 Hz, 2H), 2.76 (s, 3H), 1.74 (s, 3H)	290		MS (ESI) m/z 576.13 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.26 (bs, 1H), 8.87 (d, J = 4.6 Hz, 1H), 8.37 (s, 1H), 8.05 (dd, J = 8.7, 2.0 Hz, 1H), 7.93 (s, 1H), 7.88 (d, J = 2.0 Hz, 1H), 7.52 (d, J = 3.1 Hz, 1H), 7.5 (s, 1H), 4.5 (t, J = 4.8 Hz, 2H), 4.25 (t, J = 4.6 Hz, 2H), 1.69 (s, 3H)
286		MS (ESI) m/z 538.22 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.85 (s, 1H), 8.80 (d, J = 4.8 Hz, 1H), 8.43 (d, J = 0.8 Hz, 1H), 8.33 (d, J = 0.8 Hz, 1H), 7.87 (d, J = 8.8 Hz, 1H), 7.62 (dd, J = 8.8, 2.0 Hz, 1H), 7.52 (d, J = 2.0 Hz, 1H), 7.45 (d, J = 4.8, 1H), 6.49-6.42 (m,1H), 5.97 (d, J = 16 Hz, 1H), 4.71 (d, J = 4.8 Hz, 1H), 2.39 (s 3H)	293		MS (ESI) m/z 613.15 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.81 (d, J = 4.80 Hz, 1H), 8.75 (bs, 1H), 8.30 (d, J = 8.36 Hz, 1H), 7.60 (dd, J = 8.96, 6.52, Hz, 1H), 7.90-7.42 (m, 2H), 7.38 (d, J = 8.88 Hz, 1H), 4.43 (t, J = 5.84 Hz, 2H), 4.30 (t, J = 4.24 Hz, 2H), 3.67 (s, 3H), 2.11 (s, 3H)

297		MS (ESI) m/z 658.33 [M+1]+; 1H NMR (400 MHz, DMSO-d6): δ 13.34 (bs, 1H), 8.80 (d, J = 4.7 Hz, 1H), 8.65 (d, J = 4.32 Hz, 1H), 8.61 (d, J = 8.72 Hz, 1H), 8.48 (s, 1H), 8.37 (d, J = 7.88 Hz, 1H), 8.26 (t, J = 7.76 Hz, 1H), 7.96 (d, J = 8.76 Hz, 1H), 7.77-7.74 (m, 1H), 7.58-7.55 (m, 1H), 7.46-7.44 (m, 2H), 7.30 (d, J = 8.96 Hz, 1H), 4.34 (d, J = 4.68 Hz, 2H), 4.20 (d, J = 4.40 Hz, 2H), 1.75 (s, 3H)
298		MS (ESI) m/z 602.95 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 13.13 (bs, 1H), 8.82 (d, J = 4.76 Hz, 1H), 8.41 (s, 1H), 7.60 (dd, J = 2.64, 8.92 Hz, 1H), 7.48-7.34 (m, 4H), 4.42 (t, J = 4.6 Hz, 2H), 4.26 (t, J = 4.0 Hz, 2H), 1.85 (s, 3H)
302		MS (ESI) m/z 609.60 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.90 (d, J = 4.6 Hz, 1H), 8.38 (s, 1H), 7.89 (d, J = 9.76 Hz, 1H), 7.60 (dd, J = 2.4, 8.84 Hz, 1H), 7.50 (d, J = 4.60 Hz, 1H), 7.47-7.20 (m, 3H), 4.43 (t, J = 4.80 Hz, 2H), 4.26 (t, J = 4.88 Hz, 2H), 1.83 (s, 3H)
303		MS (ESI) m/z 613.08 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.03 (s, 1H), 8.78 (d, J = 4.84 Hz, 1H), 8.32 (s, 1H), 8.05 (s, J = 9.60, 1H), 7.59 (dd, J = 8.96, 2.56 Hz, 1H), 7.49-7.35 (m, 4H), 4.41 (m, 2H), 4.27 (m, 2H), 3.86 (s, 3H), 1.89 (s, 3H)
304		MS (ESI) m/z 583.20 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.96 (s,1H), 7.95 (s, 1H), 7.86-7.85 (m, 3H), 7.53 (d, J = 7.96, 1H), 7.43-7.38 (m, 2H), 7.28 (d, J = 2.6, 1H), 7.20 (d, J = 8.8 Hz, 1H), 4.30 (s, 4H), 2.18 (s, 3H)
305		MS (ESI) m/z 638.07 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.21 (bs, 1H), 8.83 (s, 1H), 8.35 (s, 1H), 7.94 (s, 1H), 7.71 (s, 1H), 7.58 (dd, J = 2.44, 8.88 Hz, 1H), 7.47 (bs, 1H), 7.43 (s, 1H), 7.33 (d, J = 8.96 Hz, 1H), 4.35 (t, J = 5.32 Hz, 2H), 4.18 (t, J = 5.08 Hz, 2H), 1.71 (s, 3H)

306		309	
MS (ESI) m/z 577.08 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.90 (d, J = 4.68 Hz, 1H), 8.39 (s, 1H), 7.61-7.58 (m, 1H), 7.48 (d, J = 4.64 Hz, 1H), 7.44-7.35 (m, 3H), 4.40 (t, J = 5.18 Hz, 2H), 4.22 (t, J = 4.48 Hz, 2H), 1.73 (s, 3H)		MS (ESI) m/z 614.07 [M+1]+. 1H NMR (400 MHz, DMSO-D2O) δ 8.76 (s, 1H), 8.21 (s, 1H), 8.03 (s, 1H), 7.87 (s, 1H), 7.53 (d, J = 12 Hz, 1H), 7.41 (s, 1H), 7.30-7.26 (m, 2H), 4.34 (s, 2H), 4.17 (s, 2H), 3.41 (s, 3H), 1.50 (s, 3H)	
307		310	
MS (ESI) m/z 629.98 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.68 (s, 1H), 8.90 (d, J = 4.80 Hz, 1H), 8.53 (s, 1H), 7.72 (dd, J =7.60, 10.68 Hz, 1H), 7.61 (dd, J = 2.56, 8.88 Hz, 1H), 7.56 (d, J = 4.84 Hz, 1H), 7.44 (d, J = 2.64 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 4.41 (t, J = 4.56 Hz, 2H), 4.23 (t, J = 4.60 Hz, 2H), 3.57 (s, 3H), 1.74 (s, 3H)		MS (ESI) m/z 600.23 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.84 (d, J = 4.8 Hz, 1H), 8.41 (s, 1H), 8.32 (s, 1H), 8.29 (s, 1H), 8.11 (s, 1H), 7.58 (dd, J = 2.5 Hz, 2.6 Hz, 1H), 7.52 (d, J = 4.7 Hz, 1H), 7.42 (d, J = 2.6 Hz, 1H), 7.36 (d, J = 8 Hz, 1H), 4.41 (t, J = 5.2 Hz, 2H), 4.21 (t, J = 5.5 Hz, 2H), 1.54 (s, 3H)	
308		311	
MS (ESI) m/z 581.97 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.09 (s, 1H), 8.83 (d, J = 4.76 Hz, 1H), 8.26 (s, 1H), 7.73 (dd, J = 7.24, 10.48 Hz, 1H), 7.59 (dd, J = 2.48, 8.88 Hz, 1H), 7.44 (d, J = 4.72 Hz, 1H), 7.40 (d, J = 2.52 Hz, 1H), 7.35 (d, J = 9.04 Hz, 1H), 4.38 (t, J = 4.28 Hz, 2H), 4.22 (t, J = 4.56 Hz, 2H), 3.88 (s, 3H), 1.75 (s, 3H)		MS (ESI) m/z 592.10 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.72 Hz, 1H), 8.29 (s, 1H), 7.62-7.60 (m, 2H), 7.48 (d, J = 4.76 Hz, 1H), 7.43 (d, J = 2.60 Hz, 1H), 7.37 (d, J = 8.96 Hz, 1H), 4.59 (s, 2H), 4.41 (t, J = 4.68 Hz, 2H), 4.25 (t, J = 4.68 Hz, 2H), 2.95 (s, 6H), 1.81 (s, 3H)	

312		MS (ESI) m/z 541.97 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.23 (bs, 1H), 8.8 (d, J = 4.8 Hz, 1H), 8.52 (s, 1H), 8.4 (d, J = 7.8 Hz, 1H), 8.06 (d, J = 7.8 Hz, 1H), 7.59 (dd, J = 8.9, 2.6 Hz, 1H), 7.46 (d, J = 4.8 Hz, 1H), 7.44 (d, J = 2.5 Hz, 1H), 7.36 (d, J = 8.9 Hz, 1H), 4.42 (t, J = 4.6 Hz, 2H), 4.28 (t, J = 4.9 Hz, 2H), 1.97 (s, 3H).	317		MS (ESI) m/z 559.99 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.34 (bs, 1H), 8.81 (d, J = 4.4 Hz, 1H), 8.45 (s, 1H), 8.28 (s, 2H), 8.20 (s, 1H), 7.87 (s, 1H), 7.59-7.57 (m, 1H), 7.50-7.40 (m, 2H), 7.35 (d, J = 8.8 Hz, 1H), 4.49-4.30 (m, 2H), 4.29-4.15 (m, 2H), 1.77 (s, 3H)
313		MS (ESI) m/z 600.97 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.23 (bs, 1H), 8.77 (d, J = 4.76 Hz, 1H), 8.55 (s, 1H), 8.02 (d, J = 8.28 Hz, 1H), 7.92 (d, J = 7.24 Hz, 1H), 7.58 (dd, J = 2.56, 8.88 Hz, 1H), 7.46-7.44 (m, 2H), 7.35 (d, J = 8.96 Hz, 1H), 4.41 (t, J = 5.32 Hz, 2H), 4.26 (t, J = 4.52 Hz, 2H), 1.90 (s, 3H).	318		MS (ESI) m/z 662.04 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.03 (s, 1H), 8.78 (d, J = 4.76 Hz, 1H), 8.47 (s, 1H), 8.43 (s, 1H), 7.60-7.58 (m, 1H), 7.47-7.44 (m, 2H), 7.38 (d, J = 8.92 Hz, 1H), 4.44 (s, 4H), 3.27 (s, 3H), 2.33 (s, 3H)
316		MS (ESI) m/z 560.39 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.8 Hz, 1H), 8.40 (s, 1H), 8.17 (s, 1H), 7.92 (d, J = 8.36 Hz, 2H), 7.69 (d, J = 8.52 Hz, 1H), 7.60-7.58 (m, 1H), 7.48 (d, J = 4.84 Hz, 1H), 7.44 (d, J = 2.68 Hz, 1H), 7.35 (d, J = 8.96 Hz, 1H), 4.39 (t, J = 4.48 Hz, 2H), 4.23 (t, J = 4.48 Hz, 2H), 1.72 (s, 3H)	334		MS (ESI) m/z 586.3 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ / ppm = 9.20 (b, 2H), 8.30 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.55 (s, 1H), 7.44 (s, 1H), 7.39-7.35 (m, 2H), 4.53-4.48 (m, 2H), 4.41 (bt, 2H), 4.26 (bt, 2H), 3.57 (2H; observed by HSQC, signal is obscured by water peak in 1H-NMR), 3.22 (bt, 2H), 2.73 (s, 3H), 1.97 (s, 3H)

335		MS (ESI) m/z 600.7 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ / ppm = 10.30 (b, 1H), 8.27 (bs, 1H), 7.63-7.58 (m, 1H), 7.52 (bs, 1H), 7.45-7.34 (m, 4H), 4.88-4.12 (m, 6H), 3.04 (s, 3H), 2.72 (s, 3H), 1.92 (s, 3H) [remaining signals obscured by water or solvent peak]	345a	MS (ESI) m/z 676.6 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ / ppm = 8.31 (s, 1H), 8.19 (s, 1H), 8.07-8.04 (m, 1H), 7.93-7.88 (m, 1H), 7.80-7.74 (m, 2H), 7.59 (dd, J = 8.9, 2.6 Hz, 1H), 7.45 (s, 1H), 7.42 (d, J = 2.6 Hz, 1H), 7.35 (d, J = 8.9 Hz, 1H), 4.41 (t, J = 4.8 Hz, 2H), 4.27 (t, J = 4.8 Hz, 2H), 2.74 (s, 3H), 1.82 (s, 3H)
336		MS (ESI) m/z 600.3 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ / ppm = 10.46-10.14 (b, 1H), 8.26 (s, 1H), 7.60 (dd, J = 9.0, 2.8 Hz, 1H), 7.54 (s, 1H), 7.43 (s, 1H), 7.40-7.35 (m, 2H), 4.93-3.38 (m, 6H; partially obscured by water peak), 4.43-4.35 (b, 2H), 3.38-3.27 (b, 2H), 3.10 (s, 3H), 2.73 (s, 3H), 1.93 (s, 3H)	345b	MS (ESI) m/z 694.1 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ / ppm = 8.29 (s, 1H), 8.07 (s, 1H), 8.01-7.95 (b, 1H), 7.88 (dd, J = 7.7, 1.7 Hz, 1H), 7.65-7.55 (m, 3H), 7.46-7.39 (m, 3H), 7.33 (d, J = 9.0 Hz, 1H), 7.21-7.15 (b, 1H), 4.40 (t, J = 4.7 Hz, 2H), 4.27-4.20 (b, 2H), 2.74 (s, 3H), 1.74 (s, 3H)
337		MS (ESI) m/z 575.0 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ / ppm = 9.07 (d, J = 1.9 Hz, 1H), 8.30 (s, 1H), 8.16 (d, J = 1.9 Hz, 1H), 7.59 (dd, J = 8.9, 2.6 Hz, 1H), 7.43-7.41 (m, 2H), 7.35 (d, J = 8.9 Hz, 1H), 4.39 (t, J = 5.0 Hz, 2H), 4.26 (t, J = 5.0 Hz, 2H), 2.70 (s, 3H), 1.80 (s, 3H)	346	MS (ESI) m/z 681.3 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ / ppm = 8.33 (s, 1H), 8.23 (s, 1H), 7.62-7.56 (m, 2H), 7.51 (dt, J = 7.6, 1.4 Hz, 1H), 7.46-7.42 (m, 2H), 7.40-7.35 (m, 1H), 7.35 (d, J = 9.0 Hz, 1H), 7.32-7.28 (m, 1H), 4.43-4.34 (m, 2H), 4.29-4.18 (m, 4H), 2.73 (s, 3H), 1.81 (s, 3H)

351a	MS (ESI) m/z 590.0 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) d / ppm = 11.72 (s, 1H), 8.44 (s, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.42 (d, J = 2.7 Hz, 1H), 7.40 (s, 1H), 7.34 (d, J = 8.9 Hz, 1H), 7.17-7.16 (m, 1H), 7.07-7.05 (m, 1H), 4.40 (t, J = 4.9 Hz, 1H), 4.25 (t, J = 4.9 Hz, 2H), 2.68 (s, 3H), 1.88 (s, 3H)	355	MS (ESI) m/z 615.0 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.87 – 8.84 (m, 2H), 7.61 – 7.57 (m, 2H), 7.53 – 7.51 (m, 2H), 7.38 (d, J = 9.0 Hz, 1H), 7.35 (s, 1H), 4.23 (t, J = 5.5 Hz, 2H), 3.74 (t, J = 5.4 Hz, 2H), 2.75 (s, 3H), 1.07 (s, 6H)
351b	MS (ESI) m/z 574.0 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) d / ppm = 8.35 (s, 1H), 8.18-8.14 (m, 1H), 7.76-7.71 (m, 1H), 7.58 (dd, J = 8.9, 2.8 Hz, 1H), 7.42 (d, J = 2.8 Hz, 1H), 7.40 (s, 1H), 7.34 (d, J = 8.9 Hz, 1H), 4.38 (t, J = 4.9 Hz, 2H), 4.24 (t, J = 4.9 Hz, 2H), 2.69 (s, 3H), 1.84 (s, 3H)	357	MS (ESI) m/z 598.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.8 Hz, 1H), 8.51 (s, 1H), 8.27 – 8.26 (m, 1H), 8.16 (dd, J = 1.5, 0.6 Hz, 1H), 7.56 (dd, J = 8.9, 2.7 Hz, 1H), 7.49 (d, J = 4.8 Hz, 1H), 7.41 (d, J = 2.7 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 4.23 (t, J = 6.1 Hz, 2H), 3.62 (s, 3H), 2.89 (t, J = 6.1 Hz, 2H), 1.85 (s, 3H)
353	MS (ESI) m/z 584.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.77 (d, J = 4.9 Hz, 1H), 8.61 (s, 1H), 8.18 – 8.17 (m, 1H), 8.16 – 8.15 (m, 1H), 7.67 (s, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.47 (s, 1H), 7.46 (d, J = 2.3 Hz, 1H), 7.38 (d, J = 9.0 Hz, 1H), 4.30 (t, J = 6.2 Hz, 2H), 3.70 (s, 3H), 2.71 (t, J = 6.2 Hz, 2H)	358	MS (ESI) m/z 585.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.76 (d, J = 4.8 Hz, 1H), 8.63 (s, 1H), 8.24 (d, J = 7.9 Hz, 1H), 8.06 (d, J = 7.8 Hz, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.48 – 7.43 (m, 2H), 7.37 (d, J = 9.0 Hz, 1H), 4.44 (t, J = 5.1 Hz, 2H), 4.29 (t, J = 5.1 Hz, 2H), 1.98 (s, 3H).

359		MS (ESI) m/z 583.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.78 (d, J = 4.3 Hz, 1H), 8.55 (s, 1H), 7.97 (d, J = 8.3 Hz, 1H), 7.67 (d, J = 8.2 Hz, 1H), 7.60 (dd, J = 9.0, 2.6 Hz, 1H), 7.52 – 7.29 (m, 4H), 4.42 (t, J = 4.2 Hz, 2H), 4.26 (t, J = 4.4 Hz, 2H), 1.92 (s, 3H)	362		MS (ESI) m/z 630.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.8 Hz, 1H), 8.71 (s, 1H), 8.36 (s, 1H), 8.18 (d, J = 1.2 Hz, 1H), 7.57 (dd, J = 8.9, 2.7 Hz, 1H), 7.53 (d, J = 4.8 Hz, 1H), 7.46 (d, J = 2.7 Hz, 1H), 7.38 (d, J = 9.0 Hz, 1H), 4.76 (t, J = 4.4 Hz, 1H), 4.73 – 4.66 (m, 1H), 4.64 (s, 2H), 4.21 (t, J = 6.3 Hz, 2H), 2.93 (t, J = 6.3 Hz, 2H), 2.02 (s, 3H)
360		MS (ESI) m/z 567.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.77 (d, J = 4.8 Hz, 1H), 8.55 (s, 1H), 8.12 (d, J = 7.9 Hz, 1H), 8.06 (d, J = 7.8 Hz, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.51 (t, J = 54.6 Hz, 1H), 7.44 (d, J = 2.7 Hz, 1H), 7.43 (d, J = 4.7 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.42 (t, J = 5.0 Hz, 2H), 4.25 (t, J = 5.0 Hz, 2H), 1.84 (s, 3H)	366		MS (ESI) m/z 661.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.43 (s, 1H), 8.34 (s, 1H), 7.60 (dd, J = 8.9, 2.6 Hz, 1H), 7.48 (d, J = 10.1 Hz, 1H), 7.46 – 7.39 (m, 2H), 7.36 (d, J = 8.9 Hz, 1H), 4.39 (t, J= 4.9 Hz, 2H), 4.24 (t, J = 5.0 Hz, 2H), 3.83 (s, 2H), 3.06 – 2.92 (m, 4H), 2.77 (d, J = 4.0 Hz, 3H), 2.71 (s, 3H), 1.88 (s, 3H)
361		MS (ESI) m/z 632.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.8 Hz, 1H), 8.45 (s, 1H), 8.28 (s, 1H), 7.57 (dd, J = 8.9, 2.7 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.39 (d, J = 2.7 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.24 (t, J = 5.9 Hz, 2H), 3.60 (s, 3H), 2.89 (t, J = 5.9 Hz, 2H), 1.80 (s, 3H)	367		MS (ESI) m/z 648.3 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.34 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.55 (d, J = 10.1 Hz, 1H), 7.43 (s, 1H), 7.42 (d, J = 2.6 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.40 (t, J = 5.1 Hz, 2H), 4.25 (t, J = 5.1 Hz, 3H), 3.70 (bs, 4H), 2.99 (bs, 4H), 2.72 (s, 3H), 1.88 (s, 3H)

368		MS (ESI) m/z 563.3 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.39 (s, 1H), 7.60 (dd, J = 9.0, 2.7 Hz, 1H), 7.44 – 7.39 (m, 3H), 7.36 (d, J = 9.0 Hz, 1H), 4.39 (t, J = 5.1 Hz, 2H), 4.24 (t, J = 5.1 Hz, 2H), 2.72 (s, 3H), 2.50 (s, 3H), 1.91 (s, 3H)	371		MS (ESI) m/z 589.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.42 (s, 1H), 7.76 (d, J = 9.4 Hz, 1H), 7.63 (d, J = 9.2 Hz, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.44 – 7.39 (m, 2H), 7.36 (d, J = 9.0 Hz, 1H), 4.92 (hept, J = 6.0 Hz, 1H), 4.38 (t, J = 5.1 Hz, 2H), 4.21 (t, J = 5.1 Hz, 2H), 2.71 (s, 3H), 1.79 (s, 3H), 1.37 (d, J = 6.0 Hz, 6H)
369		MS (ESI) m/z 618.4 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.37 (s, 1H), 8.50 (s, 1H), 7.96 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.44 (s, 1H), 7.41 (d, J = 2.6 Hz, 1H), 7.38 (d, J = 9.0 Hz, 1H), 4.64 (d, J = 4.6 Hz, 2H), 4.43 (t, J = 5.0 Hz, 2H), 4.27 (t, J = 4.9 Hz, 2H), 2.79 (d, J = 4.0 Hz, 6H), 2.70 (s, 3H), 1.99 (s, 3H)	390		MS (ESI) m/z 666.3 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.29 (s, 1H), 8.17 (s, 1H), 8.03 (s, 1H), 7.58 (dd, J = 8.9, 2.7 Hz, 1H), 7.51 (s, 1H), 7.43 – 7.39 (m, 2H), 7.33 (d, J = 9.0 Hz, 1H), 4.68 (s, 2H), 4.37 (t, J = 4.4 Hz, 2H), 4.21 (t, J = 4.5 Hz, 2H), 2.71 (s, 3H), 1.79 (s, 3H)
370		MS (ESI) m/z 646.3 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.36 (s, 1H), 8.53 (s, 1H), 7.96 (s, 1H), 7.60 (dd, J= 8.9, 2.7 Hz, 1H), 7.44 (s, 1H), 7.42 (d, J = 2.6 Hz, 1H), 7.38 (d, J = 9.0 Hz, 1H), 4.89 (hept, J = 6.0 Hz, 1H), 4.62 (d, J = 4.9 Hz, 2H), 4.42 (t, J = 5.0 Hz, 2H), 4.26 (t, J = 5.0 Hz, 2H), 2.78 (d, J = 4.3 Hz, 6H), 2.69 (s, 3H), 1.93 (s, 3H), 1.42 (d, J = 6.0 Hz, 6H)	391		MS (ESI) m/z 631.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.31 (s, 1H), 8.05 (s, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.45 (s, 1H), 7.42 (d, J = 2.7 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.40 (t, J = 5.0 Hz, 2H), 4.24 (t, J = 5.0 Hz, 2H), 3.01 – 2.93 (m, 2H), 2.71 (s, 3H), 1.81 (s, 3H), 1.79 – 1.70 (m, 2H), 1.42 (h, J = 7.4 Hz, 2H), 0.93 (t, J = 7.3 Hz, 3H)

392		MS (ESI) m/z 674.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.66 (d, J = 2.8 Hz, 1H), 8.40 (s, 1H), 7.98 (dd, J = 9.1, 2.9 Hz, 1H), 7.90 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.45 (s, 1H), 7.43 (d, J = 2.6 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 4.42 (t, J = 5.1 Hz, 2H), 4.35 – 4.17 (m, 2H), 2.74 (s, 3H), 2.25 (s, 3H), 1.89 (s, 3H)	395		MS (ESI) m/z 656.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.66 (dd, J = 5.0, 1.7 Hz, 1H), 8.41 (s, 1H), 7.92 – 7.87 (m, 2H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.52 (dd, J = 7.7, 4.9 Hz, 1H), 7.45 (s, 1H), 7.44 (d, J = 2.7 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 4.41 (t, J = 5.0 Hz, 2H), 4.32 – 4.18 (m, 2H), 2.73 (s, 3H), 2.29 (s, 3H), 1.86 (s, 3H)
393		MS (ESI) m/z 656.0 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.76 (s, 1H), 8.42 (s, 1H), 7.86 (s, 1H), 7.64 – 7.56 (m, 2H), 7.52 (d, J = 5.0 Hz, 1H), 7.43 (s, 1H), 7.42 (d, J = 2.6 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 4.41 (t, J = 5.1 Hz, 2H), 4.26 (t, J = 5.0 Hz, 2H), 2.73 (s, 3H), 2.64 (s, 3H), 1.90 (s, 3H)	396		MS (ESI) m/z 670.0 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.39 (s, 1H), 7.87 (s, 1H), 7.69 (s, 2H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.44 (s, 1H), 7.42 (d, J = 2.7 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 4.41 (t, J = 5.1 Hz, 2H), 4.27 (t, J = 5.0 Hz, 2H), 2.73 (s, 3H), 2.70 (s, 6H), 1.91 (s, 3H)
394		MS (ESI) m/z 660.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.80 (d, J = 2.8 Hz, 1H), 8.63 (t, J = 1.7 Hz, 1H), 8.43 (s, 1H), 8.12 (ddd, J = 9.6, 2.8, 1.7 Hz, 1H), 7.87 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.43 (s, 1H), 7.41 (d, J = 2.6 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 4.41 (t, J = 5.1 Hz, 2H), 4.31 – 4.23 (m, 3H), 2.73 (s, 3H), 1.94 (s, 3H)	397		MS (ESI) m/z 685.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.44 (s, 1H), 8.24 (d, J = 2.0 Hz, 1H), 7.88 (d, J = 9.6 Hz, 1H), 7.83 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.43 (s, 1H), 7.41 (d, J = 2.6 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 7.10 (d, J = 9.2 Hz, 1H), 4.40 (t, J = 5.1 Hz, 2H), 4.26 (t, J = 5.0 Hz, 2H), 3.21 (s, 6H), 2.73 (s, 3H), 1.92 (s, 3H)

399	MS (ESI) 699.3 m/z [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.02 – 8.95 (m, 2H), 8.67 (tt, J = 7.7, 1.3 Hz, 1H), 8.36 (s, 1H), 8.22 – 8.15 (m, 2H), 7.85 (s, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.45 – 7.40 (m, 2H), 7.35 (d, J = 9.0 Hz, 1H), 6.22 (s, 2H), 4.37 (t, J = 4.9 Hz, 2H), 4.22 (t, J = 5.0 Hz, 2H), 2.71 (s, 3H), 1.87 (s, 3H)	405	MS (ESI) m/z 547.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.86 (d, J = 4.9 Hz, 1H), 8.38 (s, 1H), 7.60 (dd, J = 8.9, 2.6 Hz, 1H), 7.57 (d, J = 2.5 Hz, 1H), 7.54 (d, J = 4.9 Hz, 1H), 7.43 (d, J = 2.7 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 7.11 (d, J = 2.5 Hz, 1H), 4.39 (t, J = 5.0 Hz, 2H), 4.20 (t, J = 5.0 Hz, 2H), 3.99 (s, 3H), 1.72 (s, 3H).
403	MS (ESI) m/z 547.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.8 Hz, 1H), 8.33 (s, 1H), 7.88 (d, J = 8.4 Hz, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.41 (d, J = 2.6 Hz, 1H), 7.37 (dd, J = 8.9, 2.9 Hz, 2H), 4.42 (t, J = 5.1 Hz, 2H), 4.24 (t, J = 5.1 Hz, 2H), 3.97 (s, 3H), 1.83 (s, 3H)	406	MS (ESI) m/z 601.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.9 Hz, 1H), 8.44 (s, 1H), 8.05-8.00 (m, 1H), 7.84 (d, J = 9.1 Hz, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.51 (d, J = 4.9 Hz, 1H), 7.45 (d, J = 2.6 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.41 (t, J = 4.9 Hz, 2H), 4.25 (t, J = 4.9 Hz, 2H), 1.78 (s, 3H)
404	MS (ESI) m/z 547.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.8 Hz, 1H), 8.41 (s, 1H), 7.76 (d, J = 9.3 Hz, 1H), 7.70 (d, J = 9.3 Hz, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.6 Hz, 1H), 7.36 (d, J = 8.9 Hz, 1H), 4.39 (t, J = 5.0 Hz, 2H), 4.21 (t, J = 5.0 Hz, 2H), 4.04 (s, 3H), 1.74 (s, 3H)	407	MS (ESI) m/z 569.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.8 Hz, 1H), 8.48 (s, 1H), 8.17 (d, J = 9.5 Hz, 1H), 7.60 (dd, J = 8.9, 2.6 Hz, 1H), 7.50 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.7 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 4.42 (t, J = 5.0 Hz, 2H), 4.26 (t, J = 5.0 Hz, 2H), 1.84 (s, 3H)

408		MS (ESI) m/z 617.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.8 Hz, 1H), 8.54 (s, 1H), 8.19 (s, 1H), 7.80 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.47 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.7 Hz, 1H), 7.36 (d, J = 8.9 Hz, 1H), 4.57 (bs, 2H), 4.40 (t, J = 5.0 Hz, 2H), 4.26 (t, J = 5.0 Hz, 2H), 2.87 (s, 6H), 1.80 (s, 3H)
409		MS (ESI) m/z 612.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.55 (s, 1H), 8.26 (s, 1H), 8.16 (bd, J = 1.1 Hz, 1H), 7.56 (dd, J = 8.9, 2.7 Hz, 1H), 7.44 (s, 1H), 7.40 (d, J = 2.6 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 4.23 (t, J = 6.1 Hz, 2H), 3.63 (s, 3H), 2.90 (t, J = 6.1 Hz, 2H), 2.70 (s, 3H), 1.94 (s, 3H).
412		MS (ESI) m/z 573.9 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.81 (d, J = 4.9 Hz, 2H), 8.45 (s, 1H), 8.26 (bs, 1H), 8.16 (bs, 1H), 7.59 (dd, J = 8.8, 2.6 Hz, 1H), 7.46 (bs, 1H), 7.44 (bs, 1H), 7.35 (d, J = 9.0 Hz, 1H), 4.40 (t, J = 5.3 Hz, 2H), 4.24 (t, J = 5.3 Hz, 2H), 2.87 (d, J = 4.5 Hz, 3H), 1.78 (s, 3H)
413		MS (ESI) m/z 588.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.83 (d, J = 4.8 Hz, 1H), 8.37 (s, 1H), 7.98 (d, J = 1.4 Hz, 1H), 7.65 (d, J = 2.0 Hz, 1H), 7.60 (dd, J = 8.9, 2.6 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.45 (d, J = 2.7 Hz, 1H), 7.35 (d, J = 9.0 Hz, 1H), 4.40 (t, J = 5.3 Hz, 2H), 4.23 (t, J = 5.3 Hz, 2H), 3.05 (s, 3H), 3.01 (s, 3H), 1.69 (s, 3H)
426		MS (ESI) m/z 651.6 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.70 (m, 1H), 8.41 (s, 1H), 8.03 (s, 1H), 7.99 (tdd, J = 7.7, 3.1, 1.8 Hz, 1H), 7.85 (s, 1H), 7.66 (d, J = 7.8 Hz, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.51 (m, 1H), 7.43 (d, J = 2.6 Hz, 1H), 7.42 (d, J = 2.7 Hz, 1H), 7.34 (d, J = 9.0 Hz, 1H), 4.39 (t, J = 5.0 Hz, 2H), 4.26 (t, J = 5.0 Hz, 2H), 2.69 (s, 3H), 1.85 (s, 3H)
427		MS (ESI) m/z 672.5 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.27 (s, 1H), 7.98 (s, 1H), 7.70 (s, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.41 (d, J = 2.6 Hz, 1H), 7.39 (s, 1H), 7.35 (d, J = 9.0 Hz, 1H), 4.39 (t, J = 5.1 Hz, 2H), 4.24 (t, J = 5.0 Hz, 3H), 3.59-3.50 (m, 2H), 3.26-3.10 (m, 6H), 2.93 (s, 3H), 2.69 (s, 3H), 1.84 (s, 3H)

