

COMPOUNDS AND PHARMACEUTICAL COMPOSITIONS THAT DEGRADE SWI/SNF-RELATED MATRIX-ASSOCIATED ACTIN-DEPENDENT REGULATOR OF CHROMATIN SUBFAMILY A

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit under 35 U.S.C. § 119(e) of United States Provisional Application Numbers 63/598,019, filed November 10, 2023, and 63/673,138, filed July 18, 2024, the contents of which are hereby incorporated by reference in their entireties.

Field

[0001] This disclosure provides for compounds, including pharmaceutically acceptable salts thereof, that are useful as modulators of targeted ubiquitination. The compounds disclosed herein bind to and degrade protein which is expressed from one or more SWI/SNF-related matrix-associated actin-dependent regulator of chromatin subfamily A ("SMARCA"). Also disclosed are pharmaceutical compositions comprising the compounds, and methods of using such compounds in the treatment of various SMARCA-mediated diseases or disorders.

State of the Art

[0002] Ubiquitin-Proteasome Pathway (UPP) is a critical pathway that regulates key regulator proteins and degrades misfolded or abnormal proteins. UPP is central to multiple cellular processes, and if defective or imbalanced, it leads to pathogenesis of a variety of diseases. The covalent attachment of ubiquitin to specific protein substrates is achieved through the action of E3 ubiquitin ligases.

[0003] There are over 600 E3 ubiquitin ligases which facilitate the ubiquitination of different proteins in vivo, which can be divided into four families: HECT-domain E3s, U-box E3s, monomeric RING E3s and multi-subunit E3s. See e.g., Li et al. "Genome-wide and functional annotation of human E3 ubiquitin ligases identifies MULAN, a mitochondrial E3 that regulates the organelle's dynamics and signaling." PLOS One 2008, (3) 1487; Berndsen et al. "New insights into ubiquitin E3 ligase mechanism" Nat. Struct. Mol. Biol. 2014, 21:301; Deshaies et al. "RING domain E3 ubiquitin ligases" Ann. Rev. Biochem. 2009, 78:399; Spratt et al. "RBRE3 ubiquitin ligases: new structures, new insights, new questions" Biochem. 2014, 458:421; and Wang et al., "Roles of F-box proteins in cancer" Nat. Rev. Cancer. 2014, 14:233.

[0004] UPP plays a key role in the degradation of short-lived and regulatory proteins important in a variety of basic cellular processes, including regulation of the cell cycle, modulation of cell surface receptors and ion channels, and antigen presentation. The pathway has been implicated in several forms of malignancy, in the pathogenesis of several genetic diseases (including cystic fibrosis, Angelman's syndrome, and Liddle syndrome), in immune surveillance/viral pathogenesis, and in the pathology of muscle wasting. Many diseases are associated with an abnormal UPP and negatively affect cell cycle and division, the cellular response to stress and to extracellular modulators, morphogenesis of neuronal networks, modulation of cell surface receptors, ion channels, the secretory pathway, DNA repair, and biogenesis of organelles.

[0005] Aberrations in the process have recently been implicated in the pathogenesis of several diseases, both inherited and acquired. These diseases fall into two major groups: (a) those that result from loss of function with the resultant stabilization of certain proteins, and (b) those that result from gain of function, i.e. abnormal or accelerated degradation of the protein target.

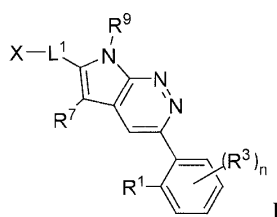
[0006] The UPP is used to induce selective protein degradation, including use of fusion proteins to artificially ubiquitinate target proteins and synthetic small-molecule probes to induce proteasome-dependent degradation. Compounds that act as molecular glues can induce or stabilize protein-protein interactions between a target protein and an E3 ubiquitin ligase ligand, leading to protein ubiquitination and subsequent proteasome-mediated degradation via the recruitment to E3 ubiquitin ligase and subsequent ubiquitination. These drug-like molecules offer the possibility of temporal control over protein expression. Such compounds are capable of inducing the inactivation of a protein of interest upon addition to cells or administration to an animal or human, and could be useful as biochemical reagents and lead to a new paradigm for the treatment of diseases by removing pathogenic or oncogenic proteins. See e.g., Crews, Chem. & Biol. 2010, 17 (6): 551; Schneekloth and Crews, Chem Bio Chem., 2005, 6 (1): 40.

[0007] An ongoing need exists in the art for effective treatments for disease, especially hyperplasias and cancers. However, non-specific effects, and the inability to target and modulate certain classes of proteins altogether, such as transcription factors, remain as obstacles to the development of effective anti-cancer agents. As such, small molecule therapeutic agents that leverage E3 ligase mediated protein degradation to target cancer-associated proteins, such as one or more SWESNF-related matrix-associated actin-dependent regulator of chromatin subfamily A ("SMARCA") and/or polybromo-1 ("PBI") protein, hold promise as therapeutic agents. Accordingly, there remains a need to find compounds that are degraders of protein which is expressed from the SMARCA gene useful as therapeutic agents.

Summary

[0008] Disclosed are compounds and pharmaceutically acceptable salts thereof, pharmaceutical compositions comprising said compounds or pharmaceutically acceptable salts thereof, and methods for use of said compounds, pharmaceutically acceptable salts thereof, and pharmaceutical compositions thereof, which find utility as inducers of targeted ubiquitination of protein which is expressed from the SMARCA gene, which are then degraded and/or inhibited by the monovalent compounds as described herein. An advantage of the compounds provided herein is that a broad range of pharmacological activities are possible, consistent with the degradation/inhibition of protein which is expressed from the SMARCA gene. In addition, the disclosure provides methods of using an effective amount of the compounds as described herein for the treatment or amelioration of a disease condition, such as cancer, e.g., lung cancer, in a subject in need thereof.

[0009] Provided herein is a compound of Formula I:



or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein:

n is 0, 1, or 2;

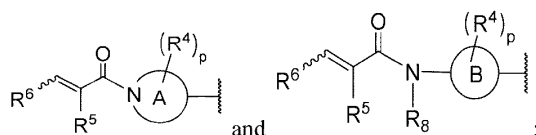
R¹ is OR¹², halo, cyano, C₁₋₄ alkoxy, N(R²)₂, or C(O)CH(C₁₋₄ alkyl)N(R²)₂;

each R² is independently hydrogen, C₁₋₄ alkyl, or C₃₋₆ cycloalkyl, wherein each alkyl or cycloalkyl is unsubstituted or substituted with one to three Z¹;

each R³ is independently halo, cyano, C₁₋₆ alkyl, or C₁₋₃ haloalkyl;

L¹ is a bond, C₁₋₄ alkylene, -C₁₋₄ alkylene-heteroaryl-, C₂₋₃ alkenylene, C₂₋₃ alkynylene, or -C(O)-;

X is selected from:



p is 0, 1, or 2;

Ring A is a monocyclic, spirocyclic, fused bicyclic, or bridged bicyclic 4-10 membered heterocyclyl or a monocyclic or fused bicyclic 5-10 membered heteroaryl;

Ring B is a monocyclic, spirocyclic, fused bicyclic, or bridged bicyclic 3-10 membered cycloalkyl, a monocyclic, spirocyclic, fused bicyclic, or bridged bicyclic 4-10 membered heterocyclyl, or a monocyclic or fused bicyclic 5-10 membered heteroaryl; wherein the nitrogen atom and L¹ may be attached via any atom on Ring B, including on the same carbon atom;

each R⁴ is independently oxo, halo, cyano, -NO₂, -SF₅, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, -C(O)R¹¹, -C(O)OR¹¹, -S(O)₀₋₂R¹¹, -NR¹¹S(O)₀₋₂R¹¹, -S(O)₀₋₂N(R¹¹)₂, -NR¹¹S(O)₀₋₂N(R¹¹)₂, -NR¹¹C(O)N(R¹¹)₂, -C(O)N(R¹¹)₂, -NR¹¹C(O)R¹¹, -OC(O)N(R¹¹)₂, or -NR¹¹C(O)OR¹¹; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z¹;

R⁵ is hydrogen, halo, cyano, or C₁₋₆ alkyl optionally substituted with one to three Z¹;

R⁶ is hydrogen, halo, cyano, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, -C(O)R¹¹, -C(O)OR¹¹, -S(O)₀₋₂R¹¹, -NR¹¹S(O)₀₋₂R¹¹, -S(O)₀₋₂N(R¹¹)₂, -NR¹¹S(O)₀₋₂N(R¹¹)₂, -NR¹¹C(O)N(R¹¹)₂, -C(O)N(R¹¹)₂, -NR¹¹C(O)R¹¹, -OC(O)N(R¹¹)₂, or -NR¹¹C(O)OR¹¹; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z¹;

R^7 is hydrogen, halo, cyano, $-\text{NO}_2$, $-\text{SF}_5$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, heteroaryl, $-\text{N}(\text{R}^{11})_2$, $-\text{OR}^{11}$, $-\text{C}(\text{O})\text{R}^{11}$, $-\text{C}(\text{O})\text{OR}^{11}$, $-\text{S}(\text{O})_{0-2}\text{R}^{11}$, $-\text{NR}^{11}\text{S}(\text{O})_{0-2}\text{R}^{11}$, $-\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{C}(\text{O})\text{N}(\text{R}^{11})_2$, $-\text{C}(\text{O})\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{C}(\text{O})\text{R}^{11}$, $-\text{OC}(\text{O})\text{N}(\text{R}^{11})_2$, or $-\text{NR}^{11}\text{C}(\text{O})\text{OR}^{11}$; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z^1 ;

R^8 is hydrogen or C_{1-6} alkyl optionally substituted with one to three Z^1 ;

R^9 is hydrogen, $-\text{C}(\text{O})\text{R}^{13}$, $-\text{C}(\text{R}^{13})_2\text{OC}(\text{O})\text{R}^{15}$, $-\text{C}(\text{O})\text{OCH}_2\text{OC}(\text{O})\text{R}^{15}$, $-\text{C}(\text{O})\text{OCH}(\text{CH}_3)\text{OC}(\text{O})\text{R}^{15}$, $-\text{C}(\text{O})\text{OCH}_2\text{OC}(\text{O})\text{R}^{15}$, $-\text{C}(\text{O})\text{OCH}(\text{CH}_3)\text{OC}(\text{O})\text{R}^{15}$, $-(\text{CH}_2)_m\text{OP}(\text{O})(\text{OR}^{14})_2$, $-\text{CH}(\text{CH}_3)\text{OP}(\text{O})(\text{OR}^{14})_2$, $-(\text{CH}_2)_m\text{OP}(\text{O})(\text{R}^{14})(\text{OR}^{14})$, $-\text{CH}(\text{CH}_3)\text{OP}(\text{O})(\text{R}^{14})(\text{OR}^{14})$, $-(\text{CH}_2)_m\text{OP}(\text{O})(\text{N}(\text{R}^{14})_2)(\text{OR}^{14})$, $-\text{CH}(\text{CH}_3)\text{OP}(\text{O})(\text{N}(\text{R}^{14})_2)(\text{OR}^{14})$, $-(\text{CH}_2)_m\text{OP}(\text{O})(\text{R}^{14})(\text{N}(\text{R}^{14})_2)$, $-(\text{CH}_2)_m\text{OP}(\text{O})(\text{N}(\text{R}^{14})_2)_2$, or $-\text{C}(\text{CH}_3)\text{OP}(\text{O})(\text{N}(\text{R}^{14})_2)_2$;

m is 1 or 2;

each Z^1 is independently halo, cyano, $-\text{NO}_2$, $-\text{SF}_5$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, heteroaryl, $-\text{N}(\text{R}^{11})_2$, $-\text{OR}^{11}$, $-\text{P}(\text{O})(\text{OR}^{11})_2$, $-\text{C}(\text{O})\text{R}^{11}$, $-\text{C}(\text{O})\text{OR}^{11}$, $-\text{S}(\text{O})_{0-2}\text{R}^{11}$, $-\text{NR}^{11}\text{S}(\text{O})_{0-2}\text{R}^{11}$, $-\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{C}(\text{O})\text{N}(\text{R}^{11})_2$, $-\text{C}(\text{O})\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{C}(\text{O})\text{R}^{11}$, $-\text{OC}(\text{O})\text{N}(\text{R}^{11})_2$, or $-\text{NR}^{11}\text{C}(\text{O})\text{OR}^{11}$; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1a} ;

each R^{11} is independently hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1a} ;

each Z^{1a} is independently hydroxy, halo, cyano, $-\text{NO}_2$, $-\text{SF}_5$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, heteroaryl, $-\text{N}(\text{R}^{13})_2$, $-\text{OR}^{13}$, $-\text{P}(\text{O})(\text{OR}^{13})_2$, $-\text{C}(\text{O})\text{R}^{13}$, $-\text{C}(\text{O})\text{OR}^{13}$, $-\text{S}(\text{O})_{0-2}\text{R}^{13}$, $-\text{NR}^{13}\text{S}(\text{O})_{0-2}\text{R}^{13}$, $-\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{13})_2$, $-\text{NR}^{13}\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{13})_2$, $-\text{NR}^{13}\text{C}(\text{O})\text{N}(\text{R}^{13})_2$, $-\text{C}(\text{O})\text{N}(\text{R}^{13})_2$, $-\text{NR}^{13}\text{C}(\text{O})\text{R}^{13}$, $-\text{OC}(\text{O})\text{N}(\text{R}^{13})_2$, or $-\text{NR}^{13}\text{C}(\text{O})\text{OR}^{13}$; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1b} ;

R^{12} is hydrogen, $-\text{C}(\text{O})\text{R}^{13}$, $-\text{C}(\text{O})\text{N}(\text{R}^{14})_2$, $-\text{P}(\text{O})(\text{OR}^{14})_2$, $-\text{CH}_2\text{OP}(\text{O})(\text{OR}^{14})_2$, $-\text{CH}(\text{CH}_3)\text{OP}(\text{O})(\text{OR}^{14})_2$, $-\text{P}(\text{O})(\text{R}^{14})(\text{OR}^{14})$, $-\text{CH}_2\text{OP}(\text{O})(\text{R}^{14})(\text{OR}^{14})$, $-\text{CH}(\text{CH}_3)\text{OP}(\text{O})(\text{R}^{14})(\text{OR}^{14})$, $-\text{P}(\text{O})(\text{N}(\text{R}^{14})_2)(\text{OR}^{14})$, $-\text{CH}_2\text{OP}(\text{O})(\text{N}(\text{R}^{14})_2)(\text{OR}^{14})$, $-\text{CH}(\text{CH}_3)\text{OP}(\text{O})(\text{N}(\text{R}^{14})_2)(\text{OR}^{14})$, $-\text{P}(\text{O})(\text{R}^{14})(\text{N}(\text{R}^{14})_2)$, $-\text{CH}_2\text{OP}(\text{O})(\text{R}^{14})(\text{N}(\text{R}^{14})_2)$, $-\text{CH}(\text{CH}_3)\text{OP}(\text{O})(\text{R}^{14})(\text{N}(\text{R}^{14})_2)$, $-\text{P}(\text{O})(\text{N}(\text{R}^{14})_2)_2$, $-\text{CH}_2\text{OP}(\text{O})(\text{N}(\text{R}^{14})_2)_2$, or $-\text{CH}(\text{CH}_3)\text{OP}(\text{O})(\text{N}(\text{R}^{14})_2)_2$;

each R^{13} is independently hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1b} ;

each R¹⁴ is independently hydrogen, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, aryl, heteroaryl, or heterocyclyl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, or heterocyclyl is independently optionally substituted with one to five Z^{1b}; or two R¹⁴ together with the atom to which they are attached form a heterocyclyl; wherein said heterocyclyl is independently optionally substituted one to five Z^{1b};

R¹⁵ is independently R¹⁶, -OR¹⁶, -SR¹⁶, or -N(R¹⁶)₂;

each R¹⁶ is independently hydrogen, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, aryl, heteroaryl, or heterocyclyl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, or heterocyclyl is independently optionally substituted with one to five Z^{1b};

each Z^{1b} is independently halo, cyano, hydroxy, -SH, -NH₂, -NO₂, -SF₅, -P(O)(OH)₂, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -L-C₁₋₆ alkyl, -L-C₂₋₆ alkenyl, -L-C₂₋₆ alkynyl, -L-C₁₋₆ haloalkyl, -L-C₃₋₁₀ cycloalkyl, -L-heterocyclyl, -L-aryl, or -L-heteroaryl; and

each L is independently -O-, -NH-, -S-, -S(O)-, -S(O)₂-, -N(C₁₋₆ alkyl)-, -N(C₂₋₆ alkenyl)-, -N(C₂₋₆ alkynyl)-, -N(C₁₋₆ haloalkyl)-, -N(C₃₋₁₀ cycloalkyl)-, -N(heterocyclyl)-, -N(aryl)-, -N(heteroaryl)-, -C(O)-, -C(O)O-, -C(O)NH-, -C(O)N(C₁₋₆ alkyl)-, -C(O)N(C₂₋₆ alkenyl)-, -C(O)N(C₂₋₆ alkynyl)-, -C(O)N(C₁₋₆ haloalkyl)-, -C(O)N(C₃₋₁₀ cycloalkyl)-, -C(O)N(heterocyclyl)-, -C(O)N(aryl)-, -C(O)N(heteroaryl)-, -NHC(O)-, -NHC(O)O-, -NHC(O)NH-, -NHS(O)-, -S(O)₂NH-, -P(O)(OH)O-, -P(O)(O-C₁₋₆ alkyl)O-, -P(O)(O-C₂₋₆ alkenyl)O-, -P(O)(O-C₂₋₆ alkynyl)O-, -P(O)(OC₁₋₆ haloalkyl)O-, -P(O)(OC₃₋₁₀ cycloalkyl)O-, -P(O)(O-heterocyclyl)O-, -P(O)(O-aryl)O-, or -P(O)(O-heteroaryl)O-;

wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, and heteroaryl of Z^{1b} and L is further independently optionally substituted with one to five hydroxy, halo, cyano, hydroxy, -SH, -NH₂, -NO₂, -SF₅, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkoxy, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl.

[0010] In some embodiments, the compound is not 1-[3-[3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl]-1-azetidiny]-2-propen-1-one.

[0011] In some embodiments, the compounds as described herein modulate protein which is expressed from the SMARCA gene. In some embodiments, the compounds as described herein degrade protein which is expressed from the SMARCA gene. In some embodiments, the protein which is modulated or degraded is expressed from the SMARCA gene member 2 (SMARCA2). In some embodiments, the protein which is modulated or degraded is expressed by the SMARCA gene member 4 (SMARCA4).

[0012] In some embodiments, this disclosure provides a pharmaceutical composition comprising a pharmaceutically acceptable excipient and an effective amount of a compound of Formula I or any subformula thereof, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopically enriched analog, tautomer thereof.

[0013] In some embodiments, this disclosure provides a method for modulating or degrading protein which is expressed from the SMARCA gene, which method comprises contacting the protein with an

effective amount of a compound of Formula I or any subformula thereof under conditions wherein the protein which is expressed from the SMARCA gene is bound to said compound and modulated or degraded. In some embodiments, the protein which is modulated or degraded is the protein which is expressed from the SMARCA2 gene. In some embodiments, the protein which is modulated or degraded is the protein which is expressed from the SMARCA4 gene.

[0014] In some embodiments, this disclosure provides a method for modulating or degrading protein which is expressed from the SMARCA gene in a subject, which method comprises administering to said subject an effective amount of a compound of Formula I or any subformula thereof, or a pharmaceutical composition comprising a pharmaceutically acceptable excipient and an effective amount of a compound of Formula I or any subformula thereof under conditions wherein the protein which is expressed from the SMARCA gene is bound to said compound and modulated or degraded. In some embodiments, the protein which is modulated or degraded in a subject is the protein which is expressed from the SMARCA2 gene. In some embodiments, the protein which is modulated or degraded in a subject is the protein which is expressed from the SMARCA4 gene.

[0015] In some embodiments, this disclosure provides a method for treating hyperplasia in a subject in need thereof, which method comprises administering to said subject an effective amount of a compound of Formula I or any subformula thereof, or a pharmaceutical composition comprising a pharmaceutically acceptable excipient and an effective amount of a compound of Formula I or any subformula thereof.

[0016] In some embodiments, this disclosure provides a method for treating cancer in a subject in need thereof, which method comprises administering to said subject an effective amount of a compound of Formula I or any subformula thereof, or a pharmaceutical composition comprising a pharmaceutically acceptable excipient and an effective amount of a compound of Formula I or any subformula thereof.

Detailed Description

[0017] This disclosure provides for compounds, pharmaceutical compositions comprising such compounds, and methods of using such compounds and compositions to treat diseases, disorders, or conditions mediated, at least in part, by SMARCA2 or SMARCA4 transcription factors. However, prior to providing a detailed description of the disclosure, the following terms will first be defined. If not defined, terms used herein have their generally accepted scientific meaning.

[0018] The terminology used herein is for the purpose of describing particular embodiments only and is not intended to be limiting of the disclosure. As used herein, the singular forms “a”, “an,” and “the” are intended to include the plural forms as well, unless the context clearly indicates otherwise.

[0019] A dash (“-”) that is not between two letters or symbols is used to indicate a point of attachment for a substituent. For example, -C(O)NH₂ is attached through the carbon atom. A dash at the front or end of a chemical group is a matter of convenience; chemical groups may be depicted with or without one or more dashes without losing their ordinary meaning. A wavy line or a dashed line drawn through a line in a structure indicates a specified point of attachment of a group. Unless chemically or structurally required, no directionality or stereochemistry is indicated or implied by the order in which a chemical group is written or named.

[0020] The prefix “C_{u-v}” indicates that the following group has from u to v carbon atoms. For example, “C₁₋₆ alkyl” indicates that the alkyl group has from 1 to 6 carbon atoms.

[0021] The term “about” when used before a numerical designation, e.g., temperature, time, amount, concentration, and such other, including a range, indicates approximations which may vary by (+) or (-) 10%, 5%, 1%, or any subrange or subvalue there between. In one embodiment, the term “about” when used with regard to a dose amount means that the dose may vary by +/- 10%.

[0022] “Comprising” or “comprises” is intended to mean that the compositions and methods include the recited elements, but not excluding others.

[0023] “Consisting essentially of” when used to define compositions and methods, shall mean excluding other elements of any essential significance to the combination for the stated purpose. Thus, a composition consisting essentially of the elements as defined herein would not exclude other materials or steps that do not materially affect the basic and novel characteristic(s) of the claimed disclosure.

[0024] “Consisting of” shall mean excluding more than trace elements of other ingredients and substantial method steps. Embodiments defined by each of these transition terms are within the scope of this disclosure.

[0025] “Alkyl” refers to an unbranched or branched saturated hydrocarbon chain. As used herein, alkyl has 1 to 20 carbon atoms (i.e., C₁₋₂₀ alkyl), 1 to 12 carbon atoms (i.e., C₁₋₁₂ alkyl), 1 to 8 carbon atoms (i.e., C₁₋₈ alkyl), 1 to 6 carbon atoms (i.e., C₁₋₆ alkyl), or 1 to 4 carbon atoms (i.e., C₁₋₄ alkyl). Examples of alkyl groups include, e.g., methyl, ethyl, propyl, isopropyl, n-butyl, sec-butyl, iso-butyl, tert-butyl, pentyl, 2-pentyl, isopentyl, neopentyl, hexyl, 2-hexyl, 3-hexyl, and 3-methylpentyl. When an alkyl residue having a specific number of carbons is named by chemical name or identified by molecular formula, all positional isomers having that number of carbons may be encompassed; thus, for example, “butyl” includes n-butyl (i.e., -(CH₂)₃CH₃), sec-butyl (i.e., -CH(CH₃)CH₂CH₃), isobutyl (i.e., -CH₂CH(CH₃)₂), and tert-butyl (i.e., -C(CH₃)₃); and “propyl” includes n-propyl (i.e., -(CH₂)₂CH₃) and isopropyl (i.e., -CH(CH₃)₂).

[0026] Certain commonly used alternative chemical names may be used. For example, a divalent group such as a divalent “alkyl” group, a divalent “aryl” group, a divalent heteroaryl group, etc., may also be referred to as an “alkylene” group or an “alkylenyl” group (for example, methylenyl, ethylenyl, and propylenyl), an “arylene” group or an “arylenyl” group (for example, phenylenyl or naphthylenyl, or quinolinyl for heteroarylene), respectively. Also, unless indicated explicitly otherwise, where combinations of groups are referred to herein as one moiety, e.g., arylalkyl or aralkyl, the last mentioned group contains the atom by which the moiety is attached to the rest of the molecule.

[0027] “Alkenyl” refers to an alkyl group containing at least one (e.g., 1-3, or 1) carbon-carbon double bond and having from 2 to 20 carbon atoms (i.e., C₂₋₂₀ alkenyl), 2 to 12 carbon atoms (i.e., C₂₋₁₂ alkenyl), 2 to 8 carbon atoms (i.e., C₂₋₈ alkenyl), 2 to 6 carbon atoms (i.e., C₂₋₆ alkenyl), or 2 to 4 carbon atoms (i.e., C₂₋₄ alkenyl). Examples of alkenyl groups include, e.g., ethenyl, propenyl, butadienyl (including 1,2-butadienyl and 1,3-butadienyl).

[0028] “Alkynyl” refers to an alkyl group containing at least one (e.g., 1-3, or 1) carbon-carbon triple bond and having from 2 to 20 carbon atoms (i.e., C₂₋₂₀ alkynyl), 2 to 12 carbon atoms (i.e., C₂₋₁₂ alkynyl), 2 to 8 carbon atoms (i.e., C₂₋₈ alkynyl), 2 to 6 carbon atoms (i.e., C₂₋₆ alkynyl), or 2 to 4 carbon atoms (i.e., C₂₋₄ alkynyl). The term “alkynyl” also includes those groups having one triple bond and one double bond.

[0029] “Alkoxy” refers to the group “alkyl-O-”. Examples of alkoxy groups include, e.g., methoxy, ethoxy, n-propoxy, iso-propoxy, n-butoxy, tert-butoxy, sec-butoxy, n-pentoxy, n-hexoxy, and 1,2-dimethylbutoxy.

[0030] “Alkylthio” refers to the group “alkyl-S-”. “Alkylsulfinyl” refers to the group “alkyl-S(O)-”. “Alkylsulfonyl” refers to the group “alkyl-S(O)₂-”. “Alkylsulfonylalkyl” refers to -alkyl-S(O)₂-alkyl.

[0031] “Acyl” refers to a group -C(O)R^y, wherein R^y is hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, heteroalkyl, or heteroaryl; each of which may be unsubstituted or substituted, as defined herein. Examples of acyl include, e.g., formyl, acetyl, cyclohexylcarbonyl, cyclohexylmethylcarbonyl, and benzoyl.

[0032] “Amido” refers to both a “C-amido” group which refers to the group -C(O)NR^yR^z and an “N-amido” group which refers to the group -NR^yC(O)R^z, wherein R^y and R^z are independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, heteroalkyl, or heteroaryl; each of which may be unsubstituted or substituted, as defined herein, or R^y and R^z are taken together to form a cycloalkyl or heterocyclyl; each of which may be unsubstituted or substituted, as defined herein.

[0033] “Amino” refers to the group -NR^yR^z wherein R^y and R^z are independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, heteroalkyl, or heteroaryl; each of which may be unsubstituted or substituted, as defined herein.

[0034] “Amidino” refers to -C(NR^y)(NR^z)₂, wherein R^y and R^z are independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, heteroalkyl, or heteroaryl; each of which may be unsubstituted or substituted, as defined herein.

[0035] “Aryl” refers to an aromatic carbocyclic group having a single ring (e.g., monocyclic) or multiple rings (e.g., bicyclic or tricyclic) including fused systems. As used herein, aryl has 6 to 20 ring carbon atoms (i.e., C₆₋₂₀ aryl), 6 to 12 carbon ring atoms (i.e., C₆₋₁₂ aryl), or 6 to 10 carbon ring atoms (i.e., C₆₋₁₀ aryl). Examples of aryl groups include, e.g., phenyl, naphthyl, fluorenyl, and anthryl. Aryl, however, does not encompass or overlap in any way with heteroaryl defined below. If one or more aryl groups are fused with a heteroaryl, the resulting ring system is heteroaryl regardless of point of attachment. If one or more aryl groups are fused with a heterocyclyl, the resulting ring system is heterocyclyl regardless of point of attachment. If one or more aryl groups are fused with a cycloalkyl, the resulting ring system is cycloalkyl regardless of point of attachment.

[0036] “Carbamoyl” refers to both an “O-carbamoyl” group which refers to the group -O-C(O)NR^yR^z and an “N-carbamoyl” group which refers to the group -NR^yC(O)OR^z, wherein R^y and R^z are independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, heteroalkyl, or heteroaryl; each of which may be unsubstituted or substituted, as defined herein.

[0037] “Carboxyl ester” or “ester” refer to both $-\text{OC}(\text{O})\text{R}^x$ and $-\text{C}(\text{O})\text{OR}^x$, wherein R^x is alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, heteroalkyl, or heteroaryl; each of which may be unsubstituted or substituted, as defined herein.