436		MS (ESI) m/z 666.5 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.71 (bs, 2H), 8.33 (s, 1H), 8.32 (s, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.54 (br, 1H), 7.45 (s, 1H), 7.44 (d, J = 2.6 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.40 (t, J = 4.5 Hz, 2H), 4.27 (d, J = 4.5 Hz, 2H), 2.74 (s, 3H), 2.06 (bs, 3H), 1.84 (s, 3H)	439b		MS (ESI) m/z 597.0 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.44 (s, 1H), 7.72 (s, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.42 (d, J = 2.7 Hz, 1H), 7.41 (s, 1H), 7.35 (d, J = 9.0 Hz, 1H), 7.15 (t, J = 54.2 Hz, 1H), 4.38 (t, J = 5.0 Hz, 3H), 4.21 (t, J = 5.0 Hz, 3H), 2.69 (s, 3H), 1.78 (s, 3H)
438		MS (ESI) m/z 690.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.65 (d, J = 2.9 Hz, 1H), 8.41 (s, 1H), 7.98 (s, 1H), 7.88 (dd, J = 9.0, 2.9 Hz, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.45 (s, 1H), 7.43 (d, J = 2.7 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 6.89 (t, J = 53.7 Hz, 1H), 4.48-4.38 (m, 2H), 4.37 – 4.19 (m, 2H), 2.73 (s, 3H), 2.18 (s, 3H), 1.89 (s, 3H)	440		MS (ESI) m/z 671.9 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.73 (dd, J = 5.2, 1.7 Hz, 1H), 8.41 (s, 1H), 7.98 (bd, J = 5.9 Hz, 2H), 7.64 – 7.56 (m, 2H), 7.45 (s, 1H), 7.44 (d, J = 2.7 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 6.84 (t, J = 53.7 Hz, 1H), 4.48 – 4.37 (m, 2H), 4.37 – 4.16 (m, 2H), 2.72 (s, 3H), 2.27 (s, 3H), 1.87 (s, 3H).
439a		MS (ESI) m/z 624.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.44 (s, 1H), 7.77 (s, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.42 (d, J = 2.7 Hz, 1H), 7.41 (s, 1H), 7.36 (d, J = 9.0 Hz, 1H), 7.16 (t, J = 54.4 Hz, 1H), 4.39 (t, J = 5.0 Hz, 2H), 4.22 (t, J = 5.0 Hz, 2H), 2.97 (s, 6H), 2.69 (s, 3H), 1.82 (s, 3H)	449		MS (ESI) m/z 656.6 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.36 (s, 1H), 8.05 (s, 1H), 7.70 – 7.17 (m, 5H), 4.49 (s, 2H), 4.42 (t, J = 5.0 Hz, 2H), 4.27 (t, J = 5.0 Hz, 2H), 2.86 (s, 6H), 2.72 (s, 3H), 1.87 (s, 3H)

451		MS (ESI) m/z 731.3 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.08 (s, 1H), 9.79 (s, 1H), 8.40 (s, 1H), 7.97 (s, 1H), 7.62 (dd, J = 8.9, 2.7 Hz, 1H), 7.51 (s, 1H), 7.44 – 7.36 (m, 2H), 7.25 (s, 1H), 4.51 (s, 2H), 4.43 (d, J = 5.3 Hz, 2H), 4.27 (d, J = 5.1 Hz, 2H), 3.56 (s, 3H), 2.85 (s, 6H), 2.74 (s, 3H), 1.83 (s, 3H)	458		MS (ESI) m/z 640.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.78 (d, J = 4.8 Hz, 1H), 8.39 (s, 1H), 8.04 (s, 1H), 7.63 – 7.17 (m, 5H), 4.54 – 4.42 (m, 2H), 4.39 (t, J = 5.0 Hz, 2H), 4.24 (t, J = 5.0 Hz, 2H), 2.83 (s, 6H), 1.79 (s, 3H)
456		MS (ESI) m/z 601.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.80 (d, J = 4.7 Hz, 1H), 8.35 (s, 1H), 8.07 – 8.03 (m, 1H), 7.60 – 7.56 (m, 1H), 7.55 (d, J = 2.7 Hz, 1H), 7.45 (d, J = 4.8 Hz, 1H), 7.41 (d, J = 2.7 Hz, 1H), 7.32 (d, J = 9.0 Hz, 1H), 4.36 (t, J = 5.0 Hz, 2H), 4.20 (t, J = 5.0 Hz, 2H), 1.70 (s, 3H)	460		LCMS: 708.6 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ 8.25 (s, 1H), 8.05 (s, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.44 – 7.38 (m, 2H), 7.35 (d, J = 8.9 Hz, 1H), 4.38 (t, J = 5.0 Hz, 2H), 4.24 (t, J = 5.0 Hz, 2H), 2.75 (d, J = 1.6 Hz, 3H), 2.69 (s, 3H), 1.78 (s, 3H)
457		MS (ESI) m/z 604.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.78 (d, J = 4.8 Hz, 1H), 8.36 (s, 1H), 7.78 (d, J = 9.3 Hz, 1H), 7.70 (d, J = 9.2 Hz, 1H), 7.57 (dd, J = 9.0, 2.7 Hz, 1H), 7.44 (d, J = 4.8 Hz, 1H), 7.39 (d, J = 2.7 Hz, 1H), 7.33 (d, J = 9.0 Hz, 1H), 4.68 – 4.55 (m, 2H), 4.36 (t, J = 5.1 Hz, 2H), 4.20 (d, J = 5.2 Hz, 2H), 3.62 (s, 2H), 2.96 – 2.87 (m, 7H), 1.77 (s, 3H)	461		LCMS: 652.5 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ 8.76 (s, 2H), 8.34 (s, 1H), 8.28 (s, 1H), 8.01 (d, J = 7.9 Hz, 1H), 7.61 (d, J = 11.7, 8.4, 3.8 Hz, 2H), 7.46 – 7.41 (m, 2H), 7.36 (d, J = 9.0 Hz, 1H), 4.41 (t, J = 5.0 Hz, 2H), 4.27 (t, J = 5.0 Hz, 2H), 2.72 (s, 3H), 1.84 (s, 3H)

462		LCMS: 652.5.6 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ 8.69 (dd, J = 4.9, 1.6 Hz, 1H), 8.40 (s, 1H), 8.30 (s, 1H), 8.03 (td, J = 7.7, 1.8 Hz, 1H), 7.84 (d, J = 8.0 Hz, 1H), 7.61 – 7.52 (m, 2H), 7.45 – 7.41 (m, 2H), 7.35 (d, J = 9.0 Hz, 1H), 4.40 (t, J = 5.0 Hz, 2H), 4.27 (t, J = 5.1 Hz, 2H), 2.70 (s, 3H), 1.82 (s, 3H)	467		LCMS: 651.8 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ 8.36 (s, 1H), 8.24 (s, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.53 (s, 5H), 7.43 (d, J = 3.1 Hz, 2H), 7.36 (d, J = 9.0 Hz, 1H), 4.40 (t, J = 5.0 Hz, 2H), 4.26 (t, J = 4.9 Hz, 2H), 2.71 (s, 3H), 1.83 (s, 3H)
463		LCMS: 666.6 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ 8.76 (d, J = 5.5 Hz, 1H), 8.31 (d, J = 6.8 Hz, 2H), 7.67 (s, 1H), 7.59 (dd, J = 8.9, 2.8 Hz, 2H), 7.45 – 7.41 (m, 2H), 7.35 (d, J = 9.0 Hz, 1H), 4.40 (t, J = 5.0 Hz, 2H), 4.27 (t, J = 5.0 Hz, 2H), 2.73 (s, 3H), 2.67 (s, 3H), 1.84 (s, 3H)	488		LCMS: 635.9 [M+H]+; 1H NMR (400 MHz, Methanol-d4) δ 8.40 (s, 1H), 7.93 (d, J = 9.8 Hz, 1H), 7.58 – 7.51 (m, 2H), 7.42 (d, J = 2.6 Hz, 1H), 7.29 (d, J = 8.9 Hz, 1H), 7.23 (s, 1H), 4.48 (t, J = 4.8 Hz, 2H), 4.40 (t, J = 4.7 Hz, 2H), 2.91 (s, 3H), 2.11 (s, 3H)
464		LCMS: 652.5 [M+H]+; 1H NMR (400 MHz, DMSO-d6); 1H NMR (400 MHz, DMSO-d6) δ 8.84 (s, 2H), 8.35 (s, 1H), 8.30 (s, 1H), 7.69 (d, J = 5.5 Hz, 2H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.46 – 7.41 (m, 2H), 7.36 (d, J = 9.0 Hz, 1H), 4.40 (t, J = 4.9 Hz, 2H), 4.27 (t, J = 4.9 Hz, 2H), 2.73 (s, 3H), 1.84 (s, 3H)	490		MS (ESI) m/z 593.7 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.14 (dd, J = 7.3, 1.5 Hz, 1H), 8.04 (d, J = 9.7 Hz, 1H), 7.61 (dd, J = 8.9, 2.7 Hz, 1H), 7.58 (s, 1H), 7.51 – 7.46 (m, 1H), 7.39 (s, 1H), 7.36 (d, J = 4.1 Hz, 1H), 7.33 (d, J = 2.6 Hz, 1H), 7.31 – 7.25 (m, 1H), 7.22 (s, 0H), 4.50 – 4.08 (m, 4H), 2.78 (s, 3H), 1.84 (s, 3H)

493		MS (ESI) m/z 627.12 [M-1]-; 1H NMR (400 MHz, DMSO-d6) δ 13.29 (bs, 1H), 8.84 (d, J = 4.68, 1H), 8.38 (s, 1H), 7.89 (s, 1H), 7.60 (dd, J = 2.56, 9.3 Hz, 1H), 7.47 (d, J = 4.6 Hz, 1H), 7.42 (d, J = 1.96 Hz, 1H),7.34 (d, J = 8.84 Hz, 1H) 4.39 (t, J = 4.7 Hz, 2H), 4.23 (t, J = 4.76, 2H), 3.60 (s, 3H), 1.75 (s, 3H)	499		MS (ESI) m/z 593.13 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.03 (s, 1 H), 8.85 (d, J = 4.8 Hz, 1H), 7.83 (d, J = 3.6 Hz, 2H), 7.64 (s, 1H), 7.60 (dd, J = 8.8Hz, 2.46 Hz, 1H), 7.32 (d, J = 8.8 Hz, 1H), 6.98 (s, 1H), 3.63 (t, J = 6.8 Hz, 2H), 2.90 (t, J = 7.2 Hz, 2H), 2.39 (s, 3H)
497		MS (ESI) m/z 619.47 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.80 (d, J = 4.8 Hz, 1H), 8.54 (s, 1H), 8.28 (s, 1H), 7.60 (dd, J = 8.88, 2.68 Hz 1H), 7.47-7.21 (m, 4H), 4.42 (t, J = 5.12, 2H), 4.28 (t, J = 4.88 Hz, 2H), 1.89 (s, 3H)	500		MS (ESI) m/z 599.53 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.77 (d, J = 4.92 Hz, 1H), 8.08 (d, J = 9.72 Hz, 1H), 7.61 (dd, J = 8.80, 2.64 Hz, 1H), 7.53 (d, J = 4.96 Hz, 1H), 7.49-7.22 (m, 3H), 4.44 (t, J = 5.40 Hz, 2H), 4.29 (t, J = 4.84 Hz, 2H). 2.60-2.40 (merged, 3H), 1.96 (s, 3H)
498		MS (ESI) m/z 619.47 [M+1]+. 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.8Hz, 1H), 8.44 (s, 1H), 7.66-7.59 (m, 5H), 4.42 (t, J = 9.04 Hz, 2H), 4.27 (t, J = 8.6Hz, 2H), 1.84 (s, 3H)	504		MS (ESI) m/z 603.0 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.80 Hz, 1H), 8.46 (s, 1H), 8.05 (d, J = 9.60 Hz, 1H), 7.65 (d, J = 8.32 Hz, 1H), 7.56 (d, J = 11.32 Hz, 1H), 7.51-7.36 (m, 2H), 4.45 (t, J = 4.72 Hz, 2H), 4.28 (t, J = 6.96 Hz, 2H), 1.86 (s, 3H)

506		MS (ESI) m/z 571.10 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.84 (d, J = 4.48 Hz, 1H), 8.41 (s, 1H), 7.74-7.70 (m, 1H), 7.62 (d, J = 8.36 Hz, 1H), 7.55 (d, J = 11.28 Hz, 1H), 7.48 (d, J = 4.48 Hz, 1H), 4.42 (t, J = 4.20 Hz, 2H). 4.23 (t, J = 4.20 Hz, 2H), 1.75 (s, 3H)	
507		MS (ESI) m/z 588.17 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 13.30 (bs, 1H), 9.71 (bs, 1H), 8.81 (d, J = 4.76 Hz ,1H), 8.35 (s, 1H), 7.91(d, J = 8.52 Hz,1H),7.68 (d, J = 8.4 Hz, 1H), 7.60 (dd, J = 2.40, 8.84 Hz, 1H), 7.46 (d, J = 4.72 Hz, 1H),7.42 (d, J = 2.5 Hz, 1H) ,7.37 (d, J = 8.88 Hz, 1H), 4.40 (s, 2H), 4.25 (s, 2H), 3.4-3.41 (m, 2H), 3.33 (t, J = 3.84 Hz ,2H), 2.92 (s, 6H) ,1.83 (s, 3H)	
508		MS (ESI) m/z 592.16 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 10.23 (bs, 1H), 8.81 (d, J = 4.60 Hz, 1H), 8.34 (s, 1H), 8.09 (d, J = 10.08 Hz, 1H), 7.61-7.58 (m, 1H), 7.48 (d, J = 4.64 Hz, 1H), 7.42 (d, J = 2.0 Hz, 1H), 7.38 (d, J = 8.88 Hz, 1H), 4.58 (bs, 2H), 4.43 (t, J = 6.08 Hz, 2H), 4.28 (t, J = 5.24 Hz, 2H), 2.90 (s, 6H), 1.87 (s, 3H)	
509		MS (ESI) m/z 608.16 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.24 (bs, 1H), 8.82 (d, J = 4.72 Hz, 1H), 8.35 (bs, 1H), 7.79 (bs, 1H), 7.60 (dd, J = 2.44, 8.84 Hz, 1H), 7.47 (d, J = 4.72 Hz, 1H), 7.42 (d, J = 2.56 Hz, 1H), 7.35 (d, J = 8.92 Hz, 1H), 4.39 (t, J = 5.4 Hz, 2H), 4.23 (t, J = 6.12 Hz, 2H), 3.75 (bs, 2H), 2.26 (bs, 6H), 1.77 (s, 3H)	
510		MS (ESI) m/z 599.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ, 8.84 (d, J = 4.76 Hz, 1H), 8.26 (s, 2H), 7.61 (dd, J = 8.84, 2.52 Hz, 1H), 7.48 (d, J = 4.76, Hz, 1H), 7.43 (d, J = 2.56 Hz, 1H), 7.37 (d, J = 8.96 Hz, 1H), 4.55 (bs, 2H), 4.42 (bs, 2H), 4.27 (b s, 2H), 2.90 (bs, 6H), 1.82 (s, 3H)	
511		MS (ESI) m/z 598.21 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 8.84 (d, J = 4.72 Hz,1H), 8.32 (s, 1H), 8.24 (s, 1H), 7.59 (dd, J = 2.44, 2.48 Hz, 1H), 7.45 (d, J = 4.72 Hz, 1H), 7.40-7.36 (m, 2H), 6.06 (s, 1H), 4.59 (bs, 2H), 4.43 (t, J = 4.36 Hz, 2H), 4.24 (t, J = 4.68 Hz, 2H), 2.93 (bs, 6H), 1.69 (s, 3H)	

512		515		MS (ESI) m/z 624.14 [M+1]+. 1H-NMR (400 MHz, DMSO-d6) δ 9.69 (bs, 1H), 8.80 (d, J = 4.4 Hz, 1H), 8.46 (s, 1H), 8.05 (bs, 1H), 7.68-7.35 (m, 5H), 4.64 (bs, 2H), 4.41 (s, 2H), 4.26 (s, 2H), 2.83 (bs, 6H), 1.79 (s, 3H)
513		MS (ESI) m/z 574.38.[M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 9.96 (bs, 1H), 8.82 (d, J = 4.72 Hz, 1H), 8.36 (s, 1H), 8.08 (s, 1H), 7.83 (s, 1H), 7.61 (dd, J = 2.32, 8.84 Hz, 1H), 7.49 (d, J = 4.68 Hz),7.44 (d, J= 2.32, 1H),7.38 (d = 8.96 Hz), 4.46 (s, 2H), 4.41 (t, J = 5.12 Hz, 2H), 4.25 (t, J = 5.08 Hz, 2H), 2.83 (s, 6H), 1.79 (s, 3H)
514		MS (ESI) m/z 588.22 [M+1]+. 1H-NMR (400 MHz, DMSO-d6) δ 9.49 (bs, 1H), 8.86 (dd, J = 4.76, 8.85 Hz, 1H), 8.28 (s, 1H), 7.97 (s, 1H), 7.60 (s, 1H),7.59 (d, J = 7.59 Hz, 1H), 7.45 (d, J = 2.28, Hz, 1H), 7.42 (d, J = 2.52 Hz, 1H), 7.35 (d, J = 8.92 Hz, 1H), 4.40 (t, J = 5.76 Hz, 2H), 4.22 (t, J = 6.32 Hz, 2H), 3.51 (t, J = 4.56. Hz, 2H), 3.18 (t, J = 8.0 Hz, 2H), 2.88 (s, 6H), 1.75 (s, 3H)
516		MS (ESI) m/z 607.9 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.81 (d, J = 4.76 Hz, 1H), 8.39 (s, 1H), 7.75 (s, 1H), 7.59 (dd, J = 8.8, 2.4 Hz, 1H), 7.46 (d, J = 4.76 Hz, 1H), 7.42 (d, J = 2.56 Hz, 1H), 7.35 (d, J = 9.0 Hz, 1H), 4.39 (t, J = 5.8 Hz, 2H), 4.23 (t, J = 5.3 Hz, 2H), 3.63 (s, 2H), 2.28 (s, 6H), 1.77 (s, 3H)
517		MS (ESI) m/z 592.02 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.98 (bs, 1H), 8.81 (d, J = 4.68 Hz, 1H), 8.41 (s, 1H), 8.00 (d, J = 6.56 Hz, 1H), 7.60 (dd, J = 8.76, 2.28 Hz, 1H), 7.47 (d, J = 4.68 Hz, 1H), 7.42 (d, J = 2.23 Hz, 1H), 7.37 (d, J = 8.96 Hz, 1H), 4.53 (s, 2H), 4.41 (t, J = 6.24 Hz, 2H), 4.26 (t, J = 6.28 Hz, 2H), 2.89 (s, 6H), 1.80 (s, 3H)

518		MS (ESI) m/z 642.14 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.79 (d, J = 4.4 Hz, 1H), 8.45 (s, 1H), 7.49 (m, 5H), 4.63 (bs, 2H), 4.43 (bs, 2H), 4.29 (bs, 2H), 2.83 (bs, 6H), 1.86 (s, 3H)	530 MS (ESI) m/z 623.97 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.28 (bs, 1H), 8.80 (d, J = 4.72 Hz, 1H), 8.27 (s, 1H), 7.95 (s, 1H), 7.62-7.32 (m, 5H), 4.62 (s, 2H), 4.41 (t, J = 4.92 Hz, 2H), 4.26 (t, J = 5.40 Hz, 2H), 2.87 (s, 6H), 1.79 (s, 3H)
520		MS (ESI) m/z 678.03 [M+1]+. 1H NMR (400 MHz, DMSO-d6) δ 12.65 (bs, 1H), 8.89 (d, J = 4.12 Hz, 1H), 8.48 (s, 1H), 7.90 (s, 1H), 7.65-7.35 (m, 5H), 4.40 (t, J = 5.18 Hz, 2H), 4.23 (t, J = 6.72 Hz, 2H), 3.56 (s, 3H), 1.71 (s, 3H)	531 MS (ESI) m/z 640.12 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 13.40 (bs, 1H), 9.88 (bs,1H), 8.83 (d, J = 4.48 Hz, 1H), 8.34 (s, 1H),7.74-7.35 (m, 6H), 4.54 (s, 2H), 4.41 (t, J = 5.6 Hz, 2H), 4.25 (t, J = 5.6 Hz, 2H), 2.94 (s, 6H), 1.76 (s, 3H)
529		MS (ESI) m/z 638.20 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.59 (bs, 1H), 8.38 (s, 1H), 8.04 (d, J = 8.72 Hz, 1H), 7.77 (d, J = 8.20 Hz, 1H), 7.80-7.55 (m, 1H), 7.42-7.40 (m, 2H), 7.35 (d, J = 9.00 Hz, 1H), 4.40 (t, J = 4.52 Hz, 2H), 4.25 (t, J = 5.16 Hz, 2H), 2.69 (s, 3H), 2.60-2.20 (merged, 8H), 1.83 (s, 3H)	532 MS (ESI) m/z 658.20 [M+1]+. 1H NMR (400 MHz, DMSO-d6) δ 10.03 (bs, 1H), 8.84 (d, J = 3.04 Hz, 1H), 8.28 (s, 1H), 7.60 (bs, 2H), 7.47-7.35 (m, 3H), 4.59 (s, 2H), 4.41 (t, J = 4.92 Hz, 2H), 4.26 (t, J = 4.72 Hz, 2H), 2.90 (s, 6H), 1.76 (s, 3H)

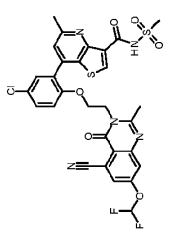
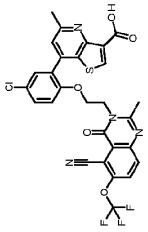
533		MS (ESI) m/z 578.18 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.76 Hz, 1H), 8.37 (s, 1H), 7.67 (d, J = 10.08Hz, 1H), 7.59-7.56 (dd, J = 2.6, 2.56 Hz, 1H), 7.45 (d, J = 4.64 Hz, 1H), 7.40-7.35 (m, 2H), 5.97 (s, 1H), 4.69 (s, 2H), 4.40 (t, J = 4.64 Hz, 2H), 4.21 (t, J = 4.64 Hz, 2H), 3.42 (s, 3H), 1.68 (s, 3H)	537		MS (ESI) m/z 615.03 [M-1] ; 1H NMR (400 MHz, DMSO-d6) δ 8.85 (d, J = 4.5 Hz, 1H), 8.49 (s, 1H), 7.76-7.33 (m, 6H), 4.88 (t, J = 5.4 Hz, 2H), 4.23 (t, J = 6.1 Hz, 2H), 1.69 (s, 3H)
534		MS (ESI) m/z 594.04. [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.81 (d, J = 4.72 Hz, 1H), 8.37 (s, 1H), 7.73 (d, J = 10.16 Hz, 1H), 7.58-7.56 (dd, J = 2.48, 2.28 Hz, 1H), 7.44-7.37 (m, 3H), 5.98 (s, 1H) 4.40 (t, J = 5.30 Hz, 2H), 4.20 (t, J = 4.54 Hz, 2H), 3.98 (s, 2H), 2.04 (s, 3H), 1.66 (s, 3H)	538		MS (ESI) m/z 608.15 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.39 (bs, 1H), 8.85 (d, J = 4.7 Hz, 1H), 8.43 (s, 1H), 7.83-7.33 (m, 6H), 4.39 (bs, 2H), 4.25 (bs, 2H), 1.72 (s, 3H)
536		MS (ESI) m/z 601.05 [M+1]+. 1H NMR (400 MHz, DMSO-d6) δ 8.85 (d, J = 4.72 Hz, 1H), 8.47 (s, 1H), 7.72-7.34 (m, 6H), 4.39 (t, J = 6.4 Hz, 2H), 4.22 (t, J = 6.4 Hz, 2H), 1.71 (s, 3H)	539		MS (ESI) m/z 633.2 [M+1]+. 1H NMR (400 MHz, DMSO-d6) δ 13.49 (bs, 1H), 8.84 (d, J = 4.8 Hz, 1H), 8.49 (s, 1H), 7.75-7.24 (m, 7H), 4.39 (t, J = 4.16 Hz, 2H), 4.24 (t, J = 5.0 Hz, 2H), 1.70 (s, 3H)

540		MS (ESI) m/z 651.13 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.85 (d, J = 4.76 Hz, 1H), 8.48 (s, 1H), 7.78-7.48 (m, 4H), 7.44 (d, J = 2.6 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.39 (t, J = 4.56 Hz, 2H), 4.29 (t, J = 4.52 Hz, 2H), 1.70 (s, 3H)	543		MS (ESI) m/z 626.11 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 8.85 (d, J = 4.76 Hz, 1H), 8.34 (s, 1H), 7.76 (s, 1H), 7.60 (dd, J =8.80, 2.44 Hz, 1H), 7.49 (d, J = 4.68 Hz, 1H), 7.43 (d, J = 2.48 Hz, 1H), 7.35 (d, J = 8.96 Hz, 1H) 4.40 (t, J = 4.32 Hz, 2H), 4.25 (t, J = 4.12 Hz, 2H), 1.74 (s, 3H)
541		MS (ESI) m/z 649.16 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.85 (d, J = 4.76, 1H), 8.47 (s, 1H), 7.93 (s, 1H), 7.93 (s, 1H), 7.59 (dd, J = 8.88, 2.52 , 1H), 7.48-6.83 (m, 5H), 4.38 (t, J = 5.48 Hz, 2H), 4.22 (t, J=4.84, 2H), 1.73(s, 3H)	544		MS (ESI) m/z 626.11 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 8.85 (d, J = 4.76 Hz, 1H), 8.34 (s, 1H), 7.76 (s, 1H), 7.60 (dd, J =8.80, 2.44 Hz, 1H), 7.49 (d, J = 4.68 Hz, 1H), 7.43 (d, J = 2.48 Hz, 1H), 7.35 (d, J = 8.96 Hz, 1H) 4.40 (t, J = 4.32 Hz, 2H), 4.25 (t, J = 4.12 Hz, 2H), 1.74 (s, 3H)
542		MS (ESI) m/z 635.09 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.33 (bs, 1H), 8.83 (d, J = 4.76 Hz, 1H), 8.367 (s, 1H), 7.76 (d, J = 1.32, 1H), 7.58 (dd, J = 2.6 Hz, J = 8.88 Hz, 1H), 7.48 (d, J = 4.76 Hz, 1H), 7.43 (d, J = 1.76 Hz, 1H) 7.34 (d, J = 8.92 Hz, 1H), 4.39 (s, 2H), 4.23 (s, 2H), 1.74 (s, 3H)	545		MS (ESI) m/z 601.18 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.76 Hz, 1H), 8.44 (s, 1H), 7.69 (d, J = 10.76 Hz, 1H), 7.60 (dd, J = 2.64, 8.76 Hz, 1H), 7.48 (d, J = 4.68 Hz, 1H), 7.42 (d, J = 2.68 Hz, 1H), 7.41 (t, J = 71.52 Hz, 1H), 7.35 (d, J = 8.92 Hz, 1H), 4.38 (t, J = 4.44 Hz, 2H), 4.23 (t, J = 4.44 Hz, 2H), 1.77 (s, 3H)

546		MS (ESI) m/z 617.13 [M+1]+. 1H NMR (400 MHz, DMSO-d6) δ 8.84 (d, J = 4.68 Hz, 1H), 8.41 (s, 1H), 7.92 (s, 1H), 7.60 (dd, J = 2.60, 9.52 Hz, 1H), 7.50 (d, J = 4.56 Hz, 1H), 7.42 (d, J = 1.84 Hz, 1H), 7.36 (bs, 1H), 7.35 (t, J = 71.96 Hz, 1H), 4.39 (t, J = 5.08 Hz, 2H), 4.23 (t, J = 5.08 Hz, 2H), 1.76 (s, 3H)	
547		MS (ESI) m/z 608.10 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.25 (bs, 1H), 8.86-8.79 (m, 1H), 8.60-8.49 (m, 2H), 7.72-7.33 (m, 5H), 4.46-4.36 (m, 2H), 4.33-4.24 (m, 2H), 1.94 (s, 3H)	
548		MS (ESI) m/z 633.07 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.77 (d, J = 4.76 Hz, 1H), 8.57 (s, 1H), 8.04 (s, 1H), 7.81-7.35 (m, 6H), 4.41 (t, J = 5.04 Hz, 2H), 4.25 (t, J = 4.84 Hz, 2H), 1.81 (s, 3H)	
550		MS (ESI) m/z 635.09 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8. 84 (d, J = 4.8 Hz, 1H), 8.41 (s, 1H), 8.00 (s, 1H), 7.60 (dd, J =2.52 Hz, 8.84 Hz, 1H), 7.50 (d, J = 4.76, 1H), 7.45 (d, J = 2.48, 1H), 7.36 (d, J = 8.96 Hz, 1H), 4.40 (t, J = 4.48 Hz, 2H), 4.24 (t, J = 4.32 Hz, 2H), 1.75 (s, 3H)	
551		MS (ESI) m/z 650.9 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.76 Hz, 1H), 8.38 (s, 1H), 8.04 (s, 1H), 7.59 (dd, J = 8.92, 2.40 Hz, 1H), 7.48-7.19 (m, 4H), 4.40 (t, J = 5.6 Hz, 2H), 4.25 (t, J = 5.6 Hz, 2), 1.76 (s, 3H).	
552		MS (ESI) m/z 658.16 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.80 (d, J = 4.7Hz, 1H), 8.48 (s, 1H), 8.17 (s, 1H), 7.62-7.59 (m, 1H), 7.46 (t, J = 4.2Hz, 2H), 7.37 (d, J = 8.9Hz, 1H), 4.5 (bs, 2H), 4.41 (t, J = 4.3Hz, 2H), 4.26 (t, J = 4.3Hz, 2H), 2.86 (s, 6H), 1.80 (s, 3H).	

557		MS (ESI) m/z 579.03 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.96 (bs, 1H), 8.73 (d, J = 4.7 Hz, 1H), 8.66 (s, 1H), 8.13 (d, J = 9.7 Hz, 1H), 7.76 (d, J = 9.0 Hz, 1H), 7.68 (m, 2H), 7.53 (d, J = 4.7 Hz, 1H), 7.37 (t, J = 53.7 Hz, 1H), 4.88 (s, 2H), 2.22 (s, 3H)	570		MS (ESI) m/z 676.14 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.34 (bs, 1H), 8.80 (s, 1H), 8.12 (d, J = 10.0 Hz, 1H), 7.56 (dd, J = 8.8 Hz 2.80 Hz, 1H), 7.49-7.22 (m, 4H), 4.38 (t, J = 5.20 Hz, 2H), 4.245 (t, J = 4.40 Hz , 2H), 2.63 (s, 3H). 1.98 (s, 3 H), 1.75 (s, 3H)
566		MS (ESI) m/z 676.15 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.93 (bs, 1H), 8.06 (d, J = 9.72 Hz, 1H), 7.60 (dd, J = 8.80, 2.40 Hz, 1H), 7.48-7.22 (m, 4H), 4.43 (t, J = 4.6 Hz, 2H), 4. 28 (t, J = 4.8Hz, 2H), 3.5 (s, 3H), 2.69 (s, 3H), 1.94 (s, 3H)	572		MS (ESI) m/z 531.22 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.80 (d, J = 4.72 Hz, 1H), 8.39 (s, 1H), 7.83 (d, J = 8.64 Hz, 1H), 7.58 (d, J = 8.64 Hz, 2H), 7.48 (d, J = 4.84 Hz, 1H), 7.42 (d, J = 2.52 Hz, 1H), 7.35 (d, J = 9.0 Hz, 1H), 4.41-4.38 (m, 2H), 4.24-4.23 (m, 2H), 2.60 (s, 3H), 1.79 (s, 3H)
567		MS (ESI) m/z 644.09 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.99 (s, 1H), 8.48 (s, 1H), 7.73 (dd, J = 7.88, 10.80 Hz, 1H), 7.60 (dd, J = 2.44, 8.88 Hz, 1H), 7.48 (s, 1H), 7.40 (d, J = 2.60 Hz, 1H), 7.36 (d, J = 9.2 Hz, 1H), 4.41 (t, J = 5.12 Hz, 2H). 4.23 (t, J = 4.28 Hz, 2H), 3.57 (s, 3H), 2.71 (s, 3H), 1.80 (s, 3H)	573		MS (ESI) m/z 531.18 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.04 Hz , 1H), 8.30 (s, 1H), 7.79 (s, 1H), 7.58 (d, J = 8.88 Hz, 1H), 7.46 (m, 2H), 7.41 (m, 2H), 7.35 (d, J = 9.08 Hz, 1H), 4.35 (s, 2H), 4.19 (s, 2H), 2.49 (s, 3H), 1.81 (s, 3H)

574		MS (ESI) m/z 531.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.26 (bs, 1H), 8.80 (d, J= 4.68 Hz, 1H), 8.43(s, 1H), 7.82 (d, J = 7.56, 1H), 7.55 (d, J = 7.68, 1H), 7.59 (dd, J = 2.44, 2.48 Hz,1H), 7.46 (d, J = 4.68 Hz, 1H), 7.41 (d, J = 2.4 Hz, 1H), 7.37 (d, J = 8.96 Hz, 1H), 4.42 (s, 2H), 4.23 (s, 2H), 3.38 (s, 3H), 1.815 (s, 3H)	577		MS (ESI) m/z 637.22 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.16-7.87 (m, 3H), 7.33 (d, J = 9.2 Hz, 1H), 7.66 (d, J = 8.5 Hz, 1H), 7.53 (dd, J = 2.6, 8.8 Hz, 1H), 7.37-7.30 (m, 3H), 4.31 (t, J = 5.6 Hz, 2H), 4.17 (t, J = 5.6 Hz, 2H), 3.09 (t, J = 6.9 Hz, 2H), 2.56 (t, J = 6.8 Hz, 2H), 2.32 (s, 6H), 1.73 (s, 3H)
575		MS (ESI) m/z 654.14 [M+1]+. 1H NMR (400 MHz, DMSO-d6) δ, 8.27 (s, 1H), 8.04-7.67 (3, 2H), 7.63 (d, J = 8.4 Hz, 1H), 7.59-7.56 (m, 1H), 7.42 (m, 1H), 7.35 (d, J = 9.2 Hz, 1H), 7.10 (s, 1H), 4.39 (t, J = 4.8 Hz, 2H), 4.24 (t, J = 5.6 Hz, 2H), 3.07(t, J = 7.2 Hz, 2H), 2.58 (t, J = 7.2 Hz, 2H), 2.22 (s, 6H), 1.75 (s, 3H)	578		MS (ESI) m/z 655.24 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.00 (s, 1H), 7.88-7.85 (m, 2H), 7.68 (d, J = 8.48 Hz, 1H), 7.54 (dd, J = 2.60, 8.88 Hz, 1H), 7.41-7.38 (m, 2H), 7.30 (d, J = 8.92 Hz, 1H), 4.34 (t, J = 4.36 Hz, 2H), 4.19 (t, J = 4.96 Hz, 2H), 3.07 (t, J = 7.20 Hz, 2H), 2.65-2.62 (m, 2H), 2.27 (s, 6H), 1.66 (s, 3H)
576		MS (ESI) m/z 601.30 [M+1]+., 1H-NMR (400 MHz, DMSO-d6) δ 12.96 (bs, 1H), 7.90 (d, J = 8.44 Hz, 1H), 7.83 (s, 1H), 7.78 (d, J = 8.44 Hz, 1H),7.48 (dd, J = 2.44, 8.76 Hz,1H), 7.27-7.22 (m, 3H), 7.10 (d, J = 7.28 Hz, 1H), 4.32 (t, J = 4.8 Hz, 2H), 4.20 (t, J = 4.8 Hz, 2H), 2.86 (s, 6H), 2.68 (s, 3H), 1.72 (s, 3H)	579		MS (ESI) m/z 597.17 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.66 (bs, 1H), 8.43 (s, 1H), 7.84 (s, 1H), 7.71-7.33 (m, 6H), 4.39-4.37 (m, 2H), 4.23-4.21 (m, 2H), 2.70 (s, 3H), 1.81 (s, 3H)

580		MS (ESI) m/z 674.19 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.07 (bs, 1H), 8.44 (s, 1H), 7.85 (s, 1H), 7.71 to 7.41 (m, 4H), 7.36 to 7.32 (m, 2H), 4.4 (bs, 2H), 4.21 (bs, 2H), 3.56 (s, 3H), 2.71 (s, 3H), 1.79 (s, 3H)	583 	MS (ESI) m/z 615.05 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.5 (bs, 1H), 8.41 (s, 1H), 8.02 (d, J = 8.8 Hz, 1H), 7.81 (d, J = 9.08, 1H), 7.59 (dd, J = 2.44, 8.80, 1H), 7.42-7.41 (m, 1H), 7.35 (d, J = 8.96, 1H), 4.39 (t, J = 5.08 Hz, 2H), 4.24 (t, J = 4.52, 2H), 2.69 (s, 3H), 1.83 (s, 3H)
581		MS (ESI) m/z 674.19 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.07 (bs, 1H), 8.44 (s, 1H), 7.85 (s, 1H), 7.71 to 7.41 (m, 4H), 7.36 to 7.32 (m, 2H), 4.4 (bs, 2H), 4.21 (bs, 2H), 3.56 (s, 3H), 2.71 (s, 3H), 1.79 (s, 3H)	584	MS (ESI) m/z 602.18 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.74 (bs, 1H), 8.33 (s, 1H), 7.91 (d, J = 8.8 Hz, 1H), 7.67 (d, J = 8.4 Hz, 1H), 7.61-7.58 (m, 1H), 7.41-7.35 (m, 3H), 4.41 (t, J = 4.8 Hz, 2H), 4.26 (t, J = 5.6 Hz, 2H), 3.41 (t, J = 9.6 Hz, 2H), 3.37 (t, J = 3.2 Hz, 2H), 2.91 (s, 6H), 2.70 (s, 3H), 1.87 (s, 3H)
582		MS (ESI) m/z 599.27 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.55 (bs, 1H), 8.37 (s, 1H), 7.89 (s, 1H), 7.60 (dd, J = 1.88 Hz, 8.84 Hz, 1H), 7.41 (s, 2H), 7.35 (d, J = 8.84 Hz, 1H), 4.40-4.38 (m , 2H), 4.24-4.22 (m, 2H), 2.70 (s, 3H), 1.82 (s, 3H)	585	MS (ESI) m/z 615.29 [M+1]+ ; 1H NMR (400 MHz, DMSO-d6) δ 13.68 (bs, 1H), 8.43 (s, 1H), 7.60-7.55 (m, 2H), 7.54 (t, J = 71.72 Hz, 1H), 7.43 (s, 1H), 7.40 (d, J = 4.00 Hz, 1H), 7.34 (d, J = 9.04 Hz, 1H), 4.38 (t, J = 4.68 Hz, 2H), 4.23 (t, J = 4.60 Hz, 2H), 2.71 (s, 3H), 1.78 (s, 3H)

586		MS (ESI) m/z 615.07 [M+1]+. 1H-NMR (400 MHz, DMSO-d6) δ 8.39 (s, 1H), 7.83 (s, 1H), 7.63-7.34 (m, 5H), 4.40 (t, J = 4.0 Hz, 2H), 4.25 (t, J = 4.4 Hz, 2H), 2.70 (s, 3H), 1.83 (s, 3H)	
587		MS (ESI) m/z 599.20 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.5 (s, 1H), 8.44 (s, 1H), 8.04 (d, J = 9.24 Hz, 1H), 7.62-7.58 (m, 1H), 7.47-7.21 (m, 4H), 4.41 (bs, 2H), 4.28 (bs, 2H), 2.69 (s, 3H), 1.94 (s, 3H)	
588		MS (ESI) m/z 581.17 [M-1]-; 1H NMR (400 MHz, DMSO-d6) δ 8.47 (s, 1H), 8.15 (d, J = 9.32 Hz, 1H), 7.59 (dd, J = 2.44, 8.88 Hz, 1H), 7.40-7.35 (m, 3H), 4.41 (t, J = 6.24 Hz, 2H), 4.27 (t, J = 5.44 Hz, 2H), 2.70 (s, 3H), 1.93 (s, 3H)	
592		MS (ESI) m/z 668.20 [M+1]+; UPLC: 92.22 %; 1H NMR (400 MHz, DMSO-d6) δ: 8.32 (s, 1H), 7.78-7.33 (m, 6H), 4.38 (t, J = 4.7 Hz, 2H), 4.22 (t, J = 4.3 Hz, 2H), 3.06-3.04 (m, 2H), 2.76-2.69 (m, 5H), 2.23 (s, 6H), 1.82 (s, 3H)	
593		MS (ESI) m/z [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.61 (s, 1H), 8.01 (d, J = 9.60 Hz, 1H), 7.88 (s, 1H), 7.67 (dd, J = 8.96, 2.52 Hz, 1H), 7.51 (d, J = 2.52 Hz, 1H), 7.49-7.22 (m, 2H), 4.46 (t, J = 4.84 Hz, 2H), 4.33 (t, J = 4.52 Hz, 2H), 2.94 (s, 3H), 2.07 (s, 3H)	
594		MS (ESI) m/z 669 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 11.93 (s, 1H), 8.45 (s, 1H), 8.01 (d, J = 9.76 Hz, 1H), 7.59 (dd, J = 8.88, 2.40, 1H), 7.47-7.20 (m, 4H), 4.40 (t, J = 4.36 Hz, 2H), 4.28 (t, J = 4.76 Hz, 2H), 3.11 (bs, 6H), 2.67 (s, 3H), 1.99 (s, 3H)	

596		MS (ESI) m/z 532.14 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.85 (s, 1H), 8.42 (s, 1H), 8.37 (s, 1H), 7.59 (dd, J=8.84 Hz, 2.56 Hz, 1H), 7.41 (t, J= 4.44 Hz, 2H), 7.33 (d, J=8.92, 1H), 4.38 (t, J=6.12Hz, 2H), 4.27 (t, J=6.2 Hz, 2H), 2.70 (s, 3H), 1.86 (s, 3H)	
598		MS (ESI) m/z 608.90 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.95 (s, 1H), 8.86 (s, 1H), 8.50 (s, 1H), 8.42 (s, 1H), 7.60 (dd, J = 7.24 Hz, 2.64Hz, 1H), 7.45 (s, 1H), 7.41 (d, J = 2.6 Hz, 1H), 7.35 (d, J = 8.96 Hz, 1H), 4.26 (t, J = 6.04 Hz, 2H), 4.26 (t, J = 4.52 Hz, 2H), 3.59 (s, 3H), 2.71 (s, 3H), 1.88 (s, 3H)	
599		MS (ESI) m/z 526.15 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.02 (bs, 1H), 8.45 (bs, 2H), 7.74 (s, 1H), 7.67 (d, J = 8.4 Hz, 2H), 7.40 (bs, 1H), 4.88 (s, 2H), 2.66 (s, 3H), 2.19 (s, 3H).	
606		MS (ESI) m/z 650.24 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.75 (bs, 1H), 9.50-9.30 (m, 1H), 8.29 (s, 1H), 7.64 (s, 1H), 7.60 (dd, J = 8.92, 2.56 Hz, 1H), 7.45 (s, 1H), 7.40 (d, J = 2.56 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H), 4.40 (t, J = 5.04 Hz, 2H), 4.24 (t, J = 4.48 Hz, 2H), 3.28-3.15 (m, 2H), 2.93 (t, J = 7.64 Hz, 2H), 2.83 (d, J = 4.60, 6H), 2.72 (s, 3H), 2.18-2.07 (m, 2H), 1.84 (s, 3H)
607		MS (ESI) m/z 668.24 [M+1]+; UPLC: 97.83 %; 1H NMR (400 MHz, DMSO-d6) δ 8.25 (s, 1H), 7.66 (s, 1H), 7.58 (dd, J = 8.68 Hz, J = 2.36 Hz, 1H), 7.47-7.12 (m, 4H), 4.41 (t, J = 4.5 Hz, 2H), 4.24 (t, J = 4.3 Hz, 2H), 3.46 (t, J = 6.0 Hz, 2H), 3.18 (t, J = 8.0 Hz, 2H), 2.89 (s, 6H), 2.70 (s, 3H), 1.81 (s, 3H)
608		MS (ESI) m/z 620.22 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.44 (s, 1H), 7.81 (d, J = 10.8 Hz, 1H), 7.58 (dd, J = 2.36 Hz, 9.0 Hz, 1H), 7.39-7.35 (m, 3H), 4.40 (t, J = 4.88 Hz, 2H), 4.25 (t, J = 4.44 Hz, 2H), 3.07 (t, J = 7.36 HZ, 2H), 2.69 (s, 5H), 2.28 (s, 6H), 1.94 (s, 3H)

609	MS (ESI) m/z 636.04 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.32 (s, 1H), 7.74 (s, 1H), 7.59-7.57 (m, 1H), 7.40-7.33 (m, 3H), 4.38 (t, J = 5.0 Hz, 2H), 4.22 (t, J = 3.92 Hz, 2H), 3.50 (s, 2H), 3.21 (t, J = 7.96 Hz, 2H) 2.69 (s, 3H), 2.26 (s, 6H), 1.84 (s, 3H)	613	MS (ESI) m/z 614.24 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.35 (s, 1H), 7.59-7.56 (dd, J = 2.52, 2.56 Hz, 1H), 7.48 (s, 1H), 7.40 (d, J = 2.4 Hz, 1H), 7.36-7.33 (m, 2H), 4.49 (t, J = 7.52 Hz, 1H), 4.41-4.19 (m, 4H), 3.14-2.98 (m, 2H), 2.67. (s, 3H), 2.20 (s, 6H), 2.12-2.05 (m, 2H), 1.89 (s, 3H)
611	MS (ESI) m/z 614.21 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.24 (s, 1H), 7.61 (dd, J1=2.5 Hz, J2 =8.8 Hz, 1H), 7.48 (s, 1H), 7.42 (s, 1H),7.38 (s, 1H), 7.36 (S, 1H), 4.40 (S , 2H), 4.39-4.30 (m, 1H),4.20 (s, 2H), 3.61-3.54 (m, 2H), 3.45-3.20 (m, 2H), 2.9 (s, 6H), 2.71 (s, 3H), 1.93 (s, 3H)	618	MS (ESI) m/z 696.40 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 13.57 (bs, 1H), 8.41 (s, 1H), 7.90 (s, 1H), 7.60-7.57(dd, J = 2.25, 8.8 Hz, 1H), 7.41-7.32 (m, 4H), 4.39 (t, J = 5.28 Hz, 2H), 4.23 (t, J = 5.28 Hz, 2H), 3.71 (s, 2H), 2.68 (s, 3H), 2.11 (s, 3H), 1.82 (s, 3H), 1.15 (s, 9H)
612	MS (ESI) m/z 614.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.63 (bs, 1H), 9.72 (bs, 1H), 8.16 (s, 1H), 7.61-7.59 (m, 2H), 7.44-7.36 (m, 3H), 5.19-5.08 (m, 1H), 4.50-4.35 (m, 2H), 4.35-4.18 (m, 2H), 3.23-3.07 (m, 2H), 2.93-2.73 (m, 6H), 2.73 (s, 3H), 1.90 (s, 1H)	619	MS (ESI) m/z 682.24 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 8.83 (bs, 1H), 8.36 (s , 1H), 8.01 (s, 1H), 7.69-7.33 (m, 5H), 4.42 (t, J = 4.72 Hz, 2H), 4.28 (m, 4H), 2.72 (s, 3H). 1.92 (s, 3H). 1.42 (s, 9H)

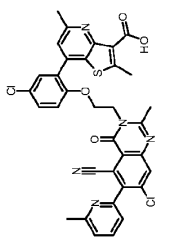
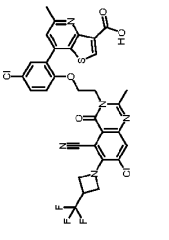
620	MS (ESI) m/z 631.21 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.76 Hz, 1H), 8.24 (s, 1H), 7.67 (s, 1H), 7.61 (dd, J = 2.64, J = 8.88 Hz, 1H), 7.47 (d, J = 4.80 Hz, 1H), 7.43 (d, J = 2.64 Hz, 1H), 7.35 (d, J = 9.04 Hz, 1H), 4.65 (s, 2H), 4.39 (t, J = 4.48 Hz, 2H), 4.21 (t, J = 4.32 Hz, 2H), 2.87 (s, 6H), 1.77 (s, 3H)	623	MS (ESI) m/z 636.00 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.76 (s, 1H), 8.59 (s, 1H), 8.06 (s, 1H), 7.76 (d, J = 8.92, 1H), 7.68 (d, J = 1.8 Hz, 2H), 7.53 (s, 1H), 4.87 (s, 2H), 3.70 (s, 2H), 2.23 (s, 6H), 2.12 (s, 3H)
621	MS (ESI) m/z 634.99 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.84 (d, J=4.74 Hz, 1H), 8.25 (s, 1H), 7.65 (s, 1H), 7.60 (dd, J=8.84, 2.48 Hz, 1H), 7.48 (d, J = 4.72 Hz, 1H), 7.43 (d, J=2.48, 1H), 7.35 (d, J=8.96, 1H), 4.55(, 2H), 4.39 (bs, 2H), 4.24 (bs, 2H), 2.92 (s, 6H), 1.78 (s, 3H).	625	MS (ESI) m/z 512.12 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.0 (s, 1H), 8.74 (d, J = 4.8 Hz, 1H), 8.6 (s, 1H), 8.43 (s, 1H), 7.75 (d, J = 8.9 Hz, 1H), 7.68 (m, 2H), 7.51 (d, J = 4.6 Hz, 1H), 4.87 (s, 2H), 2.17 (s, 3H)
622	MS (ESI) m/z 617.93 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.72 (d, J = 4.72 Hz, 1H), 8.60 (s, 1H), 8.09 (s, 1H), 7.76 (d, J = 8.92 Hz, 1H), 7.69-7.65 (m, 2H), 7.54-7.38 (m, 2H), 4.90 (s, 2H), 4.63 (bs, 2H), 2.88 (s, 6H), 2.14 (s, 3H)	626	MS (ESI) m/z 634.10 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.14 (bs, 1H), 8.74 (d, J = 4.72 Hz, 1H), 8.65 (s, 1H), 8.19 (s, 1H), 7.77-7.60 (m, 3H), 7.57-7.24 (m, 2H), 4.88 (s, 2H), 4.53 (s, 2H), 2.88 (s, 6H), 2.16 (s, 3H)

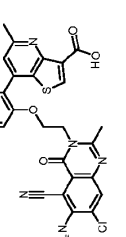
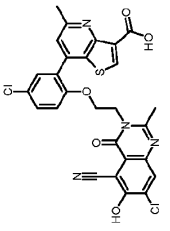
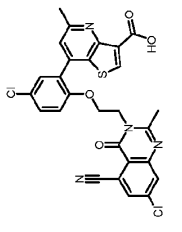
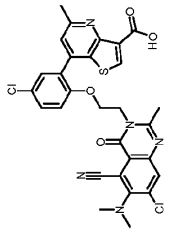
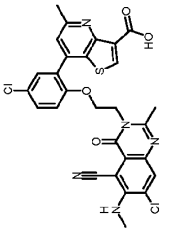
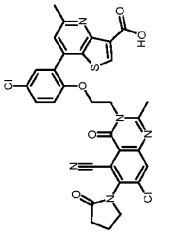
627		MS (ESI) m/z 594.95 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.36 (s, 1H), 7.80 (s, 1H), 7.60 (dd, J=2.36, J=2.52,1H), 7.20 – 7.40 (m, 4H), 4.40 (bs, 2H), 4.25 (bs, 2H), 2.68 (s, 3H), 2.65 (s , 3H), 1.88 (s, 3H)	639		MS (ESI) m/z 667.15 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.35 (s, 1H), 7.74 (bs, 1H), 7.59 (dd, J = 2.46 Hz, 8.88 Hz, 1H), 7.49-7.31 (m, 4H), 4.39 (bs, 2H), 4.23 (bs, 2H), 3.58 (bs, 2H), 3.02 (q, J = 7.52 Hz, 2H), 2.25(s, 6H), 1.78 (s, 3H), 1.35 (t, J= 7.24 Hz, 3H)
628		MS (ESI) m/z 559.06 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.34 (s, 1H), 7.59 (dd, J = 2.6 Hz, 2.56 Hz, 1H), 7.44 (s, 1H), 7.35-7.39 (m, 3H), 4.39 (s, 2H), 4.23 (s, 2H), 2.70 (s, 3H), 2.51 (s, 3H), 2.437 (s, 3H), 1.9 (s, 3H)	646		MS (ESI) m/z 693.21 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ, 9.41 (bs, 1H), 8.33 (s, 1H), 7.86 (s, 1H), 7.69-7.35 (m, 5H), 4.41 (t, J = 6.4 Hz, 2H), 4.26 (t, J = 6.4 Hz, 2H), 4.00 (s, 2H), 3.41 (d, J = 12.0 Hz, 2H), 3.02-2.94 (m, 4H), 2.79 (d, J = 3.6 Hz, 3H), 2.64 (s, 3H),2.49 (bs, 2H), 1.85 (s, 3H)
635		MS (ESI) m/z 656.12 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.48 (s, 1H), 8.38 (s, 1H), 7.92 (s, 1H), 7.59 (dd, J = 8.88, 2.52 Hz, 1H), 7.40-7.34 (m, 3H), 4.39 (t, J = 4.6 Hz, 2H), 4.25 (t, J = 4.6 Hz, 2H), 3.68 (s, 2H), 2.69 (s, 3H), 2.22 (s, 6H), 1.90 (s, 3H)	647		MS (ESI) m/z 642.99 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 8.37 (s, 1H), 7.92 (d, J = 8.52 Hz, 1H), 7.64 (d, J = 8.48 Hz, 1H), 7.58 (dd, J = 8.84, 2.44 Hz, 1H), 7.41-7.34(m, 3H), 4.42-4.37 (m, 2H), 4.27-4.21 (m, 2H), 3.75 (s, 3H), 2.68 (s, 3H), 2.50-2.30 (m, 6H), 2.21-2.16 (s, 4H), 1.85 (s, 3H)

648		MS (ESI) m/z 599.20 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.45 (s, 1H), 7.77 (d, J = 10.56 Hz, 1H), 7.60 (m, 1H), 7.40-7.35 (m, 3H), 4.41 (bs, 2H), 4.26 (bs, 2H), 2.69 (s, 3H), 2.58 (s, 3H), 1.98 (s, 3H)	653 MS (ESI) m/z 642.01 [M+1]+; 1H NMR (400 MHz, DMSO-d6) 8.76-8.73 (m, 2H), 8.45 (s, 1H), 8.03 (d, J = 7.84 Hz, 1H), 7.86 (s,1H), 7.67-7.64 (m, 1H), 7.59 (dd, J = 8.8, 2.44 Hz, 1H), 7.45-7.40 (m, 2H), 7.36 (d, J = 8.96 Hz, 1H), 4.40 (t, J = 4.28 Hz, 2H), 4.26 (t, J = 3.76 Hz, 2H), 2.72 (s, 3H), 1.90 (s, 3H)
650		MS (ESI) m/z 602.03 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.36 (s, 1H), 7.86 (s, 1H), 7.61 (dd, J = 8.92 Hz, 2.48 Hz, 1H), 7.43 (s, 1H), 7.41 (d, J = 2.52, 1H), 7.38 (d, J = 9.00 Hz, 1H), 4.54 (s, 2H), 4.43 (t, J = 5.72 , 2H), 4.27 (t, J = 4.2 Hz, 2H), 2.87 (s, 6H), 2.71 (s, 3H), 2.67 (s, 3H), 1.95 (s, 3H)	654 MS (ESI) m/z 608.35 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 9.20 (bs, 1H), 8.74 (bs, 1H), 8.45 (d, J = 7.96 Hz, 1H), 8.39 (s, 1H), 8.32 (s, 1H), 8.00 (s, 1H), 7.66 (m, 1H), 7.61-7.57 (dd, J = 2.26, 8.56 Hz, 1H),7.45 (s, 1H), 7.41 (d, J = 2.48 Hz, 1H), 7.38 (d, J = 8.96 Hz, 1H), 4.44 (t, J = 5.20 Hz, 2H), 4.26 (t, J = 4.60 2H), 2.71 (s, 3H), 1.84 (s, 3H),
651		MS (ESI) m/z 721.31 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 8.81 (d, J = 8.80 Hz, 1H), 8.47 (s, 1H), 8.23 (s, 1H), 8.03 (s, 1H), 7.61 (dd, J = 2.52, 8.84 Hz 1H), 7.47-7.19 (m, 4H), 4.41-4.40 (m, 6H), 4.21 (s, 2H), 4.10 (s, 3H), 2.67 (s, 3H). 1.82 (s, 3H)	657 LCMS (ESI) m/z 552.3 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ 8.70 (dd, J = 8.7, 1.1 Hz, 1H), 8.62 (d, J = 4.8 Hz, 1H), 8.25 (d, J = 8.6 Hz, 1H), 8.16 (s, 1H), 8.07 (dd, J = 7.4, 1.1 Hz, 1H), 7.95 (dd, J = 8.3, 7.4 Hz, 1H), 7.55 (dd, J = 8.9, 2.7 Hz, 1H), 7.38 (d, J = 1Hz, 1H), 7.36 (d, J = 5.2 Hz, 1H), 7.33 (d, J = 2.3 Hz, 1H), 7.16 – 7.06 (m, 2H), 7.01 – 6.92 (m, 1H), 4.56 – 4.50 (m, 4H)

658		LCMS (ESI) m/z 529.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.78 (s, 1H), 9.10 (s, 1H), 8.62 – 8.51 (m, 2H), 8.25 (dd, J = 8.0, 1.3 Hz, 1H), 8.08 (s, 1H), 7.95 (ddd, J = 8.3, 7.2, 1.4 Hz, 1H), 7.80 (ddd, J = 8.1, 7.3, 1.1 Hz, 1H), 7.56 (dd, J = 9.0, 2.7 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 7.33 – 7.26 (m, 2H), 4.61 (t, J = 5.2 Hz, 2H), 4.50 (t, J = 5.1 Hz, 2H)
659		LCMS (ESI) m/z 543.9 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 10.20 – 10.15 (m, 1H), 9.83 (s, 1H), 8.76 (d, J = 4.8 Hz, 1H), 8.36 (d, J = 8.5 Hz, 1H), 8.21 (s, 1H), 8.03 (d, J = 8.5 Hz, 1H), 7.55 (dd, J = 8.9, 2.7 Hz, 1H), 7.43 – 7.30 (m, 2H), 4.42 (d, J = 5.1 Hz, 1H), 4.30 (t, J = 4.9 Hz, 1H), 2.44 – 2.38 (m, 1H), 1.94 (s, 3H)
665		LCMS (ESI) m/z 592.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.68 (d, J = 4.8 Hz, 1H), 8.67 (s, 1H), 8.33 (s, 1H), 8.17 (s, 1H), 7.64 (d, J = 8.4 Hz, 1H), 7.62 – 7.56 (m, 2H), 7.46 (d, J = 4.8 Hz, 1H), 3.76 (s, 3H), 3.49 (s, 2H), 2.03 (s, 4H)
669		LCMS (ESI) m/z 626.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.73 – 8.63 (m, 2H), 8.35 (s, 1H), 7.68 – 7.53 (m, 3H), 7.47 (d, J = 4.8 Hz, 1H), 3.77 (s, 1H), 2.05 (d, J = 4.3 Hz, 1H), 2.04 (s, 1H)
671		LCMS (ESI) m/z 558.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 10.23 (d, J = 0.7 Hz, 1H), 9.92 (d, J = 1.5 Hz, 1H), 8.41 (d, J = 8.5 Hz, 1H), 8.28 (s, 1H), 8.09 (dd, J = 8.6, 0.7 Hz, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.47 – 7.34 (m, 3H), 4.46 (s, 5H), 4.34 (s, 5H), 2.65 (s, 3H), 2.04 (s, 3H)
676		LCMS (ESI) m/z 673.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.30 (s, 1H), 8.10 (s, 1H), 7.56 (dd, J = 8.9, 2.7 Hz, 1H), 7.42 – 7.35 (m, 2H), 7.31 (d, J = 9.0 Hz, 1H), 4.35 (t, J = 5.1 Hz, 2H), 4.19 (t, J = 4.9 Hz, 2H), 3.19 (m, 4H), 2.88 (d, J = 4.1 Hz, 3H), 2.67 (s, 3H), 1.75 (s, 3H)

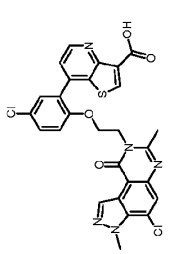
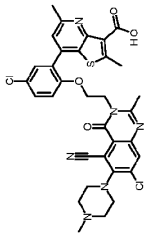
677		LCMS (ESI) m/z 673.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.78 (s, 1H), 8.31 (s, 1H), 8.09 (s, 1H), 7.56 (dd, J = 8.9, 2.7 Hz, 1H), 7.42 – 7.35 (m, 2H), 7.31 (d, J = 9.0 Hz, 1H), 4.35 (t, J = 5.0 Hz, 2H), 4.19 (d, J = 10.1 Hz, 1H), 3.58 (d, J = 11.8 Hz, 4H), 3.29 – 3.13 (m, 4H), 2.88 (d, J = 3.4 Hz, 3H), 2.67 (s, 3H), 1.75 (s, 3H)
678		LCMS (ESI) m/z 605.0 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.78 (s, 1H), 7.66 – 7.51 (m, 1H), 7.47 – 7.36 (m, 1H), 7.37 – 7.27 (m, 1H), 4.52 (d, J = 13.9 Hz, 1H), 4.33 (t, J = 5.1 Hz, 1H), 4.16 (t, J = 5.1 Hz, 1H), 3.54 (d, J = 11.8 Hz, 1H), 3.20 (d, J = 13.0 Hz, 1H), 3.18 – 3.03 (m, 1H), 2.84 (d, J = 3.6 Hz, 2H), 2.67 (s, 1H), 1.73 (s, 1H)
679		LCMS (ESI) m/z 550.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.50 (s, 1H), 7.62 – 7.52 (m, 2H), 7.43 (d, J = 2.7 Hz, 1H), 7.40 – 7.30 (m, 2H), 7.19 (d, J = 9.2 Hz, 1H), 4.36 (t, J = 5.0 Hz, 2H), 4.18 (t, J = 5.0 Hz, 2H), 3.12 (s, 6H), 2.70 (s, 3H), 1.73 (s, 3H)
680		LCMS (ESI) m/z 609.0 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.59 (s, 1H), 8.16 (s, 1H), 7.56 (dd, J = 8.9, 2.6 Hz, 1H), 7.45 – 7.38 (m, 2H), 7.33 (d, J = 9.0 Hz, 1H), 4.40 (t, J = 5.0 Hz, 2H), 4.24 (t, J = 5.1 Hz, 2H), 4.11 (s, 1H), 2.67 (s, 3H), 1.96 (s, 3H (m, 2H), 7.43 (d, J = 2.7 Hz, 1H), 7.40 – 7.30 (m, 2H), 7.19 (d, J = 9.2 Hz, 1H), 4.36 (t, J = 5.0 Hz, 2H), 4.18 (t, J = 5.0 Hz, 2H), 3.12 (s, 6H), 2.70 (s, 3H), 1.73 (s, 3H)
681		LCMS (ESI) m/z 650.7 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.69 (s, 1H), 8.00 (s, 1H), 7.96 (t, J = 7.8 Hz, 1H), 7.75 (d, J = 8.3 Hz, 1H), 7.71 – 7.63 (m, 2H), 7.54 (d, J = 7.7 Hz, 1H), 7.48 (s, 1H), 7.44 (d, J = 7.8 Hz, 1H), 4.86 (s, 2H), 2.64 (s, 3H), 2.56 (s, 3H), 2.17 (s, 3H)
682		LCMS (ESI) m/z 653.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.86 (s, 1H), 8.75 (d, J = 4.8 Hz, 1H), 8.60 (s, 1H), 8.29 (s, 1H), 7.75 (d, J = 9.2 Hz, 1H), 7.71 – 7.65 (m, 2H), 7.54 (d, J = 4.8 Hz, 1H), 4.86 (s, 2H), 3.64 (dd, J = 24.2, 12.1 Hz, 5H), 3.30 (d, J = 13.5 Hz, 7H), 2.92 (s, 3H), 2.12 (s, 3H)