[0038] “Cycloalkyl” refers to a saturated or partially unsaturated cyclic alkyl group having a single ring or multiple rings including fused, bridged, and spiro ring systems. The term “cycloalkyl” includes cycloalkenyl groups (i.e., the cyclic group having at least one double bond) and carbocyclic fused ring systems having at least one sp^3 carbon atom (i.e., at least one non-aromatic ring). As used herein, cycloalkyl has from 3 to 20 ring carbon atoms (i.e., C_{3-20} cycloalkyl), 3 to 14 ring carbon atoms (i.e., C_{3-14} cycloalkyl), 3 to 12 ring carbon atoms (i.e., C_{3-12} cycloalkyl), 3 to 10 ring carbon atoms (i.e., C_{3-10} cycloalkyl), 3 to 8 ring carbon atoms (i.e., C_{3-8} cycloalkyl), or 3 to 6 ring carbon atoms (i.e., C_{3-6} cycloalkyl). Monocyclic groups include, for example, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, and cyclooctyl. Polycyclic groups include, for example, bicyclo[2.2.1]heptanyl, bicyclo[2.2.2]octanyl, adamantyl, norbornyl, decalanyl, 7,7-dimethyl-bicyclo[2.2.1]heptanyl, and the like. Further, the term cycloalkyl is intended to encompass any non-aromatic ring which may be fused to an aryl ring, regardless of the attachment to the remainder of the molecule. Still further, cycloalkyl also includes “spirocycloalkyl” when there are two positions for substitution on the same carbon atom, for example spiro[2.5]octanyl, spiro[4.5]decanyl, or spiro[5.5]undecanyl.

[0039] “Imino” refers to a group $-\text{C}(\text{NR}^y)\text{R}^z$, wherein R^y and R^z are each independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, heteroalkyl, or heteroaryl; each of which may be unsubstituted or substituted, as defined herein.

[0040] “Imido” refers to a group $-\text{C}(\text{O})\text{NR}^y\text{C}(\text{O})\text{R}^z$, wherein R^y and R^z are each independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, heteroalkyl, or heteroaryl; each of which may be unsubstituted or substituted, as defined herein.

[0041] “Halogen” or “halo” refers to atoms occupying group VIIA of the periodic table, such as fluoro, chloro, bromo, or iodo.

[0042] “Haloalkyl” refers to an unbranched or branched alkyl group as defined above, wherein one or more (e.g., 1 to 6 or 1 to 3) hydrogen atoms are replaced by a halogen. For example, where a residue is substituted with more than one halogen, it may be referred to by using a prefix corresponding to the number of halogen moieties attached. Dihaloalkyl and trihaloalkyl refer to alkyl substituted with two (“di”) or three (“tri”) halo groups, which may be, but are not necessarily, the same halogen. Examples of haloalkyl include, e.g., trifluoromethyl, difluoromethyl, fluoromethyl, trichloromethyl, 2,2,2-trifluoroethyl, 1,2-difluoroethyl, 3-bromo-2-fluoropropyl, 1,2-dibromoethyl, and the like.

[0043] “Haloalkoxy” refers to an alkoxy group as defined above, wherein one or more (e.g., 1 to 6 or 1 to 3) hydrogen atoms are replaced by a halogen.

[0044] “Hydroxyalkyl” refers to an alkyl group as defined above, wherein one or more (e.g., 1 to 6 or 1 to 3) hydrogen atoms are replaced by a hydroxy group.

[0045] “Heteroalkyl” refers to an alkyl group in which one or more of the carbon atoms (and any associated hydrogen atoms), excluding any terminal carbon atom(s), are each independently replaced

with the same or different heteroatomic group, provided the point of attachment to the remainder of the molecule is through a carbon atom. The term “heteroalkyl” includes unbranched or branched saturated chain having carbon and heteroatoms. By way of example, 1, 2 or 3 carbon atoms may be independently replaced with the same or different heteroatomic group. Heteroatomic groups include, but are not limited to, -NR^y-, -O-, -S-, -S(O)-, -S(O)₂-, and the like, wherein R^y is hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, heteroalkyl, or heteroaryl; each of which may be unsubstituted or substituted, as defined herein. Examples of heteroalkyl groups include, e.g., ethers (e.g., -CH₂OCH₃, -CH(CH₃)OCH₃, -CH₂CH₂OCH₃, -CH₂CH₂OCH₂CH₂OCH₃, etc.), thioethers (e.g., -CH₂SCH₃, -CH(CH₃)SCH₃, -CH₂CH₂SCH₃, -CH₂CH₂SCH₂CH₂SCH₃, etc.), sulfones (e.g., -CH₂S(O)₂CH₃, -CH(CH₃)S(O)₂CH₃, -CH₂CH₂S(O)₂CH₃, -CH₂CH₂S(O)₂CH₂CH₂OCH₃, etc.), and amines (e.g., -CH₂NR^yCH₃, -CH(CH₃)NR^yCH₃, -CH₂CH₂NR^yCH₃, -CH₂CH₂NR^yCH₂CH₂NR^yCH₃, etc., where R^y is hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, heteroalkyl, or heteroaryl; each of which may be unsubstituted or substituted, as defined herein). As used herein, heteroalkyl includes 2 to 10 carbon atoms, 2 to 8 carbon atoms, or 2 to 4 carbon atoms; and 1 to 3 heteroatoms, 1 to 2 heteroatoms, or 1 heteroatom.

[0046] “Heteroaryl” refers to an aromatic group having a single ring, multiple rings or multiple fused rings, with one or more ring heteroatoms independently selected from nitrogen, oxygen, and sulfur. As used herein, heteroaryl includes 1 to 20 ring carbon atoms (i.e., C₁₋₂₀ heteroaryl), 3 to 12 ring carbon atoms (i.e., C₃₋₁₂ heteroaryl), or 3 to 8 carbon ring atoms (i.e., C₃₋₈ heteroaryl), and 1 to 5 ring heteroatoms, 1 to 4 ring heteroatoms, 1 to 3 ring heteroatoms, 1 to 2 ring heteroatoms, or 1 ring heteroatom independently selected from nitrogen, oxygen, and sulfur. In certain instances, heteroaryl includes 5-10 membered ring systems, 5-7 membered ring systems, or 5-6 membered ring systems, each independently having 1 to 4 ring heteroatoms, 1 to 3 ring heteroatoms, 1 to 2 ring heteroatoms, or 1 ring heteroatom independently selected from nitrogen, oxygen, and sulfur. Examples of heteroaryl groups include, e.g., acridinyl, benzimidazolyl, benzothiazolyl, benzindolyl, benzofuranyl, benzothiazolyl, benzothiadiazolyl, benzonaphthofuranyl, benzoxazolyl, benzothienyl (benzothiophenyl), benzotriazolyl, benzo[4,6]imidazo[1,2-a]pyridyl, carbazolyl, cinnolyl, dibenzofuranyl, dibenzothiophenyl, furanyl, isothiazolyl, imidazolyl, indazolyl, indolyl, indazolyl, isoindolyl, isoquinolyl, isoxazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, 1-oxidopyridinyl, 1-oxidopyrimidinyl, 1-oxidopyrazinyl, 1-oxidopyridazinyl, phenazinyl, phthalazinyl, pteridinyl, purinyl, pyrrolyl, pyrazolyl, pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, quinazolinyl, quinoxalinyl, quinolyl, quinuclidinyl, isoquinolyl, thiazolyl, thiadiazolyl, thiophenyl (i.e., thienyl), triazolyl, tetrazolyl, and triazinyl. Examples of the fused-heteroaryl rings include, but are not limited to, benzo[d]thiazolyl, quinolyl, isoquinolyl, benzo[b]thiophenyl, indazolyl, benzo[d]imidazolyl, pyrazolo[1,5-a]pyridinyl, and imidazo[1,5-a]pyridinyl, where the heteroaryl can be bound *via* either ring of the fused system. Any aromatic ring, having a single or multiple fused rings, containing at least one heteroatom, is considered a heteroaryl regardless of the attachment to the remainder of the molecule (i.e., through any one of the fused rings). Heteroaryl does not encompass or overlap with aryl as defined above.

[0047] “Heterocyclyl” – used interchangeably with “heterocycloalkyl” – refers to a saturated or partially unsaturated cyclic alkyl group, with one or more ring heteroatoms independently selected from nitrogen, oxygen, and sulfur. The term “heterocyclyl” includes heterocycloalkenyl groups (i.e., the heterocyclyl group having at least one double bond), bridged-heterocyclyl groups, fused-heterocyclyl groups, and spiro-heterocyclyl groups. A heterocyclyl may be a single ring or multiple rings wherein the multiple rings may be fused, bridged, or spiro, and may comprise one or more (e.g., 1 to 3) oxo (=O) or N-oxide (-O-) moieties. Any non-aromatic ring containing at least one heteroatom is considered a heterocyclyl, regardless of the attachment (i.e., can be bound through a carbon atom or a heteroatom). Further, the term heterocyclyl is intended to encompass any non-aromatic ring containing at least one heteroatom, which ring may be fused to a cycloalkyl, an aryl, or heteroaryl ring, regardless of the attachment to the remainder of the molecule. As used herein, heterocyclyl has 2 to 20 ring carbon atoms (i.e., C₂₋₂₀ heterocyclyl), 2 to 12 ring carbon atoms (i.e., C₂₋₁₂ heterocyclyl), 2 to 10 ring carbon atoms (i.e., C₂₋₁₀ heterocyclyl), 2 to 8 ring carbon atoms (i.e., C₂₋₈ heterocyclyl), 3 to 12 ring carbon atoms (i.e., C₃₋₁₂ heterocyclyl), 3 to 8 ring carbon atoms (i.e., C₃₋₈ heterocyclyl), or 3 to 6 ring carbon atoms (i.e., C₃₋₆ heterocyclyl); having 1 to 5 ring heteroatoms, 1 to 4 ring heteroatoms, 1 to 3 ring heteroatoms, 1 to 2 ring heteroatoms, or 1 ring heteroatom independently selected from nitrogen, sulfur, or oxygen. Examples of heterocyclyl groups include, e.g., azetidiny, azepiny, benzodioxoly, benzo[b][1,4]dioxepiny, 1,4-benzodioxany, benzopyrany, benzodioxiny, benzopyranony, benzofuranony, dioxolany, dihydropyrany, hydropyrany, thienyl[1,3]dithianyl, decahydroisoquinolyl, furanony, imidazoliny, imidazolidiny, indoliny, indoliziny, isoindoliny, isothiazolidiny, isoxazolidiny, morpholiny, octahydroindolyl, octahydroisoindolyl, 2-oxopiperaziny, 2-oxopiperidiny, 2-oxopyrrolidiny, oxazolidiny, oxirany, oxetany, phenothiaziny, phenoxaziny, piperidiny, piperaziny, 4-piperidony, pyrrolidiny, pyrazolidiny, quinuclidiny, thiazolidiny, tetrahydrofuryl, tetrahydropyrany, trithianyl, tetrahydroquinoliny, thiomorpholiny, thiamorpholiny, 1-oxo-thiomorpholiny, and 1,1-dioxo-thiomorpholiny. The term “heterocyclyl” also includes “spiroheterocyclyl” when there are two positions for substitution on the same carbon atom. Examples of the spiro-heterocyclyl rings include, e.g., bicyclic and tricyclic ring systems, such as oxabicyclo[2.2.2]octany, 2-oxa-7-azaspiro[3.5]nonany, 2-oxa-6-azaspiro[3.4]octany, and 6-oxa-1-azaspiro[3.3]heptany. Examples of the fused-heterocyclyl rings include, but are not limited to, 1,2,3,4-tetrahydroisoquinoliny, 4,5,6,7-tetrahydrothieno[2,3-c]pyridiny, indoliny, and isoindoliny, where the heterocyclyl can be bound *via* either ring of the fused system. In some embodiments, the heterocycloalkyl may be substituted with oxo group(s) on a heteroatom (e.g., S=O, S(=O)₂).

[0048] “Oxime” refers to the group -CR^y(=NOH) wherein R^y is hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, heteroalkyl, or heteroaryl; each of which may be unsubstituted or substituted, as defined herein.

[0049] “Oxo” refers to the moiety =O.

[0050] “Sulfonyl” refers to the group -S(O)₂R^z, where R^z is hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, heteroalkyl, or heteroaryl; each of which may be unsubstituted or

substituted, as defined herein. Examples of sulfonyl are methylsulfonyl, ethylsulfonyl, phenylsulfonyl, and toluenesulfonyl.

[0051] “Sulfinyl” refers to the group $-S(O)R^y$, where R^y is hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, heteroalkyl, or heteroaryl; each of which may be unsubstituted or substituted, as defined herein. Examples of sulfinyl are methylsulfinyl, ethylsulfinyl, phenylsulfinyl, and toluenesulfinyl.

[0052] “Sulfonamido” refers to the groups $-SO_2NR^yR^z$ and $-NR^ySO_2R^z$, where R^y and R^z are each independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, heteroalkyl, or heteroaryl; each of which may be unsubstituted or substituted, as defined herein.

[0053] The terms “optional” or “optionally” means that the subsequently described event or circumstance may or may not occur and that the description includes instances where said event or circumstance occurs and instances in which it does not. Also, the term “unsubstituted or substituted” refers to any one or more (e.g., 1 to 5 or 1 to 3) hydrogen atoms on the designated atom or group may or may not be replaced by a moiety other than hydrogen.

[0054] The term “substituted” used herein means any of the above groups (i.e., alkyl, alkenyl, alkynyl, alkylene, alkoxy, haloalkyl, haloalkoxy, cycloalkyl, aryl, heterocyclyl, heteroaryl, and/or heteroalkyl) wherein at least one (e.g., 1 to 5 or 1 to 3) hydrogen atom is replaced by a bond to a non-hydrogen atom such as, but not limited to alkyl, alkenyl, alkynyl, alkoxy, alkylthio, acyl, amido, amino, amidino, aryl, aralkyl, azido, carbamoyl, carboxyl, carboxyl ester, cyano, cycloalkyl, cycloalkylalkyl, guanadino, halo, haloalkyl, haloalkoxy, hydroxyalkyl, heteroalkyl, heteroaryl, heteroarylalkyl, heterocyclyl, heterocyclylalkyl, $-NHNH_2$, $=NNH_2$, imino, imido, hydroxy, oxo, oxime, nitro, sulfonyl, sulfinyl, alkylsulfonyl, alkylsulfinyl, thiocyanate, $-S(O)OH$, $-S(O)_2OH$, sulfonamido, thiol, thioxo, N-oxide, or $-Si(R^y)_3$, wherein each R^y is independently hydrogen, alkyl, alkenyl, alkynyl, heteroalkyl, cycloalkyl, aryl, heteroaryl, or heterocyclyl.

[0055] In certain embodiments, “substituted” includes any of the above alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl groups in which one or more (e.g., 1 to 5 or 1 to 3) hydrogen atoms are independently replaced with deuterium, halo, cyano, nitro, azido, oxo, alkyl, alkenyl, alkynyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, $-NR^gR^h$, $-NR^gC(O)R^h$, $-NR^gC(O)NR^gR^h$, $-NR^gC(O)OR^h$, $-NR^gS(O)_{1-2}R^h$, $-C(O)R^g$, $-C(O)OR^g$, $-OC(O)OR^g$, $-OC(O)R^g$, $-C(O)NR^gR^h$, $-OC(O)NR^gR^h$, $-OR^g$, $-SR^g$, $-S(O)R^g$, $-S(O)_2R^g$, $-OS(O)_{1-2}R^g$, $-S(O)_{1-2}OR^g$, $-NR^gS(O)_{1-2}NR^gR^h$, $=NSO_2R^g$, $=NOR^g$, $-S(O)_{1-2}NR^gR^h$, $-SF_5$, $-SCF_3$, or $-OCF_3$. In certain embodiments, “substituted” also means any of the above groups in which one or more (e.g., 1 to 5 or 1 to 3) hydrogen atoms are replaced with $-C(O)R^g$, $-C(O)OR^g$, $-C(O)NR^gR^h$, $-CH_2SO_2R^g$, or $-CH_2SO_2NR^gR^h$. In the foregoing, R^g and R^h are the same or different and independently hydrogen, alkyl, alkenyl, alkynyl, alkoxy, thioalkyl, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, haloalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, and/or heteroarylalkyl. In certain embodiments, “substituted” also means any of the above groups in which one or more (e.g., 1 to 5 or 1 to 3) hydrogen atoms are replaced by a bond to an amino, cyano, hydroxy, imino, nitro, oxo, thioxo, halo, alkyl, alkoxy, alkylamino, thioalkyl, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, haloalkyl, heterocyclyl,

N-heterocyclyl, heterocyclylalkyl, heteroaryl, and/or heteroarylalkyl, or two of R^g and R^h are taken together with the atoms to which they are attached to form a heterocyclyl ring unsubstituted or substituted with oxo, halo, or alkyl unsubstituted or substituted with oxo, halo, amino, hydroxy, or alkoxy.

[0056] Polymers or similar indefinite structures arrived at by defining substituents with further substituents appended ad infinitum (e.g., a substituted aryl having a substituted alkyl which is itself substituted with a substituted aryl group, which is further substituted by a substituted heteroalkyl group, etc.) are not intended for inclusion herein. Unless otherwise noted, the maximum number of serial substitutions in compounds described herein is three. For example, serial substitutions of substituted aryl groups with two other substituted aryl groups are limited to ((substituted aryl)substituted aryl) substituted aryl. Similarly, the above definitions are not intended to include impermissible substitution patterns (e.g., methyl substituted with 5 fluorines or heteroaryl groups having two adjacent oxygen ring atoms). Such impermissible substitution patterns are well known to the skilled artisan. When used to modify a chemical group, the term “substituted” may describe other chemical groups defined herein.

[0057] In certain embodiments, as used herein, the phrase “one or more” refers to one to five. In certain embodiments, as used herein, the phrase “one or more” refers to one to three.

[0058] Any compound or structure given herein, is also intended to represent unlabeled forms as well as isotopically labeled forms of the compounds. These forms of compounds may also be referred to as “isotopically enriched analogs.” Isotopically labeled compounds have structures depicted herein, except that one or more atoms are replaced by an atom having a selected atomic mass or mass number. Examples of isotopes that can be incorporated into the disclosed compounds include isotopes of hydrogen, carbon, nitrogen, oxygen, phosphorous, fluorine, chlorine, and iodine, such as ²H, ³H, ¹¹C, ¹³C, ¹⁴C, ¹⁵N, ¹⁵N, ¹⁵O, ¹⁷O, ¹⁸O, ³¹P, ³²P, ³⁵S, ¹⁸F, ³⁶Cl, ¹²³I, and ¹²⁵I, respectively. Various isotopically labeled compounds of the present disclosure, for example those into which radioactive isotopes such as ³H and ¹⁴C are incorporated. Such isotopically labelled compounds may be useful in metabolic studies, reaction kinetic studies, detection or imaging techniques, such as positron emission tomography (PET) or single-photon emission computed tomography (SPECT) including drug or substrate tissue distribution assays or in radioactive treatment of patients.

[0059] The term “isotopically enriched analogs” includes “deuterated analogs” of compounds described herein in which one or more hydrogens is/are replaced by deuterium, such as a hydrogen on a carbon atom. Such compounds exhibit increased resistance to metabolism and are thus useful for increasing the half-life of any compound when administered to a mammal, particularly a human. See, for example, Foster, “Deuterium Isotope Effects in Studies of Drug Metabolism,” Trends Pharmacol. Sci. 5(12): 524-527 (1984). Such compounds are synthesized by means well known in the art, for example by employing starting materials in which one or more hydrogens have been replaced by deuterium.

[0060] Accordingly, in some embodiments, the terms C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, and heteroaryl comprise isotopically enriched analogs thereof, such as, but not limited to, deuterated versions thereof.

[0061] Deuterium labelled or substituted therapeutic compounds of the disclosure may have improved DMPK (drug metabolism and pharmacokinetics) properties, relating to absorption, distribution, metabolism, and excretion (ADME). Substitution with heavier isotopes such as deuterium may afford certain therapeutic advantages resulting from greater metabolic stability, for example increased *in vivo* half-life, reduced dosage requirements, and/or an improvement in therapeutic index. An ^{18}F , ^3H , or ^{11}C labeled compound may be useful for PET or SPECT or other imaging studies. Isotopically labeled compounds of this disclosure and prodrugs thereof can generally be prepared by carrying out the procedures disclosed in the schemes or in the examples and preparations described below by substituting a readily available isotopically labeled reagent for a non-isotopically labeled reagent. It is understood that deuterium in this context is regarded as a substituent in a compound described herein.

[0062] The concentration of such a heavier isotope, specifically deuterium, may be defined by an isotopic enrichment factor. In the compounds of this disclosure any atom not specifically designated as a particular isotope is meant to represent any stable isotope of that atom. Unless otherwise stated, when a position is designated specifically as “H” or “hydrogen,” the position is understood to have hydrogen at its natural abundance isotopic composition. Accordingly, in the compounds of this disclosure any atom specifically designated as a deuterium (D) is meant to represent deuterium.

[0063] In many cases, the compounds of this disclosure are capable of forming acid and/or base salts by virtue of the presence of amino, and/or carboxyl groups, or groups similar thereto.

[0064] Provided are also or a pharmaceutically acceptable salt, isotopically enriched analog, deuterated analog, stereoisomer, mixture of stereoisomers, and prodrugs of the compounds described herein. “Pharmaceutically acceptable” or “physiologically acceptable” refer to compounds, salts, compositions, dosage forms, and other materials which are useful in preparing a pharmaceutical composition that is suitable for veterinary or human pharmaceutical use.

[0065] The term “pharmaceutically acceptable salt” of a given compound refers to salts that retain the biological effectiveness and properties of the given compound and which are not biologically or otherwise undesirable. “Pharmaceutically acceptable salts” or “physiologically acceptable salts” include, for example, salts with inorganic acids, and salts with an organic acid. In addition, if the compounds described herein are obtained as an acid addition salt, the free base can be obtained by basifying a solution of the acid salt. Conversely, if the product is a free base, an addition salt, particularly a pharmaceutically acceptable addition salt, may be produced by dissolving the free base in a suitable organic solvent and treating the solution with an acid, in accordance with conventional procedures for preparing acid addition salts from base compounds. Those skilled in the art will recognize various synthetic methodologies that may be used to prepare nontoxic pharmaceutically acceptable addition salts. Pharmaceutically acceptable acid addition salts may be prepared from inorganic or organic acids. Salts derived from inorganic acids include, e.g., hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid, and the like. Salts derived from organic acids include, e.g., acetic acid, propionic acid, gluconic acid, glycolic acid, pyruvic acid, oxalic acid, malic acid, malonic acid, succinic acid, maleic acid, fumaric acid, tartaric acid, citric acid, benzoic acid, cinnamic acid, mandelic acid, methanesulfonic

acid, ethanesulfonic acid, p-toluene-sulfonic acid, salicylic acid, and the like. Likewise, pharmaceutically acceptable base addition salts can be prepared from inorganic or organic bases. Salts derived from inorganic bases include, by way of example only, sodium, potassium, lithium, aluminum, ammonium, calcium, and magnesium salts. Salts derived from organic bases include, but are not limited to, salts of primary, secondary, and tertiary amines, such as alkyl amines (i.e., $\text{NH}_2(\text{alkyl})$), dialkyl amines (i.e., $\text{HN}(\text{alkyl})_2$), trialkyl amines (i.e., $\text{N}(\text{alkyl})_3$), substituted alkyl amines (i.e., $\text{NH}_2(\text{substituted alkyl})$), di(substituted alkyl) amines (i.e., $\text{HN}(\text{substituted alkyl})_2$), tri(substituted alkyl) amines (i.e., $\text{N}(\text{substituted alkyl})_3$), alkenyl amines (i.e., $\text{NH}_2(\text{alkenyl})$), dialkenyl amines (i.e., $\text{HN}(\text{alkenyl})_2$), trialkenyl amines (i.e., $\text{N}(\text{alkenyl})_3$), substituted alkenyl amines (i.e., $\text{NH}_2(\text{substituted alkenyl})$), di(substituted alkenyl) amines (i.e., $\text{HN}(\text{substituted alkenyl})_2$), tri(substituted alkenyl) amines (i.e., $\text{N}(\text{substituted alkenyl})_3$), mono-, di- or tri- cycloalkyl amines (i.e., $\text{NH}_2(\text{cycloalkyl})$, $\text{HN}(\text{cycloalkyl})_2$, $\text{N}(\text{cycloalkyl})_3$), mono-, di- or tri- arylamines (i.e., $\text{NH}_2(\text{aryl})$, $\text{HN}(\text{aryl})_2$, $\text{N}(\text{aryl})_3$), or mixed amines, etc. Specific examples of suitable amines include, by way of example only, isopropylamine, trimethyl amine, diethyl amine, tri(iso-propyl) amine, tri(n-propyl) amine, ethanolamine, 2-dimethylaminoethanol, piperazine, piperidine, morpholine, N-ethylpiperidine, and the like.

[0066] A “solvate” is formed by the interaction of a solvent and a compound. Solvates of salts of the compounds described herein are also provided. A hydrate is an example of a solvate, where the solvent is water.

[0067] Some of the compounds exist as tautomers. Tautomers are in equilibrium with one another. For example, amide containing compounds may exist in equilibrium with imidic acid tautomers. Regardless of which tautomer is shown and regardless of the nature of the equilibrium among tautomers, the compounds are understood by one of ordinary skill in the art to comprise both amide and imidic acid tautomers. Thus, the amide containing compounds are understood to include their imidic acid tautomers. Likewise, the imidic acid containing compounds are understood to include their amide tautomers.

[0068] The compounds, or their pharmaceutically acceptable salts include an asymmetric center 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 disclosure 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/or 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.

[0069] 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 disclosure

contemplates various stereoisomers, or mixtures thereof, and includes “enantiomers,” which refers to two stereoisomers whose molecules are nonsuperimposable mirror images of one another.

[0070] “Diastereomers” are stereoisomers that have at least two asymmetric atoms, but which are not mirror-images of each other.

[0071] Relative centers of the compounds as depicted herein are indicated graphically using the “thick bond” style (bold or parallel lines) and absolute stereochemistry is depicted using wedge bonds (bold or parallel lines).

[0072] “Prodrug” means any compound which releases an active parent drug according to a structure described herein *in vivo* when such prodrug is administered to a mammalian subject. Prodrugs of a compound described herein are prepared by modifying functional groups present in the compound described herein in such a way that the modifications may be cleaved *in vivo* to release the parent compound. Prodrugs may be prepared by modifying functional groups present in the compounds in such a way that the modifications are cleaved, either in routine manipulation or *in vivo*, to the parent compounds. Prodrugs include compounds described herein wherein a hydroxy, amino, carboxyl, or sulfhydryl group in a compound described herein is bonded to any group that may be cleaved *in vivo* to regenerate the free hydroxy, amino, or sulfhydryl group, respectively. Examples of prodrugs include, but are not limited to esters (e.g., acetate, formate, and benzoate derivatives), amides, guanidines, carbamates (e.g., N,N-dimethylaminocarbonyl) of hydroxy functional groups in compounds described herein, and the like. Preparation, selection, and use of prodrugs is discussed in T. Higuchi and V. Stella, “Pro-drugs as Novel Delivery Systems,” Vol. 14 of the A.C.S. Symposium Series; “Design of Prodrugs,” ed. H. Bundgaard, Elsevier, 1985; and in Bioreversible Carriers in Drug Design, ed. Edward B. Roche, American Pharmaceutical Association and Pergamon Press, 1987, each of which are hereby incorporated by reference in their entirety.

[0073] “Subject” refers to a mammal. The mammal can be a human or non-human mammalian organism. A “patient” refers to a human subject.

[0074] “Treating” or “treatment” of a disease or disorder in a subject refers to 1) preventing the disease or disorder from occurring in a subject that is predisposed or does not yet display symptoms of the disease or disorder; 2) inhibiting the disease or disorder or arresting its development; or 3) ameliorating or causing regression of the disease or disorder.

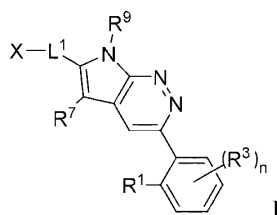
[0075] “Effective amount” refers to the amount of a compound described herein that is sufficient to treat the disease or disorder afflicting a subject or to prevent such a disease or disorder from arising in said subject or patient.

[0076] “Administration” refers to any art recognized form of administration to a subject including oral (including oral gavage), pulmonary, transdermal, sublingual, injection (e.g., intravenous, intramuscular), transmucosal (e.g., vaginal, nasal, etc.), and the like. The route of administration is selected by the attending clinician and is based on factors such as the age, weight and general health of the patient as well as the severity of the condition. In one embodiment, the compounds and pharmaceutical compositions described herein are administered orally.

[0077] The term “ubiquitin ligase” refers to a family of proteins that facilitate the transfer of ubiquitin to a specific substrate protein, targeting the substrate protein for degradation. For example, an E3 ubiquitin ligase protein that alone or in combination with an E2 ubiquitin-conjugating enzyme causes the attachment of ubiquitin to a lysine on a target protein, and subsequently targets the specific protein substrates for degradation by the proteasome. Thus, E3 ubiquitin ligase alone or in complex with an E2 ubiquitin conjugating enzyme is responsible for the transfer of ubiquitin to targeted proteins. In general, the ubiquitin ligase is involved in polyubiquitination such that a second ubiquitin is attached to the first; a third is attached to the second, and so forth. Polyubiquitination marks proteins for degradation by the proteasome. However, there are some ubiquitination events that are limited to mono-ubiquitination, in which only a single ubiquitin is added by the ubiquitin ligase to a substrate molecule. Mono-ubiquitinated proteins are not targeted to the proteasome for degradation, but may instead be altered in their cellular location or function, for example, via binding other proteins that have domains capable of binding ubiquitin. Further complicating matters, different lysines on ubiquitin can be targeted by an E3 to make chains. The most common lysine is Lys48 on the ubiquitin chain. This is the lysine used to make polyubiquitin, which is recognized by the proteasome.