683		689	
LCMS (ESI) m/z 670.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 7.89 (t, J = 7.8 Hz, 1H), 7.78 (s, 1H), 7.56 (dd, J = 8.9, 2.7 Hz, 1H), 7.45 – 7.35 (m, 4H), 7.33 (d, J = 9.0 Hz, 1H), 4.38 (t, J = 5.0 Hz, 2H), 2.68 (s, 3H), 2.53 (d, J = 11.1 Hz, 6H), 1.93 (s, 3H)		LCMS (ESI) m/z 688.0 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.47 (d, J = 0.4 Hz, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.51 (s, 1H), 7.42 (s, 1H), 7.41 (d, J = 2.7 Hz, 1H), 7.36 (d, J = 8.9 Hz, 1H), 4.84 (t, J = 9.3 Hz, 2H), 4.63 (dd, J = 9.6, 5.0 Hz, 2H), 4.37 (t, J = 5.1 Hz, 2H), 4.18 (t, J = 5.1 Hz, 2H), 3.67 (d, J = 9.1 Hz, 0H), 2.73 (s, 3H), 1.81 (s, 3H)	
685		690	
LCMS (ESI) m/z 546.9 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.36 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.45 – 7.38 (m, 3H), 7.36 (d, J = 9.0 Hz, 1H), 4.39 (d, J = 5.1 Hz, 2H), 4.26 (d, J = 5.1 Hz, 2H), 2.71 (s, 3H), 2.64 (s, 3H), 1.90 (s, 3H)		LCMS (ESI) m/z 670.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.47 (d, J = 0.4 Hz, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.51 (s, 1H), 7.42 (s, 1H), 7.41 (d, J = 2.7 Hz, 1H), 7.36 (d, J = 8.9 Hz, 1H), 4.84 (t, J = 9.3 Hz, 2H), 4.63 (dd, J = 9.6, 5.0 Hz, 2H), 4.37 (t, J = 5.1 Hz, 2H), 4.18 (t, J = 5.1 Hz, 2H), 3.67 (d, J = 9.1 Hz, 0H), 2.73 (s, 3H), 1.81 (s, 3H)	
688		691	
LCMS (ESI) m/z 656.1, 658.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.44 (s, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.55 (s, 1H), 7.43 – 7.38 (m, 2H), 7.36 (d, J = 9.0 Hz, 1H), 5.03 (t, J = 12.6 Hz, 4H), 4.38 (m, 2H), 4.19 (m, 2H), 2.72 (s, 3H), 1.83 (s, 3H)		LCMS (ESI) m/z 648.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 7.56 (dd, J = 8.9, 2.7 Hz, 1H), 7.45 – 7.27 (m, 3H), 4.33 (t, J = 5.0 Hz, 2H), 4.28 (bs, 2H), 4.14 (t, J = 5.0 Hz, 2H), 2.69 (s, 2H), 1.76 (s, 2H), 1.27 (s, 3H)	

692		LCMS (ESI) m/z 580.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.41 (s, 1H), 7.60 – 7.51 (m, 2H), 7.43 – 7.34 (m, 2H), 7.31 (d, J = 9.0 Hz, 1H), 6.45 (s, 2H), 4.33 (t, J = 5.0 Hz, 2H), 4.15 (t, J = 4.9 Hz, 2H), 2.67 (s, 3H), 1.69 (s, 3H)	695 	LCMS (ESI) m/z 581.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.42 (s, 1H), 7.69 (s, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.43 – 7.39 (m, 2H), 7.35 (d, J = 9.0 Hz, 1H), 4.37 (t, J = 5.0 Hz, 2H), 4.20 (d, J = 5.1 Hz, 2H), 2.70 (s, 3H), 1.74 (s, 3H)
693		LCMS (ESI) m/z 567.0 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.39 (s, 1H), 8.10 (d, J = 2.1 Hz, 1H), 7.71 (d, J = 2.0 Hz, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.44 – 7.40 (m, 2H), 7.35 (d, J = 9.0 Hz, 1H), 4.39 (t, J = 5.1 Hz, 2H), 4.23 (t, J = 5.1 Hz, 2H), 2.71 (s, 3H), 1.83 (s, 3H)	696 	LCMS (ESI) m/z 608.0 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.44 (d, J = 0.4 Hz, 1H), 7.65 (s, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.46 – 7.39 (m, 2H), 7.36 (d, J = 9.0 Hz, 1H), 4.38 (s, 2H), 4.20 (s, 2H), 3.03 (s, 6H), 2.72 (s, 3H), 1.81 (s, 3H)
694		LCMS (ESI) m/z 594.2 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.46 (d, J = 0.4 Hz, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.54 (s, 1H), 7.44 – 7.40 (m, 2H), 7.35 (d, J = 8.9 Hz, 1H), 6.57 (d, J = 13.4 Hz, 1H), 4.37 (t, J = 5.0 Hz, 4H), 4.18 (t, J = 5.0 Hz, 2H), 3.24 (s, 3H), 2.72 (s, 3H), 1.74 (s, 3H)	697 	LCMS (ESI) m/z 648.2 [M+1]+; 1H NMR (400 MHz, Methanol-d4) δ 8.44 (s, 1H), 7.83 (s, 1H), 7.54 (dd, J = 8.9, 2.6 Hz, 1H), 7.52 (s, 1H), 7.33 (d, J = 2.6 Hz, 1H), 7.29 (d, J = 8.9 Hz, 1H), 4.53 – 4.28 (m, 2H), 4.06 – 3.97 (m, 2H), 3.92 – 3.84 (m, 2H), 2.87 (s, 3H), 2.65 (t, J = 7.8 Hz, 2H), 2.40 (q, J = 7.5 Hz, 2H), 2.04 (s, 3H)

698		LCMS (ESI) m/z 636.3 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.45 (s, 1H), 7.55 (dd, J = 8.9, 2.7 Hz, 1H), 7.43 (s, 1H), 7.41 – 7.28 (m, 3H), 4.79 (ddd, J = 9.4, 6.7, 1.3 Hz, 2H), 4.43 (tt, J = 6.7, 4.2 Hz, 1H), 4.36 – 4.24 (m, 4H), 4.14 (t, J = 5.1 Hz, 2H), 2.68 (s, 3H), 1.74 (s, 3H)
699		LCMS (ESI) m/z 659.3 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.48 (s, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.46 (s, 1H), 7.44 – 7.39 (m, 2H), 7.35 (d, J = 9.0 Hz, 1H), 4.89 – 4.75 (m, 2H), 4.50 – 4.45 (m, 2H), 4.36 (t, J = 5.0 Hz, 2H), 4.31 (dd, J = 10.5, 4.2 Hz, 2H), 4.17 (t, J = 5.1 Hz, 2H), 2.72 (s, 3H), 1.77 (s, 3H)
700		LCMS (ESI) m/z 656.9 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.31 (s, 1H), 8.46 (s, 1H), 8.32 (s, 1H), 8.25 (s, 1H), 7.87 (s, 1H), 7.66 – 7.60 (m, 2H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.47 – 7.40 (m, 2H), 7.36 (d, J = 9.0 Hz, 1H), 4.40 (t, J = 5.0 Hz, 2H), 4.24 (t, J = 4.9 Hz, 2H), 2.71 (s, 3H), 1.80 (s, 3H)
701		LCMS (ESI) m/z 650.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.44 (s, 1H), 7.55 (dd, J = 8.9, 2.7 Hz, 1H), 7.44 (s, 1H), 7.40 – 7.28 (m, 3H), 4.76 (dd, J = 10.0, 6.5 Hz, 2H), 4.38 (dd, J = 9.8, 3.5 Hz, 2H), 4.32 (d, J = 5.3 Hz, 2H), 4.22 – 4.12 (m, 3H), 3.25 (s, 3H), 2.68 (s, 3H), 1.75 (s, 3H)
702		LCMS (ESI) m/z 698.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.48 (s, 1H), 7.59 (dd, J = 8.9, 2.6 Hz, 1H), 7.52 (s, 1H), 7.44 – 7.32 (m, 3H), 4.90 (t, J = 9.4 Hz, 2H), 4.79 (dd, J = 10.1, 4.9 Hz, 2H), 4.43 – 4.31 (m, 3H), 4.18 (t, J = 5.0 Hz, 2H), 3.12 (s, 3H), 2.72 (s, 3H), 1.80 (s, 3H)
703		LCMS (ESI) m/z 664.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.43 (s, 1H), 7.55 (dd, J = 8.9, 2.7 Hz, 1H), 7.41 (s, 1H), 7.40 – 7.34 (m, 2H), 7.31 (d, J = 9.0 Hz, 1H), 4.40 (d, J = 8.7 Hz, 2H), 4.32 (t, J = 5.0 Hz, 2H), 4.19 – 4.09 (m, 4H), 3.40 (s, 2H), 2.67 (s, 3H), 1.72 (s, 3H), 1.22 (s, 3H)

704		LCMS (ESI) m/z 666.4 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 7.58 (s, 1H), 7.51 (d, J = 9.8 Hz, 2H), 7.34 (s, 1H), 7.28 (d, J = 9.1 Hz, 1H), 7.17 (s, 1H), 6.66 (bs, 1H), 4.89 (t, J = 8.8 Hz, 2H), 4.39 (s, 2H), 4.93 - 4.36 (m, 2H), 4.30 (s, 2H), 4.15 (s, 3H), 3.72 (s, 1H), 2.62 (s, 3H), 2.51 (s, 2H), 2.12 (s, 3H), 1.84 (s, 4H), 1.73 (d, J = 8.4 Hz, 3H)	715		MS (ESI) m/z 786.00 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.27 (s, 1H), 7.70 (s, 1H), 7.54 (dd, J = 8.84, 2.48 Hz, 1H), 7.36 (d, J = 2.52 Hz, 1H), 7.30 (d, J = 8.96 Hz, 1H), 7.20 (s, 1H), 5.09 (t, J= 4.6 Hz, 1H), 4.89 (d, J = 3.88 Hz, 2H), 4.33 (d, J= 4.52 Hz, 2H), 4.19 (s, 2H), 2.62 (s, 3H), 1.69 (s, 3H), 1.61 (s, 9H)
710		MS (ESI) m/z 668.20 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 10.10 (bs, 1H), 8.35 (s, 1H), 8.12 (s, 1H), 7.61 (dd, J = 2.56, 8.84 Hz, 1H), 7.56-7.21 (m, 4H), 4.84-4.82 (m, 1H), 4.47-4.17 (m, 4H), 2.90 (s, 3H), 2.71 (s, 3H), 2.66 (s, 3H), 1.78 (s, 6H)	716		MS (ESI) m/z 784.32 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 10.10 (s, 1H), 8.29 (s, 1H), 7.79 (s, 1H), 7.54 (dd, J = 8.8, 2.5 Hz, 1H), 7.36 (d, J = 2.52 Hz, 1H), 7.30 (d, J = 8.92 Hz, 1H), 7.21 (s, 1H), 4.35 (t, J = 4.28 Hz, 2H), 4.20 (t, J = 4.0 Hz, 2H), 2.62 (s, 3H), 1.73 (s, 3H), 1.61 (s, 9H)
712		MS (ESI) m/z 586.04 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 10.95 (bs, 1H), 8.30 (s, 1H), 7.66 (s, 1H), 7.60 (dd, J = 8.84, 2.56 Hz, 1H), 7.42 (s, 1H), 7.39-7.35 (m, 2H), 4.92 (bs, 4H), 4.40 (t, J = 4.40 Hz, 2H), 4.26 (t, J = 4.80 Hz, 2H), 3.13 (s, 3H), 2.71 (s, 3H), 1.93 (s, 3H)	718		MS (ESI) m/z 657.11 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.54 (bs, 1H), 8.30 (s, 1H), 7.58 (dd, J=8.92 Hz, 2.6 Hz, 1H), 7.48 (s, 1H), 7.39-7.34 (m, 3H), 4.38 (t, J = 5.88 Hz, 2H), 4.22 (t, J = 4.32 Hz, 2H), 3.75 (s, 2H), 2.68 (s, 3H), 2.56 (s, 3H), 2.45 (bs, 4H,), 2.28 (bs, 4H), 2.12 (s, 3H), 1.89 (s, 3H)

720		MS (ESI) m/z 579.93 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.80 (d, J = 4.88 Hz, 1H), 8.48 (s, 1H), 8.32 (s, 1H), 7.59 (dd, J = 8.92, 2.68 Hz, 1H), 7.50-7.44 (m, 2H), 7.40 (d, J = 2.6 Hz, 1H), 7.35 (d, J = 8.96 Hz, 1H), 4.49-4.38 (m, 5H), 4.33-4.27 (m, 2H), 1.85 (s, 3H)	741		MS (ESI) m/z 677.17 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 14.31 (bs, 1H), 7.71 (bs, 1H), 7.60 (dd, J = 2.48, 8.8 Hz 1H), 7.41 (s, 1H), 7.39-7.18 (m, 2H), 4.38 (t, J = 4.12 Hz, 2H), 4.24 (t, J = 4.6 Hz, 2 H), 3.81-3.21 (m, 8H), 2.93 (s, 3H), 2.71 (s, 3H), 2.50 (s, 3H), 2.02 (s, 3H)
724		MS (ESI) m/z 577.00 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.36 (s, 1H), 7.64 (s, 1H), 7.59 (dd, J=8.8 Hz, 2.56 Hz, 1H), 7.39-7.35 (m, 3H), 5.68 (d, 46.72 Hz, 2H), 4.40 (t, 4.40 Hz, 2H), 4.25 (t, 4.56 Hz, 2H), 2.69 (s, 3H), 2.53 (s, 3H), 1.95 (s, 3H)	743		MS (ESI) m/z 622.01 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.69 (d, J=3.88 Hz, 1H), 8.02 (t, J = 6.20 Hz, 1H), 7.81 (d, J = 7.76 Hz, 2H), 7.51-7.47 (m, 2H), 7.30-7.08 (m, 3H), 7.03 (bs, 1H), 4.32 (t, J = 6.04 Hz, 2H), 4.21 (t, J = 5.4 Hz, 2H), 2.76 (s, 3H), 2.66 (s, 3H), 1.93 (s, 3H)
729		MS (ESI) m/z 622.01 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (bs, 1H), 8.71 (bs, 1H), 8.07 (d, J=7.84 Hz, 1H), 7.93 (s, 1H), 7.62-7.56 (m, 1H), 7.53-7.49 (m, 1H), 7.30-7.28 (m, 3H), 7.12 (d, J=7.6 Hz, 1H), 4.42 (t, J = 4.76 Hz, 2H), 4.21 (t, J = 6.16 Hz, 2H), 2.72 (s, 3H), 2.66 (s, 3H), 1.93 (s, 3H)	744		MS (ESI) m/z 579.36 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 13.59 (bs, 1H), 8.90 (s, 1H), 8.44 (s, 1H), 7.57 (d, J = 8.84 Hz, 1H), 7.41 (s, 1H), 7.38 (s, 1H), 7.33 (d, J = 8.84 Hz, 1H), 4.39 (t, J = 5.4 Hz, 2H), 4.21 ((t, J = 4.32 Hz, 2H)), 2.68 (s, 3H), 2.35-2.32 (m, 1H), 1.78 (s, 3H), 1.29-1.07 (m, 4H)

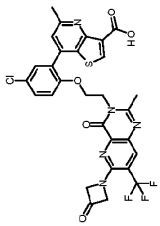
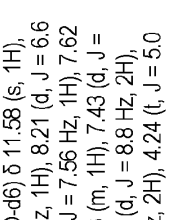
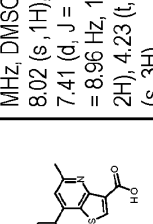
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746	MS (ESI) m/z 536.27 [M+1] +; 1H-NMR NMR (400 MHz, DMSO-d6) δ 13.58 (bs, 1H), 8.49 (s, 1H), 7.59 (d, J = 8.72 Hz, 1H), 7.40-7.38 (m, 2H), 7.35 (d, J = 8.84 Hz, 1H), 4.39 (bs, 2H), 4.22 (bs, 2H), 2.69 (s, 3H), 2.67 (s, 3H), 2.65 (s, 3H), 1.82 (s, 3H)	752	MS (ESI) m/z 620.00 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.45 (s, 1H), 7.58 (dd, J = 2.56, 8.80 Hz, 1H), 7.46 (s, 1H), 7.40 (d, J = 2.56 Hz, 1H), 7.38 (s, 1H), 7.34 (d, J = 9.04 Hz, 1H), 4.60 (t, J= 7.60 Hz, 4H), 4.35 (t, J = 5.12 Hz, 2H), 4.16 (t, J = 4.12 Hz, 2H), 2.70 (s, 3H), 2.32-2.26 (m, 2H), 1.77 (s, 3H)
748	MS (ESI) m/z 571.01 [M+1]+. 1H-NMR (400 MHz, DMSO-d6) δ 8.34 (s, 1H), 7.59 (dd, J = 8.80, 2.80 Hz 1H), 7.44-7.40 (m, 2H), 7.40-7.34 (m, 2H), 4.39 (t, J = 4.96 Hz, 2H), 4.24 (t, J = 4.52 Hz, 2H), 3.10 (t, J = 7.12 Hz, 4H), 2.71 (s, 3H), 2.21-2.14 (m, 2H), 1.96 (s, 3H)		

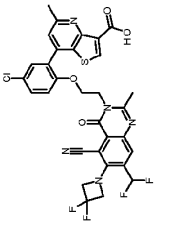
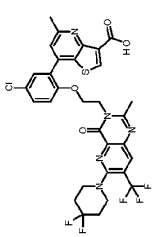
755		MS (ESI) m/z 1136.89 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.81 (d, J = 4.8 Hz, 1H), 8.41 (s, 1H), 8.20 (s, 1H), 7.98 (s, 1H), 7.72 (bs, 1H), 7.61-7.58 (m, 1H), 7.54-7.35 (m, 5H), 6.40 (s, 1H), 6.35 (s, 1H), 4.46-4.12 (m, 11H), 3.47-3.33 (m, 13H), 3.04-3.01 (m, 4H), 2.66-2.50 (m, 4H), 2.03-2.00 (m, 4H), 1.81 (s, 3H), 1.58-1.55 (m, 4H), 1.47-1.43 (m, 4H), 1.25-1.20 (m, 2H)
758		MS (ESI) m/z 692.00 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.56 (bs, 1H), 8.47 (s, 1H), 8.28 (t, J = 7.84 Hz, 1H), 7.94 (d, J = 7.72 Hz, 1H), 7.91-7.86 (m, 2H), 7.59 (dd, J = 8.88, 2.56 Hz, 1H), 7.44-7.39 (m, 2H), 7.35 (d, J = 8.96 Hz, 1H), 7.04 (t, J = 54.68 Hz, 1H), 4.39 (t, J = 4.64 Hz, 2H), 4.25 (t, J = 5.44 Hz, 2H), 2.71 (s, 3H), 1.86 (s, 3H)
761		MS (ESI) m/z 651.05 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.49 (s, 1H), 8.80 (d, J = 5.8Hz, 2H), 8.57 (s, 1H), 7.63 (d J = 5.56 Hz, 2H), 7.59 (dd, J = 8.92 Hz, 2.56, 1H), 7.44 (d, J = 2.6 Hz, 1H), 7.40 (s, 1H), 7.36 (d, J=8.96, 1H), 4.42 (t, J = 5.4 Hz, 2H), 4.32 (t, J = 4.24 Hz, 2H), 2.71 (s, 3H), 2.00 (s, 3H)

759		MS (ESI) m/z 622.07 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.63 (bs, 1H), 8.77 (s, 1H), 8.71 (s, 1H), 8.35 (s, 1H), 8.03 (d, J = 6.96 Hz, 1H), 7.61-7.59 (m, 2H), 7.52 (s, 1H), 7.43-7.36 (m, 3H), 4.42 (t, J = 5.76 Hz, 2H), 4.26 (t, J = 5.48 Hz, 2H), 2.71 (s, 3H), 2.5 (s, 3H, not visible, merged with moisture peak), 1.87 (s, 3H)	
760		MS (ESI) m/z 589.98 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.51 (s, 1H), 7.59 (dd, J = 8.88, 2.6 Hz, 1H), 7.42 (d J = 2.56 Hz, 1H), 7.39 (s, 1H), 7.35 (d, J = 8.96 Hz, 1H), 4.40 (t, J = 4.72 Hz, 2H), 4.28 (t, J = 4.8 Hz, 2H), 2.79 (s, 3H), 2.69 (s, 3H), 1.98 (s, 3H)	
764		MS (ESI) m/z 652.95 [M+1]+, 1H NMR (400 MHz, DMSO-d6) δ 13.57 (bs, 1H), 9.09 (s, 1H), 8.84 (d, J = 2.44 Hz, 1H), 8.80 (bs, 1H), 8.37 (s, 1H), 8.35 (s, 1H), 7.58 (dd, J = 2.56, 8.88 Hz, 1H), 7.43 (bs, 2H), 7.35 (d, J= 8.96 Hz, 1H), 4.41 (t, J = 4.96 Hz, 2H), 4.28 (t, J = 4.36 Hz, 2H), 2.70 (s, 3H), 1.83 (s, 3H)	
765		MS (ESI) m/z 652.95 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.61 (bs, 1H), 9.02 (d, J = 4.92 Hz, 2H), 8.40 (s, 1H), 8.34 (s, 1H), 7.70 (t, J = 4.92 Hz, 1H), 7.58 (dd, J = 8.92, 2.52 Hz, 1H), 7.43 (d, J = 2.48 Hz, 1H), 7.41 (s, 1H), 7.34 (d, J = 8.96 Hz, 1H), 4.39-4.37 (m, 2H), 4.30-4.23 (m, 2H), 2.69 (s, 3H), 1.80 (s, 3H)	
766		MS (ESI) m/z 630.01 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.40 (s, 1H), 7.89 (s, 1H), 7.59 (dd, J = 90.20, 2.52 Hz, 1H), 7.42 (s, 2H), 7.34 (d, J = 8.96 Hz, 1H), 4.36 (t, J = 5.64 Hz, 2H), 4.22-4.18 (m, 6H), 2.70 (s, 3H), 2.36-2.30 (m, 2H), 1.72 (s, 3H)	
769		MS (ESI) m/z 667.07 [M+1]+ ; 1H NMR (400 MHz, DMSO-d6) δ 13.57 (bs, 1H), 8.95 (d, J = 5.12 Hz, 1H), 8.37 (s, 1H), 8.33 (s, 1H), 7.75 (d, J = 5.08 Hz, 1H), 7.59 (dd, J = 2.52, 8.84 Hz, 1H), 7.42 (t, J = 2.64 Hz, 2H), 7.35 (d, J = 8.96 Hz, 1H), 4.40 (t, J = 6.64 Hz, 2H), 4.27 (t, J = 6.6 Hz, 2H), 2.71 (s, 6H), 1.81 (s, 3H)	

767		MS (ESI) m/z 652.92 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.57 (bs, 1H) 9.35 (d, J = 0.88 Hz, 1H), 9.08 (d, J = 5.16 Hz, 1H), 8.37 (s, 1H), 8.35 (s, 1H), 7.98 (dd, J = 4.04, 1.52 Hz, 1H), 7.59 (dd, J = 9.20, 2.40, Hz, 1H), 7.43-7.41 (m, 2H), 7.35 (d, J = 8.96 Hz, 1H), 4.40 (t, J = 3.76 Hz, 2H), 4.27 (t, J = 4.48 Hz, 2H), 2.70 (s, 3H), 1.83 (s, 3H)	778		MS (ESI) m/z 639.97 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.80 (d, J = 5.28 Hz, 1H), 8.43 (s, 1H), 7.76 (s, 1H), 7.70 (d, J = 4.88, 1H), 7.61-7.58 (m, 2H), 7.43 (s, 1H), 7.41 (d, J = 2.48 Hz, 1H), 7.37 (d, J = 8.96 Hz, 1H), 4.41 (t, J = 5.32 Hz, 2H), 4.27 (t, J = 4.28 Hz, 2H), 2.73 (s, 3H), 2.67 (s, 3H), 1.94 (s, 3H)
768		MS (ESI) m/z 653.01 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.55 (bs, 1H), 9.38 (s, 1H), 9.03 (s, 2H), 8.31 (d, J = 2.88 Hz, 1H), 7.59 (dd, J = 8.80, 2.40 Hz, 1H), 7.43-7.41 (m, 2H), 7.35 (d, J = 8.96 Hz, 1H), 4.41 (t, J = 4.80 Hz, 2H), 4.27 (t, J = 4.80 Hz, 2H), 2.72 (s, 3H), 1.85 (s, 3H)	780		MS (ESI) m/z 616.97 [M+1]+;1H NMR (400 MHz, DMSO-d6) δ 13.58 (s, 1H), 8.32 (s, 1H), 8.25 (s, 1H), 7.60 (dd, J = 2.56, 8.84 Hz 1H), 7.42-7.41 (m, 2H), 7.36 (d, J = 8.96 Hz, 1H), 4.41 (t, J = 4.56 Hz, 2H), 4.28 (t, J = 4.28 Hz, 2H), 2.72 (s, 3H), 2.71 (s, 3H), 1.81 (s, 3H)
781		MS (ESI) m/z 646.02 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.38 (s, 1H), 8.27 (s, 1H), 7.62-7.57 (dd, J = 2.6, 8.8 Hz, 1H), 7.44-7.43 (m, 2H), 7.36 (d, J = 9.2 Hz, 1H), 4.39 (t, J = 4.4 Hz, 2H), 4.25 (t, J = 4.4 Hz, 2H), 3.06 (s, 3H), 2.79 (s, 3H), 2.71 (s, 3H), 1.78 (s, 3H)	784		MS (ESI) m/z 612.97 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 8.28 (s, 1H), 8.08 (s , 1H), 7.59 (dd, J = 2.48, 8.88 Hz, 1H), 7.41 (d, J = 2.6 Hz, 2H), 7.35 (d, J = 8.96 Hz, 1H), 4.37 (t, J = 4.48 Hz, 2H), 4.23 (t, J = 4.92 Hz, 2H), 2.69 (s, 3H), 2.19 (s, 3H), 1.76 (s, 3H)

782		MS (ESI) m/z 653.03 [M+1]+. 1H NMR (400 MHz, DMSO-d6) δ 13.5 (bs, 1H), 8.40 (s, 1H), 8.32 (s, 1H), 7.59 (d, J = 8.0 Hz, 1H), 7.41 (s, 2H), 7.33 (d, J = 9.0 Hz, 1H), 4.40 (bs, 2H), 4.27 (bs, 2H), 3.54 (s, 3H), 2.70 (s, 3H), 1.78 (s, 3H)	
783		MS (ESI) m/z 598.95 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.57 (bs, 1H), 8.29 (s, 1H), 8.13 (s, 1H), 7.60-7.57 (dd, J = 8.84, 2.4 Hz, 2H), 7.41 (d, J = 3.48 Hz 1H), 7.34 (d, J = 8.92 Hz, 1H), 4.89 (s, 1H), 4.38 (t, J = 3.84 Hz, 2H), 4.24 (t, J = 4.52 Hz, 2H), 2.69 (s, 3H), 1.76 (s, 3H)	
787		MS (ESI) m/z 654.99 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.60 (bs, 1H), 8.35 (s, 1H), 8.20 (s, 1H), 7.82 (d, J = 1.96 Hz, 1H), 7.58 (dd, J = 8.88, 2.48 Hz, 1H), 7.42 (d, J = 2.52 Hz, 1H), 7.40 (s, 1H), 7.34 (d, J = 8.96 Hz, 1H), 6.70 (d, J = 2.0 Hz, 1H), 4.39 (t, J = 4.40 Hz, 2H), 4.25 (t, J = 4.00 Hz, 2H), 3.94 (s, 3H), 2.68 (s, 3H), 1.77 (s, 3H)	
785		MS (ESI) m/z 600.0 [M+1]+. 1H-NMR (400 MHz, DMSO-d6)) δ 8.33 (s, 1H), 8.24 (s ,1H), 7.60 (dd, J = 2.52, 8.84 Hz, 1H), 7.43 (s, 1H), 7.41 (d, J = 2.52 Hz, 1H), 7.35 (d, J = 8.96 Hz, 1H), 4.40 (t, J = 4.4 Hz, 2H), 4.27 (t, J = 6.0 Hz, 2H), 2.70 (s, 3H), 1.75 (s, 3H)	
786		MS (ESI) m/z 615.29 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.41 (s, 1H), 8.00 (s, 1H), 7.59 (d, J = 7.72 Hz, 1H), 7.42 (d, J = 1.92 Hz, 1H), 7.40 (s, 1H), 7.34 (d, J = 9.04 Hz, 1H), 4.37 (t, J = 4.12 Hz, 2H), 4.19 (t, J = 5.04 Hz, 2H), 3.01 (s, 6H), 2.69 (s, 1H), 1.72 (s, 3H)	
795		MS (ESI) m/z 615.04 [M+1]+ ; 1H NMR (400 MHz, DMSO-d6) δ 13.58 (bs, 1H), 8.32 (s, 1H), 8.03 (s, 1H), 7.59 (dd, J = 2.40, 8.76 Hz, 1H), 7.42 (d, J = 2.52 Hz, 1H), 7.39 (s, 1H), 7.33 (d, J = 8.96 Hz, 1H), 4.37 (bs, 2H), 4.21 (bs, 2H), 2.68 (s, 3H), 2.37-2.32 (m, 1H), 1.76 (s, 3H), 1.19-1.13 (m,4H)	

788Fa		MS (ESI) m/z 676.01 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 11.58 (s, 1H), 8.43 (d, J = 5.0 Hz, 1H), 8.21 (d, J = 6.6 Hz, 2H), 8.11 (d, J = 7.56 Hz, 1H), 7.62 (s, 1H), 7.60-7.56 (m, 1H), 7.43 (d, J = 2.6 Hz, 2H), 7.35 (d, J = 8.8 Hz, 2H), 4.40 (t, J = 6.7 Hz, 2H), 4.24 (t, J = 5.0 Hz, 2H), 2.58 (s, 3H), 1.71 (s, 3H)	796		MS (ESI) m/z 644.27 [M+1]+; 1H-NMR (400 MHz, DMSO-d6) δ 13.60 (bs, 1H), 8.34 (s, 1H), 8.02 (s ,1H), 7.59 (dd, J = 2.52, 8.88 Hz, 1H), 7.41 (d, J = 2.52 Hz, 1H),7.39 (s, 1H), 7.35 (d, J = 8.96 Hz, 1H), 5.03 (s, 4H), 4.37 (t, J = 5.28 Hz, 2H), 4.23 (t, J = 6.32 Hz, 2H), 2.70 (s, 3H), 1.75 (s, 3H)
788Fb		MS (ESI) m/z 694.03 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.69 (s, 1H), 8.63 (d, J = 4.9 Hz, 1H), 8.40 (s, 1H), 7.80 (s, 1H), 7.75 (s, 1H), 7.61 (d, J = 7.4 Hz, 1H), 7.52 (dd, J = 2.4, 4.9 Hz, 1H), 7.45 (s, 1H), 7.37 (s, 2H), 7.31-7.29 (m, 1H), 7.26 (s, 2H), 4.35 (bs, 2H), 4.24 (bs, 2H), 2.58 (s, 3H), 1.75 (s, 3H)	797		MS (ESI) m/z 644.0 [M-1]-; 1H-NMR (400 MHz, DMSO-d6)) δ 13.59 (bs, 1H), 8.39 (s, 1H), 7.90 (s ,1H), 7.59 (dd, J = 2.44, 8.88 Hz, 1H), 7.41 (d, J = 2.48 Hz, 1H), 7.38 (s, 1H), 7.33 (d, J = 8.96 Hz, 1H), 5.70 (d, J = 5.84 Hz, 1H), 4.57-4.56 (m , 1H), 4.38-4.32 (m, 4H), 4.18 (d, J = 4.2 Hz, 2H), 3.96-3.92 (m, 2H), 2.68 (s, 3H), 1.71 (s, 3H)
798		MS (ESI) m/z 725.97 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.45 (s, 1H), 7.66 (s, 1H), 7.58 (dd, J = 8.88, 2.56 Hz 1H), 7.43-7.38 (m, 2H), 7.35 (d, J = 8.96 Hz, 1H), 4.37 (t, J = 6.00 Hz, 2H), 4.20 (t, J = 4.28 Hz, 2H), 3.55-3.44 (m, 4H), 2.70 (s, 3H), 2.05-1.94 (m, 4H), 1.81 (s, 3H)	801		MS (ESI) m/z 686.30 [M+1]+ ; 1H NMR (400 MHz, DMSO-d6) δ 13.58 (bs, 1H), 8.38 (s, 1H), 8.02 (s, 1H), 7.59 (dd, J = 2.60, 8.92 Hz, 1H), 7.42 (d, J = 2.56 Hz, 1H), 7.39 (s, 1H), 7.33 (d, J = 8.96 Hz, 1H), 4.37 (t, J = 4.64 Hz, 2H), 4.20 (t, J = 5.56 Hz, 2H), 3.23 (t, J = 5.16 Hz, 4H), 2.68 (s, 3H), 1.78 (s, 3H), 1.48 (t, J = 5.2 Hz, 4H), 0.99 (s, 6H)