Compounds

[0078] In one embodiment, this disclosure provides a compound of Formula I:



or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein:

n is 0, 1, or 2;

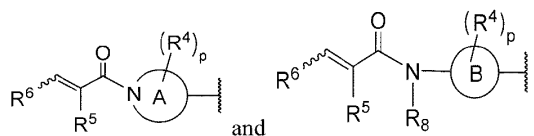
R¹ is OR¹², halo, cyano, C₁₋₄ alkoxy, N(R²)₂, or C(O)CH(C₁₋₄ alkyl)N(R²)₂;

each R² is independently hydrogen, C₁₋₄ alkyl, or C₃₋₆ cycloalkyl, wherein each alkyl or cycloalkyl is unsubstituted or substituted with one to three Z¹;

each R³ is independently halo, cyano, C₁₋₆ alkyl, or C₁₋₃ haloalkyl;

L¹ is a bond, C₁₋₄ alkylene, -C₁₋₄ alkylene-heteroaryl-, C₂₋₃ alkenylene, C₂₋₃ alkynylene, or -C(O)-;

X is selected from:



p is 0, 1, or 2;

Ring A is a monocyclic, spirocyclic, fused bicyclic, or bridged bicyclic 4-10 membered heterocyclyl or a monocyclic or fused bicyclic 5-10 membered heteroaryl;

Ring B is a monocyclic, spirocyclic, fused bicyclic, or bridged bicyclic 3-10 membered cycloalkyl, a monocyclic, spirocyclic, fused bicyclic, or bridged bicyclic 4-10 membered heterocyclyl, or a monocyclic or fused bicyclic 5-10 membered heteroaryl; wherein the nitrogen atom and L¹ may be attached via any atom on Ring B, including on the same carbon atom;

each R⁴ is independently oxo, halo, cyano, -NO₂, -SF₅, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, -C(O)R¹¹, -C(O)OR¹¹, -S(O)₀₋₂R¹¹, -NR¹¹S(O)₀₋₂R¹¹, -S(O)₀₋₂N(R¹¹)₂, -NR¹¹S(O)₀₋₂N(R¹¹)₂, -NR¹¹C(O)N(R¹¹)₂, -C(O)N(R¹¹)₂, -NR¹¹C(O)R¹¹, -OC(O)N(R¹¹)₂, or -NR¹¹C(O)OR¹¹; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z¹;

R⁵ is hydrogen, halo, cyano, or C₁₋₆ alkyl optionally substituted with one to three Z¹;

R⁶ is hydrogen, halo, cyano, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, -C(O)R¹¹, -C(O)OR¹¹, -S(O)₀₋₂R¹¹, -NR¹¹S(O)₀₋₂R¹¹, -S(O)₀₋₂N(R¹¹)₂, -NR¹¹S(O)₀₋₂N(R¹¹)₂, -NR¹¹C(O)N(R¹¹)₂, -C(O)N(R¹¹)₂, -NR¹¹C(O)R¹¹, -OC(O)N(R¹¹)₂, or -NR¹¹C(O)OR¹¹; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z¹;

R⁷ is hydrogen, halo, cyano, -NO₂, -SF₅, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, -C(O)R¹¹, -C(O)OR¹¹, -S(O)₀₋₂R¹¹, -NR¹¹S(O)₀₋₂R¹¹, -S(O)₀₋₂N(R¹¹)₂, -NR¹¹S(O)₀₋₂N(R¹¹)₂, -NR¹¹C(O)N(R¹¹)₂, -C(O)N(R¹¹)₂, -NR¹¹C(O)R¹¹, -OC(O)N(R¹¹)₂, or -NR¹¹C(O)OR¹¹; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z¹;

R⁸ is hydrogen or C₁₋₆ alkyl optionally substituted with one to three Z¹;

R⁹ is hydrogen, -C(O)R¹³, -C(R¹³)₂OC(O)R¹⁵, -C(O)OCH₂OC(O)R¹⁵, -C(O)OCH(CH₃)OC(O)R¹⁵, -C(O)OCH₂OC(O)R¹⁵, -C(O)OCH(CH₃)OC(O)R¹⁵, -(CH₂)_mOP(O)(OR¹⁴)₂, -CH(CH₃)OP(O)(OR¹⁴)₂, -(CH₂)_mOP(O)(R¹⁴)(OR¹⁴), -CH(CH₃)OP(O)(R¹⁴)(OR¹⁴), -(CH₂)_mOP(O)(N(R¹⁴)₂)(OR¹⁴), -CH(CH₃)OP(O)(N(R¹⁴)₂)(OR¹⁴), -(CH₂)_mOP(O)(R¹⁴)(N(R¹⁴)₂), -(CH₂)_mOP(O)(N(R¹⁴)₂), or -C(CH₃)OP(O)(N(R¹⁴)₂)₂;

m is 1 or 2;

each Z¹ is independently halo, cyano, -NO₂, -SF₅, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, -P(O)(OR¹¹)₂, -C(O)R¹¹, -C(O)OR¹¹, -S(O)₀₋₂R¹¹, -NR¹¹S(O)₀₋₂R¹¹, -S(O)₀₋₂N(R¹¹)₂, -NR¹¹S(O)₀₋₂N(R¹¹)₂, -NR¹¹C(O)N(R¹¹)₂, -C(O)N(R¹¹)₂, -NR¹¹C(O)R¹¹, -OC(O)N(R¹¹)₂, or -NR¹¹C(O)OR¹¹; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1a};

each R¹¹ is independently hydrogen, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl,

C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1a};

each Z^{1a} is independently hydroxy, halo, cyano, -NO₂, -SF₅, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹³)₂, -OR¹³, -P(O)(OR¹³)₂, -C(O)R¹³, -C(O)OR¹³, -S(O)₀₋₂R¹³, -NR¹³S(O)₀₋₂R¹³, -S(O)₀₋₂N(R¹³)₂, -NR¹³S(O)₀₋₂N(R¹³)₂, -NR¹³C(O)N(R¹³)₂, -C(O)N(R¹³)₂, -NR¹³C(O)R¹³, -OC(O)N(R¹³)₂, or -NR¹³C(O)OR¹³; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1b};

R¹² is hydrogen, -C(O)R¹³, -C(O)N(R¹⁴)₂, -P(O)(OR¹⁴)₂, -CH₂OP(O)(OR¹⁴)₂, -CH(CH₃)OP(O)(OR¹⁴)₂, -P(O)(R¹⁴)(OR¹⁴)₂, -CH₂OP(O)(R¹⁴)(OR¹⁴)₂, -CH(CH₃)OP(O)(R¹⁴)(OR¹⁴)₂, -P(O)(N(R¹⁴)₂)(OR¹⁴)₂, -CH₂OP(O)(N(R¹⁴)₂)(OR¹⁴)₂, -CH(CH₃)OP(O)(N(R¹⁴)₂)(OR¹⁴)₂, -P(O)(R¹⁴)(N(R¹⁴)₂)₂, -CH₂OP(O)(R¹⁴)(N(R¹⁴)₂)₂, -CH(CH₃)OP(O)(R¹⁴)(N(R¹⁴)₂)₂, -P(O)(N(R¹⁴)₂)₂, -CH₂OP(O)(N(R¹⁴)₂)₂, or -CH(CH₃)OP(O)(N(R¹⁴)₂)₂;

each R¹³ is independently hydrogen, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1b};

each R¹⁴ is independently hydrogen, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, aryl, heteroaryl, or heterocyclyl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, or heterocyclyl is independently optionally substituted with one to five Z^{1b}; or two R¹⁴ together with the atom to which they are attached form a heterocyclyl; wherein said heterocyclyl is independently optionally substituted one to five Z^{1b};

R¹⁵ is independently R¹⁶, -OR¹⁶, -SR¹⁶, or -N(R¹⁶)₂;

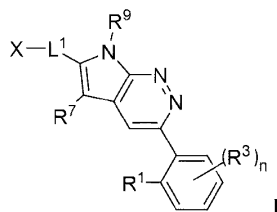
each R¹⁶ is independently hydrogen, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, aryl, heteroaryl, or heterocyclyl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, or heterocyclyl is independently optionally substituted with one to five Z^{1b};

each Z^{1b} is independently halo, cyano, hydroxy, -SH, -NH₂, -NO₂, -SF₅, -P(O)(OH)₂, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -L-C₁₋₆ alkyl, -L-C₂₋₆ alkenyl, -L-C₂₋₆ alkynyl, -L-C₁₋₆ haloalkyl, -L-C₃₋₁₀ cycloalkyl, -L-heterocyclyl, -L-aryl, or -L-heteroaryl; and

each L is independently -O-, -NH-, -S-, -S(O)-, -S(O)₂-, -N(C₁₋₆ alkyl)-, -N(C₂₋₆ alkenyl)-, -N(C₂₋₆ alkynyl)-, -N(C₁₋₆ haloalkyl)-, -N(C₃₋₁₀ cycloalkyl)-, -N(heterocyclyl)-, -N(aryl)-, -N(heteroaryl)-, -C(O)-, -C(O)O-, -C(O)NH-, -C(O)N(C₁₋₆ alkyl)-, -C(O)N(C₂₋₆ alkenyl)-, -C(O)N(C₂₋₆ alkynyl)-, -C(O)N(C₁₋₆ haloalkyl)-, -C(O)N(C₃₋₁₀ cycloalkyl)-, -C(O)N(heterocyclyl)-, -C(O)N(aryl)-, -C(O)N(heteroaryl)-, -NHC(O)-, -NHC(O)O-, -NHC(O)NH-, -NHS(O)-, -S(O)₂NH-, -P(O)(OH)O-, -P(O)(O-C₁₋₆ alkyl)O-, -P(O)(O-C₂₋₆ alkenyl)O-, -P(O)(O-C₂₋₆ alkynyl)O-, -P(O)(OC₁₋₆ haloalkyl)O-, -P(O)(OC₃₋₁₀ cycloalkyl)O-, -P(O)(O-heterocyclyl)O-, -P(O)(O-aryl)O-, or -P(O)(O-heteroaryl)O-;

wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, and heteroaryl of Z^{1b} and L is further independently optionally substituted with one to five hydroxy, halo, cyano, hydroxy, -SH, -NH₂, -NO₂, -SF₅, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkoxy, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl.

[0079] In one embodiment, this disclosure provides a compound of Formula I:



or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein:

n is 0, 1, or 2;

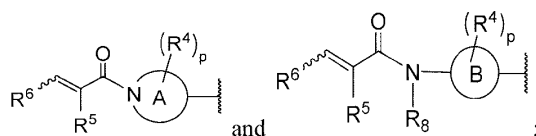
R¹ is -OR¹², halo, cyano, C₁₋₄ alkoxy, or -N(R²)₂;

each R² is independently hydrogen, C₁₋₄ alkyl, or C₃₋₆ cycloalkyl, wherein each alkyl or cycloalkyl is unsubstituted or substituted with one to three Z¹;

each R³ is independently halo, cyano, C₁₋₆ alkyl, or C₁₋₃ haloalkyl;

L¹ is a bond, C₁₋₄ alkylene, -C₁₋₄ alkylene-heteroaryl-, C₂₋₃ alkenylene, C₂₋₃ alkynylene, or -C(O)-;

X is selected from:



p is 0, 1, or 2;

Ring A is a monocyclic, spirocyclic, fused bicyclic, or bridged bicyclic 4-10 membered heterocyclyl or a monocyclic or fused bicyclic 5-10 membered heteroaryl;

Ring B is a monocyclic, spirocyclic, fused bicyclic, or bridged bicyclic 3-10 membered cycloalkyl, a monocyclic, spirocyclic, fused bicyclic, or bridged bicyclic 4-10 membered heterocyclyl, or a monocyclic or fused bicyclic 5-10 membered heteroaryl; wherein the nitrogen atom and L¹ may be attached via any atom on Ring B, including on the same carbon atom;

each R⁴ is independently oxo, halo, cyano, -NO₂, -SF₅, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, -C(O)R¹¹, -C(O)OR¹¹, -S(O)₀₋₂R¹¹, -NR¹¹S(O)₀₋₂R¹¹, -S(O)₀₋₂N(R¹¹)₂, -NR¹¹S(O)₀₋₂N(R¹¹)₂, -NR¹¹C(O)N(R¹¹)₂, -C(O)N(R¹¹)₂, -NR¹¹C(O)R¹¹, -OC(O)N(R¹¹)₂, or -NR¹¹C(O)OR¹¹; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z¹;

R⁵ is hydrogen, halo, cyano, or C₁₋₆ alkyl optionally substituted with one to three Z¹;

R⁶ is hydrogen, halo, cyano, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, -C(O)R¹¹, -C(O)OR¹¹, -S(O)₀₋₂R¹¹, -NR¹¹S(O)₀₋₂R¹¹, -S(O)₀₋₂N(R¹¹)₂,

$-\text{NR}^{11}\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{C}(\text{O})\text{N}(\text{R}^{11})_2$, $-\text{C}(\text{O})\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{C}(\text{O})\text{R}^{11}$, $-\text{OC}(\text{O})\text{N}(\text{R}^{11})_2$, or $-\text{NR}^{11}\text{C}(\text{O})\text{OR}^{11}$; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z^1 ;

R^7 is hydrogen, halo, cyano, $-\text{NO}_2$, $-\text{SF}_5$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, heteroaryl, $-\text{N}(\text{R}^{11})_2$, $-\text{OR}^{11}$, $-\text{C}(\text{O})\text{R}^{11}$, $-\text{C}(\text{O})\text{OR}^{11}$, $-\text{S}(\text{O})_{0-2}\text{R}^{11}$, $-\text{NR}^{11}\text{S}(\text{O})_{0-2}\text{R}^{11}$, $-\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{C}(\text{O})\text{N}(\text{R}^{11})_2$, $-\text{C}(\text{O})\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{C}(\text{O})\text{R}^{11}$, $-\text{OC}(\text{O})\text{N}(\text{R}^{11})_2$, or $-\text{NR}^{11}\text{C}(\text{O})\text{OR}^{11}$; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z^1 ;

R^8 is hydrogen or C_{1-6} alkyl optionally substituted with one to three Z^1 ;

R^9 is hydrogen, $-\text{C}(\text{O})\text{R}^{13}$, $-\text{C}(\text{R}^{13})_2\text{OC}(\text{O})\text{R}^{15}$, $-\text{C}(\text{O})\text{OCH}_2\text{OC}(\text{O})\text{R}^{15}$, $-\text{C}(\text{O})\text{OCH}(\text{CH}_3)\text{OC}(\text{O})\text{R}^{15}$, $-(\text{CH}_2)_m\text{OP}(\text{O})(\text{OR}^{14})_2$, $-\text{CH}(\text{CH}_3)\text{OP}(\text{O})(\text{OR}^{14})_2$, $-(\text{CH}_2)_m\text{OP}(\text{O})(\text{R}^{14})(\text{OR}^{14})$, $-\text{CH}(\text{CH}_3)\text{OP}(\text{O})(\text{R}^{14})(\text{OR}^{14})$, $-(\text{CH}_2)_m\text{OP}(\text{O})(\text{N}(\text{R}^{14})_2)(\text{OR}^{14})$, $-\text{CH}(\text{CH}_3)\text{OP}(\text{O})(\text{N}(\text{R}^{14})_2)(\text{OR}^{14})$, $-(\text{CH}_2)_m\text{OP}(\text{O})(\text{R}^{14})(\text{N}(\text{R}^{14})_2)$, $-(\text{CH}_2)_m\text{OP}(\text{O})(\text{N}(\text{R}^{14})_2)_2$, or $-\text{C}(\text{CH}_3)\text{OP}(\text{O})(\text{N}(\text{R}^{14})_2)_2$;

m is 1 or 2;

each Z^1 is independently halo, cyano, $-\text{NO}_2$, $-\text{SF}_5$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, heteroaryl, $-\text{N}(\text{R}^{11})_2$, $-\text{OR}^{11}$, $-\text{P}(\text{O})(\text{OR}^{11})_2$, $-\text{C}(\text{O})\text{R}^{11}$, $-\text{C}(\text{O})\text{OR}^{11}$, $-\text{S}(\text{O})_{0-2}\text{R}^{11}$, $-\text{NR}^{11}\text{S}(\text{O})_{0-2}\text{R}^{11}$, $-\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{C}(\text{O})\text{N}(\text{R}^{11})_2$, $-\text{C}(\text{O})\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{C}(\text{O})\text{R}^{11}$, $-\text{OC}(\text{O})\text{N}(\text{R}^{11})_2$, or $-\text{NR}^{11}\text{C}(\text{O})\text{OR}^{11}$; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1a} ;

each R^{11} is independently hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1a} ;

each Z^{1a} is independently hydroxy, halo, cyano, $-\text{NO}_2$, $-\text{SF}_5$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, heteroaryl, $-\text{N}(\text{R}^{13})_2$, $-\text{OR}^{13}$, $-\text{P}(\text{O})(\text{OR}^{13})_2$, $-\text{C}(\text{O})\text{R}^{13}$, $-\text{C}(\text{O})\text{OR}^{13}$, $-\text{S}(\text{O})_{0-2}\text{R}^{13}$, $-\text{NR}^{13}\text{S}(\text{O})_{0-2}\text{R}^{13}$, $-\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{13})_2$, $-\text{NR}^{13}\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{13})_2$, $-\text{NR}^{13}\text{C}(\text{O})\text{N}(\text{R}^{13})_2$, $-\text{C}(\text{O})\text{N}(\text{R}^{13})_2$, $-\text{NR}^{13}\text{C}(\text{O})\text{R}^{13}$, $-\text{OC}(\text{O})\text{N}(\text{R}^{13})_2$, or $-\text{NR}^{13}\text{C}(\text{O})\text{OR}^{13}$; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1b} ;

R^{12} is hydrogen, $-\text{C}(\text{O})\text{R}^{13}$, $-\text{C}(\text{O})\text{N}(\text{R}^{14})_2$, $-\text{P}(\text{O})(\text{OR}^{14})_2$, $-\text{CH}_2\text{OP}(\text{O})(\text{OR}^{14})_2$, $-\text{CH}(\text{CH}_3)\text{OP}(\text{O})(\text{OR}^{14})_2$, $-\text{P}(\text{O})(\text{R}^{14})(\text{OR}^{14})$, $-\text{CH}_2\text{OP}(\text{O})(\text{R}^{14})(\text{OR}^{14})$, $-\text{CH}(\text{CH}_3)\text{OP}(\text{O})(\text{R}^{14})(\text{OR}^{14})$, $-\text{P}(\text{O})(\text{N}(\text{R}^{14})_2)(\text{OR}^{14})$, $-\text{CH}_2\text{OP}(\text{O})(\text{N}(\text{R}^{14})_2)(\text{OR}^{14})$, $-\text{CH}(\text{CH}_3)\text{OP}(\text{O})(\text{N}(\text{R}^{14})_2)(\text{OR}^{14})$, $-\text{P}(\text{O})(\text{R}^{14})(\text{N}(\text{R}^{14})_2)$, $-\text{CH}_2\text{OP}(\text{O})(\text{R}^{14})(\text{N}(\text{R}^{14})_2)$, $-\text{CH}(\text{CH}_3)\text{OP}(\text{O})(\text{R}^{14})(\text{N}(\text{R}^{14})_2)$, $-\text{P}(\text{O})(\text{N}(\text{R}^{14})_2)_2$, $-\text{CH}_2\text{OP}(\text{O})(\text{N}(\text{R}^{14})_2)_2$, or $-\text{CH}(\text{CH}_3)\text{OP}(\text{O})(\text{N}(\text{R}^{14})_2)_2$;

each R^{13} is independently hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl,

C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1b};

each R¹⁴ is independently hydrogen, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, aryl, heteroaryl, or heterocyclyl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, or heterocyclyl is independently optionally substituted with one to five Z^{1b}; or two R¹⁴ together with the atom to which they are attached form a heterocyclyl; wherein said heterocyclyl is independently optionally substituted one to five Z^{1b};

R¹⁵ is independently R¹⁶, -OR¹⁶, -SR¹⁶, or -N(R¹⁶)₂;

each R¹⁶ is independently hydrogen, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, aryl, heteroaryl, or heterocyclyl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, or heterocyclyl is independently optionally substituted with one to five Z^{1b};

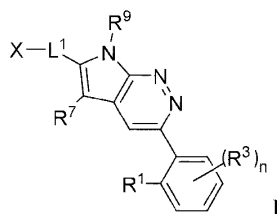
each Z^{1b} is independently halo, cyano, hydroxy, -SH, -NH₂, -NO₂, -SF₅, -P(O)(OH)₂, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -L-C₁₋₆ alkyl, -L-C₂₋₆ alkenyl, -L-C₂₋₆ alkynyl, -L-C₁₋₆ haloalkyl, -L-C₃₋₁₀ cycloalkyl, -L-heterocyclyl, -L-aryl, or -L-heteroaryl; and

each L is independently -O-, -NH-, -S-, -S(O)-, -S(O)₂-, -N(C₁₋₆ alkyl)-, -N(C₂₋₆ alkenyl)-, -N(C₂₋₆ alkynyl)-, -N(C₁₋₆ haloalkyl)-, -N(C₃₋₁₀ cycloalkyl)-, -N(heterocyclyl)-, -N(aryl)-, -N(heteroaryl)-, -C(O)-, -C(O)O-, -C(O)NH-, -C(O)N(C₁₋₆ alkyl)-, -C(O)N(C₂₋₆ alkenyl)-, -C(O)N(C₂₋₆ alkynyl)-, -C(O)N(C₁₋₆ haloalkyl)-, -C(O)N(C₃₋₁₀ cycloalkyl)-, -C(O)N(heterocyclyl)-, -C(O)N(aryl)-, -C(O)N(heteroaryl)-, -NHC(O)-, -NHC(O)O-, -NHC(O)NH-, -NHS(O)-, -S(O)₂NH-, -P(O)(OH)O-, -P(O)(O-C₁₋₆ alkyl)O-, -P(O)(O-C₂₋₆ alkenyl)O-, -P(O)(O-C₂₋₆ alkynyl)O-, -P(O)(OC₁₋₆ haloalkyl)O-, -P(O)(OC₃₋₁₀ cycloalkyl)O-, -P(O)(O-heterocyclyl)O-, -P(O)(O-aryl)O-, or -P(O)(O-heteroaryl)O-;

wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, and heteroaryl of Z^{1b} and L is further independently optionally substituted with one to five hydroxy, halo, cyano, hydroxy, -SH, -NH₂, -NO₂, -SF₅, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkoxy, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl.

[0080] In some embodiments, the compound is not 1-[3-[3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl]-1-azetidiny]-2-propen-1-one.

[0081] In some embodiments, provided is a compound of Formula I:



or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein:

n is 0, 1, or 2;

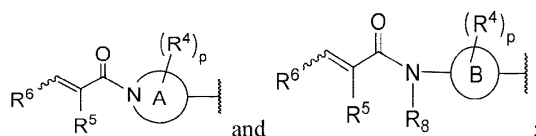
R¹ is hydroxy, halo, cyano, C₁₋₄ alkoxy, or N(R²)₂;

each R² is independently hydrogen, C₁₋₄ alkyl, or C₃₋₆ cycloalkyl;

each R³ is independently halo, cyano, C₁₋₆ alkyl, or C₁₋₃ haloalkyl;

L¹ is a bond, C₁₋₄ alkylene, -C₁₋₄ alkylene-heteroaryl-, C₂₋₃ alkenylene, C₂₋₃ alkynylene, or -C(O)-;

X is selected from:



p is 0, 1, or 2;

Ring A is a monocyclic, spirocyclic, fused bicyclic, or bridged bicyclic 4-10 membered heterocyclyl;

Ring B is a monocyclic, spirocyclic, fused bicyclic, or bridged bicyclic 3-10 membered cycloalkyl; wherein the nitrogen atom and L¹ may be attached via any atom on Ring B, including on the same carbon atom;

each R⁴ is independently halo, cyano, C₁₋₆ alkyl, -OR¹¹, -C(O)N(R¹¹)₂, heterocyclyl, or heteroaryl, wherein each C₁₋₆ alkyl is independently optionally substituted with one to eight Z¹;

R⁵ is hydrogen, halo, cyano, or C₁₋₆ alkyl optionally substituted with one to three Z¹;

R⁶ is hydrogen, halo, cyano, or C₁₋₆ alkyl optionally substituted with one to three Z¹;

R⁷ is hydrogen, halo, cyano, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, or -C(O)R¹¹, wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z¹;

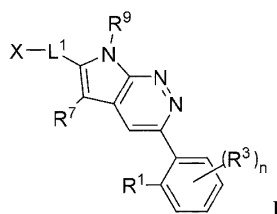
R⁸ is hydrogen or C₁₋₆ alkyl;

R⁹ is hydrogen;

each Z¹ is independently halo, cyano, -NO₂, -SF₅, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, -C(O)R¹¹, -C(O)OR¹¹, -S(O)₀₋₂R¹¹, -NR¹¹S(O)₀₋₂R¹¹, -S(O)₀₋₂N(R¹¹)₂, -NR¹¹S(O)₀₋₂N(R¹¹)₂, -NR¹¹C(O)N(R¹¹)₂, -C(O)N(R¹¹)₂, -NR¹¹C(O)R¹¹, -OC(O)N(R¹¹)₂, or -NR¹¹C(O)OR¹¹; and

each R¹¹ is independently hydrogen, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl.

[0082] In some embodiments, provided is a compound of Formula I:



or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein:

n is 0, 1, or 2;

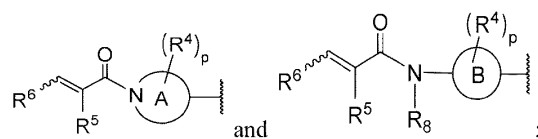
R¹ is hydroxy, halo, cyano, C₁₋₄ alkoxy, or N(R²)₂;

each R² is independently hydrogen, C₁₋₄ alkyl, or C₃₋₆ cycloalkyl;

each R³ is independently halo, cyano, C₁₋₆ alkyl, or C₁₋₃ haloalkyl;

L¹ is a bond, C₁₋₄ alkylene, -C₁₋₄ alkylene-heteroaryl-, C₂₋₃ alkenylene, C₂₋₃ alkynylene, or -C(O)-;

X is selected from:



p is 0, 1, or 2;

Ring A is a monocyclic, spirocyclic, fused bicyclic, or bridged bicyclic 4-10 membered heterocyclyl;

Ring B is a monocyclic, spirocyclic, fused bicyclic, or bridged bicyclic 3-10 membered cycloalkyl; wherein the nitrogen atom and L¹ may be attached via any atom on Ring B, including on the same carbon atom;

each R⁴ is independently halo, cyano, C₁₋₆ alkyl, -OR¹¹, or -C(O)N(R¹¹)₂, wherein each C₁₋₆ alkyl is independently optionally substituted with one to eight Z¹;

R⁵ is hydrogen, halo, cyano, or C₁₋₆ alkyl optionally substituted with one to three Z¹;

R⁶ is hydrogen, halo, cyano, or C₁₋₆ alkyl optionally substituted with one to three Z¹;

R⁷ is hydrogen, halo, cyano, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, or -C(O)R¹¹, wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z¹;

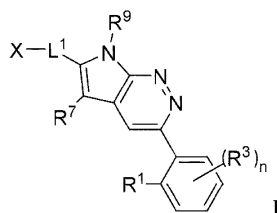
R⁸ is hydrogen or C₁₋₆ alkyl;

R⁹ is hydrogen;

each Z¹ is independently halo, cyano, -NO₂, -SF₅, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, -C(O)R¹¹, -C(O)OR¹¹, -S(O)₀₋₂R¹¹, -NR¹¹S(O)₀₋₂R¹¹, -S(O)₀₋₂N(R¹¹)₂, -NR¹¹S(O)₀₋₂N(R¹¹)₂, -NR¹¹C(O)N(R¹¹)₂, -C(O)N(R¹¹)₂, -NR¹¹C(O)R¹¹, -OC(O)N(R¹¹)₂, or -NR¹¹C(O)OR¹¹; and

each R¹¹ is independently hydrogen, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl.

[0083] In some embodiments, provided is a compound of Formula I:



or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein:

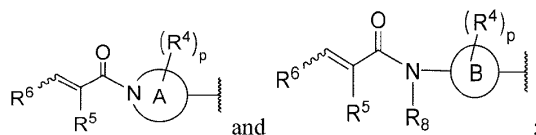
n is 0, 1, or 2;

R¹ is hydroxy;

each R³ is independently halo or C₁₋₃ haloalkyl;

L¹ is -CH₂-, -C(O)-, -CH₂-heteroaryl, or ethynyl;

X is selected from:



p is 0, 1, or 2;

Ring A is a monocyclic, spirocyclic, fused bicyclic, or bridged bicyclic 4-10 membered heterocyclyl;

Ring B is a monocyclic, spirocyclic, fused bicyclic, or bridged bicyclic 3-10 membered cycloalkyl; wherein the nitrogen atom and L¹ may be attached via any atom on Ring B, including on the same carbon atom;

each R⁴ is independently halo, cyano, -OCH₃, azetidiny, morpholino, pyridyl, or C₁₋₆ alkyl optionally substituted with cyano, -OH, -OCH₃, or -C(O)N(CH₃)₂;

R⁵ is hydrogen, halo, cyano, or C₁₋₆ alkyl;

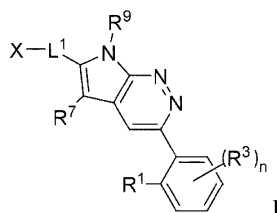
R⁶ is hydrogen, halo, cyano, or C₁₋₆ alkyl;

R⁷ is halo, -C(O)CH₃, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with halo, cyano, C₁₋₆ alkyl, -OH, -OCH₃, -OCH₂CH₃, -C(O)NH₂, -C(O)CH₃, -N(CH₃)₂, cyclopropyl, morpholino, or phenyl;

R⁸ is hydrogen or C₁₋₆ alkyl; and

R⁹ is hydrogen.

[0084] In some embodiments, provided is a compound of Formula I:



or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein:

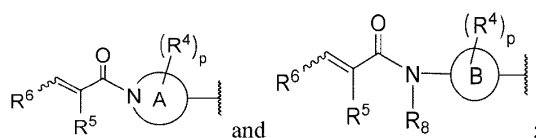
n is 0 or 1;

R¹ is hydroxy;

each R³ is independently halo or C₁₋₃ haloalkyl;

L¹ is -CH₂-, -C(O)-, -CH₂-heteroaryl, or ethynyl;

X is selected from:



p is 0, 1, or 2;

Ring A is a monocyclic, spirocyclic, fused bicyclic, or bridged bicyclic 4-10 membered heterocyclyl;

Ring B is a monocyclic, spirocyclic, fused bicyclic, or bridged bicyclic 3-10 membered cycloalkyl; wherein the nitrogen atom and L¹ may be attached via any atom on Ring B, including on the same carbon atom;

each R⁴ is independently halo, cyano, or C₁₋₆ alkyl optionally substituted with cyano, -OH, -OCH₃, or -C(O)N(CH₃)₂;

R⁵ is hydrogen, halo, cyano, or C₁₋₆ alkyl;

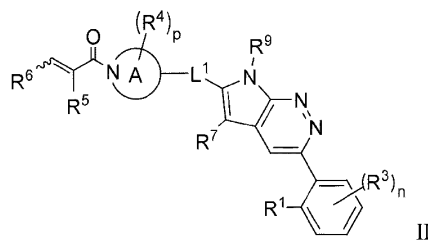
R⁶ is hydrogen, halo, cyano, or C₁₋₆ alkyl;

R⁷ is halo, -C(O)CH₃, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with halo, cyano, C₁₋₆ alkyl, -OH, -OCH₃, -OCH₂CH₃, -C(O)NH₂, -C(O)CH₃, -N(CH₃)₂, cyclopropyl, morpholino, or phenyl;

R⁸ is hydrogen or C₁₋₆ alkyl; and

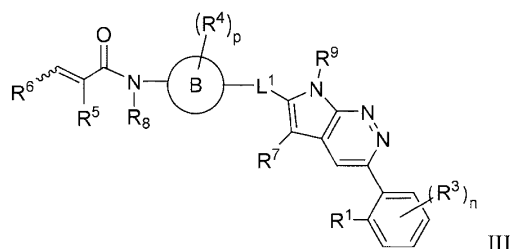
R⁹ is hydrogen.

[0085] In some embodiments, provided herein is a compound of Formula II:



or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof.

[0086] In some embodiments, provided herein is a compound of Formula III:



or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof.

[0087] In some embodiments, R^1 is $-OR^{12}$, halo, cyano, C_{1-4} alkoxy, or $-N(R^2)_2$.

[0088] In some embodiments, R^2 is hydrogen.

[0089] In some embodiments, R^1 is $-OR^{12}$.

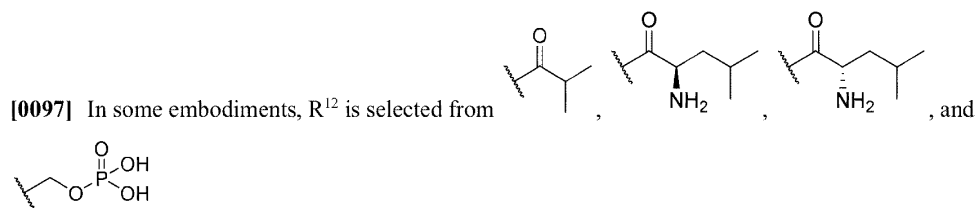
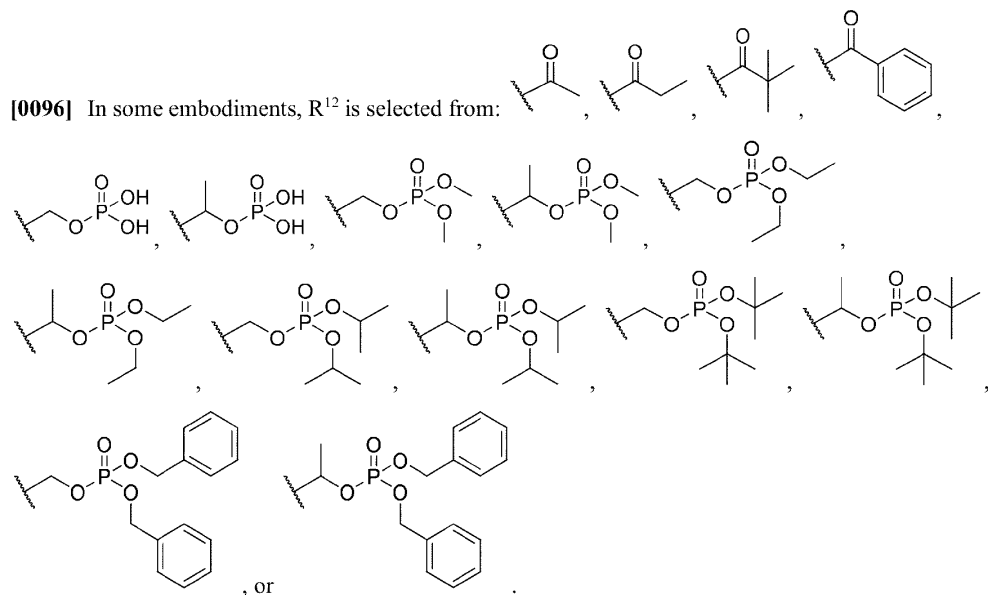
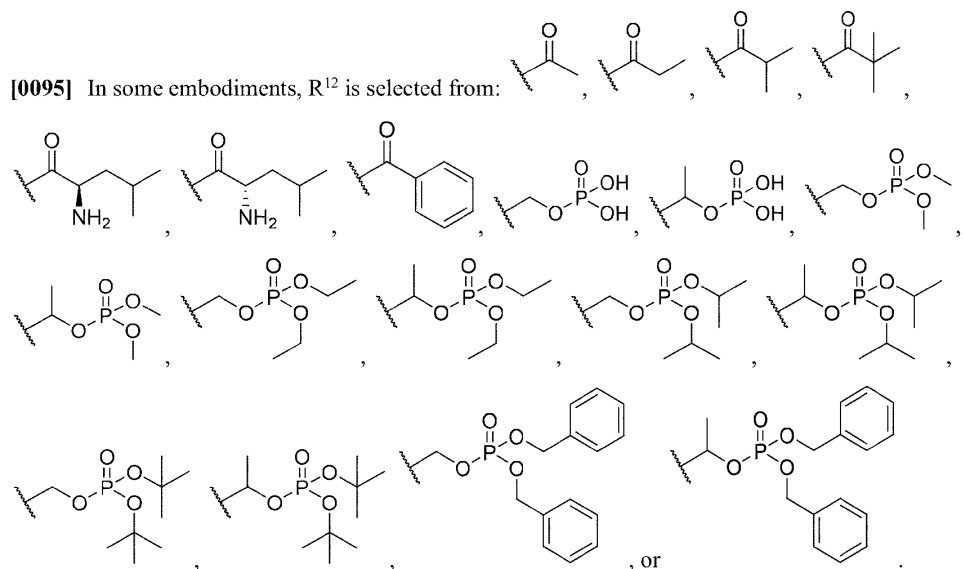
[0090] In some embodiments, R^{12} is hydrogen, $-C(O)R^{13}$, $C(O)N(R^{14})_2$, $-P(O)(OR^{14})_2$, or $-CH_2OP(O)(OR^{14})_2$, or $-CH(CH_3)OP(O)(OR^{14})_2$.

[0091] In some embodiments, R^{12} is hydrogen.

[0092] In some embodiments, R^{12} is $-C(O)R^{13}$. In some embodiments, R^{12} is $-C(O)-C_{1-6}$ alkyl, $-C(O)-C_{3-10}$ cycloalkyl, $-C(O)-aryl$, or $-C(O)-heteroaryl$.

[0093] In some embodiments, R^{12} is $-C(O)R^{13}$ wherein R^{13} is C_{1-6} alkyl optionally substituted with one to five Z^{1b} . In some embodiments, R^{12} is $-C(O)R^{13}$ wherein R^{13} is unsubstituted C_{1-6} alkyl. In some embodiments, R^{12} is $-C(O)R^{13}$ wherein R^{13} is C_{1-6} alkyl optionally substituted with one to three halo, cyano, hydroxy, or $-NH_2$. In some embodiments, R^{12} is $-C(O)R^{13}$ wherein R^{13} is C_{1-6} alkyl substituted with $-NH_2$.

[0094] In some embodiments, R^{12} is $-CH_2OP(O)(OR^{14})_2$. In some embodiments, R^{12} is $-CH_2P(O)(OH)_2$, $-CH_2P(O)(O-C_{1-6} \text{ alkyl})_2$, or $-CH_2P(O)(O-aryl)_2$. R^{12} is $-CH(CH_3)OP(O)(OR^{14})_2$. In some embodiments, R^{12} is $-CH(CH_3)OP(O)(OH)_2$, $-CH(CH_3)OP(O)(O-C_{1-6} \text{ alkyl})_2$, or $-CH(CH_3)OP(O)(O-aryl)_2$.



[0098] In some embodiments, R¹ is hydroxy.

[0099] In some embodiments, R⁹ is hydrogen, -C(O)R¹³, -(CH₂)_mP(O)(OR¹⁴)₂, -CH(CH₃)P(O)(OR¹⁴)₂, or -(CH₂)_mP(O)(R¹⁴)(OR¹⁴).

[0100] In some embodiments, R⁹ is -C(O)-C₁₋₆ alkyl, -C(O)-C₃₋₁₀ cycloalkyl, -C(O)-aryl, or -C(O)-heteroaryl.

[0101] In some embodiments, R⁹ is -CH₂P(O)(OR¹⁴)₂. In some embodiments, R⁹ is -CH₂P(O)(OH)₂, -CH₂P(O)(O-C1-6 alkyl)₂, or -CH₂P(O)(O-aryl)₂.

[illegible]

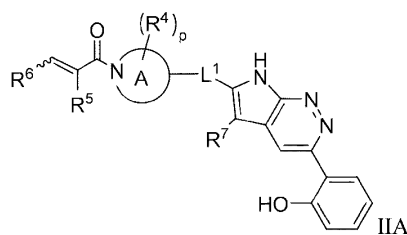
[0103] In some embodiments, n is 0 or 1. In some embodiments, n is 0. In some embodiments, n is 1.

[0104] In some embodiments, R³ is halo or cyano. In some embodiments, R³ is halo. In some embodiments, R³ is fluoro, chloro, or cyano. In some embodiments, R₃ is fluoro.

[0105] In some embodiments, n is 1 and R³ is halo or cyano. In some embodiments, n is 1 and R³ is halo. In some embodiments, n is 1 and R³ is fluoro.

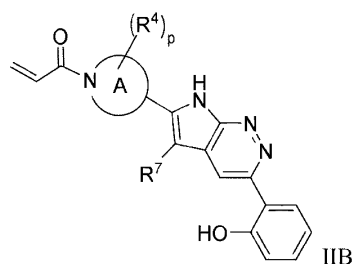
[0106] In some embodiments, R⁹ is hydrogen.

[0107] In some embodiments, provided herein is a compound of Formula IIA:



or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof.

[0108] In some embodiments, provided herein is a compound of Formula IIB:



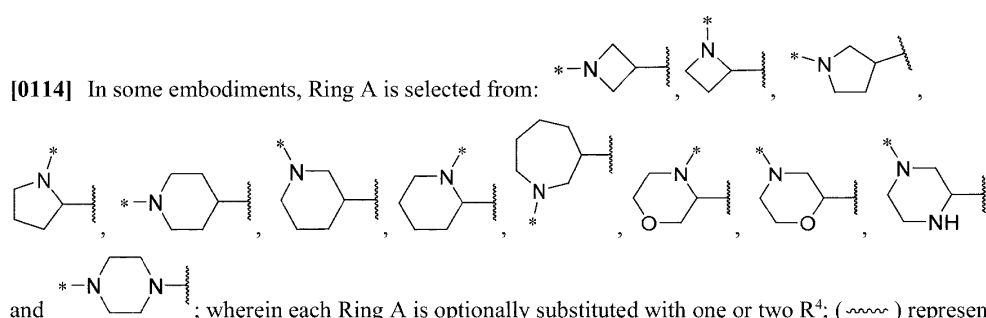
[0109] In some embodiments, Ring A is a monocyclic, spirocyclic, fused bicyclic, or bridged bicyclic 4-10 membered heterocyclyl or a monocyclic or fused bicyclic 5-10 membered heteroaryl, wherein each Ring A is optionally substituted with one or two R^4 .

[0110] In some embodiments, Ring A is a monocyclic 5-10 membered heteroaryl optionally substituted with one or two R^4 . In some embodiments, Ring A is a fused bicyclic 5-10 membered heteroaryl optionally substituted with one or two R^4 .

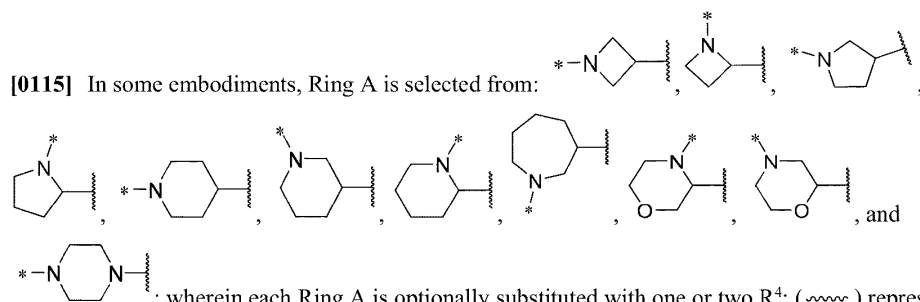
[0111] In some embodiments, Ring A is a monocyclic, spirocyclic, fused bicyclic, or bridged bicyclic 4-10 membered heterocyclyl optionally substituted with one or two R^4 . In some embodiments, Ring A is a monocyclic 4-10 membered heterocyclyl optionally substituted with one or two R^4 . In some embodiments, Ring A is a spirocyclic 4-10 membered heterocyclyl optionally substituted with one or two R^4 . In some embodiments, Ring A is a fused bicyclic 5-10 membered heterocyclyl optionally substituted with one or two R^4 . In some embodiments, Ring A is a bridged bicyclic 5-10 membered heterocyclyl optionally substituted with one or two R^4 . In some embodiments, Ring A is a monocyclic 4-10 membered heterocyclyl optionally substituted with one or two R^4 .

[0112] In some embodiments, Ring A is a monocyclic 4-7 membered heterocyclic optionally substituted with one or two R^4 . In some embodiments, Ring A is azetidiny, pyrrolidinyl, piperidinyl, or azepanyl, wherein each Ring A is optionally substituted with one or two R^4 .

[0113] In some embodiments, Ring A is morpholinyl or piperazinyl, wherein each Ring A is optionally substituted with one or two R^4 .



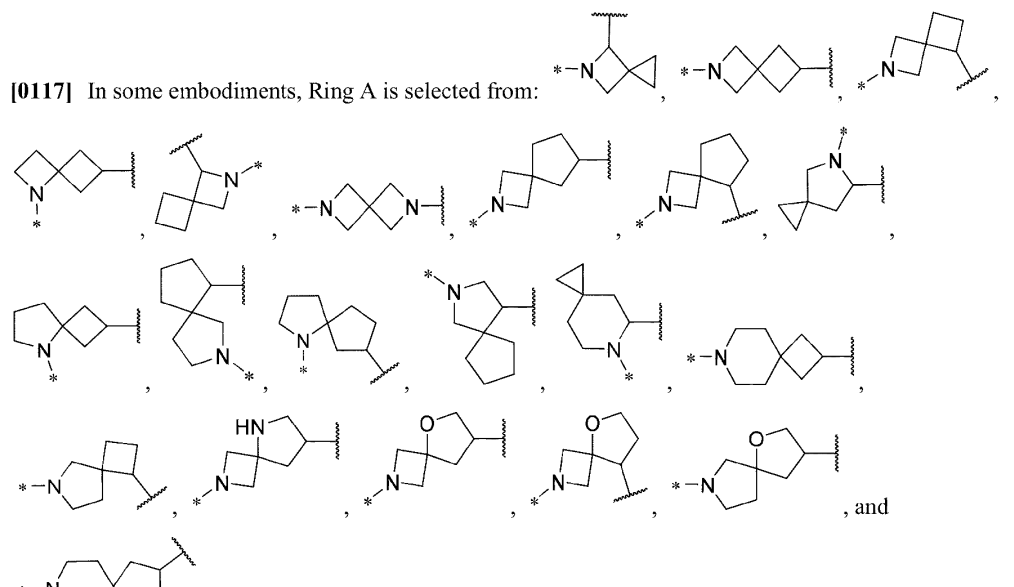
[0115] In some embodiments, Ring A is selected from:



; wherein each Ring A is optionally substituted with one or two R^4 ; (~~~~) represents the point of attachment to L^1 or the 7H-pyrrolo[2,3-c]pyridazine moiety; and (*) represents the point of attachment to the carbonyl moiety.

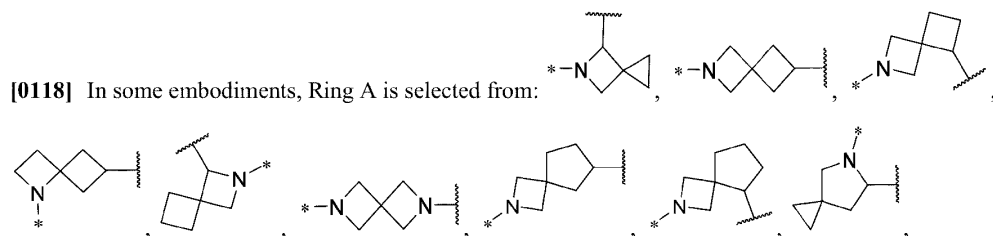
[0116] In some embodiments, Ring A is a spirocyclic 4-10 membered heterocyclyl optionally substituted with one or two R^4 .

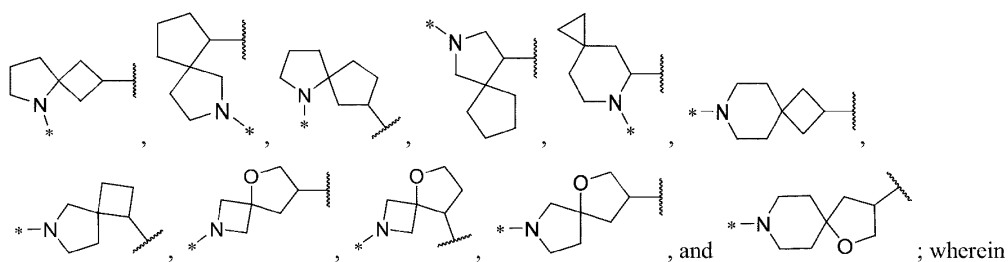
[0117] In some embodiments, Ring A is selected from:



; wherein each Ring A is optionally substituted with one or two R^4 ; (~~~~) represents the point of attachment to L^1 or the 7H-pyrrolo[2,3-c]pyridazine moiety; and (*) represents the point of attachment to the carbonyl moiety.

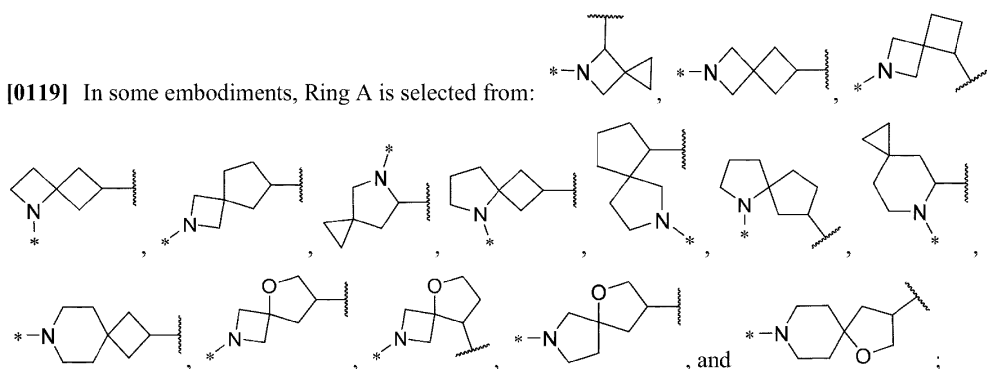
[0118] In some embodiments, Ring A is selected from:





each Ring A is optionally substituted with one or two R^4 ; (~~~~) represents the point of attachment to L^1 or the 7H-pyrrolo[2,3-c]pyridazine moiety; and (*) represents the point of attachment to the carbonyl moiety.

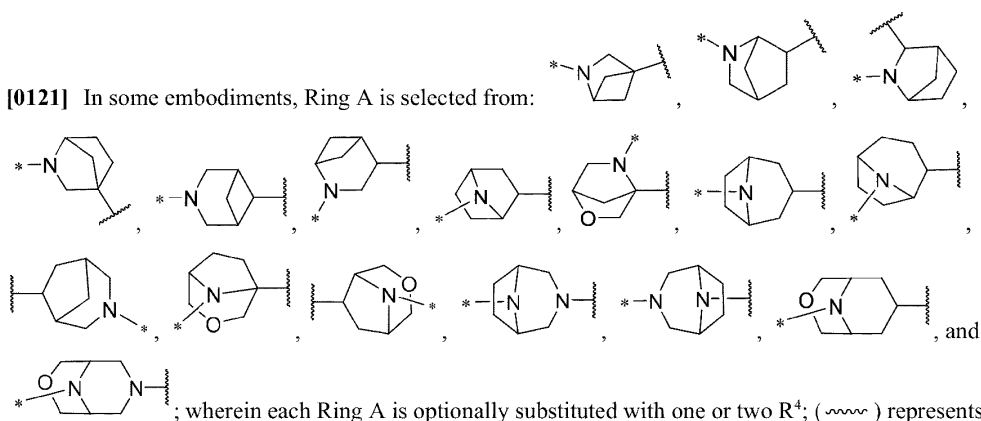
[0119] In some embodiments, Ring A is selected from:



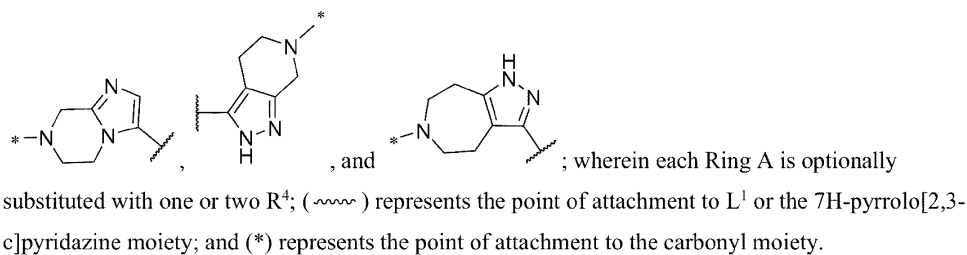
wherein each Ring A is optionally substituted with one or two R^4 ; (~~~~) represents the point of attachment to L^1 or the 7H-pyrrolo[2,3-c]pyridazine moiety; and (*) represents the point of attachment to the carbonyl moiety.

[0120] In some embodiments, Ring A is a bridged bicyclic 4-10 membered heterocyclyl optionally substituted with one or two R^4 .

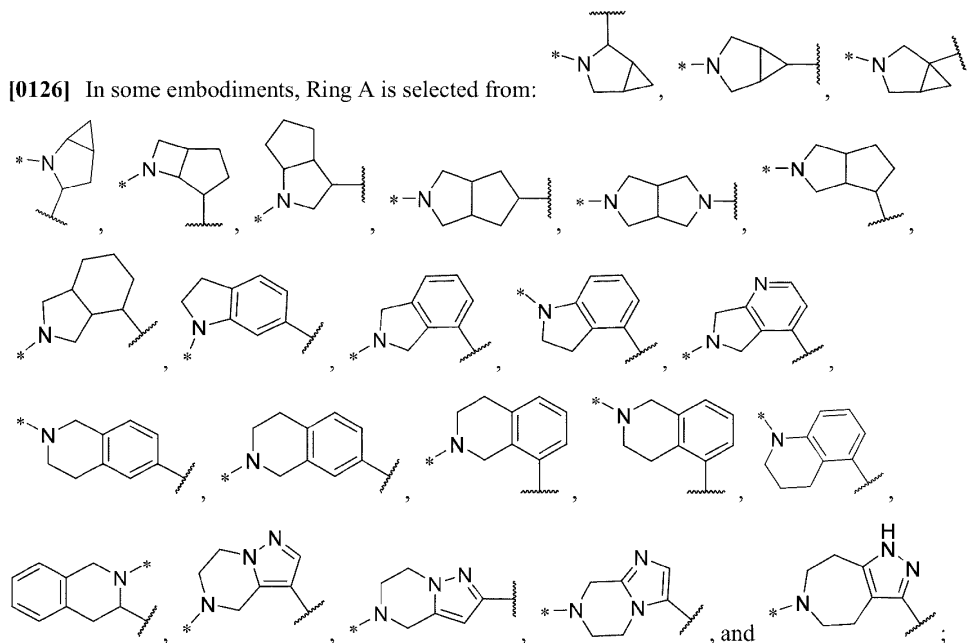
[0121] In some embodiments, Ring A is selected from:



; wherein each Ring A is optionally substituted with one or two R^4 ; (~~~~) represents the point of attachment to L^1 or the 7H-pyrrolo[2,3-c]pyridazine moiety; and (*) represents the point of attachment to the carbonyl moiety.

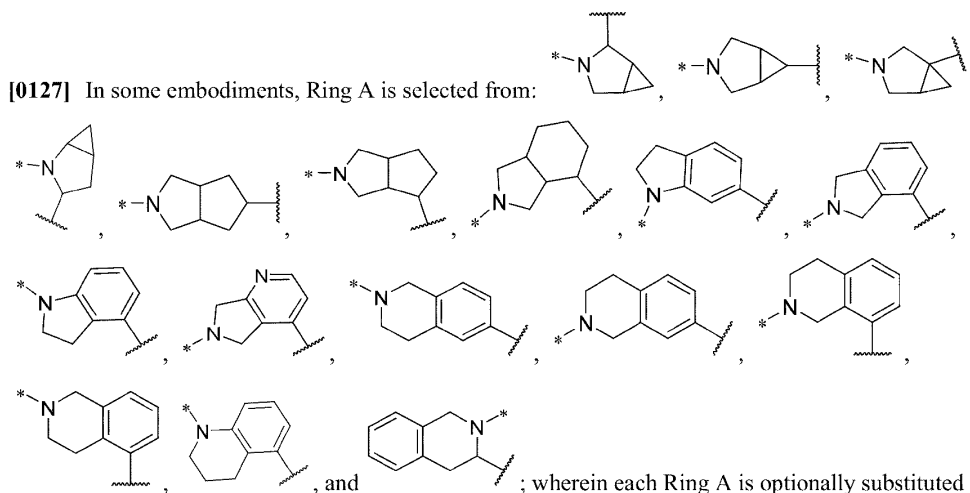


[0126] In some embodiments, Ring A is selected from:



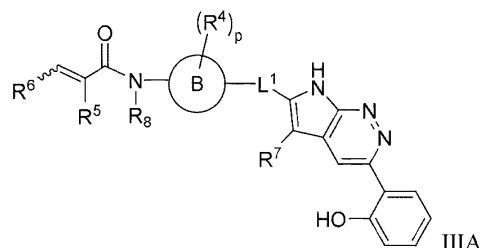
wherein each Ring A is optionally substituted with one or two R^4 ; (~~~~) represents the point of attachment to L^1 or the 7H-pyrrolo[2,3-c]pyridazine moiety; and (*) represents the point of attachment to the carbonyl moiety.

[0127] In some embodiments, Ring A is selected from:



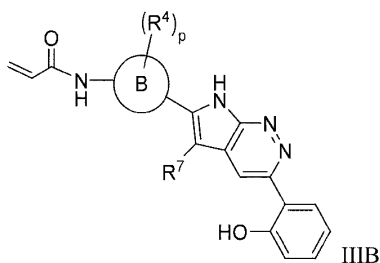
with one or two R^4 ; (~~~~) represents the point of attachment to L^1 or the 7H-pyrrolo[2,3-c]pyridazine moiety; and (*) represents the point of attachment to the carbonyl moiety.

[0128] In some embodiments, provided herein is a compound of Formula IIIA:



or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof.