799		802	
MS (ESI) m/z 671.94 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.55 (bs, 1H), 8.42 (s, 1H), 7.69 (s, 1H), 7.58 (dd, J = 2.36, 8.84 Hz, 1H), 7.40 (d, J = 2.52 Hz, 1H), 7.39 (s, 1H), 7.35 (d, J = 9.00 Hz, 1H), 7.33 (t, J = 54.04 Hz, 1H), 4.92 (t, J = 12.44 Hz, 4H), 4.38 (t, J = 5.36 Hz, 2H), 4.20 (t, J = 5.80 Hz, 2H), 2.70 (s, 3H), 1.82 (s, 3H)		MS (ESI) m/z 694.06 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.57 (bs, 1H), 8.33 (s, 1H), 8.10 (s, 1H), 7.58 (d, J = 7.08, 1H), 7.41-7.32 (m, 3H), 4.38 (t, J = 3.64 Hz, 2H), 4.21 (t, J = 5.68 Hz, 2H), 3.35 (t, J = 5.08 Hz, 4H), 2.68 (s, 3H), 2.14 (t, J = 13.4 Hz, 4H), 1.76 (s, 3H)	
800		803	
MS (ESI) m/z 672.15 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.38 (s, 1H), 8.03 (s, 1H), 7.59 (dd, J = 2.56, 8.88 Hz, 1H), 7.42 (d, J = 2.56 Hz, 1H), 7.39 (s, 1H), 7.33 (d, J = 8.96 Hz, 1H), 4.37 (t, J = 5.48 Hz, 2H), 4.20 (t, J = 4.32 Hz, 2H), 3.55 (d, J = 12.44 Hz, 2H), 2.90 (t, J = 11.90 Hz, 2H), 2.68 (s, 3H), 1.74-1.72 (m, 5H), 1.58 (bs, 1H), 1.31-1.23 (m, 2H), 0.97 (d, J = 6.44 Hz, 3H)		MS (ESI) m/z 725.97 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.38 (s, 1H), 8.06 (s, 1H), 7.58 (d, J = 8.60 Hz, 1H), 7.41 (s, 2H), 7.34 (d, J = 8.96 Hz, 1H), 4.38 (t, J = 5.16 Hz, 2H), 4.21 (t, J = 5.52 Hz, 2H), 3.62 (d, J = 12.52 Hz, 2H), 2.97 (t, J = 12.12 Hz, 2H), 2.70 (s, 3H), 1.94 (d, J = 11.96 Hz, 2H), 1.76 (s, 3H), 1.64-159 (m, 2H)	
804		810	
MS (ESI) m/z 681.96 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.56 (s, 1H), 8.59 (d, J = 3.56, 1H), 8.35 (s, 1H), 8.14 (s, 1H) 7.87 (t, J = 6.92 Hz, 1H), 7.59-7.53 (m, 2H), 7.42-7.40 (m, 2H), 7.38-7.33 (m, 2H), 5.66 (s, 2H), 4.39 (t, J = 4.36 Hz, 2H), 4.22 (t, J = 4.04 Hz, 2H), 2.70 (s, 3H), 1.75 (s, 3H)		MS (ESI) m/z 605.8 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.49 (d, J = 0.8 Hz, 1H), 8.44 (s, 1H), 7.58 (dd, J = 8.9, 2.7 Hz, 1H), 7.42 (d, J = 2.7 Hz, 1H), 7.36 (s, 1H), 7.34 (d, J = 9.0 Hz, 1H), 7.11 (d, J = 0.9 Hz, 1H), 4.48 (d, J = 12.6 Hz, 2H), 4.36 (t, J = 5.1 Hz, 2H), 4.21 (t, J = 5.1 Hz, 2H), 3.56 (bd, J = 11.0 Hz, 2H), 3.25-3.04 (m, 4H), 2.88 (d, J = 3.5 Hz, 3H), 2.69 (s, 3H), 1.83 (s, 3H)	

805		MS (ESI) m/z 614.99 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.44 (s, 1H), 7.59 (dd, J = 8.80, 2.40 Hz, 1H), 7.43-7.41 (m, 3H), 7.36 (d, J = 8.80 Hz, 1H), 6.19 (s, 1H), 4.38 (t, J = 4.92 Hz, 2H), 4.22 (t, J = 6.00 Hz, 2H), 2.78-2.50 (m, 5H), 2.09-2.01 (m, 4H), 1.86 (s, 3H)	811		MS (ESI) m/z 604.8 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.44 (s, 1H), 7.57 (td, J = 8.9, 2.8 Hz, 2H), 7.42 (d, J = 2.7 Hz, 1H), 7.39 – 7.27 (m, 4H), 4.36 (t, J = 5.1 Hz, 2H), 4.22 (t, J = 5.0 Hz, 2H), 3.97 (d, J = 13.2 Hz, 2H), 3.57 (d, J = 12.3 Hz, 2H) 3.29 – 3.13 (m, 2H), 3.04 (t, J = 12.6 Hz, 2H), 2.89 (d, J = 4.0 Hz, 3H), 2.68 (s, 3H), 1.82 (s, 3H).
806		MS (ESI) m/z 583.01 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.89 (bs, 1H), 8.07 (bs, 1H), 7.89 (d, J = 7.6 Hz, 1H), 7.85 (s, 1H), 7.52-7.12 (m, 6H), 4.35 (s, 4H), 4.13 (s, 2H), 2.56 (bs, 6H), 2.14 (s, 3H)	812		MS (ESI) m/z 643.6 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 7.70 (d, J = 9.0 Hz, 1H), 7.64 – 7.57 (m, 2H), 7.43 – 7.34 (m, 3H), 4.41 (t, J = 5.0 Hz, 2H), 4.24 (t, J = 5.1 Hz, 2H), 3.82 – 3.55 (m, 4H), 3.25 (bd, J = 9.1 Hz, 4H), 2.92 (s, 3H), 2.70 (s, 3H), 2.48 (s, 3H), 1.95 (s, 3H)
841		MS (ESI) m/z = 580.3 [M+1]+; 1H-NMR (400 MHz, d6-DMSO) δ /ppm = 9.74-9.62 (b, 1H), 8.84 (d, J = 4.7 Hz, 1H), 8.52 (s, 1H), 8.44 (s, 1H), 8.38 (s, 1H), 7.59 (dd, J = 8.9, 2.7 Hz, 1H), 7.46-7.43 (m, 2H), 7.32 (d, J = 8.9 Hz, 1H), 4.54 (t, J = 4.4 Hz, 2H), 4.34 (t, J = 4.9 Hz, 2H), 4.18 (t, J = 4.9 Hz, 2H), 3.61-3.56 (m, 2H), 2.98 (d, J = 4.4 Hz, 6H), 1.80 (s, 3H)	877		LCMS (ESI) m/z 671.1 [M+1]+. 1H NMR (400 MHz, DMSO-d6) δ 8.62 (s, 1H), 8.18 (d, J = 8.8 Hz, 1H), 8.07 (s, 1H), 7.63 (s, 1H), 7.56 (dd, J = 8.9, 2.7 Hz, 1H), 7.41 – 7.28 (m, 2H), 4.37 (t, J = 5.0 Hz, 1H), 4.22 (d, J = 5.0 Hz, 1H), 3.38 (d, J = 12.0 Hz, 1H), 3.09 (d, J = 12.0 Hz, 1H), 2.67 (s, 2H), 2.17 (s, 2H), 1.94 (t, J = 11.8 Hz, 1H), 1.81 (s, 3H)

849		LCMS: 672.9 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ 9.79 (s, 1H), 8.48 (s, 1H), 8.41 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.43 (d, J = 2.7 Hz, 1H), 7.40 – 7.31 (m, 2H), 4.41 (t, J = 5.1 Hz, 2H), 4.27 (t, J = 5.2 Hz, 2H), 3.37 – 3.12 (m, 6H), 2.93 (d, J = 2.7 Hz, 3H), 2.69 (s, 3H), 1.99 (s, 3H)	880		LCMS (ESI) m/z 643.1 [M+1]+. 1H NMR (400 MHz, DMSO-d6) δ 8.77 (d, J = 4.8 Hz, 1H), 8.26 (s, 1H), 8.20 (s, 1H), 8.06 (s, 1H), 7.70 (s, 1H), 7.56 (dd, J = 8.9, 2.7 Hz, 1H), 7.45 – 7.37 (m, 2H), 7.32 (d, J = 9.0 Hz, 1H), 4.36 (t, J = 5.0 Hz, 2H), 4.21 (t, J = 5.1 Hz, 2H), 3.19 (s, 1H), 3.09 (d, J = 11.9 Hz, 2H), 1.94 (q, J = 13.5, 12.6 Hz, 4H), 1.79 (s, 3H)
858		LCMS: 631.4 [M+H]+; 1H NMR (400 MHz, DMSO-d6) δ 9.77 – 9.57 (m, 1H), 8.79 (d, J = 4.8 Hz, 1H), 8.19 (s, 1H), 8.11 (s, 1H), 7.70 (s, 1H), 7.56 (dd, J = 8.9, 2.7 Hz, 1H), 7.41 (dd, J = 12.9, 3.7 Hz, 2H), 7.32 (d, J = 9.0 Hz, 1H), 4.36 (t, J = 5.1 Hz, 2H), 4.22 (t, J = 5.0 Hz, 2H), 3.34 (t, J = 6.2 Hz, 2H), 3.20 (dd, J = 11.3, 5.4 Hz, 2H), 2.88 (d, J = 4.3 Hz, 6H), 1.78 (s, 3H)	881		LCMS (ESI) m/z 657.0 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.78 (d, J = 4.8 Hz, 1H), 8.24 (s, 1H), 8.02 (s, 1H), 7.70 (s, 1H), 7.56 (dd, J = 8.9, 2.7 Hz, 1H), 7.45 – 7.37 (m, 2H), 7.32 (d, J = 9.0 Hz, 1H), 4.36 (t, J = 5.0 Hz, 2H), 4.21 (t, J = 5.0 Hz, 2H), 3.21 – 3.11 (m, 3H), 2.82 (d, J = 4.6 Hz, 3H), 1.99 (s, 3H), 1.78 (s, 3H)
896		MS (ESI) m/z 668.21 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.34 (s, 1H), 7.74 (bs, 1H), 7.60 (dd, J = 2.4, 8.8 Hz, 1H), 7.49-7.13 (m, 4H), 4.39 (bs, 2H), 4.23 (bs, 2H), 3.58 (bs, 2H), 3.03-2.98 (m, 2H), 2.25 (bs, 6H), 1.78 (s, 3H), 1.37 (t, J = 7.6 Hz, 3H)	920		MS (ESI) m/z 662.15 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.38 (s, 1H), 7.74 (d, J = 8.72 Hz, 1H), 7.57 (dd, J = 2.12, 8.76 Hz, 1H), 7.41 (d, J = 2.08 Hz, 1H), 7.39 (bs, 1H), 7.34(d, J = 8.92 Hz, 1H), 4.37 (bs, 2H), 4.19 (bs, 2H), 3.60-3.57 (m, 1H), 3.47-3.41 (m, 1H), 2.69 (s, 3H), 2.10-2.05 (m, 2H), 1.89-1.86 (m, 2H), 1.79 (s, 3H), 1.25 (s, 3H), 1.12 (s, 3H)

918	MS (ESI) m/z 648.12 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.32 (bs, 1H), 8.37 (s, 1H), 7.62-7.57 (m, 2H), 7.42-7.33 (m, 3H), 4.41-4.37 (m, 4H), 4.18 (s, 2H), 2.69 (s, 3H), 2.25 (t, J=7.52 Hz, 2H), 1.74 (s, 3H), 1.53 (s, 6H).	921	MS (ESI) m/z 646.03 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.45 (s, 1H), 8.02 (s, 1H), 7.59 (dd, J = 2.56 Hz, J = 8.88 Hz, 1H), 7.55 (d, J = 10.16 Hz, 1H), 7.43 (s, 1H), 7.41 (d, J = 2.56 Hz, 1H), 7.36 (d, J = 8.96 Hz, 1H), 4.40 (t, J = 5.88 Hz, 2H), 4.25 (t, J = 4.44 Hz, 2H), 2.79 (s, 3H), 2.72 (s, 3H), 1.90 (s, 3H)
919	MS (ESI) m/z 684.04 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.40 (s, 1H), 7.68 (s, 1H), 7.59 (dd, J = 2.48, 8.84 Hz, 1H), 7.40 (bs, 2H), 7.35 (d, J = 8.92 Hz, 1H), 4.38 (t, J = 5.92 Hz, 2H), 4.22 (t, J = 6.52 Hz, 2H), 3.45 (t, J = 5.96 Hz, 4H), 2.71 (s, 3H), 2.21-2.16 (m, 4H), 1.86 (s, 3H)	932	MS (ESI) m/z 654.10 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.41 (s, 1H), 7.69-7.55 (m, 4H), 7.43 (s, 1H), 7.40 (d, J = 2.52 Hz, 1H), 7.32 (d, J = 8.96 Hz, 1H), 4.44-4.38 (m, 2H) 4.26 (t, J=5.40 Hz, 2H), 2.73 (s, 3H), 2.65 (s, 6H), 1.93 (s, 3H)
933	MS (ESI) m/z 668.23 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.39 (s, 1H), 7.79 (s, 1H), 7.60 (dd, J = 8.84, 2.6 Hz, 1H), 7.51 (bs, 2H), 7.42 (s, 1H), 7.40 (d, J = 2.56 Hz, 1H), 7.37 (d, J= 9 Hz, 1H), 5.32 (d, J= 46.4 Hz, 2H), 4.41 (t, J = 3.04 Hz, 2H), 4.27 (t, J = 5.12 Hz, 2H), 2.72 (s, 3H), 2.64 (s, 6H), 1.96 (s, 3H)	938	MS (ESI) m/z 633.05 [M+1]+. 1H NMR (400 MHz, DMSO-d6) δ 13.56 (s, 1H), 8.38 (s, 1H), 8.14 (s, 1H), 7.57 (bs, 1H), 7.42-7.33 (m, 3H), 5.36 (bs, 1H), 4.39 (bs, 2H), 4.23 (bs, 2H), 2.67 (s, 3H), 1.79 (s, 3H), 1.58 (s, 6H)

935		MS (ESI) m/z 625.09 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.59 (bs, 1H), 8.46 (s, 1H), 7.58-7.51 (m, 7H), 7.42 (s, 2H), 7.37 (d, J = 8.44 Hz, 1H), 4.40 (t, J = 3.72, 2H), 4.25 (t, J = 5.12, 2H), 2.72 (s, 3H), 1.85 (s, 3H).	
936		MS (ESI) m/z 646.04 [M+1]+, 1H NMR (400 MHz, DMSO-d6) δ 9.29 (s, 1H), 8.45 (s, 1H), 7.61-7.57 (m, 2H), 7.43 (bs, 2H), 7.33 (t, J=19.2Hz, 1H), 4.40 (t, J=5.68 Hz, 2H), 4.25 (d, J=4.48 Hz, 2H), 2.72 (s, 3H), 2.30 (s, 3H), 1.85 (s, 3H).	
939		MS (ESI) m/z 671.98 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.61 (bs, 1H), 9.19 (s, 1H), 8.35 (s, 1H), 7.58 (dd, J = 8.88, 2.56 Hz, 1H), 7.44 (s, 2H), 7.35 (d, J =9.0 Hz, 1H), 4.40 (t, J=5.0 Hz, 2H), 4.26 (t, J = 5.44, 2H), 2.72 (s, 3H), 2.20 (s, 3H), 1.81 (s, 3H)	
955		MS (ESI) m/z 650.12 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.54 (s, 1H), 8.34 (s, 1H), 7.72 (s, 1H), 7.58 (dd, J = 1.48 Hz, J = 7.80 Hz, 1H), 7.42 (d, J = 1.76 Hz, 1H), 7.40 (s, 1H), 7.50 (d, J = 8.88, 1H), 4.38 (t, J = 5.80, 2H), 4.20 (t, J = 4.32, 2H), 2.90 (s, 3H), 2.70 (s, 3H), 1.77 (s, 3H), 1.25 (s, 9H)	
956		MS (ESI) m/z 636.11 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.47 (s, 1H), 8.38 (s, 1H), 7.73 (s, 1H), 7.58 (dd, J = 2.32 Hz, J = 8.80 Hz, 1H), 7.43 (d, J = 2.28 Hz, 1H), 7.40 (s, 1H), 7.35 (d, J = 8.96 Hz, 1H), 4.55 (s, 1H), 4.37 (t, J = 5.12 Hz, 2H), 4.19 (t, J = 6.04 Hz, 2H), 2.69 (s, 3H), 1.74 (s, 3H), 1.32 (s, 9H)	
959		MS (ESI) m/z 685.17 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.58 (s, 1H), 8.41 (s, 1H), 8.17 (s, 1H), 7.92 (s, 1H), 7.62-7.59 (m, 3H), 7.44 (s, 2H), 7.37 (d, J = 8.96 Hz, 1H), 4.40 (t, J = 2.76 Hz, 2H), 4.26 (t, J = 3.72 Hz, 2H), 3.44 (s, 3H), 2.73 (s, 3H), 2.57 (s, 3H), 1.85 (s, 3H)	

957		MS (ESI) m/z 634.13 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.4 (s, 1H), 8.39 (s, 1H), 7.69 (s, 1H), 7.59 (dd, J = 8.84, 2.44 Hz, 1H), 7.42 (d, J = 2.4 Hz, 1H), 7.38 (s, 1H), 7.35 (d, J = 8.92 Hz, 1H), 4.37 (bs, 2H), 4.19 (bs, 2H), 3.08 (t, J = 10.36 Hz, 1H), 3.02 (s, 3H), 2.69 (s, 3H), 1.78 (s, 3H), 0.63 (d, J = 4.92 Hz, 2H), 0.37 (bs, 2H)	960		MS (ESI) m/z 671.27 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.25 (s, 1H), 8.45 (s, 1H), 8.20 (d, J = 2.20, 1H), 7.86 (s, 1H), 7.69 (s, 1H), 7.60 (dd, J = 2.32 Hz, J = 8.72 Hz, 2H), 7.43-7.42 (m, 2H), 7.36 (d, J = 8.92 Hz, 1H), 4.39 (t, J = 5.56 Hz, 2H), 4.24 (t, J = 3.56 Hz, 2H), 2.71 (s, 3H), 2.55 (s, 3H), 1.81 (s, 3H)
958		MS (ESI) m/z 620.03 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ8.46 (s, 1H), 7.59 (d, J = 2.2Hz, 1H), 7.54 (s, 1H), 7.43 (d, J = 2.4 Hz, 2H), 7.36 (d, J = 8.92 Hz, 1H), 6.66 (s, 1H), 4.36 (bs, 2H), 4.10 (bs, 2H), 3.16 (d, J = 6.84 Hz, 1H), 2.70 (s, 3H), 1.80 (s, 3H), 0.867-0.82 (m, 2H), 0.65-0.62 (m, 2H)	961		MS (ESI) m/z 689.15 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.43 (s, 1H), 8.01 (s, 1H), 7.91 (s, 1H), 7.79 (s, 1H), 7.59 (d, J = 8.80 Hz, 1H), 7.44 (s, 2H), 7.36 (d, J = 8.80 Hz, 1H), 7.04 (d, J = 12.04 Hz, 1H), 4.39 (s, 2H), 4.25 (s, 2H), 3.39 (s , 3H), 2.73 (s, 3H), 1.80 (s, 3H)
962		MS (ESI) m/z 675.07 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.07 (s, 1H), 8.45 (s, 1H), 8.09 (s, 1H), 8.03 (d, J = 2.04, 1H), 7.85 (s, 1H), 7.59 (dd, J = 8.84 Hz, 2.36 Hz, 1H), 7.44 (s, 2H), 7.36 (d, J = 8.92 Hz, 1H), 7.04 (d, J = 11.12 Hz, 1H), 4.39 (t, J = 4.64 Hz, 2H), 4.22 (t, J = 4.48 Hz, 2H), 2.72 (s, 3H), 1.75 (s, 3H)	1001		MS (ESI) m/z [M+1]+, 1H NMR (400 MHz, DMSO-d6) δ 9.08 (s, 1H), 8.64 (s, 1H), 8.38 (s, 1H), 8.02 (d, J = 6.96 Hz,1H), 7.59 (d, J = 6.76 Hz, 1H), 7.39-7.35 (m, 3H), 6.18 (s, 1H), 4.37 (s, 2H), 4.22 (s, 2H), 2.68 (s, 3H), 2.30 (s, 3H), 1.78 (s, 3H), 1.05 (t, J = 7.16 Hz, 1H).

990		MS (ESI) m/z 721.31 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.63 (bs, 1H), 9.18 (s, 1H), 9.13 (s, 1H), 8.46 (s, 1H), 8.32 (s, 1H), 7.58 (dd, J = 2.52, 8.88 Hz, 1H), 7.44 -7.43 (m, 2H), 7.34 (d, J = 8.96 Hz, 1H), 4.39 (t, J = 5.00 Hz, 2H), 4.26 (t, J = 4.36 Hz, 2H), 2.70 (s, 3H), 1.82 (s, 3H)
1000		MS (ESI) m/z [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.12 (s, 1H), 8.49 (s, 1H), 7.86 (t, J = 9.12 Hz, 1H), 7.74-7.66 (m, 2H), 7.54-7.38 (m, 3H),6.21 (s, 1H), 4.40 (t, J = 4.48, 2H), 4.24 (t, J = 4.64, 2H), 2.69 (s, 3H), 2.54 (s, 3H), 1.69 (s, 3H).
1005		MS (ESI) m/z 562.18 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.64 (bs, 1H), 8.58 (s, 1H), 8.56 (s, 1H), 7.62-7.56 (m, 1H), 7.43-7.39 (m, 2H), 7.34 (d, J = 8.92 Hz, 1H), 4.35 (t, J = 4.68 Hz, 2H), 4.41 (t, J = 4.48 Hz, 2H), 3.70 (s, 3H), 2.72 (s, 3H), 1.71 (s, 3H)
1002		MS (ESI) m/z 574 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.52 (bs, 1H), 8.57 (s, 1H), 8.49 (s, 1H), 7.57 (d, J = 8.52Hz, 1H), 7.39-7.33 (m, 3H), 5.91 (s,1H), 4.37 (t, J = 5.08 Hz, 2H), 4.16 (t, J = 4.04 Hz, 2H), 3.21 (s, 6H), 2.70 (s, 3H), 1.63 (s, 3H)
1003		MS (ESI) m/z 586.13 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.49 (bs, 1H), 8.56 (s, 1H), 8.48 (s, 1H), 7.56 (d, J = 8.84 Hz, 1H), 7.39 (s, 1H), 7.40-7.33 (m, 2 H), 5.89 (s, 1H), 4.37-4.32 (m, 6H), 4.15 (t, J = 5.36 Hz, 2H), 2.69 (s, 3H), 1.69 (s, 3H), 2.38-2.32 (m, 2H)
1018		MS (ESI) m/z 667.06 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.58 (bs, 1H), 8.95 (s, 1H), 8.68 (s, 1H), 8.36 (s, 1H), 8.32 (s, 1H), 7.58 (dd, J = 8.92, 2.40 Hz, 1H), 7.42 (s, 2H), 7.35 (d, J = 8.92 Hz, 1H), 4.40 (s, 2H), 4.27 (s, 2H), 2.70 (s, 3H), 2.62 (s, 3H), 1.81 (s, 3H)

1006		MS (ESI) m/z 632.03 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.51 (s, 1H), 8.48 (s, 1H), 7.91 (s, 1H), 7.63-7.56 (m, 2H), 7.46-7.40 (m, 2H), 7.35 (d, J = 8.96 Hz, 1H), 4.39 (t, J = 5.96 Hz, 2H), 4.24 (t, J = 5.44 Hz, 2H), 2.71 (s, 3H), 1.81 (s, 3H)	1019		MS (ESI) m/z 667.16 [M+1]+; 1H NMR (400 MHz, DMSO-d6) 13.60 (s,1H), 8.72 (d, J = 2.36 Hz, 1H), 8.61 (s, 1H), 8.39 (s, 1H), 8.37 (s, 1H), 7.58 (dd, J = 8.76, 2.36 Hz, 1H), 7.47-7.40 (m, 2H), 7.35 (d, J = 8.96 Hz, 1H), 4.40 (t, J = 4.3 Hz, 2H), 4.26 (t, J = 4.8 Hz, 2H), 2.71 (s, 3H), 2.35(s, 3H), 1.82 (s, 3H)
1007		MS (ESI) m/z 591.10 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.58 (bs, 1H), 8.69 (s, 1H), 8.46 (s, 1H), 7.59 (dd, J = 2.52, 8.64 Hz, 1H), 7.43-7.42 (m, 3H), 7.34 (s, 1H), 7.32 (s, 1H), 4.34 (t, J = 5.04 Hz, 2H), 4.15(t, J = 4.68 Hz, 2H), 2.70 (s, 3H), 1.69 (s, 3H)	1020		MS (ESI) m/z 703.10 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.56 (bs, 1H), 9.24 (s, 1H), 9.12 (s, 1H), 8.37 (d, J = 7.00 Hz, 2H), 7.60 (dd, J = 2.44, 8.88 Hz, 1H), 7.42-7.13 (m, 4H), 4.42 (t, J = 5.68 Hz, 2H), 4.28 (t, J = 5.16 Hz, 2H), 2.71 (s, 3H) 1.84 (s, 3H)
1021		MS (ESI) m/z 721.05 [M-1]; 1H NMR (400 MHz, DMSO-d6) δ 9.51 (s, 1H), 9.41 (s, 1H), 8.39 (s, 1H), 8.36 (s, 1H), 7.59 (dd, J = 2.0, 8.8 Hz, 1H), 7.42 (s, 1H), 7.36 (d, J = 8.8 Hz, 1H, 4.41 (bs, 2H), 4.29 (bs, 2H), 2.69 (s, 3H), 1.83 (s, 3H)	1024		MS (ESI) m/z 701.10 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.74 (s, 1H), 8.39 (s, 1H), 8.35 (s, 1H), 7.58 (dd, J=8.9, 2.3 Hz, 1H), 7.44 (s, 2H), 7.34 (d, J=8.9 Hz, 1H), 4.39 (t, J=9.5 Hz, 2H), 4.26 (t, J=4.5 Hz, 2H), 3.21 (s, 3H), 2.64 (s, 3H), 1.82 (s, 3H)

1022		MS (ESI) m/z 681.06. [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.62 (bs, 1H), 8.59 (s, 1H), 8.40 (s, 1H), 8.35 (s, 1H), 7.58 (dd, J = 2.48, 8.88 Hz, 1H), 7.43 (d, J = 2.5 Hz, 1H),7.43 (s, 1H), 7.34 (d, J = 8.96 Hz, 1H), 4.39 (t, J = 4.39 Hz, 2H), 4.26 (t, J = 4.12 Hz, 2H), 2.71 (s, 6H), 2.29 (s, 3H), 1.81 (s, 1H)
1040		MS (ESI) m/z 650.13 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.54 (bs, 1H), 8.34 (s, 1H), 7.59-7.52 (m, 1H), 7.50-7.45 (m, 5H), 7.40 (bs, 2H), 7.35 (d, J = 8.92 Hz, 1H), 6.99 (s, 1H), 4.36 (t, J = 5.24 Hz, 2H), 4.18 (t, J = 4.84 Hz, 2H), 2.71 (s, 3H), 2.70 (s, 6H), 1.79 (s, 3H)
1023		MS (ESI) m/z 681.21 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.48 (s, 1H), 8.39 (s, 1H), 8.34 (s, 1H), 7.58 (dd, J = 8.88, 2.56 Hz, 1H), 7.44 (d, J = 2.84 Hz, 2H), 7.35 (d, J = 8.92 Hz, 1H), 4.39 (t, J = 9.4 Hz, 2H), 4.26 (t, J = 8.32 Hz, 2H), 2.71 (s, 3H), 2.57 (s, 3H), 2.30 (s, 3H), 1.81 (s, 3H)
1047		MS (ESI) m/z 619.12 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.50 (s, 1H), 8.37 (s, 1H), 7.66 (s, 1H), 7.57 (dd, J = 2.32 Hz, J = 6.64 Hz, 1H), 7.41-7.34 (m, 3H), 4.37 (bs, 2H), 4.33-4.28 (m, 1H), 4.22 (bs, 2H), 2.81-2.73 (m, 2H), 2.69 (s, 3H), 2.50-2.48 (m, 2H), 2.10-2.03 (m, 1H), 2.01-1.84(m, 1H), 1.84 (s, 3H)
1048		MS (ESI) m/z 621.09 [M+1] +; 1H NMR (400 MHz, DMSO-d6)) δ 13.49 (bs, 1H), 8.34 (s, 1H), 7.76 (s, 1H), 7.65-7.34 (m, 5H), 4.39 (t, J = 5.8 Hz, 2H), 4.23 (t, J = 5.2 Hz, 2H), 2.69 (s, 3H), 2.20-2.09 (m, 1H), 1.85 (s, 3H), 1.25-1.18 (m, 2H), 0.97-0.88 (m, 2H)
1061		MS (ESI) m/z 672.07 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.50 (bs, 1H), 8.44 (s, 1H), 8.30 (s, 1H), 7.88 (dd, J = 8.56, 2.16 Hz, 1H), 7.87 (s, 1H), 7.59 (dd, J = 8.88, 2.16 Hz, 1H), 7.42 (s, 2H), 7.36 (d, J = 8.88 Hz, 1H), 7.03 (d, J = 8.52 Hz, 1H), 4.40 (t, J = 5.56 Hz, 2H), 4.25 (t, J = 5.20 Hz, 2H), 3.95 (s, 3H), 2.71 (s, 3H), 1.89 (s, 3H)

1050		MS (ESI) m/z 605.09 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.51 (bs, 1H), 8.34 (s, 1H), 7.68 (s, 1H), 7.58 (dd, J = 8.64, 1.96 Hz, 1H), 7.44-7.38 (m, 2H), 7.35 (d, J = 8.92 Hz, 1H), 4.37 (s, 2H), 4.21 (s, 2H), 2.69 (s, 3H), 2.08-2.03 (m, 1H), 1.84 (s, 3H), 1.26-1.20 (m, 2H), 0.92-0.86 (m, 2H)	1077		MS (ESI) m/z 580.08 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.85 (s, 1H), 8.50 (s, 1H), 7.58 (dd, J = 2.56, 11.44 Hz, 1H), 7.48 (d, J = 1.76 Hz, 1H), 7.42-7.41 (m, 2H), 7.34 (d, J = 8.96 Hz, 1H), 7.23 (d, J = 2.56 Hz, 1H), 7.18 (bs, 2H), 4.35 (t, J = 5.28 Hz, 2H), 4.24 (t, J = 4.76 Hz, 2H), 2.99 (q, J = 7.48 Hz, 2H), 1.34 (t, J = 7.52 Hz, 3H)
1054		MS (ESI) m/z 650.08 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.01 (s, 1H), 8.42 (s, 1H), 7.65 (s, 1H), 7.59 (dd, J = 10.96 Hz, 8.88 Hz, 1H), 7.33- 7.41 (m, 3H), 5.02 (s, 1H), 4.44 (s, 1H), 4.36 (bs, 2H), 4.19 (bs, 2H), 3.74-3.79 (m, 2H), 3.43-3.47 (m, 1H), 3.33 (s, 1H), 2.69 (s, 3H), 2.07-2.15 (m, 1H), 1.75-1.86 (m, 1H), 1.80 (s, 3H)	1078		MS (ESI) m/z 581.07 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.75 (bs, 1H), 8.53 (s, 1H), 7.72 (d, J = 1.60 Hz, 1H), 7.58 (dd, J = 2.56, 8.88 Hz, 1H), 7.46 (bs, 1H), 7.42 (d, J = 2.56 Hz, 2H), 7.34 (d, J = 8.96 Hz, 1H), 7.30 (d, J = 1.76 Hz, 1H), 4.35 (t, J = 5.16 Hz, 2H), 4.10 (t, J = 5.04 Hz, 2H), 2.99 (q, J = 7.48 Hz, 2H), 1.34 (t, J = 7.56 Hz, 3H)
1083		MS (ESI) m/z 686.21 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.23 (s, 1H), 7.98 (s, 1H), 7.67 (s, 1H), 7.59 (dd, J = 2.52 Hz, J = 8.84 Hz, 1H), 7.43 (bs, 2H), 7.35 (d, J = 8.96 Hz, 1H), 4.39 (t, J = 6.20 Hz, 2H), 4.23 (t, J = 6.32 Hz, 2H), 3.56 (d, J = 9.80 Hz, 2H), 3.25-3.13 (m, 6H), 2.99 (q, J = 7.52 Hz, J = 15.04 Hz, 2H), 2.93 (bs, 3H), 1.79 (s, 3H), 1.35 (t, 7.56 Hz, 3H)	1090b		MS (ESI) m/z 689.25 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 14.28 (bs, 1H), 7.58 (dd, J = 2.28, 8.84 Hz, 1H), 7.41 (bs, 1H), 7.38 (d, J = 2.36 Hz, 1H), 7.34 (d, J = 8.92 Hz, 1H), 6.99 (d, J = 8.28 Hz, 1H), 4.38 (t, J = 5.04 Hz, 2H), 4.19 (t, J = 4.68 Hz, 2H), 3.55 (d, J = 11.64 Hz, 2H), 2.79-2.73 (m, 2H), 2.70 (s, 3H), 2.39 (s, 3H), 2.37-2.34 (m, 2H), 2.23 (s, 3H), 1.86 (s, 3H), 1.10 (d, J = 6.00 Hz, 6H)