[0129] In some embodiments, provided herein is a compound of Formula IIIB:



or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof.

[0130] In some embodiments, L^1 is a bond, C_{1-4} alkylene, $-C_{1-4}$ alkylene-heteroaryl-, C_{2-3} alkenylene, C_{2-3} alkynylene, or $-C(O)-$.

[0131] In some embodiments, L^1 is a bond.

[0132] In some embodiments, L^1 is C_{1-4} alkylene. In some embodiments, L^1 is $-CH_2-$.

[0133] In some embodiments, L^1 is C_{1-4} alkylene-heteroaryl. In some embodiments, L^1 is $-CH_2-$ heteroaryl. In some embodiments, L^1 is $-CH_2$ -pyrazolyl.

[0134] In some embodiments, L^1 is C_{2-3} alkynylene. In some embodiments, L^1 is ethynyl.

[0135] In some embodiments, L^1 is $-C(O)-$.

[0136] In some embodiments, L^1 is a bond, $-CH_2-$, $-C(O)-$, $-CH_2$ -heteroaryl, or ethynyl.

[0137] In some embodiments, L^1 is $-CH_2-$, $-C(O)-$, $-CH_2$ -heteroaryl, or ethynyl.

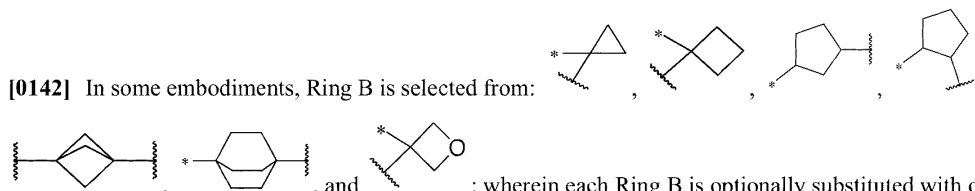
[0138] In some embodiments, Ring B is a monocyclic, spirocyclic, fused bicyclic, or bridged bicyclic 3-10 membered cycloalkyl, a monocyclic, spirocyclic, fused bicyclic, or bridged bicyclic 4-10 membered heterocyclyl, or a monocyclic or fused bicyclic 5-10 membered heteroaryl, wherein each Ring B is optionally substituted with one or two R^4 .

[0139] In some embodiments, Ring B is a monocyclic 3-10 membered cycloalkyl optionally substituted with one or two R^4 . In some embodiments, Ring B is cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, or cycloheptyl, wherein each Ring B is optionally substituted with one or two R^4 .

[0140] In some embodiments, Ring B is a bridged bicyclic 3-10 membered cycloalkyl optionally substituted with one or two R⁴. In some embodiments, Ring B is bicyclo[1.1.1]pentyl optionally substituted with one or two R⁴. In some embodiments, Ring B is bicyclo[2.2.2]octyl optionally substituted with one or two R⁴.

[0141] In some embodiments, Ring B is a monocyclic 4-10 membered heterocyclyl optionally substituted with one or two R⁴.

[0142] In some embodiments, Ring B is selected from:




 ; wherein each Ring B is optionally substituted with one or two R⁴; (~~~~~) represents the point of attachment to L¹ or the 7H-pyrrolo[2,3-c]pyridazine moiety; and (*) represents the point of attachment to the nitrogen atom.

[0143] In some embodiments, p is 0, 1, or 2. In some embodiments, p is 1 or 2. In some embodiments, p is 0. In some embodiments, p is 1. In some embodiments, p is 2.

[0144] In some embodiments, p is 1 or 2 and each R⁴ is independently oxo, halo, cyano, -NO₂, -SF₅, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, -C(O)R¹¹, -C(O)OR¹¹, -S(O)₀₋₂R¹¹, -NR¹¹S(O)₀₋₂R¹¹, -S(O)₀₋₂N(R¹¹)₂, -NR¹¹S(O)₀₋₂N(R¹¹)₂, -NR¹¹C(O)N(R¹¹)₂, -C(O)N(R¹¹)₂, -NR¹¹C(O)R¹¹, -OC(O)N(R¹¹)₂, or -NR¹¹C(O)OR¹¹; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z¹.

[0145] In some embodiments, each R⁴ is independently halo, cyano, C₁₋₆ alkyl, -OR¹¹, or -C(O)N(R¹¹)₂, wherein each C₁₋₆ alkyl is independently optionally substituted with one to eight Z¹.

[0146] In some embodiments, each R⁴ is independently halo. In some embodiments, R⁴ is fluoro.

[0147] In some embodiments, p is 1 and R⁴ is halo. In some embodiments, p is 1 and R⁴ is fluoro. In some embodiments, p is 2 and each R⁴ is independently halo. In some embodiments, p is 2 and R⁴ is fluoro.

[0148] In some embodiments, R⁴ is cyano. In some embodiments, p is 1 and R⁴ is cyano.

[0149] In some embodiments, each R⁴ is independently C₁₋₆ alkyl optionally substituted with one to three Z¹.

[0150] In some embodiments, each R⁴ is independently C₁₋₆ alkyl substituted with cyano or methoxy. In some embodiments, R⁴ is -CH₂CN. In some embodiments, R⁴ is -CH₂OCH₃. In some embodiments, p is 1 and R⁴ is -CH₂CN or -CH₂OCH₃.

[0151] In some embodiments, R⁴ is C₁₋₆ alkyl substituted with cyano.

[0152] In some embodiments, R⁴ is unsubstituted C₁₋₆ alkyl. In some embodiments, R⁴ is methyl, ethyl, or propyl. In some embodiments, R⁴ is methyl.

[0153] In some embodiments, p is 1 and R⁴ is methyl. In some embodiments, p is 2 and R⁴ is methyl.

[0154] In some embodiments, R^4 is $-OR^{11}$. In some embodiments, R^4 is $-OH$. In some embodiments, R^4 is $-OCH_3$. In some embodiments, p is 1 and R^4 is $-OH$. In some embodiments, p is 1 and R^4 is $-OCH_3$.

[0155] In some embodiments, R^4 is $-C(O)N(R^{11})_2$. In some embodiments, R^4 is $-C(O)N(CH_3)_2$. In some embodiments, p is 1 and R^4 is $-C(O)N(CH_3)_2$.

[0156] In some embodiments, R^4 is C_{3-10} cycloalkyl, aryl, heteroaryl, or heterocyclyl.

[0157] In some embodiments, R^4 is aryl. In some embodiments, R^4 is a C_{6-10} aryl. In some embodiments, p is 1 and R^4 is phenyl or naphthenyl. In some embodiments, p is 1 and R^4 is phenyl.

[0158] In some embodiments, R^4 is heteroaryl. In some embodiments, R^4 is a 5-6 membered heteroaryl containing 1-3 heteroatoms selected from N, O, and S. In some embodiments, p is 1 and R^4 is pyrrolyl, pyrazolyl, oxazolyl, oxadiazolyl, thiazolyl, thiadiazolyl, or triazolyl.

[0159] In some embodiments, R^4 is heterocyclyl. In some embodiments, R^4 is a 4-6 membered heterocyclyl containing 1-2 heteroatoms selected from N, O, and S. In some embodiments, p is 1 and R^4 is azetidyl, pyrrolidyl, piperidyl, or morpholino. In some embodiments, p is 1 and R^4 is morpholino.

[0160] In some embodiments, p is 1 and R^4 is phenyl, pyrazolyl, triazolyl, azetidyl, or morpholino.

[0161] In some embodiments, R^4 is fluoro, cyano, methyl, ethyl, propyl, $-CH_2CN$, $-CH_2OCH_3$, $-OH$, $-OCH_3$, $-C(O)N(CH_3)_2$, phenyl, pyrazolyl, triazolyl, azetidyl, or morpholino. In some embodiments, p is 1 or 2 and R^4 is fluoro, cyano, methyl, ethyl, propyl, $-CH_2CN$, $-CH_2OCH_3$, $-OH$, $-OCH_3$, $-C(O)N(CH_3)_2$, phenyl, pyrazolyl, triazolyl, azetidyl, or morpholino. In some embodiments, p is 1 and R^4 is fluoro, cyano, methyl, ethyl, propyl, $-CH_2CN$, $-CH_2OCH_3$, $-OH$, $-OCH_3$, $-C(O)N(CH_3)_2$, phenyl, pyrazolyl, triazolyl, azetidyl, or morpholino. In some embodiments, p is 2 and R^4 is fluoro or methyl.

[0162] In some embodiments, R^4 is fluoro, cyano, methyl, ethyl, propyl, $-CH_2CN$, $-OH$, $-OCH_3$, or $-C(O)N(CH_3)_2$. In some embodiments, p is 1 or 2 and R^4 is fluoro, cyano, methyl, ethyl, propyl, $-CH_2CN$, $-OH$, $-OCH_3$, or $-C(O)N(CH_3)_2$. In some embodiments, p is 1 and R^4 is fluoro, cyano, methyl, ethyl, propyl, $-CH_2CN$, $-OH$, $-OCH_3$, or $-C(O)N(CH_3)_2$. In some embodiments, p is 2 and R^4 is fluoro or methyl.

[0163] In some embodiments, R^5 is hydrogen, halo, cyano, or C_{1-6} alkyl optionally substituted with one to three Z^1 .

[0164] In some embodiments, R^5 is hydrogen. In some embodiments, R^5 is halo. In some embodiments, R^5 is fluoro. In some embodiments, R^5 is cyano.

[0165] In some embodiments, R^6 is hydrogen, halo, cyano, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, heteroaryl, $-N(R^{11})_2$, $-OR^{11}$, $-C(O)R^{11}$, $-C(O)OR^{11}$, $-S(O)_{0-2}R^{11}$, $-NR^{11}S(O)_{0-2}R^{11}$, $-S(O)_{0-2}N(R^{11})_2$, $-NR^{11}S(O)_{0-2}N(R^{11})_2$, $-NR^{11}C(O)N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-NR^{11}C(O)R^{11}$, $-OC(O)N(R^{11})_2$, or $-NR^{11}C(O)OR^{11}$; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z^1 .

[0166] In some embodiments, R^6 is hydrogen, halo, cyano, C_{3-10} cycloalkyl, or C_{1-6} alkyl optionally substituted with one to eight Z^1 .

[0167] In some embodiments, R^6 is hydrogen, halo, cyano, or C_{1-6} alkyl optionally substituted with one to eight Z^1 . In some embodiments, R^6 is hydrogen, halo, or cyano.

[0168] In some embodiments, R^6 is hydrogen.

[0169] In some embodiments, R^6 is C_{3-10} cycloalkyl. In some embodiments, R^6 is cyclopropyl.

[0170] In some embodiments, R^6 is C_{1-6} alkyl optionally substituted with one to eight Z^1 . In some embodiments, R^6 is C_{1-6} alkyl substituted with halo, $-N(R^{11})_2$, or heterocyclyl optionally substituted with one to five Z^{1a} .

[0171] In some embodiments, R^6 is C_{1-6} alkyl substituted with one to three halo. In some embodiments, R^6 is C_{1-3} alkyl substituted with one to three fluoro.

[0172] In some embodiments, R^6 is C_{1-6} alkyl substituted with heterocyclyl optionally substituted with one to five Z^{1a} . In some embodiments, R^6 is C_{1-3} alkyl substituted with heterocyclyl substituted with one or two C_{1-6} alkyl.

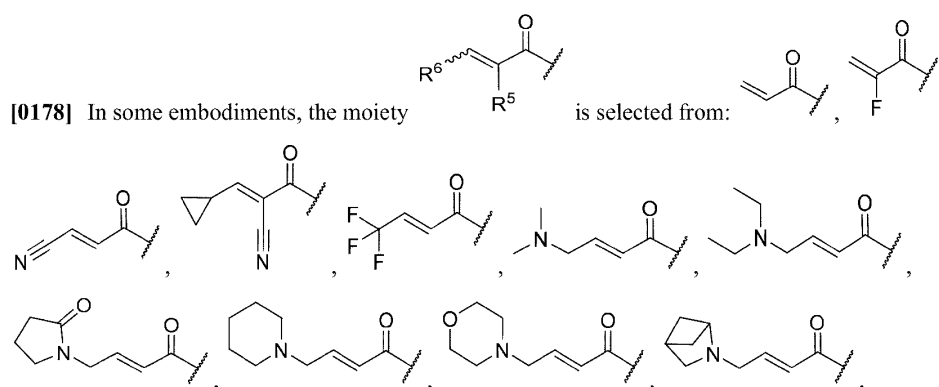
[0173] In some embodiments, R^6 is C_{1-3} alkyl substituted with a 4-10 membered heterocyclyl, wherein the heterocyclyl is optionally substituted with one or two methyl or fluoro.

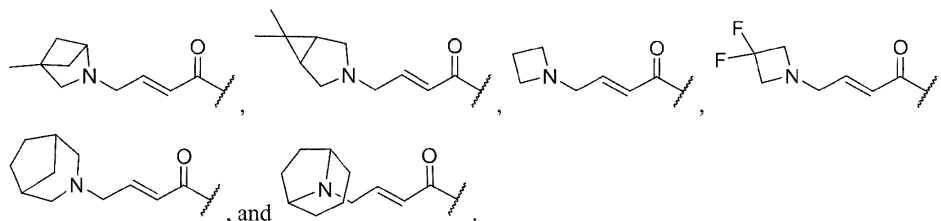
[0174] In some embodiments, R^6 is C_{1-6} alkyl substituted with $-N(R^{11})_2$. In some embodiments, R^6 is C_{1-3} alkyl substituted with $-N(CH_3)_2$ or $-N(CH_2CH_3)_2$.

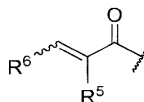
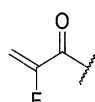
[0175] In some embodiments, R^5 is hydrogen and R^6 is hydrogen. In some embodiments, R^5 is halo and R^6 is hydrogen. In some embodiments, R^5 is fluoro and R^6 is hydrogen. In some embodiments, R^5 is hydrogen and R^6 is cyano. In some embodiments, R^5 is hydrogen and R^6 is halo, cyano, or C_{1-6} alkyl optionally substituted with one to eight Z^1 .

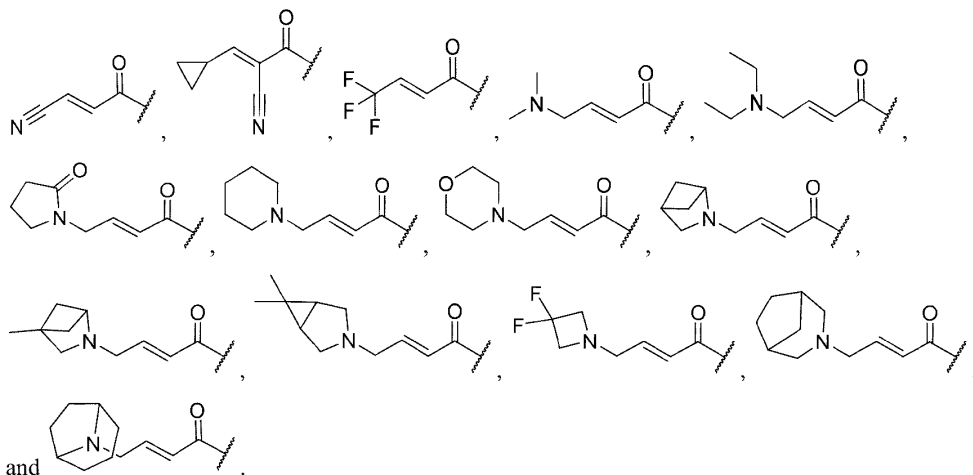
[0176] In some embodiments, R^5 is hydrogen or cyano and R^6 is halo, cyano, cyclopropyl, or C_{1-6} alkyl optionally substituted with one to three groups selected from fluoro, cyano, $-N(CH_3)_2$, $-N(CH_2CH_3)_2$, and heterocyclyl substituted with one to three Z^{1a} . In some embodiments, R^5 is hydrogen and R^6 is C_{1-3} alkyl substituted with a 4-10 membered heterocyclyl optionally substituted with one or two Z^{1a} .

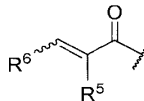
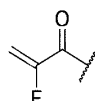
[0177] In some embodiments, R^5 is hydrogen and R^6 is halo, cyano, or C_{1-6} alkyl optionally substituted with one to three fluoro, cyano, $-N(CH_3)_2$, $-N(CH_2CH_3)_2$, or heterocyclyl substituted with one or two methyl.

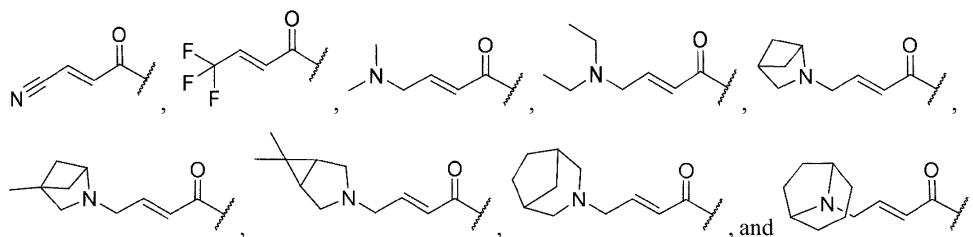




[0179] In some embodiments, the moiety  is selected from: , ,



[0180] In some embodiments, the moiety  is selected from: , ,



[0181] In some embodiments, R^8 is hydrogen. In some embodiments, R^8 is C_{1-6} alkyl. In some embodiments, R^8 is methyl.

[0182] In some embodiments, R^5 , R^6 , and R^8 are hydrogen. In some embodiments, R^5 and R^6 are hydrogen and R^8 is methyl.

[0183] In some embodiments, R^7 is hydrogen, halo, cyano, $-\text{NO}_2$, $-\text{SF}_5$, $-\text{CD}_3$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, heteroaryl, $-\text{N}(\text{R}^{11})_2$, $-\text{OR}^{11}$, $-\text{C}(\text{O})\text{R}^{11}$, $-\text{C}(\text{O})\text{OR}^{11}$, $-\text{S}(\text{O})_{0.2}\text{R}^{11}$, $-\text{NR}^{11}\text{S}(\text{O})_{0.2}\text{R}^{11}$, $-\text{S}(\text{O})_{0.2}\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{S}(\text{O})_{0.2}\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{C}(\text{O})\text{N}(\text{R}^{11})_2$, $-\text{C}(\text{O})\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{C}(\text{O})\text{R}^{11}$, $-\text{OC}(\text{O})\text{N}(\text{R}^{11})_2$, or $-\text{NR}^{11}\text{C}(\text{O})\text{OR}^{11}$; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl,

C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z¹.

[0184] In some embodiments, R⁷ is hydrogen, halo, cyano, -NO₂, -SF₅, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, -C(O)R¹¹, -C(O)OR¹¹, -NR¹¹C(O)N(R¹¹)₂, -C(O)N(R¹¹)₂, -NR¹¹C(O)R¹¹, -OC(O)N(R¹¹)₂, or -NR¹¹C(O)OR¹¹; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z¹;

[0185] In some embodiments, R⁷ is hydrogen, halo, cyano, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, -C(O)R¹¹, or -C(O)N(R¹¹)₂, wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z¹.

[0186] In some embodiments, R⁷ is hydrogen, halo, cyano, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, or -C(O)R¹¹, wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z¹.

[0187] In some embodiments, R⁷ is hydrogen.

[0188] In some embodiments, R⁷ is halo. In some embodiments, R⁷ is fluoro. In some embodiments, R⁷ is chloro. In some embodiments, R⁷ is bromo. In some embodiments, R⁷ is iodo.

[0189] In some embodiments, R⁷ is -C(O)R¹¹. In some embodiments, R⁷ is -C(O)CH₃.

[0190] In some embodiments, R⁷ is hydrogen, fluoro, chloro, bromo, iodo, or -C(O)CH₃.

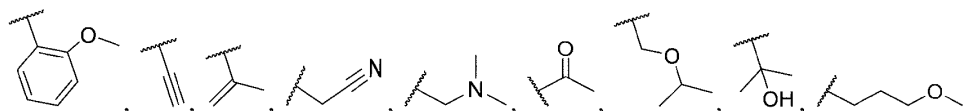
[0191] In some embodiments, R⁷ is C₁₋₆ alkyl, C₂₋₆ alkenyl, or C₂₋₆ alkynyl, wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, or C₂₋₆ alkynyl is independently optionally substituted with one to three Z¹.

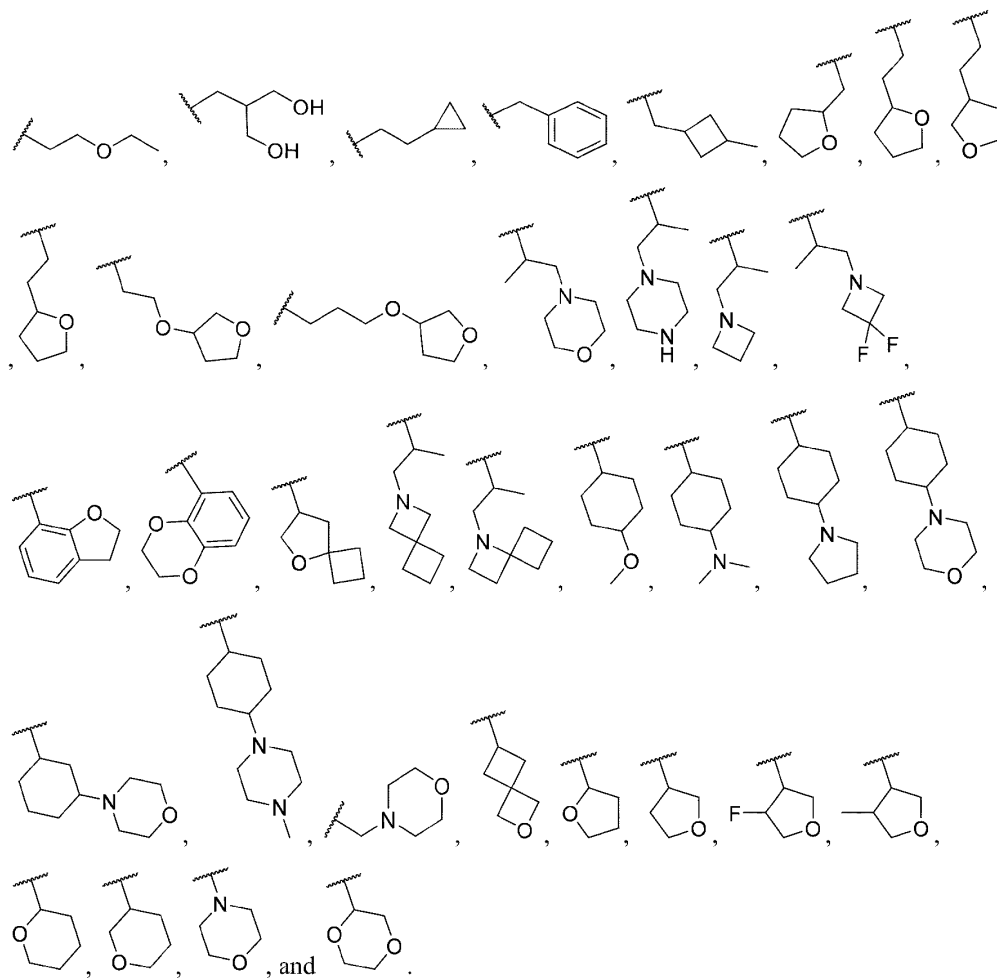
[0192] In some embodiments, R⁷ is C₁₋₆ alkyl. In some embodiments, R⁷ is methyl, ethyl, *n*-propyl, or isopropyl. In some embodiments, R⁷ is methyl. In some embodiments, R⁷ is ethyl. In some embodiments, R⁷ is isopropyl. In some embodiments, R⁷ is linear or branched butyl.

[0193] In some embodiments, R⁷ is C₁₋₆ alkyl optionally substituted with one to three Z¹. In some embodiments, R⁷ is C₁₋₆ alkyl substituted with one to three cyano, -OR¹¹, -N(R¹¹)₂, C₃₋₁₀ cycloalkyl, heterocyclyl, or aryl.

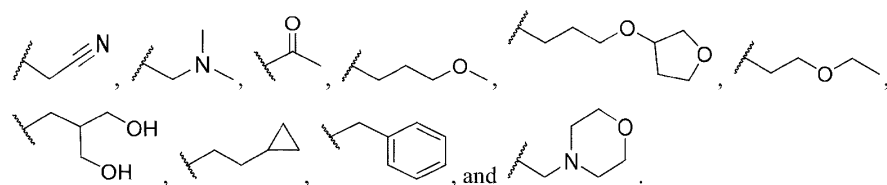
[0194] In some embodiments, R⁷ is C₁₋₆ alkyl substituted with cyano. In some embodiments, R⁷ is C₁₋₆ alkyl substituted with -OCH₃. In some embodiments, R⁷ is C₁₋₆ alkyl substituted with -OCH₂CH₃. In some embodiments, R⁷ is C₁₋₆ alkyl substituted with -OH and -OCH₂CH₃. In some embodiments, R⁷ is C₁₋₆ alkyl substituted with -N(CH₃)₂. In some embodiments, R⁷ is C₁₋₆ alkyl substituted with cyclopropyl. In some embodiments, R⁷ is C₁₋₆ alkyl substituted with a 6-membered heterocyclyl. In some embodiments, R⁷ is C₁₋₆ alkyl substituted with phenyl.

[0195] In some embodiments, R⁷ is selected from hydrogen, halo, C₁₋₄ alkyl, -CD₃, cyclopropyl, phenyl,

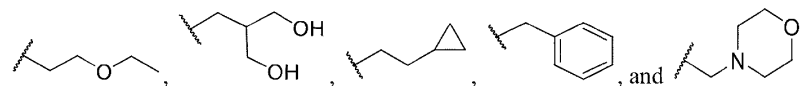




[0196] In some embodiments, R^7 is selected from:



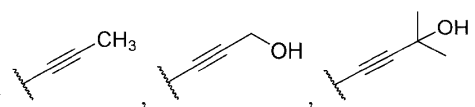
[0197] In some embodiments, R⁷ is selected from: , , , ,



[0198] In some embodiments, R⁷ is C₂₋₆alkenyl optionally substituted with one to three Z¹. In some embodiments, R⁷ is C₂₋₆alkenyl. In some embodiments, R⁷ is propenyl.

[0199] In some embodiments, R^7 is C_{2-6} alkynyl optionally substituted with one to three Z^1 . In some embodiments, R^7 is C_{2-6} alkynyl substituted with $-OR^{11}$ or C_{3-10} cycloalkyl. In some embodiments, R^7 is C_{2-6} alkynyl substituted with $-OH$. In some embodiments, R^7 is C_{2-6} alkynyl substituted with cyclopropyl.

[0200] In some embodiments, R^7 is selected from:



and



[0201] In some embodiments, R^7 is C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl, wherein each C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl is independently optionally substituted with one to three cyano, $-OH$, $-OCH_3$, $-OCH_2CH_3$, $-N(CH_3)_2$, cyclopropyl, phenyl, or morpholino.

[0202] In some embodiments, R^7 is C_{3-10} cycloalkyl or heterocyclyl, wherein each C_{3-10} cycloalkyl or heterocyclyl is independently optionally substituted with one to three Z^1 .

[0203] In some embodiments, R^7 is C_{3-10} cycloalkyl or heterocyclyl, wherein each C_{3-10} cycloalkyl or heterocyclyl is independently optionally substituted with C_{1-6} alkyl, $-C(O)N(R^{11})_2$, or $-C(O)R^{11}$.

[0204] In some embodiments, R^7 is C_{3-10} cycloalkyl optionally substituted with one to three Z^1 . In some embodiments, R^7 is C_{3-6} cycloalkyl substituted with $-C(O)N(R^{11})_2$. In some embodiments, R^7 is C_{3-6} cycloalkyl substituted with $-C(O)NH_2$. In some embodiments, R^7 is C_{3-6} cycloalkyl substituted with methoxy.

[0205] In some embodiments, R^7 is C_{3-6} cycloalkyl substituted with heterocyclyl. In some embodiments, R^7 is C_{3-6} cycloalkyl substituted with morpholinyl, piperidinyl, or pyrrolidinyl.

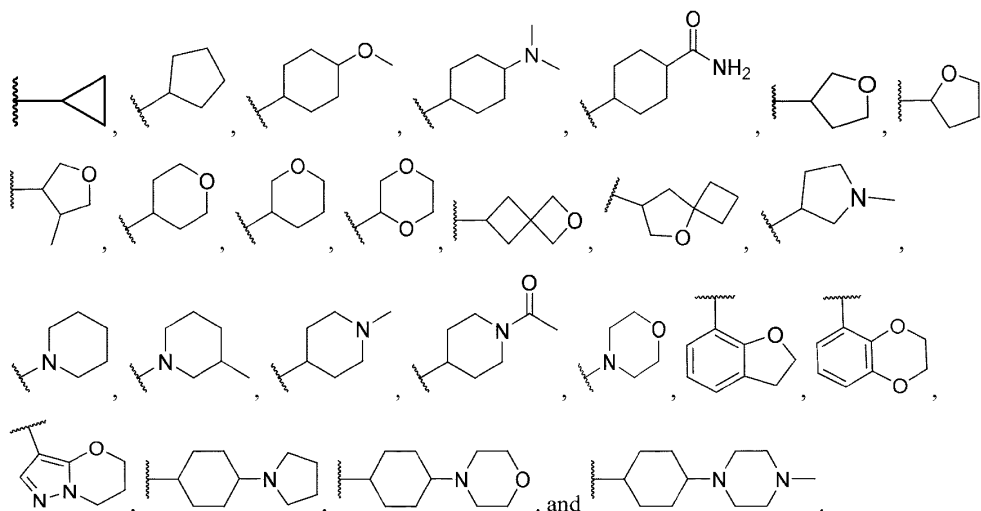
[0206] In some embodiments, R^7 is heterocyclyl optionally substituted with one to three Z^1 . In some embodiments, R^7 is a 5-6 membered heterocyclyl optionally substituted with C_{1-6} alkyl or $-C(O)R^{11}$. In some embodiments, R^7 is a 5-6 membered heterocyclyl substituted with methyl. In some embodiments, R^7 is a 5-6 membered heterocyclyl substituted with $-C(O)CH_3$.

[0207] In some embodiments, R^7 is a spirocyclic heterocyclyl optionally substituted with one to three Z^1 . In some embodiments, R^7 is unsubstituted spirocyclic heterocyclyl.

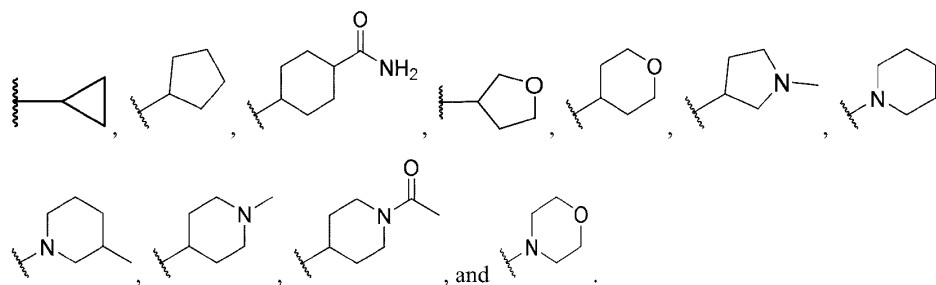
[0208] In some embodiments, R^7 is cyclopropyl, cyclopentyl, cyclohexyl, tetrahydrofuranyl, tetrahydropyranyl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzo[b][1,4]dioxinyl, pyrrolidinyl, piperidinyl, or morpholino, wherein each R^7 is optionally substituted with one to three Z^1 .

[0209] In some embodiments, R^7 is cyclopropyl, cyclopentyl, cyclohexyl, tetrahydrofuranyl, tetrahydropyranyl, pyrrolidinyl, piperidinyl, or morpholino, wherein each R^7 is optionally substituted with methyl, $-C(O)CH_3$, or $-C(O)NH_2$.

[0210] In some embodiments, R^7 is selected from:



[0211] In some embodiments, R^7 is selected from:



[0212] In some embodiments, R⁷ is phenyl or 5-6 membered heteroaryl, wherein each phenyl or 5-6 membered heteroaryl is independently optionally substituted with one to three Z¹.

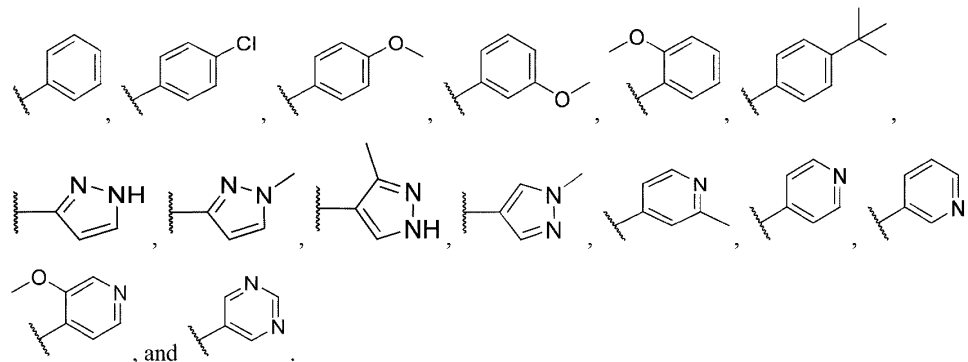
[0213] In some embodiments, R⁷ is phenyl optionally substituted with one to three Z¹. In some embodiments, R⁷ is phenyl optionally substituted with halo, C₁₋₆ alkyl, or -OR¹¹. In some embodiments, R⁷ is phenyl optionally substituted with fluoro. In some embodiments, R⁷ is phenyl optionally substituted with chloro. In some embodiments, R⁷ is phenyl optionally substituted with bromo. In some embodiments, R⁷ is phenyl optionally substituted with cyano. In some embodiments, R⁷ is phenyl optionally substituted with -OCH₃. In some embodiments, R⁷ is phenyl optionally substituted with C₁₋₃ alkyl. In some embodiments, R⁷ is phenyl optionally substituted with *tert*-butyl.

[0214] In some embodiments, R⁷ is a 5-6 membered heteroaryl optionally substituted with one to three Z¹. In some embodiments, R⁷ is a 5-membered heteroaryl optionally substituted with C₁₋₆ alkyl. In some embodiments, R⁷ is a 5-membered heteroaryl containing one or two nitrogen atoms and optionally substituted with methyl. In some embodiments, R⁷ is pyrazolyl. In some embodiments, R⁷ is 1-methylpyrazolyl. In some embodiments, R⁷ is 3-methylpyrazolyl. In some embodiments, R⁷ is a 6-membered heteroaryl optionally substituted with one to three Z¹. In some embodiments, R⁷ is a 6-membered unsubstituted heteroaryl containing one or two nitrogen atoms. In some embodiments, R⁷ is pyridinyl. In some embodiments, R⁷ is pyrimidinyl.

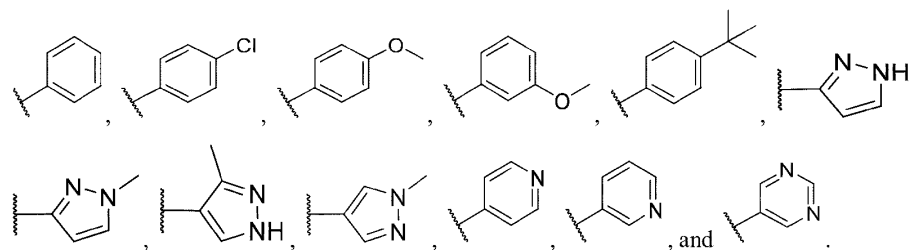
[0215] In some embodiments, R^7 is phenyl or 5-6 membered heteroaryl, wherein each phenyl or 5-6 membered heteroaryl is independently optionally substituted with halo, C_{1-6} alkyl, or $-OR^{11}$.

[0216] In some embodiments, R^7 is phenyl, pyridinyl, pyrazolyl, or pyrimidinyl, wherein each R^7 is optionally substituted with chloro, methyl, *tert*-butyl, or $-OCH_3$.

[0217] In some embodiments, R^7 is selected from:



[0218] In some embodiments, R^7 is selected from:

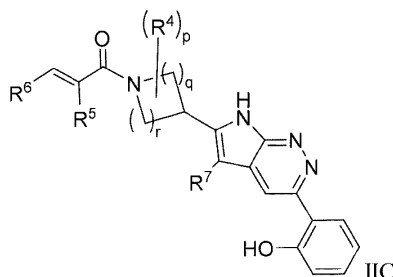


[0219] In some embodiments, R^7 is halo, $-C(O)CH_3$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with one to three Z^1 .

[0220] In some embodiments, R^7 is halo, $-C(O)CH_3$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with halo, cyano, C_{1-6} alkyl, $-OH$, $-OCH_3$, $-OCH_2CH_3$, $-C(O)NH_2$, $-C(O)CH_3$, $-N(CH_3)_2$, cyclopropyl, morpholino, or phenyl.

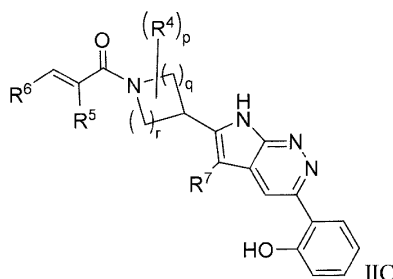
[0221] In some embodiments, each Z^1 is independently deuterium, halo, cyano, $-NO_2$, $-SF_5$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, heteroaryl, $-N(R^{11})_2$, $-OR^{11}$, $-P(O)(OR^{11})_2$, $-C(O)R^{11}$, $-C(O)OR^{11}$, $-S(O)_{0-2}R^{11}$, $-NR^{11}S(O)_{0-2}R^{11}$, $-S(O)_{0-2}N(R^{11})_2$, $-NR^{11}S(O)_{0-2}N(R^{11})_2$, $-NR^{11}C(O)N(R^{11})_2$, $-C(O)N(R^{11})_2$, $-NR^{11}C(O)R^{11}$, $-OC(O)N(R^{11})_2$, or $-NR^{11}C(O)OR^{11}$; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1a} ;

[0222] In some embodiments, provided herein is a compound of Formula IIC:



or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein q and r are each independently 0, 1, 2, 3, or 4; provided that the sum of q and r is at least 2.

[0223] In some embodiments, provided herein is a compound of Formula IIC:



or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein:

p is 0, 1, or 2;

q and r are each independently 0, 1, 2, 3, or 4; provided that the sum of q and r is at least 2;

each R⁴ is independently oxo, halo, cyano, -NO₂, -SF₅, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, -C(O)R¹¹, -C(O)OR¹¹, -S(O)₀₋₂R¹¹, -NR¹¹S(O)₀₋₂R¹¹, -S(O)₀₋₂N(R¹¹)₂, -NR¹¹S(O)₀₋₂N(R¹¹)₂, -NR¹¹C(O)N(R¹¹)₂, -C(O)N(R¹¹)₂, -NR¹¹C(O)R¹¹, -OC(O)N(R¹¹)₂, or -NR¹¹C(O)OR¹¹; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z¹;

R⁵ is hydrogen, halo, cyano, or C₁₋₆ alkyl optionally substituted with one to three Z¹;

R⁶ is hydrogen, halo, cyano, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, -C(O)R¹¹, -C(O)OR¹¹, -S(O)₀₋₂R¹¹, -NR¹¹S(O)₀₋₂R¹¹, -S(O)₀₋₂N(R¹¹)₂, -NR¹¹S(O)₀₋₂N(R¹¹)₂, -NR¹¹C(O)N(R¹¹)₂, -C(O)N(R¹¹)₂, -NR¹¹C(O)R¹¹, -OC(O)N(R¹¹)₂, or -NR¹¹C(O)OR¹¹; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z¹;

R⁷ is hydrogen, halo, cyano, -NO₂, -SF₅, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, -C(O)R¹¹, -C(O)OR¹¹, -S(O)₀₋₂R¹¹, -NR¹¹S(O)₀₋₂R¹¹, -S(O)₀₋₂N(R¹¹)₂, -NR¹¹S(O)₀₋₂N(R¹¹)₂, -NR¹¹C(O)N(R¹¹)₂, -C(O)N(R¹¹)₂, -NR¹¹C(O)R¹¹, -OC(O)N(R¹¹)₂, or -NR¹¹C(O)OR¹¹; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z¹;

each Z^1 is independently halo, cyano, $-\text{NO}_2$, $-\text{SF}_5$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, heteroaryl, $-\text{N}(\text{R}^{11})_2$, $-\text{OR}^{11}$, $-\text{P}(\text{O})(\text{OR}^{11})_2$, $-\text{C}(\text{O})\text{R}^{11}$, $-\text{C}(\text{O})\text{OR}^{11}$, $-\text{S}(\text{O})_{0-2}\text{R}^{11}$, $-\text{NR}^{11}\text{S}(\text{O})_{0-2}\text{R}^{11}$, $-\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{C}(\text{O})\text{N}(\text{R}^{11})_2$, $-\text{C}(\text{O})\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{C}(\text{O})\text{R}^{11}$, $-\text{OC}(\text{O})\text{N}(\text{R}^{11})_2$, or $-\text{NR}^{11}\text{C}(\text{O})\text{OR}^{11}$; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1a} ;

each R^{11} is independently hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1a} ;

each Z^{1a} is independently hydroxy, halo, cyano, $-\text{NO}_2$, $-\text{SF}_5$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, heteroaryl, $-\text{N}(\text{R}^{13})_2$, $-\text{OR}^{13}$, $-\text{P}(\text{O})(\text{OR}^{13})_2$, $-\text{C}(\text{O})\text{R}^{13}$, $-\text{C}(\text{O})\text{OR}^{13}$, $-\text{S}(\text{O})_{0-2}\text{R}^{13}$, $-\text{NR}^{13}\text{S}(\text{O})_{0-2}\text{R}^{13}$, $-\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{13})_2$, $-\text{NR}^{13}\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{13})_2$, $-\text{NR}^{13}\text{C}(\text{O})\text{N}(\text{R}^{13})_2$, $-\text{C}(\text{O})\text{N}(\text{R}^{13})_2$, $-\text{NR}^{13}\text{C}(\text{O})\text{R}^{13}$, $-\text{OC}(\text{O})\text{N}(\text{R}^{13})_2$, or $-\text{NR}^{13}\text{C}(\text{O})\text{OR}^{13}$; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1b} ;

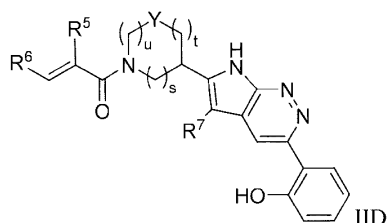
each R^{13} is independently hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1b} ;

each Z^{1b} is independently halo, cyano, hydroxy, $-\text{SH}$, $-\text{NH}_2$, $-\text{NO}_2$, $-\text{SF}_5$, $-\text{P}(\text{O})(\text{OH})_2$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, heteroaryl, $-\text{L}-\text{C}_{1-6}$ alkyl, $-\text{L}-\text{C}_{2-6}$ alkenyl, $-\text{L}-\text{C}_{2-6}$ alkynyl, $-\text{L}-\text{C}_{1-6}$ haloalkyl, $-\text{L}-\text{C}_{3-10}$ cycloalkyl, $-\text{L}-\text{heterocyclyl}$, $-\text{L}-\text{aryl}$, or $-\text{L}-\text{heteroaryl}$; and

each L is independently $-\text{O}-$, $-\text{NH}-$, $-\text{S}-$, $-\text{S}(\text{O})-$, $-\text{S}(\text{O})_2-$, $-\text{N}(\text{C}_{1-6} \text{ alkyl})-$, $-\text{N}(\text{C}_{2-6} \text{ alkenyl})-$, $-\text{N}(\text{C}_{2-6} \text{ alkynyl})-$, $-\text{N}(\text{C}_{1-6} \text{ haloalkyl})-$, $-\text{N}(\text{C}_{3-10} \text{ cycloalkyl})-$, $-\text{N}(\text{heterocyclyl})-$, $-\text{N}(\text{aryl})-$, $-\text{N}(\text{heteroaryl})-$, $-\text{C}(\text{O})-$, $-\text{C}(\text{O})\text{O}-$, $-\text{C}(\text{O})\text{NH}-$, $-\text{C}(\text{O})\text{N}(\text{C}_{1-6} \text{ alkyl})-$, $-\text{C}(\text{O})\text{N}(\text{C}_{2-6} \text{ alkenyl})-$, $-\text{C}(\text{O})\text{N}(\text{C}_{2-6} \text{ alkynyl})-$, $-\text{C}(\text{O})\text{N}(\text{C}_{1-6} \text{ haloalkyl})-$, $-\text{C}(\text{O})\text{N}(\text{C}_{3-10} \text{ cycloalkyl})-$, $-\text{C}(\text{O})\text{N}(\text{heterocyclyl})-$, $-\text{C}(\text{O})\text{N}(\text{aryl})-$, $-\text{C}(\text{O})\text{N}(\text{heteroaryl})-$, $-\text{NHC}(\text{O})-$, $-\text{NHC}(\text{O})\text{O}-$, $-\text{NHC}(\text{O})\text{NH}-$, $-\text{NHS}(\text{O})-$, $-\text{S}(\text{O})_2\text{NH}-$, $-\text{P}(\text{O})(\text{OH})\text{O}-$, $-\text{P}(\text{O})(\text{O}-\text{C}_{1-6} \text{ alkyl})\text{O}-$, $-\text{P}(\text{O})(\text{O}-\text{C}_{2-6} \text{ alkenyl})\text{O}-$, $-\text{P}(\text{O})(\text{O}-\text{C}_{2-6} \text{ alkynyl})\text{O}-$, $-\text{P}(\text{O})(\text{OC}_{1-6} \text{ haloalkyl})\text{O}-$, $-\text{P}(\text{O})(\text{OC}_{3-10} \text{ cycloalkyl})\text{O}-$, $-\text{P}(\text{O})(\text{O}-\text{heterocyclyl})\text{O}-$, $-\text{P}(\text{O})(\text{O}-\text{aryl})\text{O}-$, or $-\text{P}(\text{O})(\text{O}-\text{heteroaryl})\text{O}-$;

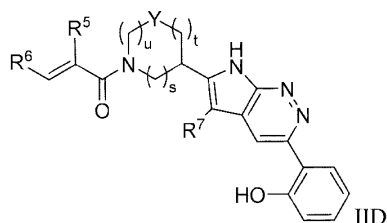
wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, and heteroaryl of Z^{1b} and L is further independently optionally substituted with one to five hydroxy, halo, cyano, hydroxy, $-\text{SH}$, $-\text{NH}_2$, $-\text{NO}_2$, $-\text{SF}_5$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl.

[0224] In some embodiments, provided herein is a compound of Formula IID:



or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein Y is O or N; s and t are each independently 0, 1, 2, or 3; and u is 1, 2, 3, or 4; provided that the sum of s, t, and u is not greater than 7.

[0225] In some embodiments, provided herein is a compound of Formula IID:



or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein:

Y is O or N;

s and t are each independently 0, 1, 2, or 3;

u is 1, 2, 3, or 4; provided that the sum of s, t, and u is not greater than 7;

R⁵ is hydrogen, halo, cyano, or C₁₋₆ alkyl optionally substituted with one to three Z¹;

R⁶ is hydrogen, halo, cyano, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, -C(O)R¹¹, -C(O)OR¹¹, -S(O)₀₋₂R¹¹, -NR¹¹S(O)₀₋₂R¹¹, -S(O)₀₋₂N(R¹¹)₂, -NR¹¹S(O)₀₋₂N(R¹¹)₂, -NR¹¹C(O)N(R¹¹)₂, -C(O)N(R¹¹)₂, -NR¹¹C(O)R¹¹, -OC(O)N(R¹¹)₂, or -NR¹¹C(O)OR¹¹; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z¹;

R⁷ is hydrogen, halo, cyano, -NO₂, -SF₅, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, -C(O)R¹¹, -C(O)OR¹¹, -S(O)₀₋₂R¹¹, -NR¹¹S(O)₀₋₂R¹¹, -S(O)₀₋₂N(R¹¹)₂, -NR¹¹S(O)₀₋₂N(R¹¹)₂, -NR¹¹C(O)N(R¹¹)₂, -C(O)N(R¹¹)₂, -NR¹¹C(O)R¹¹, -OC(O)N(R¹¹)₂, or -NR¹¹C(O)OR¹¹; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z¹;

each Z¹ is independently halo, cyano, -NO₂, -SF₅, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, -P(O)(OR¹¹)₂, -C(O)R¹¹, -C(O)OR¹¹, -S(O)₀₋₂R¹¹, -NR¹¹S(O)₀₋₂R¹¹, -S(O)₀₋₂N(R¹¹)₂, -NR¹¹S(O)₀₋₂N(R¹¹)₂, -NR¹¹C(O)N(R¹¹)₂, -C(O)N(R¹¹)₂, -NR¹¹C(O)R¹¹, -OC(O)N(R¹¹)₂, or -NR¹¹C(O)OR¹¹; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1a};

each R^{11} is independently hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1a} ;

each Z^{1a} is independently hydroxy, halo, cyano, $-NO_2$, $-SF_5$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, heteroaryl, $-N(R^{13})_2$, $-OR^{13}$, $-P(O)(OR^{13})_2$, $-C(O)R^{13}$, $-C(O)OR^{13}$, $-S(O)_{0-2}R^{13}$, $-NR^{13}S(O)_{0-2}R^{13}$, $-S(O)_{0-2}N(R^{13})_2$, $-NR^{13}S(O)_{0-2}N(R^{13})_2$, $-NR^{13}C(O)N(R^{13})_2$, $-C(O)N(R^{13})_2$, $-NR^{13}C(O)R^{13}$, $-OC(O)N(R^{13})_2$, or $-NR^{13}C(O)OR^{13}$; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1b} ;

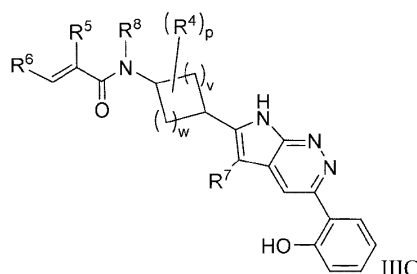
each R^{13} is independently hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1b} ;

each Z^{1b} is independently halo, cyano, hydroxy, $-SH$, $-NH_2$, $-NO_2$, $-SF_5$, $-P(O)(OH)_2$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, heteroaryl, $-L-C_{1-6}$ alkyl, $-L-C_{2-6}$ alkenyl, $-L-C_{2-6}$ alkynyl, $-L-C_{1-6}$ haloalkyl, $-L-C_{3-10}$ cycloalkyl, $-L$ -heterocyclyl, $-L$ -aryl, or $-L$ -heteroaryl; and

each L is independently $-O-$, $-NH-$, $-S-$, $-S(O)-$, $-S(O)_2-$, $-N(C_{1-6} \text{ alkyl})-$, $-N(C_{2-6} \text{ alkenyl})-$, $-N(C_{2-6} \text{ alkynyl})-$, $-N(C_{1-6} \text{ haloalkyl})-$, $-N(C_{3-10} \text{ cycloalkyl})-$, $-N(\text{heterocyclyl})-$, $-N(\text{aryl})-$, $-N(\text{heteroaryl})-$, $-C(O)-$, $-C(O)O-$, $-C(O)NH-$, $-C(O)N(C_{1-6} \text{ alkyl})-$, $-C(O)N(C_{2-6} \text{ alkenyl})-$, $-C(O)N(C_{2-6} \text{ alkynyl})-$, $-C(O)N(C_{1-6} \text{ haloalkyl})-$, $-C(O)N(C_{3-10} \text{ cycloalkyl})-$, $-C(O)N(\text{heterocyclyl})-$, $-C(O)N(\text{aryl})-$, $-C(O)N(\text{heteroaryl})-$, $-NHC(O)-$, $-NHC(O)O-$, $-NHC(O)NH-$, $-NHS(O)-$, $-S(O)_2NH-$, $-P(O)(OH)O-$, $-P(O)(O-C_{1-6} \text{ alkyl})O-$, $-P(O)(O-C_{2-6} \text{ alkenyl})O-$, $-P(O)(O-C_{2-6} \text{ alkynyl})O-$, $-P(O)(OC_{1-6} \text{ haloalkyl})O-$, $-P(O)(OC_{3-10} \text{ cycloalkyl})O-$, $-P(O)(O-\text{heterocyclyl})O-$, $-P(O)(O-\text{aryl})O-$, or $-P(O)(O-\text{heteroaryl})O-$;

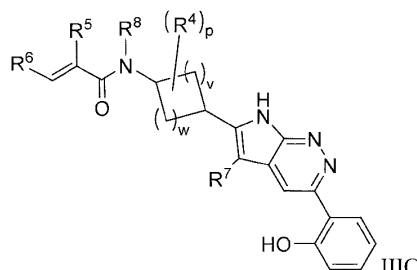
wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, and heteroaryl of Z^{1b} and L is further independently optionally substituted with one to five hydroxy, halo, cyano, hydroxy, $-SH$, $-NH_2$, $-NO_2$, $-SF_5$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl.

[0226] In some embodiments, provided herein is a compound of Formula IIIC:



or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein v and w are each independently 0, 1, 2, 3, or 4; provided that the sum of v and w is at least 1.

[0227] In some embodiments, provided herein is a compound of Formula IIIC:



or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein:

p is 0, 1, or 2;

v and w are each independently 0, 1, 2, 3, or 4; provided that the sum of v and w is at least 1;

each R⁴ is independently oxo, halo, cyano, -NO₂, -SF₅, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, -C(O)R¹¹, -C(O)OR¹¹, -S(O)₀₋₂R¹¹, -NR¹¹S(O)₀₋₂R¹¹, -S(O)₀₋₂N(R¹¹)₂, -NR¹¹S(O)₀₋₂N(R¹¹)₂, -NR¹¹C(O)N(R¹¹)₂, -C(O)N(R¹¹)₂, -NR¹¹C(O)R¹¹, -OC(O)N(R¹¹)₂, or -NR¹¹C(O)OR¹¹; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z¹;

R⁵ is hydrogen, halo, cyano, or C₁₋₆ alkyl optionally substituted with one to three Z¹;

R⁶ is hydrogen, halo, cyano, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, -C(O)R¹¹, -C(O)OR¹¹, -S(O)₀₋₂R¹¹, -NR¹¹S(O)₀₋₂R¹¹, -S(O)₀₋₂N(R¹¹)₂, -NR¹¹S(O)₀₋₂N(R¹¹)₂, -NR¹¹C(O)N(R¹¹)₂, -C(O)N(R¹¹)₂, -NR¹¹C(O)R¹¹, -OC(O)N(R¹¹)₂, or -NR¹¹C(O)OR¹¹; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z¹;

R⁷ is hydrogen, halo, cyano, -NO₂, -SF₅, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, -C(O)R¹¹, -C(O)OR¹¹, -S(O)₀₋₂R¹¹, -NR¹¹S(O)₀₋₂R¹¹, -S(O)₀₋₂N(R¹¹)₂, -NR¹¹S(O)₀₋₂N(R¹¹)₂, -NR¹¹C(O)N(R¹¹)₂, -C(O)N(R¹¹)₂, -NR¹¹C(O)R¹¹, -OC(O)N(R¹¹)₂, or -NR¹¹C(O)OR¹¹; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z¹;

R⁸ is hydrogen or C₁₋₆ alkyl optionally substituted with one to three Z¹;

each Z¹ is independently halo, cyano, -NO₂, -SF₅, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, -P(O)(OR¹¹)₂, -C(O)R¹¹, -C(O)OR¹¹, -S(O)₀₋₂R¹¹, -NR¹¹S(O)₀₋₂R¹¹, -S(O)₀₋₂N(R¹¹)₂, -NR¹¹S(O)₀₋₂N(R¹¹)₂, -NR¹¹C(O)N(R¹¹)₂, -C(O)N(R¹¹)₂, -NR¹¹C(O)R¹¹, -OC(O)N(R¹¹)₂, or -NR¹¹C(O)OR¹¹; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1a};

each R^{11} is independently hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1a} ;

each Z^{1a} is independently hydroxy, halo, cyano, $-NO_2$, $-SF_5$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, heteroaryl, $-N(R^{13})_2$, $-OR^{13}$, $-P(O)(OR^{13})_2$, $-C(O)R^{13}$, $-C(O)OR^{13}$, $-S(O)_{0-2}R^{13}$, $-NR^{13}S(O)_{0-2}R^{13}$, $-S(O)_{0-2}N(R^{13})_2$, $-NR^{13}S(O)_{0-2}N(R^{13})_2$, $-NR^{13}C(O)N(R^{13})_2$, $-C(O)N(R^{13})_2$, $-NR^{13}C(O)R^{13}$, $-OC(O)N(R^{13})_2$, or $-NR^{13}C(O)OR^{13}$; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1b} ;

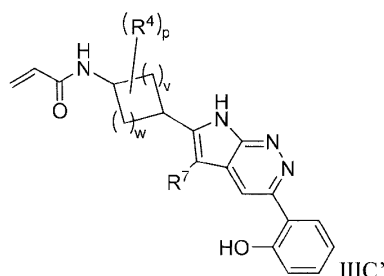
each R^{13} is independently hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1b} ;

each Z^{1b} is independently halo, cyano, hydroxy, $-SH$, $-NH_2$, $-NO_2$, $-SF_5$, $-P(O)(OH)_2$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, heteroaryl, $-L-C_{1-6}$ alkyl, $-L-C_{2-6}$ alkenyl, $-L-C_{2-6}$ alkynyl, $-L-C_{1-6}$ haloalkyl, $-L-C_{3-10}$ cycloalkyl, $-L$ -heterocyclyl, $-L$ -aryl, or $-L$ -heteroaryl; and

each L is independently $-O-$, $-NH-$, $-S-$, $-S(O)-$, $-S(O)_2-$, $-N(C_{1-6} \text{ alkyl})-$, $-N(C_{2-6} \text{ alkenyl})-$, $-N(C_{2-6} \text{ alkynyl})-$, $-N(C_{1-6} \text{ haloalkyl})-$, $-N(C_{3-10} \text{ cycloalkyl})-$, $-N(\text{heterocyclyl})-$, $-N(\text{aryl})-$, $-N(\text{heteroaryl})-$, $-C(O)-$, $-C(O)O-$, $-C(O)NH-$, $-C(O)N(C_{1-6} \text{ alkyl})-$, $-C(O)N(C_{2-6} \text{ alkenyl})-$, $-C(O)N(C_{2-6} \text{ alkynyl})-$, $-C(O)N(C_{1-6} \text{ haloalkyl})-$, $-C(O)N(C_{3-10} \text{ cycloalkyl})-$, $-C(O)N(\text{heterocyclyl})-$, $-C(O)N(\text{aryl})-$, $-C(O)N(\text{heteroaryl})-$, $-NHC(O)-$, $-NHC(O)O-$, $-NHC(O)NH-$, $-NHS(O)-$, $-S(O)_2NH-$, $-P(O)(OH)O-$, $-P(O)(O-C_{1-6} \text{ alkyl})O-$, $-P(O)(O-C_{2-6} \text{ alkenyl})O-$, $-P(O)(O-C_{2-6} \text{ alkynyl})O-$, $-P(O)(OC_{1-6} \text{ haloalkyl})O-$, $-P(O)(OC_{3-10} \text{ cycloalkyl})O-$, $-P(O)(O-\text{heterocyclyl})O-$, $-P(O)(O-\text{aryl})O-$, or $-P(O)(O-\text{heteroaryl})O-$;

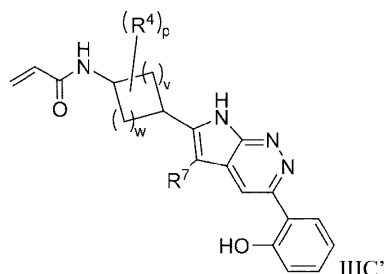
wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, and heteroaryl of Z^{1b} and L is further independently optionally substituted with one to five hydroxy, halo, cyano, hydroxy, $-SH$, $-NH_2$, $-NO_2$, $-SF_5$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl.