1084		1094	
MS (ESI) m/z 687.16 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.72 (bs, 1H), 8.30 (s, 1H), 8.10 (s, 1H), 7.59 (dd, J = 2.5, 9.1 Hz, 1H), 7.45 (s, 2H), 7.34 (d, J = 8.9 Hz, 1H), 4.38 (bs, 2H), 4.21 (bs, 2H), 3.59 (bs, 4H), 3.25 (bs, 4H), 3.03-2.97 (m, 2H), 2.90 (s, 3H), 1.72 (s, 3H), 1.34 (t, J = 7.52 Hz, 3H)		MS (ESI) m/z 675.07 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.57 (s, 1H), 8.38 (s, 1H), 7.58 (s, 2H), 7.41-7.33 (m, 3H), 4.36 (s, 2H), 4.21 (s, 2H), 3.55 (bs, 4H), 3.24 (bs, 2H), 3.06 (bs, 2H), 2.91 (s, 3H), 2.69 (s, 3H), 1.82 (s, 3H)
1090a		1095	
MS (ESI) m/z 705.26 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 14.28 (bs, 1H), 7.60 (bs, 1H), 7.58 (dd, J = 2.64, 8.96 Hz, 1H), 7.39 (bs, 1H), 7.38 (d, J = 2.60 Hz, 1H), 7.35 (d, J = 9.00 Hz, 1H), 4.37 (t, J = 4.56 Hz, 2H), 4.23 (t, J = 4.16 Hz, 2H), 3.17-3.12 (m, 5H), 2.70 (s, 3H), 2.43-2.38 (m, 4H), 2.22 (s, 3H), 1.96 (s, 3H), 1.03 (d, J = 6.08 Hz, 6H)		MS (ESI) m/z 711.15 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.42 (s, 1H), 7.57 (dd, J = 8.8, 2.5 Hz, 1H), 7.45-7.41 (m, 2H), 7.36-7.32 (m, 2H), 7.12 (d, J = 13.2 Hz, 1H), 4.35 (t, J = 9.2 Hz, 2H), 4.20 (t, J = 9.3 Hz, 2H), 3.14 (bs, 4H), 2.69 (s, 3H), 2.50 (bs, 4H), 1.79 (s, 3H), 1.23 (s, 3H)	
1096		1138	
MS (ESI) m/z 687.25 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 14.36 (bs, 1H), 8.00 (s, 1H), 8.32 (s, 1H), 7.60 (dd, J = 2.20, 8.68 Hz, 1H), 7.41 (s, 1H), 7.34 (d, J = 8.92 Hz, 1H), 4.40 (t, J = 4.32 Hz, 2H), 4.20 (t, J = 3.92 Hz, 2H), 3.23 (bs, 4H), 2.69 (s, 3H), 2.49 (bs, 4H), 2.35 (s, 3H), 2.23 (s, 3H), 1.77 (s, 3H)		MS (ESI) m/z 679.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.98 (s, 1H), 8.41 (s, 1H), 7.88 (d, J = 8.5 Hz, 1H), 7.67 (d, J = 8.5 Hz, 1H), 7.61 (dd, J = 8.9, 2.7 Hz, 1H), 7.46 – 7.37 (m, 3H), 4.42 (t, J = 5.1 Hz, 2H), 4.25 (t, J = 5.1 Hz, 2H), 3.56 (s, 3H), 3.45 – 3.37 (m, 2H), 3.37 – 3.29 (m, 2H), 2.91 (d, J = 4.5 Hz, 6H), 2.70 (s, 3H), 1.91 (s, 3H)	

1098		MS (ESI) m/z 642.01 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.84 (s, 1H), 8.73 (d, J = 3.7 Hz, 1H), 8.24 (s, 1H), 8.13 (d, J = 7.8 Hz 1H), 7.75 (s, 1H), 7.63-7.57 (m, 2H), 7.40-7.35 (m, 3H), 4.42 (t, J = 5.1 Hz, 2H), 4.27 (t, J = 4.8 Hz, 2H), 2.69 (s, 3H), 1.83 (s, 3H)	1147	MS (ESI) m/z 460.1 [M+1]+; 1H NMR (300 MHz, DMSO-d6) δ 12.95 (s, 1H), 8.00 – 7.82 (m, 5H), 7.56 – 7.49 (m, 1H), 7.45 – 7.36 (m, 2H), 7.29 (d, J = 2.7 Hz, 1H), 7.21 (d, J = 8.9 Hz, 1H), 4.34 (s, 4H), 2.19 (s, 3H)
1114		MS (ESI) m/z 683.3 [M+1]+; 1H NMR (400 MHz, Chloroform-d) δ 8.79 (d, J = 4.9 Hz, 1H), 8.66 (d, J = 0.9 Hz, 1H), 8.30 (s, 1H), 7.48 (dd, J = 8.9, 2.6 Hz, 1H), 7.32 (d, J = 4.9 Hz, 1H), 7.24 (d, J = 2.6 Hz, 1H), 7.07 (d, J = 8.9 Hz, 1H), 6.87 (d, J = 0.9 Hz, 1H), 5.23 – 5.13 (m, 1H), 4.37 (t, J = 5.0 Hz, 2H), 4.28 (t, J = 5.0 Hz, 2H), 3.88 (d, J = 12.0 Hz, 2H), 3.57 (t, J = 14.3 Hz, 2H), 3.34 – 3.24 (m, 2H), 2.97 (s, 3H), 2.51 – 2.36 (m, 2H), 2.08 – 2.02 (m, 5H), 1.80 (t, J = 19.0 Hz, 3H)	1150	MS (ESI) m/z 721.29 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 14.35 (s, 1H), 9.78 (s, 1H), 8.12 (s, 1H), 7.62 (dd, J = 8.8, 2.5 Hz, 1H), 7.45-7.42 (m, 2H), 7.38 (d, 1H), 4.41 (t, J = 4.5 Hz, 2H), 4.26 (t, J = 8.9 Hz, 2H), 3.90 (m, 2H), 3.57 (s, 5H), 3.23 (m, 4H), 2.90 (s, 3H), 2.72 (s, 3H), 2.47 (s, 3H), 1.99 (s, 3H)
1155		MS (ESI) m/z 735.80 [M+1] ;1H NMR (400 MHz, DMSO-d6) δ 12.50 (bs, 1H), 8.87 (d, J = 4.7 Hz, 1H), 8.47 (s, 1H), 8.12 (s, 1H), 7.60 (dd, J = 2.4, 8.9 Hz, 1H), 7.53 (d, J = 4.7 Hz, 1H), 7.45 (d, J = 2.4 Hz, 1H), 7.35 (d, J = 8.9 Hz, 1H), 4.39 (t, J = 5.1 Hz, 2H), 4.20 (t, J = 4.5 Hz, 2H), 3.51 (s, 3H), 3.28 (bs, 4H), 2.55 (bs, 4H), 2.28 (s, 3H), 1.69 (s, 3H)	1205	MS (ESI) m/z 661.24 [M+1]+. 1H NMR (400 MHz, DMSO-d6) δ 14.29 (bs, 1H), 7.58 (d, J = 6.8 Hz, 1H), 7.44-7.34 (m, 4H), 4.38 (t, J = 4.8 Hz, 2H), 4.26 (t, J = 5.2 Hz, 2H), 2.68 (s, 3H), 2.54 (s, 3H), 2.52-2.45 (m, 8H), 2.24 (s, 3H), 1.98 (s, 3H)

1193		MS (ESI) m/z 639.26 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.68 (s, 1H), 7.59-7.58 (m, 6H), 7.42-7.36 (m, 3H), 4.41 (t, J = 4.0 Hz, 2H), 4.25 (t, J = 4.0 Hz, 2H), 3.20 (s, 3H), 2.66 (s, 3H), 2.03 (s, 3H)	1208 MS (ESI) m/z 673.30 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 14.41 (bs, 1H), 7.59 (dd, J = 8.8, 2.4 Hz, 1H), 7.41 (s, 1H), 7.40-7.32 (m, 2H), 6.96 (s, 1H), 4.39 (s, 2H), 4.19 (s, 2H), 4.00 (s, 3H), 3.26 (s, 4H), 2.71 (s, 3H), 2.55-2.45 (merged, 4H), 2.40 (s, 3H), 2.28 (s, 3H), 1.91 (s, 3H)
1201		MS (ESI) m/z 719.23 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 14.24 (bs, 1H), 7.65 (s, 1H), 7.57 (d, J = 7.2 Hz, 1H), 7.37-7.33 (m, 3H), 4.38 (s, 2H), 4.26 (s, 2H), 2.68 (s, 6H), 2.5-2.47 (m, 8H), 1.93 (s, 3H), 1.06 (s, 9H)	1209 MS (ESI) m/z 682.30 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.43 (s, 1H), 7.96 (s, 1H), 7.93 (s, 1H), 7.58 (dd, J = 8.8, 2.4 Hz, 1H), 7.42-7.34 (m, 3H), 4.39 (s, 2H), 4.22 (s, 2H), 3.52 (s, 3H), 3.04 (s, 4H), 2.68 (s, 3H), 2.50 (merged, 4H), 2.26 (s, 3H), 1.87 (s, 3H)
1210		MS (ESI) m/z 672.17 [M+1]+; 1H NMR (400 MHz, DMSO-d6), δ 8.79 (d, J = 4.8 Hz, 1H), 8.02 (s, 1H), 7.68 (s, 1H), 7.59 (dd, J = 9.2 Hz, 2.4 Hz, 1H), 7.51 (d, J = 4.8 Hz, 1H), 7.42 (d, J = 2.4 Hz, 1H), 7.35 (d, J = 9.2 Hz, 1H), 4.40 (bs, 2H), 4.24 (bs, 2H), 3.56-3.54 (m, 2H), 3.20-3.12 (m, 6H), 2.93 (s, 3H), 2.23 (s, 3H), 1.78 (s, 3H)	1240 MS (ESI) m/z 682.34 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.14 (bs, 1H), 8.82 (d, J = 4.8, 1H), 8.32 (s, 1H), 8.05 (s, 1H), 7.57 (d, J = 6.4 Hz, 1H), 7.42 (d, J = 5.2 Hz, 2H), 7.35 (d, J = 9.2 Hz, 1H), 6.07 (s, 1H), 4.39 (s, 2H), 4.19 (s, 2H), 3.67 (bs, 4H), 2.87 (bs, 4H), 2.23 (s, 3H), 1.61 (s, 3H)

1211		MS (ESI) m/z 656.26 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.24 (s, 1H), 8.27 (s, 1H), 8.08 (s, 1H), 7.56 (dd, J = 8.4 Hz, 2.4 Hz, 1H), 7.40 (s, 1H), 7.33 (s, 1H), 7.30 (d, J = 14.8 Hz, 1H), 7.25 (s, 1H), 4.53-3.38 (m, 4H), 4.25-3.16 (m, 4H), 3.01-2.98 (m, 2H), 2.89 (s, 3H), 2.86 (s, 3H), 2.69-2.60 (m, 2H), 2.26 (s, 3H)
1267		MS (ESI) m/z 683.35 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 10.14 (bs, 1H), 8.83 (d, J = 4.8 Hz, 1H), 8.54 (s, 1H), 8.52 (d, J = 2.8 Hz, 1H), 7.91 (s, 1H), 7.62-7.55 (m, 2H), 7.46-7.43 (m, 2H), 7.30 (d, J = 8.9 Hz, 1H), 4.66-4.56 (m, 2H), 4.22 (s, 2H), 4.15-4.06 (m, 2H), 2.96 (s, 6H), 2.06 (s, 3H), 1.77 (s, 3H)
1230		MS (ESI) m/z 660.24 [M+2]+; 1H NMR (400 MHz, DMSO-d6), δ 8.1 (d, J = 4.8 Hz, 1H), 8.30 (s, 1H), 7.95 (s, 1H), 7.70 (s, 1H), 7.58 (dd, J = 8.8, 2.4 Hz, 1H), 7.45-7.42 (m, 2H), 7.34 (d, J = 9.2 Hz, 1H), 4.38 (bs, 2H), 4.23 (bs, 2H), 3.0 (bs, 8H), 2.50 (bs, 3H), 1.78 (bs, 3H)
1277		MS (ESI) m/z 688.19 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.8 Hz, 1H), 8.38 (s, 1H), 7.76 (s, 1H), 7.59 (dd, J = 2.4, 8.8 Hz, 1H), 7.50-7.20 (m, 4H), 4.39 (d, J = 4.4 Hz, 2H), 4.23 (bs, 2H), 4.05 (s, 2H), 3.85 (t, J = 12.4 Hz, 4H), 1.78 (s, 3H)
1278		MS (ESI) m/z 672.23 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.29 (bs, 1H), 8.81 (d, J = 4.8 Hz, 1H), 8.39 (s, 1H), 7.82 (s, 1H), 7.58 (dd, J = 8.8, 6.4 Hz 1H), 7.52–7.15 (m, 4H), 4.59 (d, J = 47.2 Hz, 2H), 4.40 (s, 2H), 4.23 (s, 2H), 3.76 (s, 2H), 2.89-2.71 (m, 2H), 2.30 (s, 3H), 1.79 (s, 3H)	1285		MS (ESI) m/z 696.35 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.93 (bs, 1H), 8.78 (d, J = 4.8 Hz, 1H), 8.10 (s, 1H), 7.59 (dd, J = 8.8 Hz, 2.8 Hz, 1H), 7.48 (d, J = 4.8 Hz, 1H), 7.41 (d, J = 2.8 Hz, 1H), 7.36 (d, J = 8.8 Hz, 1H), 6.13 (s, 1H), 4.41 (bs, 2H), 4.22 (bs, 2H), 3.93-3.87 (m, 2H), 3.54 (d, J = 10.8 Hz, 2H), 3.16 (d, J = 12.8 Hz, 2H), 3.09-3.06 (m, 2H), 2.90 (s, 3H), 2.37 (s, 3H), 1.70 (s, 3H)

1280		MS (ESI) m/z 616.25 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.50 (s, 1H), 7.58 (dd, J = 8.8, 2.4 Hz, 1H), 7.44-7.31 (m, 5H), 4.46-4.34 (m, 3H), 4.19 (s, 2H), 3.87-3.77 (m, 2H), 3.54 (t, J = 7.20, 1H), 3.36 (d, J = 10.4 Hz, 1H), 2.70 (s, 3H), 2.08-1.86 (m, 2H), 1.78 (s, 3H)	1290		MS (ESI) m/z 703.31 [M+1] +; 1H NMR (400 MHz, DMSO-d6) δ 8.75 (d, J = 4.8 Hz, 1H), 8.62 (s, 1H), 8.25 (s, 1H), 7.75 (d, J = 8.8 Hz, 1H), 7.69 (t, J = 3.2 Hz, 2H), 7.55 (d, J = 4.8 Hz, 1H), 6.43 (t, J = 54.4 Hz, 1H), 4.85 (s, 2H), 3.44 (s, 6H), 3.18 (bs, 4H), 2.09 (s, 3H)
1284		MS (ESI) m/z 697.27 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 14.00 (bs, 1H), 10.10 (bs, 1H), 8.77 (d, J = 4.8 Hz, 1H), 8.53 (d, J = 2.4 Hz, 1H), 7.96 (s, 1H), 7.64-7.54 (m, 2H), 7.47-7.46 (m, 2H), 7.29 (d, J = 8.9 Hz, 1H), 4.65-4.56 (m, 2H), 4.23 (s, 2H), 4.15-4.10 (m, 2H), 2.94 (s, 6H), 2.57 (s, 3H), 2.06 (s, 3H), 1.83 (s, 3H)	1294		MS (ESI) m/z 707.32 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 14.03 (bs, 1H), 9.79 (bs, 1H), 8.79 (d, J = 4.8 Hz, 1H), 8.13 (s, 1H), 7.63-7.60 (dd, J = 2.4, 8.8 Hz, 1H), 7.53 (d, J = 4.8 Hz, 1H), 7.44 (d, J = 2.4 Hz, 1H), 7.38 (d, J = 8.8 Hz, 1H), 4.42 (bs, 2H), 4.25 (bs, 2H), 3.93 (t, J = 12.0 Hz, 2H), 3.59-3.57 (m, 5H), 3.34-23 (m, 4H), 2.91 (s, 3H), 2.44 (s, 3H), 1.88 (s, 3H)
1295		MS (ESI) m/z 707.34 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 13.58 (bs, 1H), 8.39 (s, 1H), 8.10 (s, 1H), 7.61-7.58 (dd, J = 2.8, 8.8 Hz, 1H), 7.42 (s, 2H), 7.38 (d, J = 9.2 Hz, 1H), 4.41 (t, J = 4.8 Hz, 2H), 4.24 (t, J = 4.4 Hz, 2H), 3.74 (bs, 2H), 3.57 (s, 3H), 3.08 (bs, 4H), 2.87 (m, 2H), 2.71 (s, 3H), 2.32 (s, 3H), 1.87 (s, 3H)	1300		MS (ESI) m/z 735.80 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.50 (bs, 1H), 8.87 (d, J = 4.7 Hz, 1H), 8.47 (s, 1H), 8.12 (s, 1H), 7.60 (dd, J = 2.4, 8.9 Hz, 1H), 7.53 (d, J = 4.7 Hz, 1H), 7.45 (d, J = 2.4 Hz, 1H), 7.35 (d, J = 9.0 Hz, 1H), 4.39 (t, J = 5.1 Hz, 2H), 4.20 (t, J = 4.6 Hz, 2H), 3.51 (s, 3H), 3.28 (bs, 4H), 2.55 (bs, 4H), 2.28 (s, 3H), 1.69 (s, 3H)

1296		MS (ESI) m/z 693.35; 1H NMR (400 MHz, DMSO-d6) δ 13.50 (bs, 1H), 9.78 (bs, 1H), 8.84 (d, J = 4.8 Hz, 1H), 8.33 (s, 1H), 8.13 (s, 1H), 7.61 (dd, J = 8.4, 2.4, Hz, 1H), 7.49 (d, J = 4.7 Hz, 1H), 7.44 (d, J = 2.4 Hz, 1H), 7.36 (d, J = 8.1 Hz, 1H), 4.49-4.39 (m, 2H), 4.30-4.20 (m, 2H), 3.95-3.85 (m, 2 Hz), 3.62-3.50 (m, 5H), 3.40 (d, J = 12.0 Hz, 2H), 3.29-3.19 (m, 2H), 2.92 (s, 3H), 1.79 (s, 3H)
1299		MS (ESI) m/z 735.36 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 12.58 (bs, 1H), 8.83 (d, J = 4.8 Hz, 1H), 8.36 (s, 1H), 7.97 (s, 1H), 7.74 (s, 1H), 7.56 (d, J = 8.4 Hz, 1H), 7.44 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.8 Hz, 1H), 4.39 (s, 2H), 4.22 (s, 2H), 3.42 (s, 2H), 3.31 (m, 4H), 2.95 (m, 4H), 2.10 (s, 3H), 1.77 (s, 3H)
1379		MS (ESI) m/z 602.3 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 9.57 (s, 1H), 8.16 (s, 1H), 7.66 – 7.51 (m, 2H), 7.49 – 7.33 (m, 3H), 4.63 (s, 2H), 4.42 (t, J = 5.1 Hz, 2H), 4.25 (t, J = 5.0 Hz, 2H), 2.96 (s, 6H), 2.73 (s, 3H), 2.62 (s, 3H), 1.90 (s, 3H)
1331		MS (ESI) m/z 596.2 [M+1] +; 1H NMR (400 MHz, DMSO-d6) δ 13.39 (bs, 1H), 9.59 (s, 1H), 8.82 (d, J = 4.8 Hz, 1H), 8.54 (s, 1H), 8.45 (s, 1H), 8.44 (s, 1H), 7.60-7.57 (dd, J = 2.4, 8.8 Hz, 1H), 7.44 (t, J = 8.3 Hz, 2H), 7.33 (d, J = 8.8 Hz, 1H), 4.34 (d, J = 4.4 Hz, 2H), 4.19 (s, 2H), 3.43 (s, 4H), 2.90 (s, 6H), 1.83 (s, 3H)
1373		MS (ESI) m/z 535.0 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.82 (d, J = 4.8 Hz, 1H), 8.44 (s, 1H), 7.99 (dd, J = 8.4, 4.5 Hz, 1H), 7.77 (dd, J = 9.6, 8.4 Hz, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.49 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 2.7 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 4.42 (t, J = 5.1 Hz, 2H), 4.26 (t, J = 5.1 Hz, 2H), 1.87 (s, 3H)
1387		MS (ESI) m/z 676.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.80 (d, J = 2.6 Hz, 1H), 8.57 (s, 1H), 8.40 (s, 1H), 8.04 (ddd, J = 9.4, 2.8, 1.7 Hz, 1H), 7.95 (s, 1H), 7.60 (dd, J = 8.9, 2.7 Hz, 1H), 7.47 – 7.32 (m, 3H), 6.93 (t, J = 53.7 Hz, 1H), 4.42 (t, J = 5.0 Hz, 2H), 4.29 (dd, J = 5.3, 1.9 Hz, 2H), 2.73 (s, 3H), 1.92 (s, 3H)

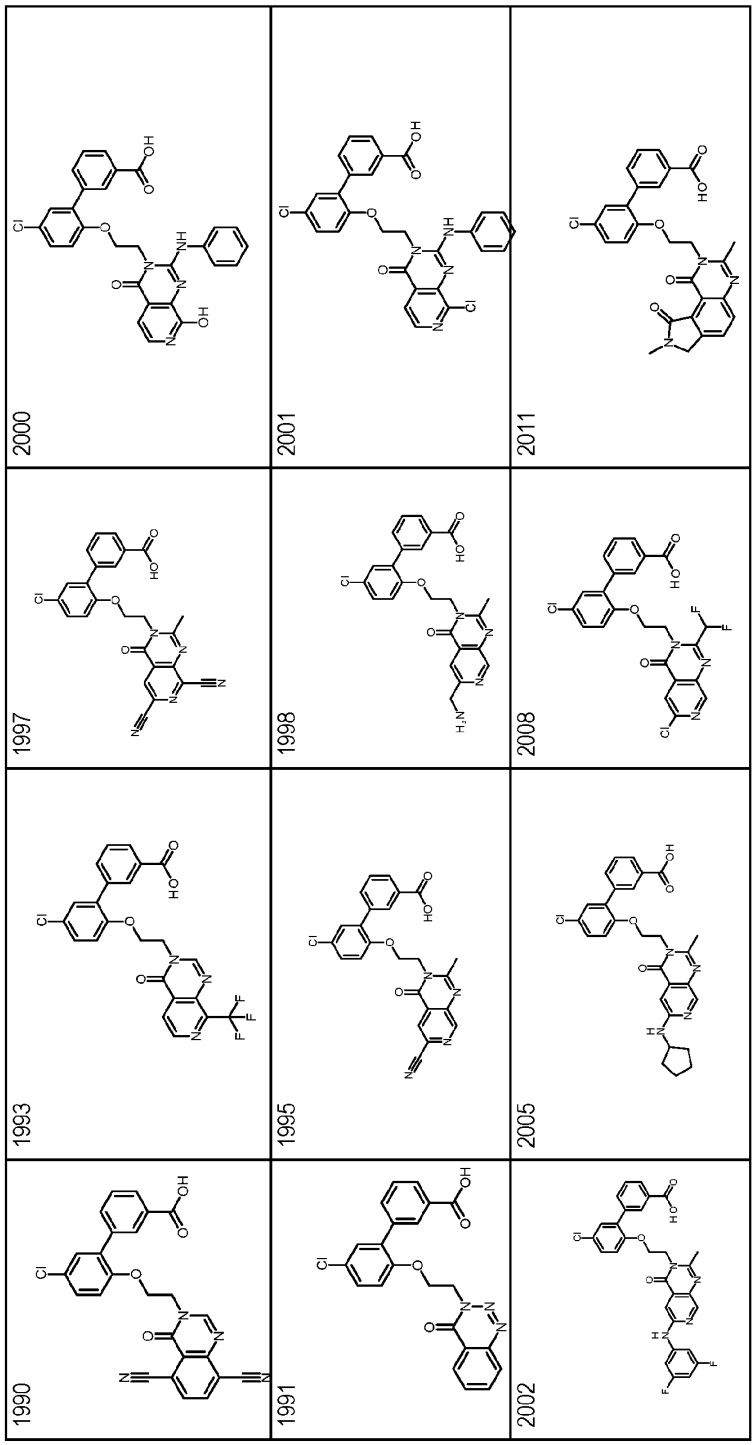
1385	MS (ESI) m/z 686.1 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.36 (s, 1H), 7.95 (s, 1H), 7.63 – 7.51 (m, 3H), 7.44 – 7.40 (m, 2H), 7.36 (d, J = 9.0 Hz, 1H), 6.90 (t, J = 53.7 Hz, 3H), 4.42 (t, J = 5.0 Hz, 2H), 4.28 (t, J = 5.0 Hz, 2H), 2.72 (s, 3H), 2.66 (s, 6H), 1.89 (s, 3H)	1935	
1386	MS (ESI) m/z 672.0 [M+1]+; 1H NMR (400 MHz, DMSO-d6) δ 8.76 (d, J = 5.4 Hz, 1H), 8.39 (s, 1H), 7.95 (s, 1H), 7.62 – 7.57 (m, 2H), 7.56 – 7.51 (m, 1H), 7.44 – 7.40 (m, 2H), 7.36 (d, J = 9.0 Hz, 1H), 6.88 (t, J = 53.8 Hz, 1H), 4.41 (t, J = 5.0 Hz, 2H), 4.28 (t, J = 4.8 Hz, 2H), 2.72 (s, 3H), 2.65 (s, 3H), 1.89 (s, 3H)	1936	
1937		1940	1943
			1946

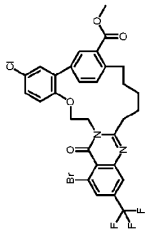
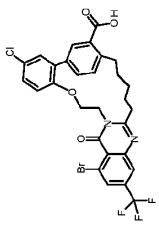
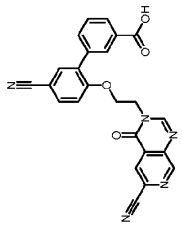
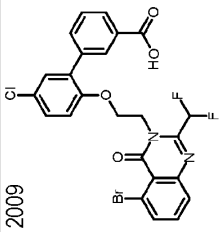
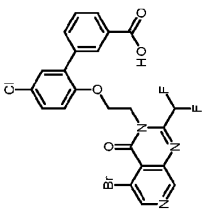
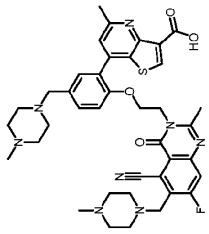
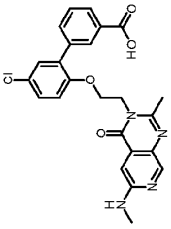
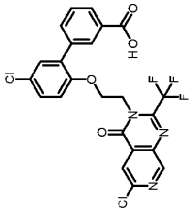
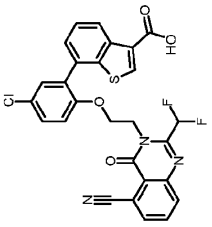
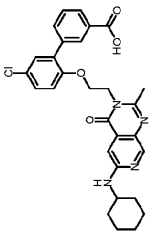
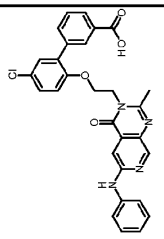
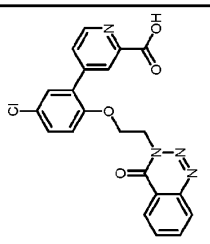
1938	1941	1944	1947
1939	1942	1945	1948
1949	1952	1955	1958

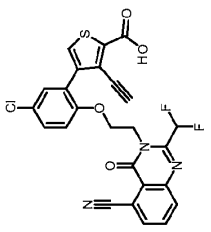
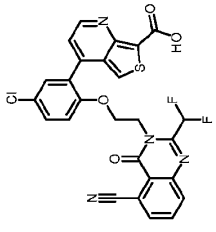
1950	1953	1956	1959
1951	1954	1957	1960
1961	1964	1967	1970

1962	1965	1968	1971
1963	1966	1969	1972
2026	1976	1979	1986

1987	1988	1999	
1980	1981	1996	
1977	1978	1992	
1974	1975	1989	


2000
2001
2011
1997
1998
2008
1993
1995
2005
1990
1991
2002

2012	2013	2026
		
2009	2010	2027
		
2006	2007	2017
		
2003	2004	2014
		

2034		MS (ESI) m/z 526.15 [M+1]+	
2035		MS (ESI) m/z 553.33 [M+1]+	

Example 5. Biological Studies

Example 5A. Fluorescence Polarization

[0509] Compounds were screened for eIF4E binding potency using a fluorescence polarization competition assay. All binding reactions were performed in fluorescence polarization buffer (FPB) containing 20 mM Tris pH 7.5, 100 mM NaCl, 1 mM DTT, and 0.02% Tween-20. Final binding reactions contained 75 nM recombinant eIF4E (Beryllium, custom order), 20 nM EDA-m^7GDP-ATTO-550 (Jena Bioscience, NU-827-550) and varying concentrations of the inhibitory compound of interest. Final DMSO concentration in each reaction was 1%.

[0510] eIF4E protein was pre-incubated with EDA-m^7GDP-ATTO-550 in FPB at 2X concentrations for 5 minutes prior to the addition of compounds. Compounds (100X) were prepared using 3-fold serial dilutions in 100% DMSO, and subsequently diluted 1:50 in FPB to produce 2X stocks. 50 µl of 2X eIF4E/ EDA-m^7GDP-ATTO-550 were transferred to the wells of a 96-well half-area black flat bottom polystyrene plate. 50 µl of 2X test compound were added, and binding reactions were allowed to equilibrate for 30 minutes at room temperature while protected from light. The fluorescent polarization signal was detected using a Victor 2 multi-label counter (Perkin Elmer) and the concentration necessary to achieve inhibition of eIF4E/EDA-m^7GDP-ATTO-550 binding by 50% (IC_{50}) was calculated using data from an 8-point compound dilution series.

[0511] The results of these assays are set forth in Tables 4A and 4B, below. In Table 4A, IC_{50} values of less than 0.05 µM are labelled as "+++", from 1 to 0.05 µM are labelled as "++", and greater than 1 µM are labelled as "+". Calculated IC_{50} values are shown in Table 4B. ND = not determined.