[0228] In some embodiments, provided herein is a compound of Formula IIIC':



or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein v and w are each independently 0, 1, 2, 3, or 4; provided that the sum of v and w is at least 1.

[0229] In some embodiments, provided herein is a compound of Formula IIIC':



or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein:

v and w are each independently 0, 1, 2, 3, or 4; provided that the sum of v and w is at least 1;
p is 0, 1, or 2;

each R⁴ is independently oxo, halo, cyano, -NO₂, -SF₅, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, -C(O)R¹¹, -C(O)OR¹¹, -S(O)₀₋₂R¹¹, -NR¹¹S(O)₀₋₂R¹¹, -S(O)₀₋₂N(R¹¹)₂, -NR¹¹S(O)₀₋₂N(R¹¹)₂, -NR¹¹C(O)N(R¹¹)₂, -C(O)N(R¹¹)₂, -NR¹¹C(O)R¹¹, -OC(O)N(R¹¹)₂, or -NR¹¹C(O)OR¹¹; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z¹;

R⁷ is hydrogen, halo, cyano, -NO₂, -SF₅, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, -C(O)R¹¹, -C(O)OR¹¹, -S(O)₀₋₂R¹¹, -NR¹¹S(O)₀₋₂R¹¹, -S(O)₀₋₂N(R¹¹)₂, -NR¹¹S(O)₀₋₂N(R¹¹)₂, -NR¹¹C(O)N(R¹¹)₂, -C(O)N(R¹¹)₂, -NR¹¹C(O)R¹¹, -OC(O)N(R¹¹)₂, or -NR¹¹C(O)OR¹¹; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z¹;

each Z¹ is independently halo, cyano, -NO₂, -SF₅, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, -P(O)(OR¹¹)₂, -C(O)R¹¹, -C(O)OR¹¹, -S(O)₀₋₂R¹¹, -NR¹¹S(O)₀₋₂R¹¹, -S(O)₀₋₂N(R¹¹)₂, -NR¹¹S(O)₀₋₂N(R¹¹)₂, -NR¹¹C(O)N(R¹¹)₂, -C(O)N(R¹¹)₂, -NR¹¹C(O)R¹¹, -OC(O)N(R¹¹)₂, or -NR¹¹C(O)OR¹¹; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1a};

each R¹¹ is independently hydrogen, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1a};

each Z^{1a} is independently hydroxy, halo, cyano, -NO₂, -SF₅, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹³)₂, -OR¹³, -P(O)(OR¹³)₂, -C(O)R¹³, -C(O)OR¹³, -S(O)₀₋₂R¹³, -NR¹³S(O)₀₋₂R¹³, -S(O)₀₋₂N(R¹³)₂, -NR¹³S(O)₀₋₂N(R¹³)₂, -NR¹³C(O)N(R¹³)₂, -C(O)N(R¹³)₂,

$-\text{NR}^{13}\text{C}(\text{O})\text{R}^{13}$, $-\text{OC}(\text{O})\text{N}(\text{R}^{13})_2$, or $-\text{NR}^{13}\text{C}(\text{O})\text{OR}^{13}$; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1b} ;

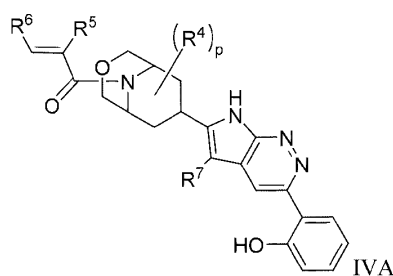
each R^{13} is independently hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1b} ;

each Z^{1b} is independently halo, cyano, hydroxy, $-\text{SH}$, $-\text{NH}_2$, $-\text{NO}_2$, $-\text{SF}_5$, $-\text{P}(\text{O})(\text{OH})_2$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, heteroaryl, $-\text{L}-\text{C}_{1-6}$ alkyl, $-\text{L}-\text{C}_{2-6}$ alkenyl, $-\text{L}-\text{C}_{2-6}$ alkynyl, $-\text{L}-\text{C}_{1-6}$ haloalkyl, $-\text{L}-\text{C}_{3-10}$ cycloalkyl, $-\text{L}-\text{heterocyclyl}$, $-\text{L}-\text{aryl}$, or $-\text{L}-\text{heteroaryl}$; and

each L is independently $-\text{O}-$, $-\text{NH}-$, $-\text{S}-$, $-\text{S}(\text{O})-$, $-\text{S}(\text{O})_2-$, $-\text{N}(\text{C}_{1-6} \text{ alkyl})-$, $-\text{N}(\text{C}_{2-6} \text{ alkenyl})-$, $-\text{N}(\text{C}_{2-6} \text{ alkynyl})-$, $-\text{N}(\text{C}_{1-6} \text{ haloalkyl})-$, $-\text{N}(\text{C}_{3-10} \text{ cycloalkyl})-$, $-\text{N}(\text{heterocyclyl})-$, $-\text{N}(\text{aryl})-$, $-\text{N}(\text{heteroaryl})-$, $-\text{C}(\text{O})-$, $-\text{C}(\text{O})\text{O}-$, $-\text{C}(\text{O})\text{NH}-$, $-\text{C}(\text{O})\text{N}(\text{C}_{1-6} \text{ alkyl})-$, $-\text{C}(\text{O})\text{N}(\text{C}_{2-6} \text{ alkenyl})-$, $-\text{C}(\text{O})\text{N}(\text{C}_{2-6} \text{ alkynyl})-$, $-\text{C}(\text{O})\text{N}(\text{C}_{1-6} \text{ haloalkyl})-$, $-\text{C}(\text{O})\text{N}(\text{C}_{3-10} \text{ cycloalkyl})-$, $-\text{C}(\text{O})\text{N}(\text{heterocyclyl})-$, $-\text{C}(\text{O})\text{N}(\text{aryl})-$, $-\text{C}(\text{O})\text{N}(\text{heteroaryl})-$, $-\text{NHC}(\text{O})-$, $-\text{NHC}(\text{O})\text{O}-$, $-\text{NHC}(\text{O})\text{NH}-$, $-\text{NHS}(\text{O})-$, $-\text{S}(\text{O})_2\text{NH}-$, $-\text{P}(\text{O})(\text{OH})\text{O}-$, $-\text{P}(\text{O})(\text{O}-\text{C}_{1-6} \text{ alkyl})\text{O}-$, $-\text{P}(\text{O})(\text{O}-\text{C}_{2-6} \text{ alkenyl})\text{O}-$, $-\text{P}(\text{O})(\text{O}-\text{C}_{2-6} \text{ alkynyl})\text{O}-$, $-\text{P}(\text{O})(\text{OC}_{1-6} \text{ haloalkyl})\text{O}-$, $-\text{P}(\text{O})(\text{OC}_{3-10} \text{ cycloalkyl})\text{O}-$, $-\text{P}(\text{O})(\text{O}-\text{heterocyclyl})\text{O}-$, $-\text{P}(\text{O})(\text{O}-\text{aryl})\text{O}-$, or $-\text{P}(\text{O})(\text{O}-\text{heteroaryl})\text{O}-$;

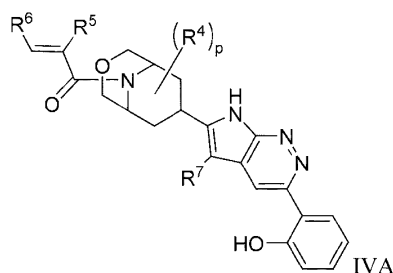
wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, and heteroaryl of Z^{1b} and L is further independently optionally substituted with one to five hydroxy, halo, cyano, hydroxy, $-\text{SH}$, $-\text{NH}_2$, $-\text{NO}_2$, $-\text{SF}_5$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl.

[0230] In some embodiments, provided herein is a compound of Formula IVA:



or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof.

[0231] In some embodiments, provided herein is a compound of Formula IVA:



or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof; wherein:

p is 0, 1, or 2;

each R^4 is independently oxo, halo, cyano, $-\text{NO}_2$, $-\text{SF}_5$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, heteroaryl, $-\text{N}(\text{R}^{11})_2$, $-\text{OR}^{11}$, $-\text{C}(\text{O})\text{R}^{11}$, $-\text{C}(\text{O})\text{OR}^{11}$, $-\text{S}(\text{O})_{0-2}\text{R}^{11}$, $-\text{NR}^{11}\text{S}(\text{O})_{0-2}\text{R}^{11}$, $-\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{C}(\text{O})\text{N}(\text{R}^{11})_2$, $-\text{C}(\text{O})\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{C}(\text{O})\text{R}^{11}$, $-\text{OC}(\text{O})\text{N}(\text{R}^{11})_2$, or $-\text{NR}^{11}\text{C}(\text{O})\text{OR}^{11}$; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z^1 ;

R^5 is hydrogen, halo, cyano, or C_{1-6} alkyl optionally substituted with one to three Z^1 ;

R^6 is hydrogen, halo, cyano, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, heteroaryl, $-\text{N}(\text{R}^{11})_2$, $-\text{OR}^{11}$, $-\text{C}(\text{O})\text{R}^{11}$, $-\text{C}(\text{O})\text{OR}^{11}$, $-\text{S}(\text{O})_{0-2}\text{R}^{11}$, $-\text{NR}^{11}\text{S}(\text{O})_{0-2}\text{R}^{11}$, $-\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{C}(\text{O})\text{N}(\text{R}^{11})_2$, $-\text{C}(\text{O})\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{C}(\text{O})\text{R}^{11}$, $-\text{OC}(\text{O})\text{N}(\text{R}^{11})_2$, or $-\text{NR}^{11}\text{C}(\text{O})\text{OR}^{11}$; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z^1 ;

R^7 is hydrogen, halo, cyano, $-\text{NO}_2$, $-\text{SF}_5$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, heteroaryl, $-\text{N}(\text{R}^{11})_2$, $-\text{OR}^{11}$, $-\text{C}(\text{O})\text{R}^{11}$, $-\text{C}(\text{O})\text{OR}^{11}$, $-\text{S}(\text{O})_{0-2}\text{R}^{11}$, $-\text{NR}^{11}\text{S}(\text{O})_{0-2}\text{R}^{11}$, $-\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{C}(\text{O})\text{N}(\text{R}^{11})_2$, $-\text{C}(\text{O})\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{C}(\text{O})\text{R}^{11}$, $-\text{OC}(\text{O})\text{N}(\text{R}^{11})_2$, or $-\text{NR}^{11}\text{C}(\text{O})\text{OR}^{11}$; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z^1 ;

each Z^1 is independently halo, cyano, $-\text{NO}_2$, $-\text{SF}_5$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, heteroaryl, $-\text{N}(\text{R}^{11})_2$, $-\text{OR}^{11}$, $-\text{P}(\text{O})(\text{OR}^{11})_2$, $-\text{C}(\text{O})\text{R}^{11}$, $-\text{C}(\text{O})\text{OR}^{11}$, $-\text{S}(\text{O})_{0-2}\text{R}^{11}$, $-\text{NR}^{11}\text{S}(\text{O})_{0-2}\text{R}^{11}$, $-\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{C}(\text{O})\text{N}(\text{R}^{11})_2$, $-\text{C}(\text{O})\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{C}(\text{O})\text{R}^{11}$, $-\text{OC}(\text{O})\text{N}(\text{R}^{11})_2$, or $-\text{NR}^{11}\text{C}(\text{O})\text{OR}^{11}$; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1a} ;

each R^{11} is independently hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1a} ;

each Z^{1a} is independently hydroxy, halo, cyano, $-\text{NO}_2$, $-\text{SF}_5$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, heteroaryl, $-\text{N}(\text{R}^{13})_2$, $-\text{OR}^{13}$, $-\text{P}(\text{O})(\text{OR}^{13})_2$, $-\text{C}(\text{O})\text{R}^{13}$, $-\text{C}(\text{O})\text{OR}^{13}$,

$-\text{S}(\text{O})_{0-2}\text{R}^{13}$, $-\text{NR}^{13}\text{S}(\text{O})_{0-2}\text{R}^{13}$, $-\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{13})_2$, $-\text{NR}^{13}\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{13})_2$, $-\text{NR}^{13}\text{C}(\text{O})\text{N}(\text{R}^{13})_2$, $-\text{C}(\text{O})\text{N}(\text{R}^{13})_2$, $-\text{NR}^{13}\text{C}(\text{O})\text{R}^{13}$, $-\text{OC}(\text{O})\text{N}(\text{R}^{13})_2$, or $-\text{NR}^{13}\text{C}(\text{O})\text{OR}^{13}$; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1b} ;

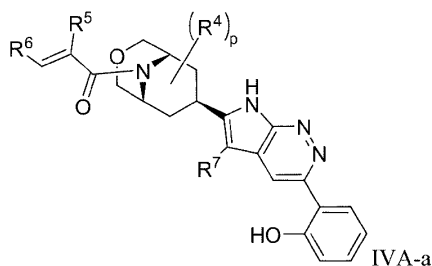
each R^{13} is independently hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1b} ;

each Z^{1b} is independently halo, cyano, hydroxy, $-\text{SH}$, $-\text{NH}_2$, $-\text{NO}_2$, $-\text{SF}_5$, $-\text{P}(\text{O})(\text{OH})_2$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, heteroaryl, $-\text{L}-\text{C}_{1-6}$ alkyl, $-\text{L}-\text{C}_{2-6}$ alkenyl, $-\text{L}-\text{C}_{2-6}$ alkynyl, $-\text{L}-\text{C}_{1-6}$ haloalkyl, $-\text{L}-\text{C}_{3-10}$ cycloalkyl, $-\text{L}-\text{heterocyclyl}$, $-\text{L}-\text{aryl}$, or $-\text{L}-\text{heteroaryl}$; and

each L is independently $-\text{O}-$, $-\text{NH}-$, $-\text{S}-$, $-\text{S}(\text{O})-$, $-\text{S}(\text{O})_2-$, $-\text{N}(\text{C}_{1-6} \text{ alkyl})-$, $-\text{N}(\text{C}_{2-6} \text{ alkenyl})-$, $-\text{N}(\text{C}_{2-6} \text{ alkynyl})-$, $-\text{N}(\text{C}_{1-6} \text{ haloalkyl})-$, $-\text{N}(\text{C}_{3-10} \text{ cycloalkyl})-$, $-\text{N}(\text{heterocyclyl})-$, $-\text{N}(\text{aryl})-$, $-\text{N}(\text{heteroaryl})-$, $-\text{C}(\text{O})-$, $-\text{C}(\text{O})\text{O}-$, $-\text{C}(\text{O})\text{NH}-$, $-\text{C}(\text{O})\text{N}(\text{C}_{1-6} \text{ alkyl})-$, $-\text{C}(\text{O})\text{N}(\text{C}_{2-6} \text{ alkenyl})-$, $-\text{C}(\text{O})\text{N}(\text{C}_{2-6} \text{ alkynyl})-$, $-\text{C}(\text{O})\text{N}(\text{C}_{1-6} \text{ haloalkyl})-$, $-\text{C}(\text{O})\text{N}(\text{C}_{3-10} \text{ cycloalkyl})-$, $-\text{C}(\text{O})\text{N}(\text{heterocyclyl})-$, $-\text{C}(\text{O})\text{N}(\text{aryl})-$, $-\text{C}(\text{O})\text{N}(\text{heteroaryl})-$, $-\text{NHC}(\text{O})-$, $-\text{NHC}(\text{O})\text{O}-$, $-\text{NHC}(\text{O})\text{NH}-$, $-\text{NHS}(\text{O})-$, $-\text{S}(\text{O})_2\text{NH}-$, $-\text{P}(\text{O})(\text{OH})\text{O}-$, $-\text{P}(\text{O})(\text{O}-\text{C}_{1-6} \text{ alkyl})\text{O}-$, $-\text{P}(\text{O})(\text{O}-\text{C}_{2-6} \text{ alkenyl})\text{O}-$, $-\text{P}(\text{O})(\text{O}-\text{C}_{2-6} \text{ alkynyl})\text{O}-$, $-\text{P}(\text{O})(\text{OC}_{1-6} \text{ haloalkyl})\text{O}-$, $-\text{P}(\text{O})(\text{OC}_{3-10} \text{ cycloalkyl})\text{O}-$, $-\text{P}(\text{O})(\text{O}-\text{heterocyclyl})\text{O}-$, $-\text{P}(\text{O})(\text{O}-\text{aryl})\text{O}-$, or $-\text{P}(\text{O})(\text{O}-\text{heteroaryl})\text{O}-$;

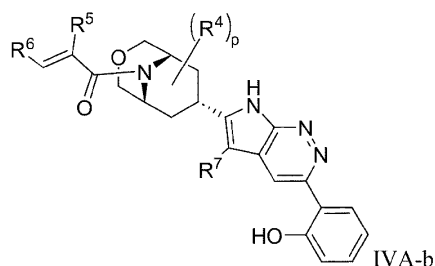
wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, and heteroaryl of Z^{1b} and L is further independently optionally substituted with one to five hydroxy, halo, cyano, hydroxy, $-\text{SH}$, $-\text{NH}_2$, $-\text{NO}_2$, $-\text{SF}_5$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl.

[0232] In some embodiments, the compound of Formula IVA is represented by Formula IVA-a:



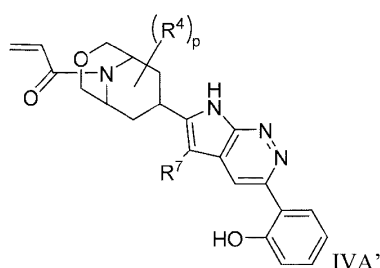
or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof.

[0233] In some embodiments, the compound of Formula IVA is represented by Formula IVA-b:



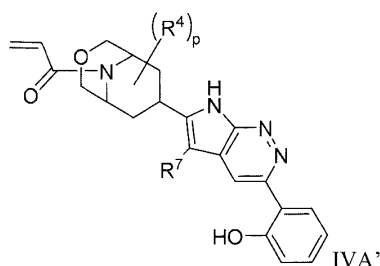
or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof.

[0234] In some embodiments, provided herein is a compound of Formula IVA':



or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof.

[0235] In some embodiments, provided herein is a compound of Formula IVA':



or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof; wherein:

p is 0, 1, or 2;

each R^4 is independently oxo, halo, cyano, $-\text{NO}_2$, $-\text{SF}_5$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, heteroaryl, $-\text{N}(\text{R}^{11})_2$, $-\text{OR}^{11}$, $-\text{C}(\text{O})\text{R}^{11}$, $-\text{C}(\text{O})\text{OR}^{11}$, $-\text{S}(\text{O})_{0-2}\text{R}^{11}$, $-\text{NR}^{11}\text{S}(\text{O})_{0-2}\text{R}^{11}$, $-\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{C}(\text{O})\text{N}(\text{R}^{11})_2$, $-\text{C}(\text{O})\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{C}(\text{O})\text{R}^{11}$, $-\text{OC}(\text{O})\text{N}(\text{R}^{11})_2$, or $-\text{NR}^{11}\text{C}(\text{O})\text{OR}^{11}$; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z^1 ;

R^7 is hydrogen, halo, cyano, $-\text{NO}_2$, $-\text{SF}_5$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, heteroaryl, $-\text{N}(\text{R}^{11})_2$, $-\text{OR}^{11}$, $-\text{C}(\text{O})\text{R}^{11}$, $-\text{C}(\text{O})\text{OR}^{11}$, $-\text{S}(\text{O})_{0-2}\text{R}^{11}$, $-\text{NR}^{11}\text{S}(\text{O})_{0-2}\text{R}^{11}$, $-\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{C}(\text{O})\text{N}(\text{R}^{11})_2$, $-\text{C}(\text{O})\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{C}(\text{O})\text{R}^{11}$, $-\text{OC}(\text{O})\text{N}(\text{R}^{11})_2$,

or $-\text{NR}^{11}\text{C}(\text{O})\text{OR}^{11}$; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z^1 ;

each Z^1 is independently halo, cyano, $-\text{NO}_2$, $-\text{SF}_5$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, heteroaryl, $-\text{N}(\text{R}^{11})_2$, $-\text{OR}^{11}$, $-\text{P}(\text{O})(\text{OR}^{11})_2$, $-\text{C}(\text{O})\text{R}^{11}$, $-\text{C}(\text{O})\text{OR}^{11}$, $-\text{S}(\text{O})_{0-2}\text{R}^{11}$, $-\text{NR}^{11}\text{S}(\text{O})_{0-2}\text{R}^{11}$, $-\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{C}(\text{O})\text{N}(\text{R}^{11})_2$, $-\text{C}(\text{O})\text{N}(\text{R}^{11})_2$, $-\text{NR}^{11}\text{C}(\text{O})\text{R}^{11}$, $-\text{OC}(\text{O})\text{N}(\text{R}^{11})_2$, or $-\text{NR}^{11}\text{C}(\text{O})\text{OR}^{11}$; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1a} ;

each R^{11} is independently hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1a} ;

each Z^{1a} is independently hydroxy, halo, cyano, $-\text{NO}_2$, $-\text{SF}_5$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, heteroaryl, $-\text{N}(\text{R}^{13})_2$, $-\text{OR}^{13}$, $-\text{P}(\text{O})(\text{OR}^{13})_2$, $-\text{C}(\text{O})\text{R}^{13}$, $-\text{C}(\text{O})\text{OR}^{13}$, $-\text{S}(\text{O})_{0-2}\text{R}^{13}$, $-\text{NR}^{13}\text{S}(\text{O})_{0-2}\text{R}^{13}$, $-\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{13})_2$, $-\text{NR}^{13}\text{S}(\text{O})_{0-2}\text{N}(\text{R}^{13})_2$, $-\text{NR}^{13}\text{C}(\text{O})\text{N}(\text{R}^{13})_2$, $-\text{C}(\text{O})\text{N}(\text{R}^{13})_2$, $-\text{NR}^{13}\text{C}(\text{O})\text{R}^{13}$, $-\text{OC}(\text{O})\text{N}(\text{R}^{13})_2$, or $-\text{NR}^{13}\text{C}(\text{O})\text{OR}^{13}$; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1b} ;

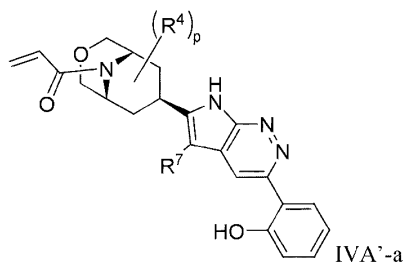
each R^{13} is independently hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl; wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1b} ;

each Z^{1b} is independently halo, cyano, hydroxy, $-\text{SH}$, $-\text{NH}_2$, $-\text{NO}_2$, $-\text{SF}_5$, $-\text{P}(\text{O})(\text{OH})_2$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, heteroaryl, $-\text{L}-\text{C}_{1-6}$ alkyl, $-\text{L}-\text{C}_{2-6}$ alkenyl, $-\text{L}-\text{C}_{2-6}$ alkynyl, $-\text{L}-\text{C}_{1-6}$ haloalkyl, $-\text{L}-\text{C}_{3-10}$ cycloalkyl, $-\text{L}-\text{heterocyclyl}$, $-\text{L}-\text{aryl}$, or $-\text{L}-\text{heteroaryl}$; and

each L is independently $-\text{O}-$, $-\text{NH}-$, $-\text{S}-$, $-\text{S}(\text{O})-$, $-\text{S}(\text{O})_2-$, $-\text{N}(\text{C}_{1-6}\text{ alkyl})-$, $-\text{N}(\text{C}_{2-6}\text{ alkenyl})-$, $-\text{N}(\text{C}_{2-6}\text{ alkynyl})-$, $-\text{N}(\text{C}_{1-6}\text{ haloalkyl})-$, $-\text{N}(\text{C}_{3-10}\text{ cycloalkyl})-$, $-\text{N}(\text{heterocyclyl})-$, $-\text{N}(\text{aryl})-$, $-\text{N}(\text{heteroaryl})-$, $-\text{C}(\text{O})-$, $-\text{C}(\text{O})\text{O}-$, $-\text{C}(\text{O})\text{NH}-$, $-\text{C}(\text{O})\text{N}(\text{C}_{1-6}\text{ alkyl})-$, $-\text{C}(\text{O})\text{N}(\text{C}_{2-6}\text{ alkenyl})-$, $-\text{C}(\text{O})\text{N}(\text{C}_{2-6}\text{ alkynyl})-$, $-\text{C}(\text{O})\text{N}(\text{C}_{1-6}\text{ haloalkyl})-$, $-\text{C}(\text{O})\text{N}(\text{C}_{3-10}\text{ cycloalkyl})-$, $-\text{C}(\text{O})\text{N}(\text{heterocyclyl})-$, $-\text{C}(\text{O})\text{N}(\text{aryl})-$, $-\text{C}(\text{O})\text{N}(\text{heteroaryl})-$, $-\text{NHC}(\text{O})-$, $-\text{NHC}(\text{O})\text{O}-$, $-\text{NHC}(\text{O})\text{NH}-$, $-\text{NHS}(\text{O})-$, $-\text{S}(\text{O})_2\text{NH}-$, $-\text{P}(\text{O})(\text{OH})\text{O}-$, $-\text{P}(\text{O})(\text{O}-\text{C}_{1-6}\text{ alkyl})\text{O}-$, $-\text{P}(\text{O})(\text{O}-\text{C}_{2-6}\text{ alkenyl})\text{O}-$, $-\text{P}(\text{O})(\text{O}-\text{C}_{2-6}\text{ alkynyl})\text{O}-$, $-\text{P}(\text{O})(\text{OC}_{1-6}\text{ haloalkyl})\text{O}-$, $-\text{P}(\text{O})(\text{OC}_{3-10}\text{ cycloalkyl})\text{O}-$, $-\text{P}(\text{O})(\text{O}-\text{heterocyclyl})\text{O}-$, $-\text{P}(\text{O})(\text{O}-\text{aryl})\text{O}-$, or $-\text{P}(\text{O})(\text{O}-\text{heteroaryl})\text{O}-$;

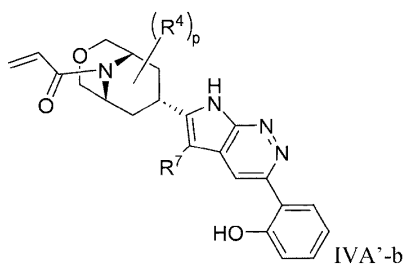
wherein each C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, heterocyclyl, aryl, and heteroaryl of Z^{1b} and L is further independently optionally substituted with one to five hydroxy, halo, cyano, hydroxy, $-\text{SH}$, $-\text{NH}_2$, $-\text{NO}_2$, $-\text{SF}_5$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{3-10} cycloalkyl, heterocyclyl, aryl, or heteroaryl.

[0236] In some embodiments, the compound of Formula IVA' is represented by Formula IVA'-a:



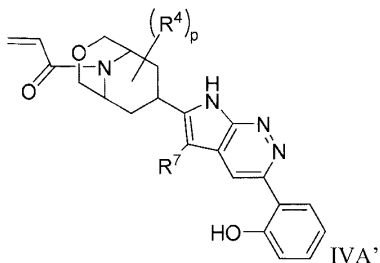
or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof.

[0237] In some embodiments, the compound of Formula IVA' is represented by Formula IVA'-b:



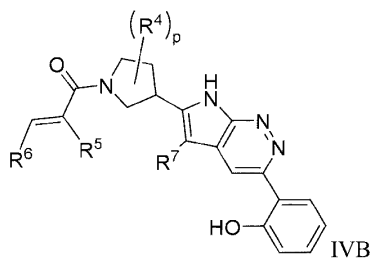
or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof.

[0238] In some embodiments, provided herein is a compound of Formula IVA':



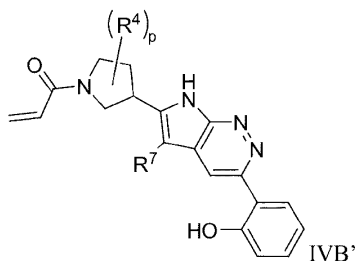
or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof.