Table 4A

Compound	eIF4E FP
1	++
2	+
3	+
4	+
5	+
6	+
7	+
8	+++
9	+
10	+
11	+
12	+
13	+
14	+
15	+
16	++++
17	++
18	++
19	++
20	+
21	++
22	+++
23	++
24	++
25	+
26	++
27	++
28	++
29	++
30	++
31	++
32	++
33	++
34	++
35	+++
36	ND
37	+++
38	++
39	++
40	+++
41	+
42	+
43	+
44	++
45	+
46	++
47	+++
48	++
49	+++
50	+++
51	+++
52	+
53	++
54	+
55	+++
56	+++
57	+++
58	++
59	+++
60	+++
61	+++
62	+++
63	+++
64	++
65	+++
66	++
67	+
68	+
69	+
70	++
71	++
72	+
73	++
74	++
75	+
76	+
77	+
78	+
79	+
80	++
81	+
82	+
83	+
84	+
85	+
86	+
87	+
88	+
89	+
90	+
91	++
92	+
93	+
94	+
95	+
96	+
97	+
98	++
99	+
100	+
101	+
102	+
103	++
104	++
105	+
106	+
107	+
108	+
109	+
110	+
111	++
112	+
113	++
114	++
115	+
116	+
117	+
118	++
119	+++
120	+++
121	+++
122	+++
123	+++
124	+
125	+
126	+
127	++
128	++
129	+
130	+
131	++
132	++
133	++
134	++
135	ND
136	++
137	++
138	++
139	+++
140	++
141	+++
142	++
143	+++
144	+++
145	++
146	++
147	+++
148	+++
149	++
150A	++
150B	++
150C	++
151	+++
152	+++
153	++
154	++
155	+++
156	+++
157	ND
158	+++
159	+++
160	+++
161	++
162	+++
163	++
164	ND
165	++
166	+++
167	++
168	+++
169	++
170	++
171	++
172	++
173	++
174	++
175	+++
176	+++
177	+++
178	++
179	+++
180	+++
181	++
182	+++
183	++
184	++
185	++
186	++
187	+++
188	++
189	+
190	++
191	++
192	+
193	+++
194	+++
195	+++
196	+++
197	++
198	++
199	++
200	+++
201	++
202	+++
203	++
204	+++
205	++
206	++
207	+++
208	++
209	+++

Compound	eIF4E FP	Compound	eIF4E FP	Compound	eIF4E FP	Compound	eIF4E FP	Compound	eIF4E FP
210	++	253	+++	296	+++	339	+++	380	+++
211	+++	254	+++	297	+++	340	+++	381	ND
212	+++	255	++	298	++	341	+++	382	ND
213	+++	256	++	299	+++	342	+++	383	ND
214	+++	257	++	300	+++	343	+++	384	+++
215	++	258	+++	301	++	344	+++	385	+++
216	++	259	++	302	++	345	+++	386	+++
217	++	260	+++	303	++	345	+++	387	++
218	+++	261	+++	304	+	346	+++	388	+++
219	++	262	+++	305	++	347	+++	389	+++
220	++	263	+++	306	++	348	+++	390	+++
221	++	264	+++	307	++	349	+++	391	+++
222	++	265	++	308	++	350	+++	392	+++
223	++	266	+++	309	++	351	++	393	+++
224	+++	267	++	310	++	351	++	394	+++
225	++	268	+++	311	++	352	+	395	+++
226	++	269	+++	312	++	353	++	396	+++
227	++	270	+++	313	+++	354	++	397	+++
228	+++	271	+++	314	+++	355	++	398	++
229	+++	272	+++	315	++	356	+	399	++
230	+++	273	+++	316	+++	357	+++	400	+++
231	+++	274	+++	317	+++	358	++	401	+++
232	+++	275	+++	318	+++	359	+++	402	++
233	+++	276	+++	319	++	360	+++	403	+++
234	+++	277	+++	320	+++	361	++	404	+++
235	+++	278	+++	321	+++	362	++	405	+++
236	+++	279	+++	322	++	363	+++	406	+++
237	++	280	+++	323	++	364	++	407	+++
238	+++	281	+++	324	++	365	+++	408	+++
239	+++	282	+++	325	++	366	+++	409	+++
240	+++	283	+++	326	+	367	+++	410	++
241	+++	284	+++	327	+++	368	+++	411	++
242	+++	285	++	328	+	369	+++	412	++
243	+++	286	++	329	+++	370	+++	413	+++
244	+++	287	+++	330	+++	371	+++	414	+++
245	+++	288	+++	331	ND	372	+++	415	+++
246	+++	289	+++	332	+++	373	+++	416	+++
247	++	290	+++	333	ND	374	+++	417	+++
248	++	291	++	334	+++	375	++	418	+++
249	+++	292	++	335	++	376	+++	419	+++
250	+++	293	++	336	+++	377	++	420	+++
251	+++	294	+++	337	+++	378	+++	421	+++
252	+++	295	++	338	+++	379	+++	422	+++

Compound	eIF4E FP	Compound	eIF4E FP	Compound	eIF4E FP	Compound	eIF4E FP	Compound	eIF4E FP
423	+++	465	+++	508	+++	551	+++	594	+
424	+++	466	+++	509	++	552	++	595	+++
425	+++	467	+++	510	++	553	+++	596	+++
426	+++	468	+++	511	++	554	+++	597	+++
427	+++	469	+++	512	++	555	+++	598	++
428	+++	470	+++	513	+++	556	+++	599	++
429	+++	471	+++	514	+++	557	+++	600	+++
430	+++	472	+++	515	+++	558	+++	601	++
431	++	473	+++	516	+++	559	+++	602	+++
432	+++	474	+++	517	+++	560	+++	603	+++
433	+++	475	+++	518	+++	561	++	604	++
434	+++	476	+++	519	+++	562	+++	605	ND
435	+++	477	+++	520	+++	563	+++	606	+++
436	+++	478	+++	521	++	564	+++	607	+++
437	+++	479	+++	522	+++	565	+++	608	+++
438	+++	480	+++	523	+++	566	+++	609	+++
439	+++	481	+++	524	+++	567	+++	610	+++
439	+++	482	+++	525	+++	568	+++	611	+++
440	+++	483	+++	526	++	569	+++	612	+++
441	+++	484	+++	527	+++	570	+++	613	+++
442	+++	485	+++	528	+++	571	++	614	++
443	++	486	+++	529	+++	572	+++	615	+++
444	+++	487	++	530	+++	573	++	616	+++
445	++	488	+++	531	+++	574	++	617	+++
446	++	489	+++	532	+++	575	+++	618	+++
447	++	490	++	533	++	576	+++	619	+++
448	+++	491	+++	534	+++	577	+++	620	+++
449	+++	492	+++	535	++	578	+++	621	++
450	+++	493	++	536	+++	579	+++	622	+++
451	+++	494	++	537	+++	580	+++	623	+++
452	+++	495	++	538	+++	581	+++	624	+++
453	+	496	+	539	+++	582	+++	625	++
454	++	497	+++	540	+++	583	+++	626	+++
455	++	498	+++	541	+++	584	+++	627	+++
456	+++	499	++	542	+++	585	+++	628	+++
457	+++	500	+++	543	+++	586	+++	629	+++
458	+++	501	+++	544	+++	587	+++	630	++
459	+++	502	+++	545	+++	588	+++	631	+++
460	+++	503	+++	546	+++	589	+++	632	+++
461	+++	504	+++	547	++	590	+++	633	+++
462	+++	505	+++	548	+++	591	+++	634	+++
463	+++	506	++	549	+++	592	+++	635	+++
464	+++	507	+++	550	++	593	+++	636	+++

Compound	eIF4E FP	Compound	eIF4E FP	Compound	eIF4E FP	Compound	eIF4E FP	Compound	eIF4E FP
637	+++	680	++	723	+++	766	+++	808	++
638	+++	681	+++	724	+++	767	+++	809	+++
639	+++	682	+++	725	+++	768	+++	810	+++
640	+++	683	+++	726	++	769	+++	811	++
641	+++	684	+++	727	+++	770	+++	812	+++
642	+++	685	+++	728	+++	771	+++	813	+++
643	+++	686	+++	729	++	772	+++	814	ND
644	+++	687	+++	730	++	773	+++	815	+++
645	+++	688	+++	731	+++	774	+++	816	+++
646	+++	689	+++	732	++	775	+++	817	+++
647	+++	690	+++	733	+	776	+++	818	+++
648	+++	691	+++	734	+++	777	++	819	+++
649	+++	692	+++	735	++	778	+++	820	+++
650	+++	693	+++	736	+++	779	+++	821	+++
651	+++	694	+++	737	+++	780	+++	822	+++
652	+++	695	+++	738	+++	781	+++	823	+++
653	+++	696	+++	739	+++	782	+++	824	+++
654	+++	697	+++	740	+++	783	+++	825	+++
655	+++	698	+++	741	+++	784	+++	826	+++
656	+++	699	+++	742	+++	785	+++	827	+++
657	+++	700	+++	743	++	786	+++	828	+++
658	+	701	+++	744	+++	787	+++	829	+++
659	+++	702	+++	745	+++	788Fa	+	830	+++
660	++	703	+++	746	+++	788Fb	+++	831	+++
661	+++	704	++	747	+++	789	+++	832	ND
662	++	705	+++	748	+++	790	+++	833	++
663	++	706	++	749	+	791	+++	834	+++
664	++	707	+++	750	+++	792	+++	835	+++
665	+++	708	++	751	++	793	+++	836	+++
666	++	709	++	752	+++	794	+++	837	+++
667	+++	710	+++	753	+++	795	+++	838	+++
668	+++	711	++	754	+++	796	+++	839	+++
669	+++	712	+++	755	+++	797	+++	840	+++
670	+++	713	+++	756	+++	798	+++	841	++
671	++	714	+++	757	++	799	+++	842	+++
672	++	715	ND	758	+++	800	+++	843	+++
673	+++	716	ND	759	++	801	+++	844	+++
674	+++	717	++	760	+++	802	+++	845	+++
675	+++	718	+++	761	+++	803	++	846	+++
676	+++	719	+++	762	+++	804	+++	847	+++
677	+++	720	++	763	+++	805	+++	848	+++
678	++	721	+++	764	+++	806	+++	849	+++
679	++	722	+++	765	+++	807	+++	850	+++

Compound	eIF4E FP	Compound	eIF4E FP	Compound	eIF4E FP	Compound	eIF4E FP	Compound	eIF4E FP
851	+++	894	+++	937	+++	980	+++	1023	+++
852	+++	895	+++	938	+++	981	+++	1024	+++
853	+++	896	+++	939	+++	982	+++	1025	+++
854	+++	897	+++	940	++	983	+++	1026	+++
855	+++	898	+++	941	+++	984	+++	1027	+++
856	+++	899	+++	942	+++	985	+++	1028	+++
857	+++	900	+++	943	+++	986	+++	1029	+++
858	+++	901	+++	944	+++	987	+++	1030	+++
859	+++	902	+++	945	+++	988	+++	1031	+++
860	+++	903	+++	946	+++	989	+++	1032	+++
861	+++	904	+++	947	+++	990	+++	1033	+++
862	+++	905	+++	948	+++	991	+++	1034	+++
863	+++	906	+++	949	+++	992	++	1035	+++
864	+++	907	+++	950	+++	993	+++	1036	+++
865	+++	908	+++	951	+++	994	+++	1037	+++
866	+++	909	+++	952	+++	995	+++	1038	+++
867	+++	910	+++	953	+++	996	+++	1039	+++
868	+++	911	+++	954	+++	997	+++	1040	+++
869	+++	912	+++	955	+++	998	+++	1041	+++
870	++	913	+++	956	+++	999	+++	1042	+++
871	+++	914	+++	957	+++	1000	+++	1043	+++
872	+++	915	+++	958	+++	1001	+++	1044	+++
873	+++	916	+++	959	+++	1002	+++	1045	+++
874	+++	917	+++	960	+++	1003	+++	1046	+++
875	+++	918	+++	961	+++	1004	+++	1047	+++
876	++	919	+++	962	+++	1005	+++	1048	+++
877	++	920	+++	963	+++	1006	+++	1049	+++
878	+++	921	++	964	+++	1007	+++	1050	+++
879	+++	922	++	965	++	1008	+++	1051	+++
880	++	923	+++	966	+++	1009	+++	1052	+++
881	+++	924	+++	967	+++	1010	+++	1053	+++
882	+++	925	+++	968	+++	1011	+++	1054	+++
883	+++	926	+++	969	+++	1012	+++	1055	+++
884	+++	927	+++	970	++	1013	+++	1056	+++
885	+++	928	+++	971	++	1014	+++	1057	+++
886	+++	929	+++	972	+++	1015	+++	1058	+++
887	+++	930	+++	973	++	1016	+++	1059	+++
888	+++	931	+++	974	+++	1017	+++	1060	++
889	+++	932	+++	975	+++	1018	+++	1061	+++
890	+++	933	++	976	+++	1019	+++	1062	+++
891	+++	934	+++	977	+++	1020	+++	1063	+++
892	+++	935	+++	978	+++	1021	+++	1064	+++
893	+++	936	ND	979	+++	1022	+++	1065	+++

Compound	eIF4E FP
1066	++
1067	+++
1068	+++
1069	+++
1070	+++
1071	++
1072	+++
1073	++
1074	+++
1075	+++
1076	+++
1077	++
1078	++
1079	ND
1080	++
1081	+
1082	++
1083	+++
1084	+++
1085	++
1086	+++
1087	+++
1088	++
1089	++
1090	+++
1090	++
1091	++
1092	+++
1093	++
1094	++
1095	+++
1096	+++
1097	+++
1098	+++
1099	+++
1100	+++
1101	+++
1102	+++
1103	+++
1104	++
1105	+++
1106	+++
1107	+++

Compound	eIF4E FP
1108	+++
1109	+++
1110	+++
1111	+++
1112	+++
1113	++
1114	+++
1115	+++
1116	+++
1117	+++
1118	+++
1119	+++
1120	+++
1121	+++
1122	+++
1123	+++
1124	+++
1125	+++
1126	+++
1127	+++
1128	+++
1129	+++
1130	+++
1131	+++
1132	+++
1133	+++
1134	+++
1135	+++
1136	+++
1137	+++
1138	+++
1139	ND
1140	+++
1141	+++
1142	+++
1143	+++
1144	+++
1145	+++
1146	+++
1147	+++
1148	+++
1149	+++
1150	+++

Compound	eIF4E FP
1151	+++
1152	+++
1153	+++
1154	+++
1155	+++
1156	+++
1157	+++
1158	+++
1159	+++
1160	+++
1161	+++
1162	+++
1163	+++
1164	+++
1165	+++
1166	+++
1167	+++
1168	+++
1169	+++
1170	+++
1171	+++
1172	+++
1173	+++
1173	+++
1174	+++
1175	+++
1176	+++
1177	+++
1178	+++
1179	+++
1180	+++
1181	+++
1182	+++
1183	+++
1184	+++
1185	+++
1186	+++
1187	+++
1188	+++
1189	+++
1190	+++
1191	+++
1192	+++

Compound	eIF4E FP
1193	+++
1194	+++
1195	+++
1196	+++
1197	+++
1198	+++
1199	+++
1200	+++
1201	+++
1202	+++
1203	+++
1204	++
1205	++
1206	+++
1207	++
1208	+++
1209	++
1210	+++
1211	++
1212	+++
1213	+++
1214	+++
1215	+++
1216	+++
1217	+++
1218	+++
1219	+++
1220	+++
1221	+++
1222	+++
1223	+++
1224	++
1225	+++
1226	+++
1227	+++
1228	+++
1229	+++
1230	+++
1231	ND
1232	+++
1233	ND
1234	+++
1235	+++

Compound	eIF4E FP
1236	+++
1237	+++
1238	+++
1239	+++
1240	+++
1241	+++
1242	+++
1243	+++
1244	+++
1245	+++
1246	++
1247	+++
1248	++
1249	++
1250	++

Table 4B

Cmpd.	IC_{50} (μM)
1	0.281
2	3.10
3	4.72
4	3.52
5	7.64
6	7.39
7	12.0
8	>30.0
9	>30.0
10	6.51
11	6.85
12	2.39
13	1.07
14	>3.00
15	1.74
16	46.1
17	0.721
18	0.832
19	0.838
20	1.07
21	0.575
22	0.0249
23	0.624
24	0.184
25	12.6
26	0.919
27	0.149
28	0.0616
29	0.211
30	0.164
31	0.751
32	0.190
33	0.203
34	0.0885
35	0.0443
36	ND
37	0.0396
38	0.0555
39	0.116
40	0.540
41	3.44
42	19.8
43	>10.0
44	0.0731
45	2.89
46	0.0672
47	0.0224
48	0.631
49	>3.00
50	>3.00
51	0.0213
52	>3.00
53	0.931
54	2.28
55	0.0216
56	0.00789
57	0.0128
58	0.0502
59	0.0215
60	0.0147
61	0.0265
62	0.0249
63	0.0258
64	0.0625
65	0.0241
66	0.187
67	3.22
68	64.3
69	26.8
70	0.432
71	0.636
72	3.10
73	0.0832
74	0.423
75	1.40
76	2.30
77	1.44
78	1.63
79	1.65
80	0.110
81	4.22
82	1.66
83	2.56
84	1.25
85	1.85
86	49.7
87	1.16
88	1.68
89	>3.00
90	1.23
91	0.287
92	>3.00
93	1.40
94	1.42
95	2.86
96	2.10
97	>3.00
98	0.564
99	3.42
100	3.48
101	43.8
102	4.82
103	0.747
104	0.586
105	>3.00
106	1.38
107	3.82
108	11.2
109	19.2
110	26.9
111	0.434
112	>3.00
113	0.804
114	0.333
115	>3.00
116	>3.00
117	>3.00
118	0.416
119	0.0199
120	0.0357
121	0.0375
122	0.0244
123	0.0365
124	9.13
125	>3.00
126	8.36
127	0.0770
128	0.970
129	3.10
130	1.42
131	0.600
132	0.624
133	0.0665
134	0.116
135	ND
136	0.199
137	0.904
138	0.279
139	0.0346
140	0.0500
141	0.0442
142	0.152
143	0.0167
144	0.132
145	0.0959
146	0.259
147	0.0147
148	0.0205
149	0.110
150FA	0.0631
150FB	0.143
150FC	0.124
151	1.05
152	>3.00
153	0.0540
154	0.0972
155	0.0455
156	0.00420
157	ND
158	0.0483
159	0.0309
160	0.00883
161	0.0904
162	0.0287
163	0.0955
164	0.0164
165	0.106
166	0.0350
167	0.101
168	0.0372
169	0.234
170	0.845
171	0.194
172	0.0923
173	0.141
174	0.0521
175	0.0204
176	0.0415
177	0.0268
178	0.140
179	0.0206
180	0.0477
181	0.0623
182	0.0438
183	0.0502
184	0.144
185	0.0949
186	0.344
187	0.0483
188	0.0632
189	1.57
190	0.301
191	0.144
192	1.31
193	0.0209
194	0.0358
195	0.0274
196	0.0257

Cmpd.	IC_{50} (μM)	Cmpd.	IC_{50} (μM)	Cmpd.	IC_{50} (μM)	Cmpd.	IC_{50} (μM)	Cmpd.	IC_{50} (μM)
197	0.0524	237	0.0548	277	0.0307	317	0.0171	355	0.146
198	0.124	238	0.0380	278	0.0127	318	0.00292	356	1.22
199	0.143	239	0.0286	279	0.0178	319	0.0535	357	0.0477
200	0.0435	240	0.00978	280	0.0412	320	0.0435	358	0.0863
201	0.354	241	0.00487	281	0.0375	321	0.00489	359	0.0489
202	0.0474	242	0.0203	282	0.0171	322	0.116	360	0.0426
203	0.0806	243	0.0432	283	0.0406	323	0.0826	361	0.0684
204	0.0444	244	0.0312	284	0.0196	324	0.0933	362	0.0722
205	0.101	245	0.0256	285	0.0725	325	0.0520	363	0.0228
206	0.229	246	0.0430	286	0.183	326	1.44	364	0.107
207	0.0213	247	0.0611	287	0.0478	327	0.0437	365	0.0190
208	0.103	248	0.0523	288	0.0461	328	1.32	366	0.00666
209	0.0470	249	0.0198	289	0.0191	329	0.0464	367	0.00287
210	0.0910	250	0.0437	290	0.0427	330	0.0477	368	0.0411
211	0.0354	251	0.0311	291	0.0995	331	ND	369	0.00132
212	0.0400	252	0.0420	292	0.203	332	0.0377	370	0.0121
213	0.0356	253	0.0460	293	0.0639	333	0.0249	371	0.0200
214	0.0122	254	0.0204	294	0.0229	334	0.0104	372	0.00734
215	0.137	255	0.0785	295	0.167	335	0.0569	373	0.00643
216	0.0628	256	0.104	296	0.0375	336	0.0279	374	0.0205
217	0.0554	257	0.0692	297	0.0363	337	0.0257	375	0.0580
218	0.0169	258	0.0377	298	0.101	338	0.0453	376	0.0127
219	0.109	259	>1.00	299	0.0223	339	0.0268	377	0.0612
220	0.213	260	0.0204	300	0.0243	340	0.00501	378	0.0451
221	0.113	261	0.0420	301	0.0576	341	0.0450	379	0.0267
222	0.0674	262	0.0224	302	0.0776	342	0.0474	380	0.0297
223	0.950	263	0.0127	303	0.498	343	0.0418	381	ND
224	0.0110	264	0.0246	304	1.60	344	0.0321	382	ND
225	0.147	265	0.0771	305	0.431	345a	0.0432	383	ND
226	0.0707	266	0.0266	306	0.0912	345b	0.0253	384	0.0209
227	0.507	267	0.0741	307	0.0594	346	0.0181	385	0.0395
228	0.0235	268	0.0341	308	0.811	347	0.0321	386	0.0254
229	0.0222	269	0.0156	309	0.0525	348	0.0154	387	0.619
230	0.0149	270	0.0464	310	0.0977	349	0.00584	388	0.00629
231	0.0129	271	0.0132	311	0.0555	350	0.0142	389	0.0123
232	0.0163	272	0.0229	312	0.0756	351a	0.885	390	0.00175
233	0.0289	273	0.0302	313	0.0345	351b	0.0936	391	0.00352
234	0.0185	274	0.0188	314	0.0428	352	1.27	392	0.0251
235	0.0166	275	0.0365	315	0.582	353	0.101	393	0.0118
236	0.0203	276	0.0228	316	0.0204	354	>1.00	394	0.0218

Cmpd.	IC_{50} (μM)	Cmpd.	IC_{50} (μM)	Cmpd.	IC_{50} (μM)	Cmpd.	IC_{50} (μM)	Cmpd.	IC_{50} (μM)
395	0.00968	435	0.0167	474	0.0135	514	0.0399	554	0.0318
396	0.0181	436	0.00717	475	0.0170	515	0.0460	555	0.0108
397	0.0105	437	0.00621	476	0.0339	516	0.0344	556	0.0227
398	0.149	438	0.00916	477	0.00973	517	0.0357	557	0.00640
399	0.0699	439a	0.00287	478	0.0132	518	0.0164	558	0.0272
400	0.00468	439b	0.0320	479	0.0135	519	0.0378	559	0.00869
401	0.0474	440	0.00499	480	0.00739	520	0.0183	560	0.00477
402	0.124	441	0.0204	481	0.0105	521	0.623	561	0.0562
403	0.0126	442	0.0177	482	0.0354	522	0.0227	562	0.00878
404	0.0101	443	0.128	483	0.0421	523	0.0239	563	0.0144
405	0.0197	444	0.0308	484	0.0116	524	0.0128	564	0.0405
406	0.0114	445	0.0931	485	0.00859	525	0.0347	565	0.0297
407	0.0331	446	0.0573	486	0.0305	526	0.0641	566	0.0164
408	0.0311	447	0.0848	487	0.114	527	0.0248	567	0.0117
409	0.0133	448	0.00420	488	0.0265	528	0.0271	568	0.0141
410	0.0626	449	0.0196	489	0.0208	529	0.00578	569	0.00200
411	0.193	450	0.00784	490	0.178	530	0.00665	570	0.00557
412	0.0701	451	0.0360	491	0.0229	531	0.0429	571	0.0548
413	0.0346	452	0.0466	492	0.0297	532	0.0451	572	0.0306
414	0.0205	453	2.32	493	0.0942	533	0.0627	573	0.0547
415	0.0143	454	0.0511	494	0.0856	534	0.0302	574	0.0575
416	0.0230	455	0.473	495	0.237	535	0.244	575	0.0257
417	0.0197	456	0.0109	496	1.06	536	0.0488	576	0.0177
418	0.00907	457	0.0112	497	0.0397	537	0.0466	577	0.0394
419	0.00108	458	0.0368	498	0.0242	538	0.0223	578	0.0320
420	0.00960	459	0.0415	499	>1.00	539	0.0472	579	0.0302
421	0.0171	460	0.0255	500	0.0365	540	0.0140	580	0.0242
422	0.0115	461	0.00615	501	0.0257	541	0.0491	581	0.00608
423	0.00884	462	0.0105	502	0.0384	542	0.0202	582	0.0127
424	0.00408	463	0.00886	503	0.00867	543	0.0382	583	0.0159
425	0.0112	464	0.0214	504	0.0229	544	0.0282	584	0.0235
426	0.0412	465	0.0151	505	0.0436	545	0.00781	585	0.0296
427	0.0250	466	0.00930	506	0.0689	546	0.0436	586	0.0500
428	0.00745	467	0.0180	507	0.0490	547	0.134	587	0.0255
429	0.0382	468	0.00436	508	0.0152	548	0.0472	588	0.0493
430	0.00900	469	0.00225	509	0.125	549	0.0193	589	0.00445
431	0.226	470	0.0128	510	0.0505	550	0.0878	590	0.00226
432	0.0258	471	0.0288	511	0.0880	551	0.0292	591	0.0449
433	0.00415	472	0.0236	512	0.0718	552	0.0509	592	0.0103
434	0.00776	473	0.0145	513	0.0116	553	0.0134	593	0.0329

Cmpd.	IC_{50} (μM)	Cmpd.	IC_{50} (μM)	Cmpd.	IC_{50} (μM)	Cmpd.	IC_{50} (μM)	Cmpd.	IC_{50} (μM)
594	1.35	634	0.00562	674	0.00927	714	0.0472	754	0.0172
595	0.0248	635	0.0106	675	0.00777	715	ND	755	0.0101
596	0.0377	636	0.0332	676	0.00622	716	ND	756	0.0432
597	0.0468	637	0.0166	677	0.00544	717	0.0730	757	0.137
598	0.0572	638	0.00446	678	0.0538	718	0.0201	758	0.0131
599	0.0616	639	0.00157	679	0.160	719	0.0285	759	0.0529
600	0.0142	640	0.0240	680	0.0566	720	0.199	760	0.00644
601	0.0520	641	0.0333	681	0.0174	721	0.0206	761	0.0258
602	0.0102	642	0.00363	682	0.00621	722	0.0380	762	0.0337
603	0.0117	643	0.000832	683	0.0403	723	0.0287	763	0.00519
604	0.0707	644	0.00497	684	0.0150	724	0.0377	764	0.0106
605	ND	645	0.0313	685	0.0176	725	0.0382	765	0.00919
606	0.00412	646	0.0414	686	0.0265	726	0.0530	766	0.0451
607	0.00550	647	0.0198	687	0.0135	727	0.0294	767	0.00751
608	0.0186	648	0.0246	688	0.0228	728	0.0310	768	0.0224
609	0.0331	649	0.0150	689	0.0115	729	0.0925	769	0.0239
610	0.0139	650	0.0283	690	0.00595	730	0.0510	770	0.0140
611	0.00776	651	0.0218	691	0.00717	731	0.00597	771	0.0128
612	0.0438	652	0.00668	692	0.00597	732	0.874	772	0.0141
613	0.00789	653	0.0227	693	0.0150	733	1.73	773	0.0102
614	0.167	654	0.00312	694	0.0191	734	0.00468	774	0.00829
615	0.0163	655	0.0135	695	0.00105	735	0.0580	775	0.0483
616	0.00245	656	0.0334	696	0.00894	736	0.0170	776	0.0365
617	0.0397	657	0.0457	697	0.0102	737	0.0123	777	0.0533
618	0.00298	658	1.29	698	0.00340	738	0.0193	778	0.0000702
619	0.00634	659	0.0264	699	0.0121	739	0.0308	779	0.00954
620	0.0369	660	0.258	700	0.0224	740	0.0392	780	0.00960
621	0.0600	661	0.0121	701	0.0192	741	0.0152	781	0.00312
622	0.0438	662	0.144	702	0.0127	742	0.0325	782	0.00403
623	0.00477	663	0.332	703	0.00318	743	0.188	783	0.0148
624	0.00402	664	0.153	704	0.0890	744	0.0133	784	0.0137
625	0.0780	665	0.0165	705	0.0191	745	0.0333	785	0.0182
626	0.0104	666	0.268	706	0.140	746	0.0367	786	0.0192
627	0.00672	667	0.0467	707	0.0178	747	0.0189	787	0.0109
628	0.0285	668	0.00776	708	0.0878	748	0.0163	788Fa	1.94
629	0.00639	669	0.0364	709	0.0567	749	>100	788Fb	0.00435
630	0.0502	670	0.0180	710	0.0316	750	0.0415	789	0.00896
631	0.00341	671	0.0777	711	0.0775	751	0.0698	790	0.0178
632	0.0120	672	0.106	712	0.0196	752	0.0276	791	0.00359
633	0.0129	673	0.0253	713	0.0314	753	0.0138	792	0.00244

Cmpd.	IC_{50} (μM)	Cmpd.	IC_{50} (μM)	Cmpd.	IC_{50} (μM)	Cmpd.	IC_{50} (μM)	Cmpd.	IC_{50} (μM)
793	0.00481	833	0.111	873	0.0157	913	0.0162	953	0.0134
794	0.00341	834	0.0316	874	0.0415	914	0.0207	954	0.00829
795	0.0121	835	0.0293	875	ND	915	0.0184	955	0.0102
796	0.00327	836	0.00233	876	0.0733	916	0.00481	956	0.0165
797	0.00679	837	0.0134	877	0.234	917	0.0110	957	0.00581
798	0.00986	838	0.0387	878	0.00963	918	0.00437	958	0.0135
799	0.00935	839	0.0296	879	0.00731	919	0.0177	959	0.0148
800	0.0324	840	0.0104	880	0.0679	920	0.00576	960	0.0396
801	0.0170	841	>1.00	881	0.0204	921	0.0696	961	0.0211
802	0.0359	842	0.0209	882	0.00662	922	0.0894	962	0.00315
803	0.161	843	0.0131	883	0.0128	923	0.00371	963	0.00784
804	0.0188	844	0.0233	884	0.00585	924	0.0143	964	0.00332
805	0.0136	845	0.0127	885	0.0307	925	0.0431	965	0.118
806	0.00358	846	0.0379	886	0.0105	926	0.0183	966	0.00358
807	0.0210	847	0.0440	887	0.0201	927	0.00634	967	0.0122
808	0.0524	848	0.0269	888	0.0402	928	0.0387	968	0.00895
809	0.0160	849	0.0145	889	0.0124	929	0.0225	969	0.00556
810	0.00547	850	0.0177	890	0.0125	930	0.00688	970	0.166
811	0.157	851	0.00602	891	0.0137	931	0.0137	971	0.0578
812	0.0300	852	0.0214	892	0.0360	932	0.0178	972	0.00977
813	0.00404	853	0.0319	893	0.0201	933	0.122	973	0.0850
814	ND	854	0.0119	894	0.0216	934	0.0136	974	0.0236
815	0.00331	855	0.00477	895	0.0229	935	0.0196	975	0.0148
816	0.00687	856	0.0137	896	0.00157	936	ND	976	0.0190
817	0.00724	857	0.00462	897	0.00140	937	0.00136	977	0.0144
818	0.0131	858	0.00728	898	0.0325	938	0.00244	978	0.0207
819	0.0282	859	0.00559	899	0.00744	939	0.0121	979	0.00948
820	0.0136	860	0.0103	900	0.0112	940	0.470	980	0.0156
821	0.0142	861	0.0246	901	0.0456	941	0.0200	981	0.0416
822	0.0107	862	0.0209	902	0.0142	942	0.00693	982	0.0204
823	0.0115	863	0.0455	903	0.0112	943	0.0147	983	0.0189
824	0.0136	864	0.0479	904	0.00419	944	0.0462	984	0.0115
825	0.0143	865	0.0284	905	0.00938	945	0.0389	985	0.00669
826	0.0124	866	0.0168	906	0.0176	946	0.0277	986	0.0169
827	0.00572	867	0.00661	907	0.00776	947	0.0237	987	0.0136
828	0.00572	868	0.0172	908	0.00326	948	0.0183	988	0.0219
829	0.00453	869	0.0254	909	0.0132	949	0.0373	989	0.0198
830	0.0128	870	0.140	910	0.0175	950	0.0172	990	0.0322
831	0.0123	871	0.0164	911	0.0171	951	0.0436	991	0.0121
832	ND	872	0.0204	912	0.00898	952	0.0450	992	0.0561

Cmpd.	IC_{50} (μM)	Cmpd.	IC_{50} (μM)	Cmpd.	IC_{50} (μM)	Cmpd.	IC_{50} (μM)	Cmpd.	IC_{50} (μM)
993	0.0156	1033	0.0200	1073	0.0581	1112	0.0199	1152	0.00380
994	0.0234	1034	0.0379	1074	0.0174	1113	0.140	1153	0.0380
995	0.0157	1035	0.0197	1075	0.00664	1114	0.0499	1154	0.0140
996	0.0316	1036	0.00351	1076	0.0245	1115	0.00677	1155	0.0181
997	0.0122	1037	0.0119	1077	0.245	1116	0.0171	1156	0.0351
998	0.0451	1038	0.0389	1078	0.347	1117	0.0134	1157	0.0220
999	0.0163	1039	0.0217	1079	0.0559	1118	0.0140	1158	0.0158
1000	0.0167	1040	0.0300	1080	0.105	1119	0.0146	1159	0.0147
1001	0.0312	1041	0.00621	1081	1.04	1120	0.00951	1160	0.0172
1002	0.00237	1042	0.0265	1082	0.903	1121	0.00926	1161	0.0195
1003	0.0134	1043	0.00398	1083	0.0440	1122	0.0146	1162	0.0216
1004	0.0225	1044	0.00531	1084	0.0150	1123	0.0215	1163	0.0248
1005	0.0334	1045	0.0382	1085	0.0543	1124	0.0132	1164	0.0267
1006	0.0182	1046	0.0380	1086	0.0384	1125	0.0145	1165	0.0223
1007	0.0482	1047	0.0212	1087	0.0392	1126	0.0266	1166	0.0286
1008	0.0153	1048	0.0137	1088	0.0533	1127	0.0129	1167	0.0173
1009	0.00623	1049	0.00935	1089	0.618	1128	0.0239	1168	0.0130
1010	0.00529	1050	0.0195	1090a	0.0383	1129	0.0107	1169	0.0153
1011	0.00715	1051	0.00502	1090b	0.503	1130	0.00439	1170	0.0171
1012	0.00894	1052	0.00546	1091	0.0914	1131	0.0147	1171	0.0130
1013	0.0185	1053	0.00508	1092	0.0427	1132	0.0133	1172	0.0142
1014	0.0256	1054	0.0186	1093	0.0586	1133	0.0170	1173a	0.0192
1015	0.0197	1055	0.0117	1094	0.0716	1134	0.0153	1173b	0.0130
1016	0.00111	1056	0.0161	1095	0.0465	1135	0.0343	1174	0.00932
1017	0.00826	1057	0.0125	1096	0.0335	1136	0.0170	1175	0.0221
1018	0.00671	1058	0.0397	1097	0.0388	1137	0.0174	1176	0.0343
1019	0.0308	1059	0.0111	1098	0.0156	1138	0.0237	1177	0.0342
1020	0.0234	1060	0.0509	1099	0.0375	1139	ND	1178	0.0229
1021	0.0211	1061	0.00854	1100	0.0335	1140	0.00614	1179	0.0147
1022	0.0424	1062	0.00663	1101	0.00720	1141	0.0189	1180	0.0162
1023	0.0498	1063	0.0312	1102	0.0192	1142	0.0130	1181	0.0137
1024	0.0242	1064	0.0162	1103	0.0148	1143	0.0246	1182	0.0136
1025	0.0300	1065	0.0186	1104	0.631	1144	0.0344	1183	0.0232
1026	0.0155	1066	0.0574	1105	0.0217	1145	0.0331	1184	0.00932
1027	0.0315	1067	0.0105	1106	0.0174	1146	0.0144	1185	0.0176
1028	0.00614	1068	0.0278	1107	0.0105	1147	0.0446	1186	0.0201
1029	0.00766	1069	0.00152	1108	0.0291	1148	0.0356	1187	0.0186
1030	0.0144	1070	0.0320	1109	0.0134	1149	0.00419	1188	0.0124
1031	0.0116	1071	0.0540	1110	0.00720	1150	0.00460	1189	0.0134
1032	0.00620	1072	0.0372	1111	0.00571	1151	0.0190	1190	0.00730

Cmpd.	IC_{50} (μM)	Cmpd.	IC_{50} (μM)	Cmpd.	IC_{50} (μM)	Cmpd.	IC_{50} (μM)	Cmpd.	IC_{50} (μM)
1191	0.0128	1231	ND	1271	0.0131	1311	0.0133	1351	0.0160
1192	0.0488	1232	0.00449	1272	0.0281	1312	0.00829	1352	0.0216
1193	0.0102	1233	ND	1273	0.00748	1313	0.0426	1353	0.0172
1194	0.0153	1234	0.0302	1274	0.0402	1314	0.0181	1354	0.0216
1195	0.0131	1235	0.00632	1275	0.0587	1315	0.0131	1355	0.0248
1196	0.0306	1236	0.0339	1276	0.0135	1316	0.0328	1356	0.0232
1197	0.00593	1237	0.00668	1277	0.0384	1317	0.0335	1357	0.0159
1198	0.0130	1238	0.0130	1278	0.0106	1318	0.0344	1358	0.0183
1199	0.0182	1239	0.0182	1279	0.00891	1319	0.0136	1359	0.0397
1200	0.0148	1240	0.0155	1280	0.00426	1320	0.0277	1360	0.0168
1201	0.0228	1241	0.0173	1281	0.117	1321	0.0602	1361	0.0213
1202	0.0197	1242	0.00885	1282	0.0382	1322	0.0112	1362	0.0141
1203	0.00915	1243	0.00555	1283	0.0335	1323	0.0730	1363	0.0429
1204	0.150	1244	0.0194	1284	>1.00	1324	0.0237	1364	0.0247
1205	0.199	1245	0.0156	1285	0.0413	1325	0.0271	1365	0.0341
1206	0.0325	1246	0.106	1286	0.0342	1326	0.0128	1366	0.0143
1207	0.121	1247	0.0355	1287	0.0424	1327	0.0193	1367	0.0149
1208	0.0489	1248	0.0607	1288	0.0367	1328	0.0248	1368	0.0199
1209	0.0980	1249	0.0759	1289	0.0140	1329	0.0352	1369	0.0132
1210	0.0483	1250	0.0758	1290	0.149	1330	0.0130	1370	0.0199
1211	>1.00	1251	0.00477	1291	0.0412	1331	0.0918	1371	0.0151
1212	0.0442	1252	0.222	1292	0.0523	1332	0.0345	1372	0.0807
1213	0.0427	1253	0.00840	1293	0.0351	1333	0.0262	1373	0.0267
1214	0.00508	1254	0.0265	1294	0.0559	1334	0.0513	1374	0.0561
1215	0.0257	1255	0.150	1295	0.0134	1335	0.0128	1375	0.0839
1216	0.0103	1256	0.0247	1296	0.0270	1336	0.0130	1376	0.0136
1217	0.0242	1257	0.0525	1297	0.0378	1337	0.0519	1377	0.0440
1218	0.0131	1258	0.0615	1298	0.0383	1338	0.00950	1378	0.0300
1219	0.00399	1259	0.00538	1299	0.0321	1339	0.0364	1379	0.0180
1220	0.0131	1260	0.0130	1300	0.0181	1340	0.0442	1380	0.0266
1221	0.0300	1261	0.0336	1301	0.0155	1341	0.0215	1381	0.00796
1222	0.00302	1262	0.0106	1302	0.0307	1342	0.0304	1382	0.0216
1223	0.00279	1263	0.0106	1303	0.0366	1343	0.0406	1383	0.00503
1224	0.0760	1264	0.0124	1304	0.0185	1344	0.0183	1384	0.00686
1225	0.00312	1265	0.0115	1305	0.0265	1345	0.0345	1385	0.00724
1226	0.00663	1266	0.00907	1306	0.0389	1346	0.0197	1386	0.0128
1227	0.0128	1267	>1.00	1307	0.0542	1347	0.0414	1387	0.0228
1228	0.00111	1268	0.472	1308	0.0415	1348	0.0122	1388	0.0362
1229	0.0107	1269	0.0666	1309	0.0372	1349	0.0365	1389	1.19
1230	0.0103	1270	0.0399	1310	0.0213	1350	0.0351	1390	ND

Cmpd.	IC_{50} (μM)	Cmpd.	IC_{50} (μM)	Cmpd.	IC_{50} (μM)	Cmpd.	IC_{50} (μM)	Cmpd.	IC_{50} (μM)
1391	0.0376	1431	0.0198	1472	0.0289	1512	0.0122	1554	0.0151
1392	0.0265	1432	0.0212	1473	0.0169	1513	0.0134	1555	0.0239
1393	0.0132	1433	0.0274	1474	0.0138	1514	0.0517	1556	0.0499
1394	0.00474	1434	0.0290	1475	0.00720	1515	0.0321	1557	0.00677
1395	0.0296	1435	0.0264	1476	0.0162	1516	0.0170	1558	0.0690
1396	0.0195	1436	0.0295	1477	0.0181	1518	0.0107	1559	0.0134
1397	0.0147	1437	0.0373	1478	0.0130	1519	0.0153	1560	0.00631
1398	0.0140	1438	0.0408	1479	0.0167	1520	0.0179	1561	0.0130
1399	0.0144	1439	0.0128	1480	ND	1521	0.0183	1562	0.0168
1400	0.0278	1440	0.0690	1481	0.0208	1522	0.0177	1563	0.0130
1401	0.0127	1441	0.0298	1482	0.0166	1523	0.0131	1564	0.0106
1402	0.00658	1443	0.0316	1483	0.0137	1524	0.0125	1565	0.00799
1403	0.00876	1444	0.0252	1484	0.0229	1525	0.0151	1566	0.00439
1404	0.482	1445	0.0320	1485	0.0229	1526	0.0112	1568	0.0216
1405	0.631	1446	0.0140	1486	0.0107	1527	0.0156	1569	0.0195
1406	0.0266	1447	0.0316	1487	0.0254	1528	0.00631	1570	0.0229
1407	0.0247	1448	0.0260	1488	0.0123	1529	0.0201	1571	0.0205
1408	0.0176	1449	0.0170	1489	0.0137	1530	0.0335	1572	0.0200
1409	0.0108	1450	0.0134	1490	0.0291	1531	0.0134	1573	0.0222
1410	0.0180	1451	0.0217	1491	0.0290	1532	0.0112	1574	0.0134
1411	0.0175	1452	0.0391	1492	0.0201	1533	0.0217	1575	0.0147
1412	0.00671	1453	0.0146	1493	0.00683	1534	0.0158	1576	0.0179
1413	0.0517	1454	0.00615	1494	0.0247	1535	0.0174	1577	0.0133
1414	0.0153	1455	0.0211	1495	0.00709	1536	0.0183	1578	0.0203
1415	0.0168	1456	0.0184	1496	0.0325	1537	0.0189	1579	0.0303
1416	0.0127	1457	0.0180	1497	0.0129	1538	0.0145	1581	0.0143
1417	0.0249	1458	0.0191	1498	0.0291	1539	0.0125	1582	0.0192
1418	0.00910	1459	0.0207	1499	0.0275	1540	0.0195	1583	0.0582
1419	0.00676	1460	0.00799	1500	0.0170	1541	0.0106	1584	0.0369
1420	0.00633	1461	0.0138	1501	0.0205	1542	0.0186	1585	0.0152
1421	0.0366	1462	0.0201	1502	0.0262	1543	0.0205	1586	0.0318
1422	0.0335	1463	0.0229	1503	0.0192	1544	0.0131	1587	0.0397
1423	0.0232	1464	0.0134	1504	0.0136	1545	0.0275	1588	0.0264
1424	0.0292	1465	0.0236	1505	0.0130	1546	0.0134	1589	0.0124
1425	0.0130	1466	0.0179	1506	0.0274	1547	0.0152	1590	0.0360
1426	0.0117	1467	0.0110	1507	0.0160	1548	0.0362	1591	0.0362
1427	0.0143	1468	0.0350	1508	0.0174	1549	0.0262	1592	0.0203
1428	0.0122	1469	0.0230	1509	0.0375	1550	0.0229	1593	0.0616
1429	0.0178	1470	0.0308	1510	0.0201	1551	0.0220	1594	0.442
1430	0.0228	1471	0.0142	1511	0.0232	1553	0.0129	1595	0.0548

Cmpd.	IC_{50} (μM)	Cmpd.	IC_{50} (μM)	Cmpd.	IC_{50} (μM)	Cmpd.	IC_{50} (μM)	Cmpd.	IC_{50} (μM)
1596	0.654	1636	0.0388	1676	0.00433	1716	ND	1756	ND
1597	0.0221	1637	0.0177	1677	0.0129	1717	0.0134	1757	ND
1598	0.0375	1638	0.0388	1678	0.0280	1718	ND	1758	ND
1599	0.0167	1639	0.0305	1679	0.0293	1719	ND	1759	ND
1600	0.0203	1640	ND	1680	0.0233	1720	ND	1760	ND
1601	0.00805	1641	0.0189	1681	0.00827	1721	ND	1761	0.00565
1602	0.00388	1642	0.0245	1682	0.0151	1722	ND	1762	0.0250
1603	0.00212	1643	0.0188	1683	0.0183	1723	ND	1763	0.0233
1604	0.00396	1644	0.0145	1684	ND	1724	0.00407	1764	0.0190
1605	0.00378	1645	0.0232	1685	ND	1725	ND	1765	0.0123
1606	0.00460	1646	0.0263	1686	ND	1726	ND	1766	ND
1607	0.0146	1647	0.0196	1687	ND	1727	0.00384	1767	0.0174
1608	0.00659	1648	0.0133	1688	0.0127	1728	ND	1768	0.0313
1609	0.00488	1649	0.0183	1689	0.0222	1729	ND	1769	0.0164
1610	0.00602	1650	0.0107	1690	0.0274	1730	ND	1770	0.0175
1611	0.00385	1651	ND	1691	0.0179	1731	ND	1771	0.0266
1612	0.0137	1652	ND	1692	ND	1732	ND	1772	0.00607
1613	0.0161	1653	0.0265	1693	ND	1733	0.00811	1773	0.0475
1614	0.0314	1654	0.0210	1694	ND	1734	0.0194	1774	0.0450
1615	0.0147	1655	0.0134	1695	ND	1735	0.0336	1775	0.0321
1616	0.0115	1656	ND	1696	ND	1736	0.0126	1776	0.00365
1617	0.0156	1657	ND	1697	ND	1737	0.0143	1777	ND
1618	0.0124	1658	ND	1698	ND	1738	0.0255	1778	ND
1619	0.0316	1659	ND	1699	ND	1739	0.0333	1779	0.0351
1620	0.0179	1660	ND	1700	ND	1740	0.0126	1780	0.0109
1621	0.0721	1661	ND	1701	ND	1741	0.0110	1781	0.00832
1622	0.0173	1662	0.0221	1702	ND	1742	0.00543	1782	ND
1623	ND	1663	0.0141	1703	0.00600	1743	0.00687	1783	ND
1624	0.00417	1664	ND	1704	0.00654	1744	0.0115	1784	ND
1625	ND	1665	0.0146	1705	0.00480	1745	0.0110	1785	ND
1626	0.0303	1666	ND	1706	0.0121	1746	0.0108	1786	ND
1627	ND	1667	0.0122	1707	0.0157	1747	0.0165	1787	ND
1628	ND	1668	0.00567	1708	0.0162	1748	0.0175	1788	ND
1629	ND	1669	0.00917	1709	0.0284	1749	0.0164	1789	ND
1630	ND	1670	0.00568	1710	ND	1750	0.0161	1790	ND
1631	0.0161	1671	0.00414	1711	ND	1751	ND	1791	0.0101
1632	0.0424	1672	0.0132	1712	ND	1752	ND	1792	0.00924
1633	0.0526	1673	0.00722	1713	0.0158	1753	ND	1793	0.00729
1634	0.0174	1674	0.00650	1714	ND	1754	ND	1794	0.00928
1635	0.0215	1675	0.00411	1715	ND	1755	ND	1795	0.00896

Cmpd.	IC_{50} (μM)	Cmpd.	IC_{50} (μM)	Cmpd.	IC_{50} (μM)	Cmpd.	IC_{50} (μM)	Cmpd.	IC_{50} (μM)
1796	ND	1836	ND	1876	ND	1916	ND	1956	ND
1797	ND	1837	ND	1877	ND	1917	ND	1957	ND
1798	ND	1838	0.0123	1878	ND	1918	ND	1958	ND
1799	ND	1839	0.0345	1879	ND	1919	ND	1959	0.0463
1800	ND	1840	0.0264	1880	ND	1920	ND	1960	43.2
1801	ND	1841	ND	1881	ND	1921	ND	1961	0.211
1802	ND	1842	ND	1882	ND	1922	ND	1962	ND
1803	ND	1843	ND	1883	ND	1923	ND	1963	0.241
1804	ND	1844	ND	1884	ND	1924	ND	1964	0.0498
1805	ND	1845	ND	1885	ND	1925	ND	1965	0.0864
1806	ND	1846	ND	1886	ND	1926	ND	1966	ND
1807	0.0104	1847	ND	1887	ND	1927	ND	1967	ND
1808	0.00540	1848	ND	1888	ND	1928	ND	1968	ND
1809	0.00757	1849	ND	1889	ND	1929	ND	1969	ND
1810	0.0129	1850	ND	1890	ND	1930	0.00481	1970	0.0672
1811	0.0127	1851	ND	1891	ND	1931	0.0197	1971	0.0519
1812	0.0184	1852	ND	1892	ND	1932	0.00840	1972	0.0180
1813	ND	1853	ND	1893	ND	1933	0.0346	1973	0.0143
1814	ND	1854	ND	1894	ND	1934	0.0385	1974	0.0513
1815	ND	1855	ND	1895	0.0127	1935	0.0801	1975	0.109
1816	ND	1856	ND	1896	0.0122	1936	0.0374	1976	1.85
1817	0.0258	1857	ND	1897	0.0131	1937	0.0382	1977	>1.00
1818	0.0130	1858	ND	1898	0.0613	1938	0.0463	1978	0.0253
1819	0.00440	1859	ND	1899	0.0164	1939	0.0245	1979	ND
1820	0.0122	1860	ND	1900	2.70	1940	0.0349	1980	ND
1821	ND	1861	ND	1901	0.0357	1941	0.0616	1981	0.0238
1822	ND	1862	ND	1902	0.0842	1942	0.182	1982	0.0364
1823	ND	1863	ND	1903	0.0298	1943	0.0424	1983	0.0826
1824	ND	1864	ND	1904	0.0369	1944	0.0249	1984	ND
1825	0.0171	1865	ND	1905	0.881	1945	0.0449	1985	ND
1826	0.0184	1866	ND	1906	ND	1946	0.0447	1986	0.0785
1827	0.0148	1867	ND	1907	0.405	1947	0.0297	1987	1.29
1828	ND	1868	ND	1908	0.00517	1948	0.0356	1988	0.0495
1829	0.00627	1869	ND	1909	0.0292	1949	0.0216	1989	0.0890
1830	0.00806	1870	ND	1910	0.0474	1950	0.0417	1990	0.0581
1831	0.00500	1871	ND	1911	0.00403	1951	0.0199	1991	>300
1832	0.0205	1872	ND	1912	0.00596	1952	ND	1992	0.490
1833	0.0148	1873	ND	1913	0.0229	1953	0.0893	1993	0.412
1834	ND	1874	ND	1914	ND	1954	0.0170	1994	0.0418
1835	ND	1875	ND	1915	ND	1955	ND	1995	0.0593

Cmpd.	IC_{50} (μM)
1996	0.189
1997	0.0775
1998	0.409
1999	0.482
2000	18.2
2001	65.8
2002	0.259
2003	0.264
2004	0.639
2005	0.364
2006	0.611
2007	>300
2008	0.0961
2009	2.15
2010	1.19
2011	0.529
2012	ND
2013	>10.0
2014	12.2
2015	0.0511
2016	0.613
2017	0.0506
2018	0.0244
2019	0.0249
2020	0.0330
2021	ND
2022	ND
2023	ND
2024	ND
2025	ND
2026	0.656
2027	>1.00
2028	>1.00
2029	ND
2030	ND
2031	ND
2032	ND
2034	0.00620
2035	0.0723
2036	0.0384

Cmpd.	IC_{50} (μM)
2037	>1.00
2038	ND
2039	ND
2041	ND
2042	ND

Example 5B. Cell Proliferation Assays

[0512] MDA-MB-361 cells were maintained in DMEM supplemented with 10% FBS and 1X penicillin/streptomycin solution at 37° C in a CO_2 incubator. For cell proliferation assays, exponentially growing cells were seeded at 2,000 cells per well in 96-well flat bottom white polystyrene plates (ThermoFisher) and cultured overnight. The following day, compound was added in a 9 point 3-fold dilution series starting from a top concentration of 1 or 10 μM (as indicated) together with a DMSO control. The final DMSO concentration in samples was 0.1%.

[0513] Cells were incubated for up to 6 days hours at 37°C in a CO_2 incubator. Baseline viability of untreated cells was measured on the day of treatment and proliferation was measured after 6 days hours of treatment using CELLTITER-GLO® reagent from Promega (Madison, WI) according to the manufacturer's instructions. Response to compound was calculated relative to the DMSO control (% of control) using the formula, % of control (DMSO) = [(CTG_{cells} + inhibitor) / ($CTG_{DMSO\ control}$)] x 100. Data were plotted using Prism (GraphPad software), and IC_{50} and E_{max} values were calculated from a 4 parameter, variable slope non-linear regression model. Results are shown below and in Figures 1-3.

Compound	Mean IC50 (nM)	n
1188	46.8*	7
634	3.8	3
1141	361	2

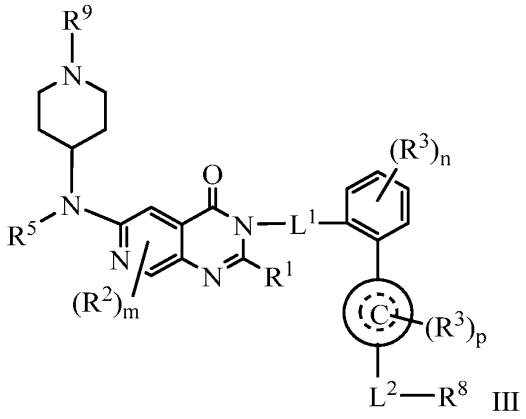
*95% CI (nM) 35.1 – 62.2, E_{max} (%), 90.2

[0514] The various embodiments described above can be combined to provide further embodiments. All of the U.S. patents, U.S. patent application publications, U.S. patent applications, foreign patents, foreign patent applications and non-patent publications referred to in this specification and/or listed in the Application Data Sheet are incorporated herein by reference, in their entirety. Aspects of the embodiments can be modified, if necessary to employ concepts of the various patents, applications and publications to provide yet further embodiments.

[0515] These and other changes can be made to the embodiments in light of the above-detailed description. In general, in the following claims, the terms used should not be construed to limit the claims to the specific embodiments disclosed in the specification and the claims, but should be construed to include all possible embodiments along with the full scope of equivalents to which such claims are entitled. Accordingly, the claims are not limited by the disclosure.

CLAIMS

1. A compound of Formula III:



III

or a pharmaceutically acceptable salt thereof, wherein:

L^1 is $–(CH_2)–$, $–(CH_2)_2–$, $–(CH_2)_3–$, $–CH((C_1\text{-}C_8)alkyl)(CH_2)–$, $–CH((C_1\text{-}C_8)alkyl)(CH_2)_2–$, $–(CH_2)_2\text{-}O–$, $–CH_2CH=CH–$, $–CH_2C\equiv C–$ or $–CH_2(cyclopropyl)–$;

L^2 is $-C(R^6)(R^6)-$, $-C(R^6)(R^6)C(R^6)(R^6)-$, $-C(R^6)=C(R^6)-$, $-N(R^5)C(R^6)(R^6)-$, $-OC(R^6)(R^6)-$, $-C(=O)-$, $-C(=O)N(R^5)C(R^6)(R^6)-$ or a bond;

Ring C is a heteroaryl;

R^1 is H, OH, halo, CN, $(C_1\text{-}C_8)$alkyl, $(C_1\text{-}C_8)$haloalkyl, $(C_3\text{-}C_6)$cycloalkyl or NR^5R^5;

R^2 is independently H, halo, CN, NO, NO_2, C≡H, $(C_1\text{-}C_8)$alkyl, $(C_1\text{-}C_8)$haloalkyl, CH_2SR^5, OR^5, NHR^5, NR^5R^5, $[(C_1\text{-}C_8)alkylene]$heterocyclyl, $[(C_1\text{-}C_8)alkylene]$heteroaryl, $[(C_1\text{-}C_8)alkylene]NHR^5$, $[(C_1\text{-}C_8)alkylene]NR^5R^5$, $[(C_1\text{-}C_8)alkylyne]NR^5R^5$, $C(O)R^5$, $C(O)OR^5$, $C(O)NHR^5$, $C(O)NR^5R^5$, SR^5, $S(O)R^5$, SO_2R^5, SO_2NHR^5, $SO_2NR^5R^5$, $NH(CO)R^6$, $NR^5(CO)R^6$, aryl, heteroaryl, cycloalkyl or heterocyclyl;

R^3 is independently OH, halo, CN, NO_2, $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$haloalkyl, $(C_1\text{-}C_6)$alkoxy, C≡H, NHR^7, NR^7R^7, CO_2H, CO_2R^7, $[(C_1\text{-}C_3)alkylene]$ $(C_1\text{-}C_3)$alkoxy, $[(C_1\text{-}C_3)alkylene]CO_2H$, $(C_3\text{-}C_5)$cycloalkyl, =O. =S, SR^7, SO_2R^7, $NH(CO)R^7$ or $NR^7(CO)R^7$;

R^5 is independently H, $(C_1\text{-}C_3)$alkyl, $(C_1\text{-}C_3)$haloalkyl, $(C_3\text{-}C_5)$cycloalkyl or heterocyclyl;

R^6 is independently H, OH, halo, CN, $(C_1\text{-}C_3)$alkyl, $(C_1\text{-}C_3)$haloalkyl, $(C_1\text{-}C_3)$alkoxy, NHR^7, NR^7R^7, CO_2H, $[(C_1\text{-}C_3)alkylene]CO_2H$, $(C_3\text{-}C_5)$cycloalkyl, SR^7, $NH(CO)R^7$ or $NR^7(CO)R^7$;

R^7 is independently H, (C_1-C_8)alkyl, (C_1-C_8)haloalkyl, cycloalkyl, heterocyclyl, aryl or heteroaryl;

R^8 is H, OH, CO_2H, CO_2R^7, $CF_2C(R^6)_2OH$, $C(R^6)_2OH$, $C(CF_3)_2OH$, SO_2H, SO_3H, $CF_2SO_2C(R^6)_3$, $CF_2SO_2N(H)R^5$, $SO_2N(H)R^5$, $SO_2N(H)C(O)R^6$, $C(O)N(H)SO_2R^5$, C(O)haloalkyl, $C(O)N(H)OR^5$, $C(O)N(R^5)OH$, $C(O)N(H)R^5$, $C(O)NR^5C(O)N(R^5)_2$, $P(O)(OR^5)OH$, $P(O)(O)N(H)R^5$, $P(O)(C(R^6)_3)C(R^6)_3$, $B(OH)_2$, heterocyclyl or heteroaryl;

R^9 is H, (C_1-C_8)alkyl, (C_1-C_8)haloalkyl, cycloalkyl or heterocyclyl;

m is 0, 1, or 2;

n is 0, 1, 2 or 3;

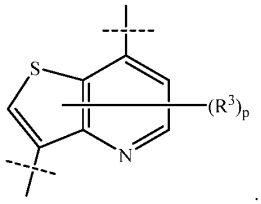
p is 0, 1, 2 or 3;

wherein any alkyl, alkylene, cycloalkyl, heterocyclyl, heteroaryl or aryl is optionally substituted with 1, 2 or 3 groups selected from OH, CN, SH, SCH_3, SO_2CH_3, SO_2NH_2, $SO_2NH(C_1$-$C_4)$alkyl, halogen, NH_2, $NH(C_1$-$C_4)$alkyl, $N[(C_1$-$C_4)alkyl]_2$, NH(aryl), $C(O)NH_2$, C(O)NH(alkyl), $CH_2C(O)NH$(alkyl), COOH, COOMe, acetyl, (C_1-C_8)alkyl, (C_1-C_8)haloalkyl, $O(C_1$-$C_8)$alkyl, $O(C_1$-$C_8)$haloalkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, thioalkyl, cyanomethylene, alkylaminyl, alkylene-$C(O)NH_2$, alkylene-C(O)-NH(Me), NHC(O)alkyl, CH_2-C(O)-(C_1-C_8)alkyl, C(O)-(C_1-C_8)alkyl, and alkylcarbonylaminyl.

2. The compound or the salt of claim 1, wherein L^1 is a bond.

3. The compound or the salt of claim 1, wherein Ring C is heteroaryl.

4. The compound or the salt of claim 1, wherein Ring C is



.

5. The compound or the salt of claim 1, wherein R^1 is H, (C_1-C_8)alkyl or (C_1-C_8)haloalkyl.

6. The compound or the salt of claim 1, wherein R^2 is halo, CN, (C_1-C_8)alkyl, (C_1-C_8)haloalkyl or OR^5.

7. The compound or the salt of claim 1, wherein R^2 is halo, CN or (C_1-C_8)haloalkyl.

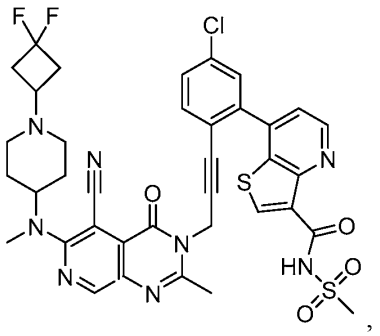
8. The compound or the salt of claim 1, wherein R^5 is H, (C_1-C_3)alkyl or (C_1-C_3)haloalkyl.

9. The compound or the salt of claim 1, wherein R^8 is CO_2H or $C(O)N(H)SO_2R^5$.

10. The compound or the salt of claim 1, wherein R^9 is cycloalkyl or heterocyclyl.

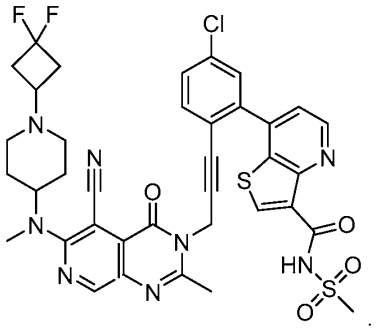
11. The compound or the salt of claim 1, wherein p = 0 or 1.

12. A compound having the formula:

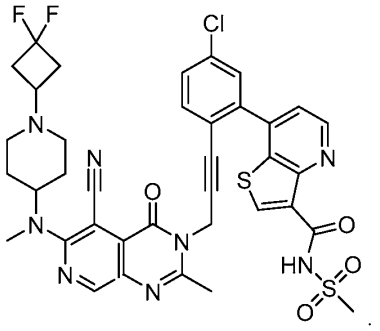


or a pharmaceutically acceptable salt thereof.

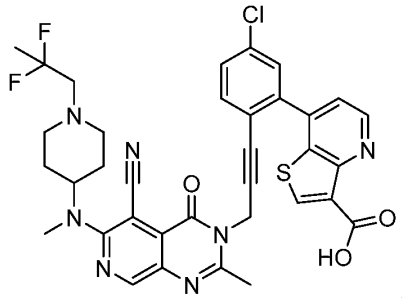
13. A compound having the formula:



14. A pharmaceutically acceptable salt of a compound having the formula:



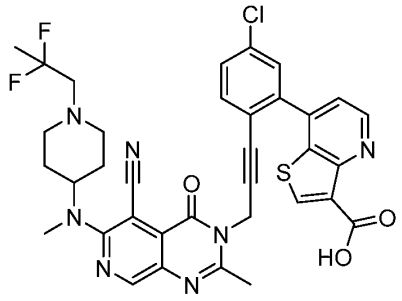
15. A compound having the formula:



,

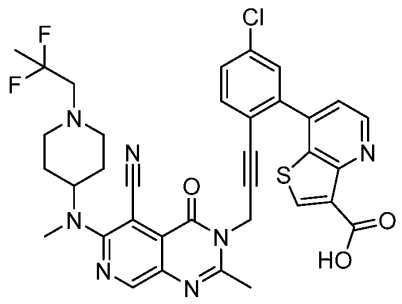
or a pharmaceutically acceptable salt thereof.

16. A compound having the formula:



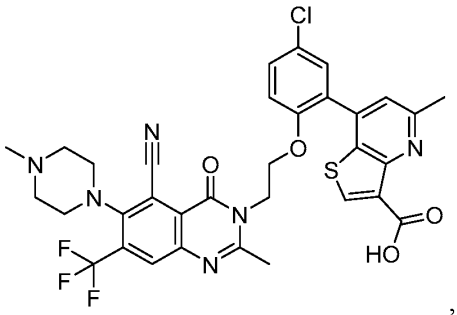
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17. A pharmaceutically acceptable salt of a compound having the formula:



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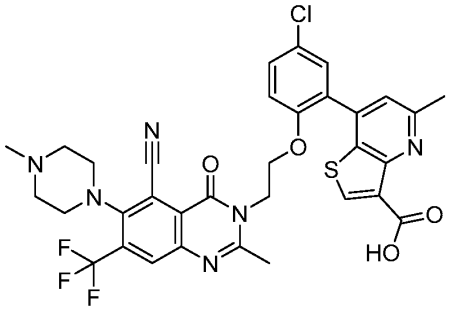
18. A compound having the formula:



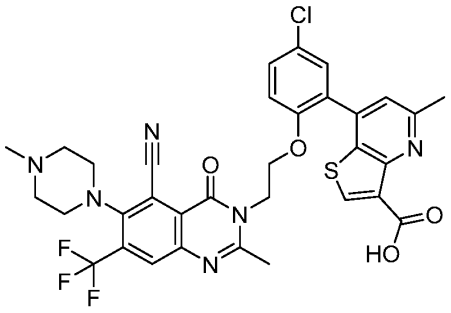
,

or a pharmaceutically acceptable salt thereof.

19. A compound having the formula:



20. A pharmaceutically acceptable salt of a compound having the formula:



21. A pharmaceutical composition comprising:

(a) a compound or a salt of any one of claims 1-20; and

(b) a pharmaceutically acceptable carrier, diluent, or excipient.

22. A method of treating cancer, comprising administering to an individual in need thereof a therapeutically effective amount of a compound or a salt of any one of claims 1-20.

23. The method of claim 22, wherein the cancer is colon cancer, gastric cancer, thyroid cancer, lung cancer, leukemia, B-cell lymphoma, T-cell lymphoma, hairy cell lymphoma, Hodgkin's lymphoma, non-Hodgkin's lymphoma, Burkitt's lymphoma, pancreatic cancer, melanoma, brain cancer, CNS cancer, renal cancer, prostate cancer, ovarian cancer, or breast cancer.

24. The method of claim 23, wherein the cancer is a metastatic cancer.

25. The method of claim 23, wherein the cancer is breast cancer, prostate cancer, or lung cancer.

26. The method of claim 25, wherein the cancer is breast cancer.

27. The method of claim 26, wherein the breast cancer is hormone receptor positive breast cancer.

28. Use of a compound or a salt of any one of claims 1-20 in the manufacture of a medicament for treating cancer.

29. The pharmaceutical composition of claim 21 for treating cancer.