[0239] In some embodiments, provided herein is a compound of Formula IVB:



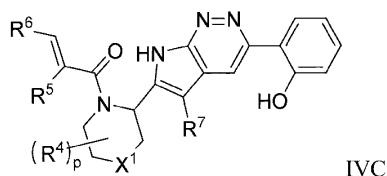
or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof.

[0240] In some embodiments, provided herein is a compound of Formula IVB':



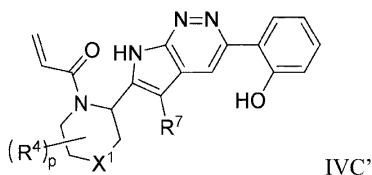
or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof.

[0241] In some embodiments, provided herein is a compound of Formula IVC:



or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof; wherein X¹ is O or CH₂.

[0242] In some embodiments, provided herein is a compound of Formula IVC':



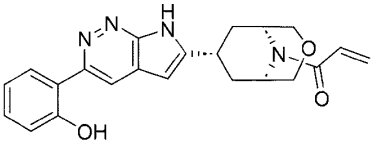
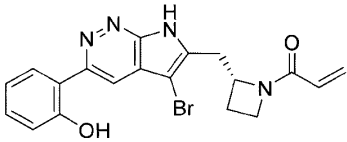
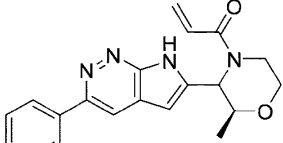
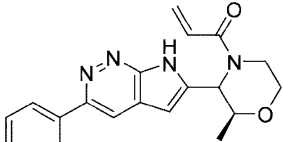
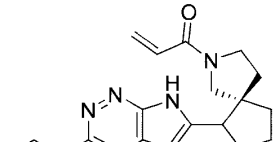
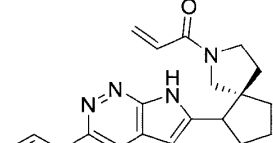
or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof; wherein X¹ is O or CH₂.

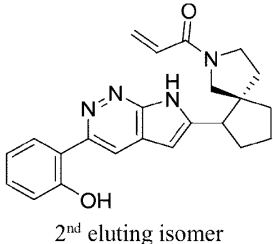
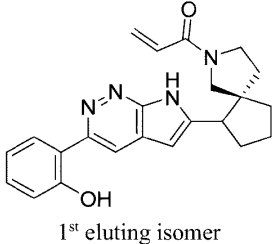
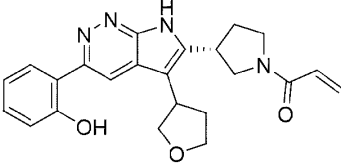
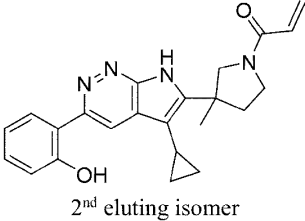
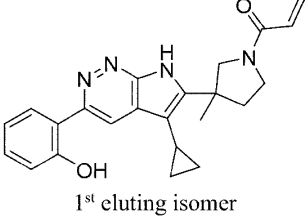
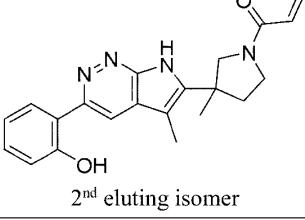
[0243] In one embodiment, provided is a compound, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, selected from Table 1.

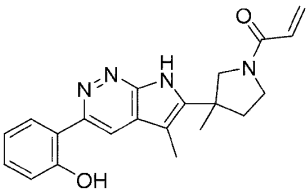
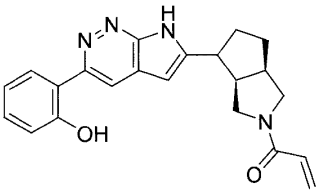
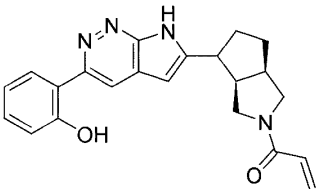
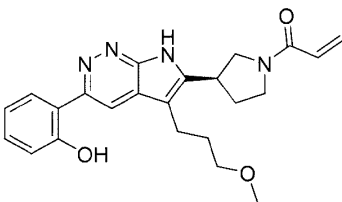
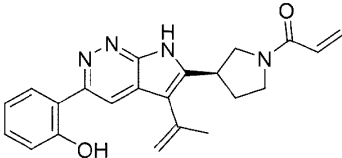
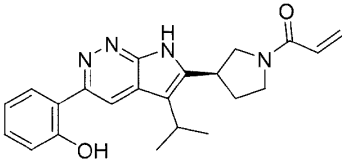
[0244] Each compound denoted as "1st eluting isomer," "2nd eluting isomer," etc. is a single unknown stereoisomer whose stereochemistry is unknown at the stereocenter depicted as racemic. Where the order of elution is not specified, the compound is a mixture of stereoisomers with respect to the stereocenter depicted as racemic.

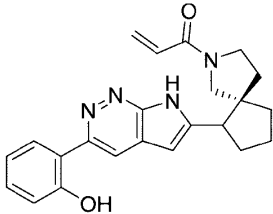
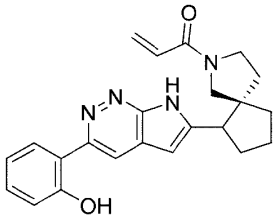
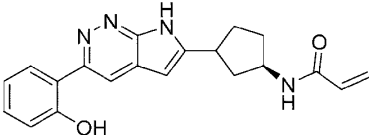
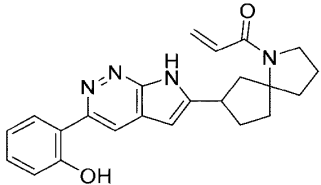
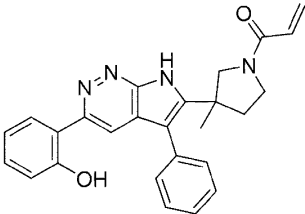
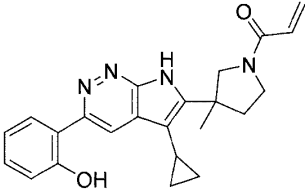
Table 1

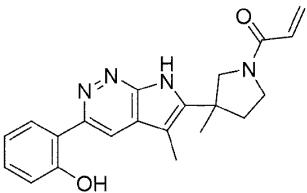
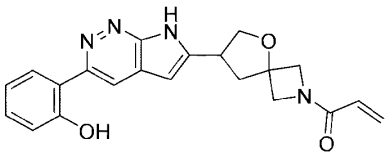
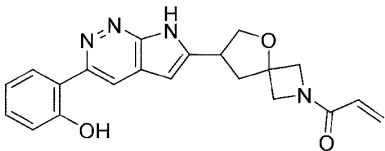
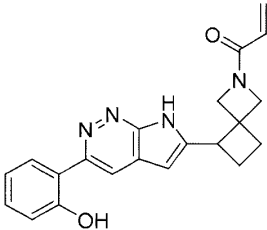
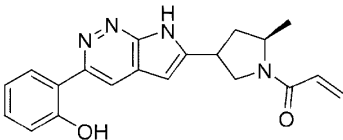
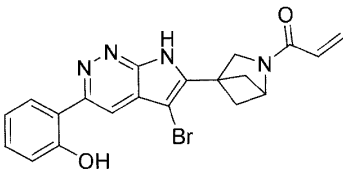
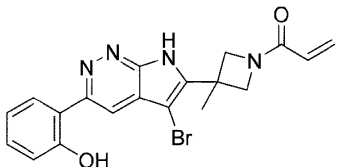
Ex.	Structure	Name
1		1-{(R)-3-[5-(o-hydroxyphenyl)-3-(1-methyl-4-pyrazolyl)-1H-1,6,7-triazainden-2-yl]-1-pyrrolidinyl}-2-propen-1-one
2		1-{(3S)-3-fluoro-4-[5-(o-hydroxyphenyl)-3-(3-pyrazolyl)-1H-1,6,7-triazainden-2-yl]-1-pyrrolidinyl}-2-propen-1-one
3		1-((1R,5S,7r)-7-(5-bromo-3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one
4		N-{(1S)-3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]cyclopentyl}acrylamide
5		1-{(2S)-3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-methyl-1-pyrrolidinyl}-2-propen-1-one
6		N-{(1R)-3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]cyclopentyl}acrylamide
7		1-{(3S)-4-[3-ethyl-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-3-fluoro-1-pyrrolidinyl}-2-propen-1-one

Ex.	Structure	Name
8		1-((1R,5S,7r)-7-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one
9		1-[(R)-2-{[3-bromo-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]methyl}-1-azetidiny]-2-propen-1-one
10	 2 nd eluting isomer	1-[(2S)-3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-methyl-4-morpholinyl]-2-propen-1-one
11	 1 st eluting isomer	1-[(2S)-3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-methyl-4-morpholinyl]-2-propen-1-one
12	 2 nd eluting isomer	1-[(5S)-6-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-aza-2-spiro[4.4]nonyl]-2-propen-1-one
13	 1 st eluting isomer	1-[(5S)-6-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-aza-2-spiro[4.4]nonyl]-2-propen-1-one

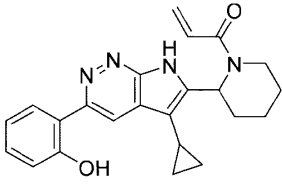
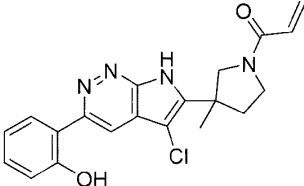
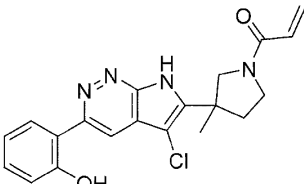
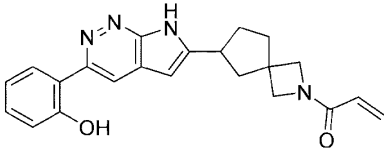
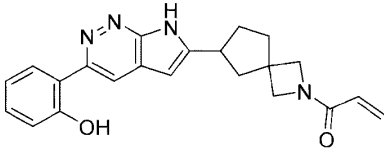
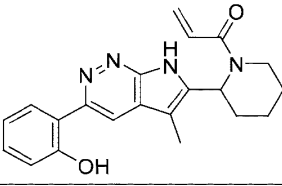
Ex.	Structure	Name
14	 2nd eluting isomer	1-{{(5R)-6-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]}-2-aza-2-spiro[4.4]nonyl}-2-propen-1-one
15	 1st eluting isomer	1-{{(5R)-6-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]}-2-aza-2-spiro[4.4]nonyl}-2-propen-1-one
16		1-{{(R)-3-[5-(o-hydroxyphenyl)-3-(tetrahydro-3-furyl)-1H-1,6,7-triazainden-2-yl]}-1-pyrrolidinyl}-2-propen-1-one
17	 2nd eluting isomer	1-{{3-[3-cyclopropyl-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]}-3-methyl-1-pyrrolidinyl}-2-propen-1-one
18	 1st eluting isomer	1-{{3-[3-cyclopropyl-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]}-3-methyl-1-pyrrolidinyl}-2-propen-1-one
19	 2nd eluting isomer	1-{{3-[5-(o-hydroxyphenyl)-3-methyl-1H-1,6,7-triazainden-2-yl]}-3-methyl-1-pyrrolidinyl}-2-propen-1-one

Ex.	Structure	Name
20	 1st eluting isomer	1-{3-[5-(o-hydroxyphenyl)-3-methyl-1H-1,6,7-triazainden-2-yl]-3-methyl-1-pyrrolidinyl}-2-propen-1-one
21	 2nd eluting isomer	1-[(1R,5R)-6-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-3-azabicyclo[3.3.0]oct-3-yl]-2-propen-1-one
22	 1st eluting isomer	1-[(1R,5R)-6-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-3-azabicyclo[3.3.0]oct-3-yl]-2-propen-1-one
23		1-[(R)-3-[5-(o-hydroxyphenyl)-3-(3-methoxypropyl)-1H-1,6,7-triazainden-2-yl]-1-pyrrolidinyl]-2-propen-1-one
24		1-[(R)-3-[5-(o-hydroxyphenyl)-3-isopropenyl-1H-1,6,7-triazainden-2-yl]-1-pyrrolidinyl]-2-propen-1-one
25		1-[(R)-3-[5-(o-hydroxyphenyl)-3-isopropyl-1H-1,6,7-triazainden-2-yl]-1-pyrrolidinyl]-2-propen-1-one

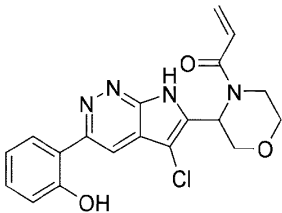
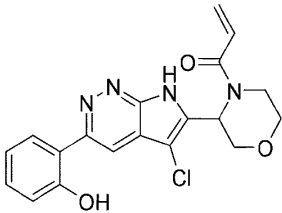
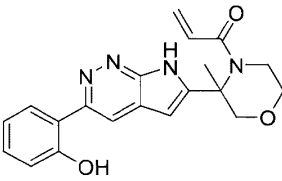
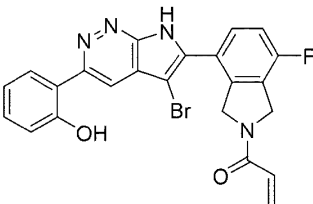
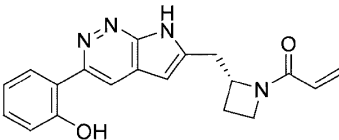
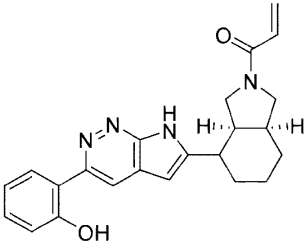
Ex.	Structure	Name
26	 2nd eluting isomer	1-((6-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-aza-2-spiro[4.4]nonyl)-2-propen-1-one
27	 1st eluting isomer	1-{6-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-aza-2-spiro[4.4]nonyl}-2-propen-1-one
28		N-((1R)-3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]cyclopentyl)acrylamide
29		1-{7-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-aza-1-spiro[4.4]nonyl}-2-propen-1-one
30		1-{3-[5-(o-hydroxyphenyl)-3-phenyl-1H-1,6,7-triazainden-2-yl]-3-methyl-1-pyrrolidinyl}-2-propen-1-one
31		1-{3-[3-cyclopropyl-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-3-methyl-1-pyrrolidinyl}-2-propen-1-one

Ex.	Structure	Name
32		1-{3-[5-(o-hydroxyphenyl)-3-methyl-1H-1,6,7-triazainden-2-yl]-3-methyl-1-pyrrolidinyl}-2-propen-1-one
33	 2nd eluting isomer	1-{7-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-5-oxa-2-aza-2-spiro[3.4]octyl}-2-propen-1-one
34	 1 st eluting isomer	1-{7-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-5-oxa-2-aza-2-spiro[3.4]octyl}-2-propen-1-one
35		1-{5-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-aza-2-spiro[3.3]heptyl}-2-propen-1-one
36		1-{(2R)-4-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-methyl-1-pyrrolidinyl}-2-propen-1-one
37		1-{4-[3-bromo-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-azabicyclo[2.1.1]hex-2-yl}-2-propen-1-one
38		1-{3-[3-bromo-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-3-methyl-1-azetidiny]-2-propen-1-one

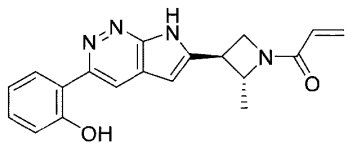
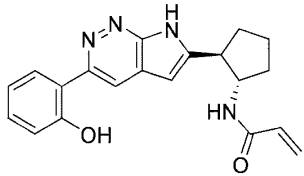
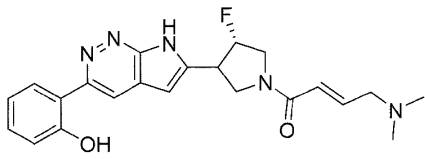
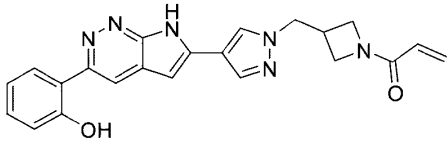
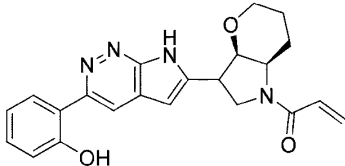
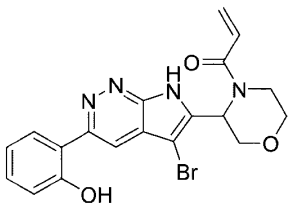
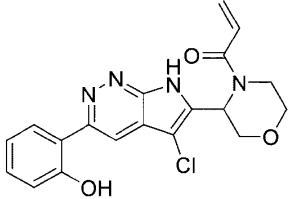
Ex.	Structure	Name
39		1-((R)-3-[5-(o-hydroxyphenyl)-3-(3-pyrazolyl)-1H-1,6,7-triazainden-2-yl]-1-pyrrolidinyl)-2-propen-1-one
40		1-{3-[3-bromo-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-3-fluoro-1-pyrrolidinyl}-2-propen-1-one
41		1-{2-[5-(o-hydroxyphenyl)-3-methyl-1H-1,6,7-triazainden-2-yl]-1-piperidyl}-2-propen-1-one
42		1-{2-[5-(o-hydroxyphenyl)-3-methyl-1H-1,6,7-triazainden-2-yl]-1-piperidyl}-2-propen-1-one
43		1-{2-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-methyl-1-pyrrolidinyl}-2-propen-1-one
44		1-{2-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-methyl-1-pyrrolidinyl}-2-propen-1-one
45		1-{2-[3-cyclopropyl-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-piperidyl}-2-propen-1-one

Ex.	Structure	Name
46	 1st eluting isomer	1-{2-[3-cyclopropyl-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-piperidyl}-2-propen-1-one
47	 2nd eluting isomer	1-{3-[3-chloro-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-3-methyl-1-pyrrolidinyl}-2-propen-1-one
48	 1st eluting isomer	1-{3-[3-chloro-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-3-methyl-1-pyrrolidinyl}-2-propen-1-one
49	 2nd eluting isomer	1-{6-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-aza-2-spiro[3.4]octyl}-2-propen-1-one
50	 1st eluting isomer	1-{6-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-aza-2-spiro[3.4]octyl}-2-propen-1-one
51		1-{2-[5-(o-hydroxyphenyl)-3-methyl-1H-1,6,7-triazainden-2-yl]-1-piperidyl}-2-propen-1-one

Ex.	Structure	Name
52		1-{3-[3-chloro-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-3-methyl-1-pyrrolidinyl}-2-propen-1-one
53		1-[(3S)-4-[3-cyclopropyl-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-3-fluoro-1-pyrrolidinyl]-2-propen-1-one
54		1-[(3S)-3-fluoro-4-[5-(o-hydroxyphenyl)-3-methyl-1H-1,6,7-triazainden-2-yl]-1-pyrrolidinyl]-2-propen-1-one
55		1-{2-[3-cyclopropyl-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-piperidyl}-2-propen-1-one
56		1-[(2S)-5-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-methyl-1-piperidyl]-2-propen-1-one
57		1-(3-{3-[(R)-3-methyl-1-piperidyl]-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl}-1-azetidiny)-2-propen-1-one
58		(2S)-1-acryloyl-4-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-pyrrolidinecarbonitrile 1 st eluting isomer

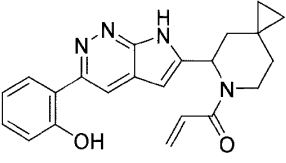
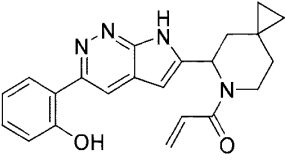
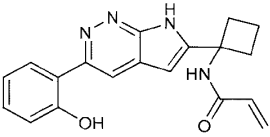
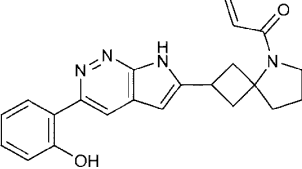
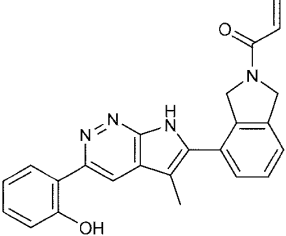
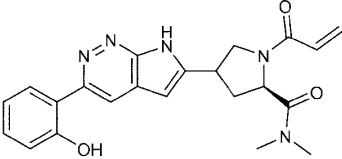
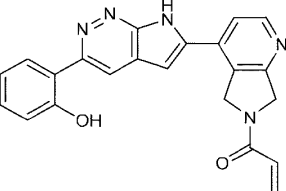
Ex.	Structure	Name
59	 2nd eluting isomer	1-{3-[3-chloro-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-4-morpholinyl}-2-propen-1-one
60	 1st eluting isomer	1-{3-[3-chloro-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-4-morpholinyl}-2-propen-1-one
61		1-{3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-3-methyl-4-morpholinyl}-2-propen-1-one
62		1-{4-[3-bromo-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-7-fluoro-2-isindoliny}-2-propen-1-one
63		1-[(R)-2-{[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]methyl}-1-azetidiny]-2-propen-1-one
64		1-{(3aS,7aS)-4-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]octahydro-1H-isindol-2-yl}-2-propen-1-one

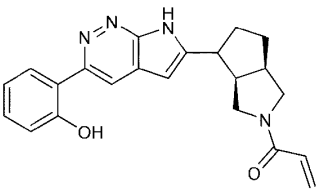
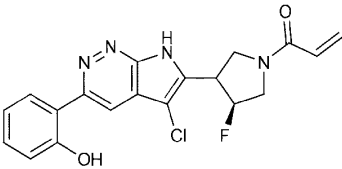
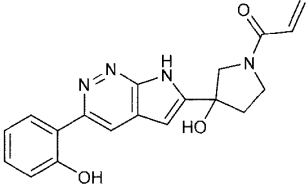
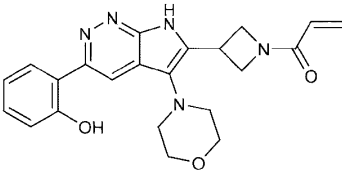
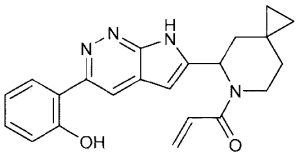
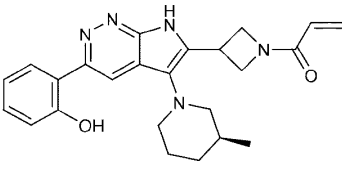
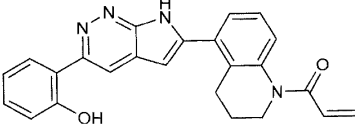
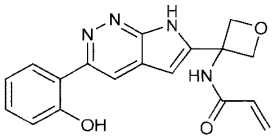
Ex.	Structure	Name
65		1-{{(3aR,7aR)-4-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]octahydro-1H-isindol-2-yl}-2-propen-1-one
66		1-{3-[5-(o-hydroxyphenyl)-3-methyl-1H-1,6,7-triazainden-2-yl]-4-morpholinyl}-2-propen-1-one
67		1-{2-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-methyl-1-pyrrolidinyl}-2-propen-1-one
68		1-(2-{[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]methyl}-1-azetidiny)-2-propen-1-one
69		1-{6-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-aza-2-spiro[3.4]octyl}-2-propen-1-one
70		1-{6-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-azabicyclo[2.2.1]hept-2-yl}-2-propen-1-one 2 nd eluting isomer
71		1-{6-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-azabicyclo[2.2.1]hept-2-yl}-2-propen-1-one 1 st eluting isomer

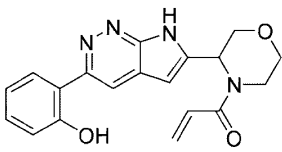
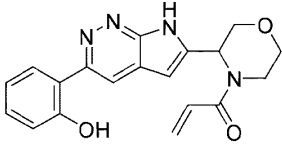
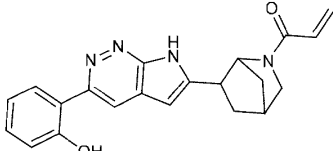
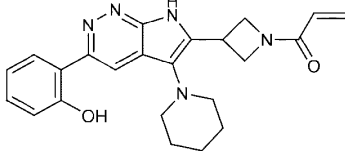
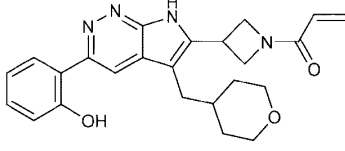
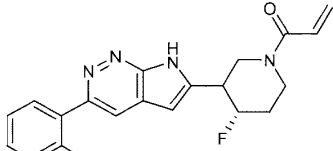
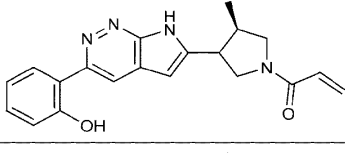
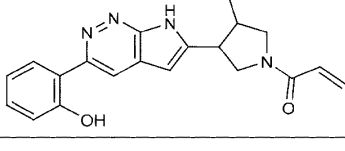
Ex.	Structure	Name
72		1-((2R)-3-((5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl)-2-methyl-1-azetidinyl)-2-propen-1-one
73		N-((1S)-2-((5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl)cyclopentyl)acrylamide
74		(E)-1-((3S)-3-fluoro-4-((5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl)-1-pyrrolidinyl)-4-(dimethylamino)-2-buten-1-one
75		1-((3-((4-((5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl)-1-pyrazolyl)methyl)-1-azetidinyl)-2-propen-1-one
76		1-((1R,3aR,7aR)-5'-(o-hydroxyphenyl)octahydro-1'H-7-oxa-1',3,6',7'-tetraaza-1,2'-biindenyl-3-yl)-2-propen-1-one
77		1-((3-((3-bromo-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl)-4-morpholinyl)-2-propen-1-one
78		1-((3-((3-chloro-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl)-4-morpholinyl)-2-propen-1-one

Ex.	Structure	Name
79		1-{7-fluoro-4-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-isoindolinyl}-2-propen-1-one
80		N-[(1R)-2-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]cyclopentyl]acrylamide
81		1-{4,4-difluoro-2-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-piperidyl}-2-propen-1-one 2 nd eluting isomer
82		1-{4,4-difluoro-2-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-piperidyl}-2-propen-1-one 1 st eluting isomer
83		1-{2-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-piperidyl}-2-propen-1-one 2 nd eluting isomer
84		1-{2-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-piperidyl}-2-propen-1-one 1 st eluting isomer

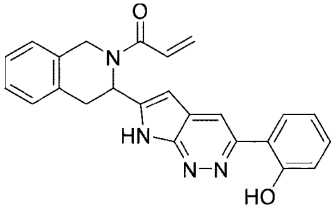
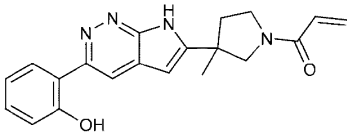
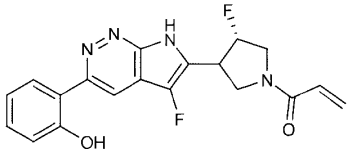
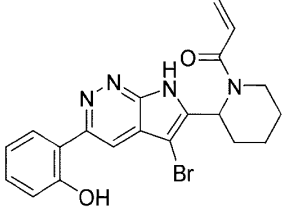
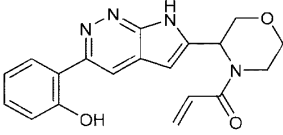
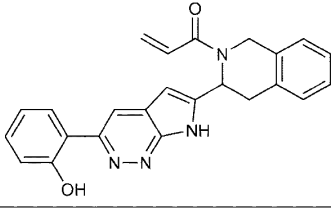
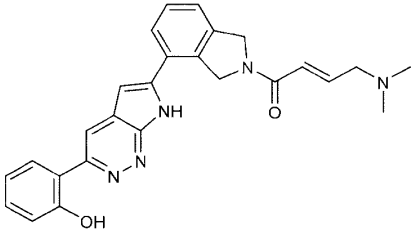
Ex.	Structure	Name
85		1-{4-[3-cyclopropyl-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-isindoliny}-2-propen-1-one
86		1-{4-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-azabicyclo[2.1.1]hex-2-yl}-2-propen-1-one
87		1-{2-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-pyrrolidiny}-2-propen-1-one 2 nd eluting isomer
88		1-{2-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-pyrrolidiny}-2-propen-1-one 1 st eluting isomer
89		1-{3-fluoro-3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-pyrrolidiny}-2-propen-1-one
90		1-{2-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-4-morpholiny}-2-propen-1-one 2 nd eluting isomer
91		1-{2-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-4-morpholiny}-2-propen-1-one 1 st eluting isomer

Ex.	Structure	Name
92	 2nd eluting isomer	1-{5-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-6-aza-6-spiro[2.5]octyl}-2-propen-1-one
93	 1st eluting isomer	1-{5-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-6-aza-6-spiro[2.5]octyl}-2-propen-1-one
94		N-{1-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]cyclobutyl}acrylamide
95		1-{2-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-5-aza-5-spiro[3.4]octyl}-2-propen-1-one
96		1-{4-[5-(o-hydroxyphenyl)-3-methyl-1H-1,6,7-triazainden-2-yl]-2-isindoliny}-2-propen-1-one
97		N,N-dimethyl-(2R)-1-acryloyl-4-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-pyrrolidinecarboxamide
98		1-{7-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2,4-diaza-2-indanyl}-2-propen-1-one

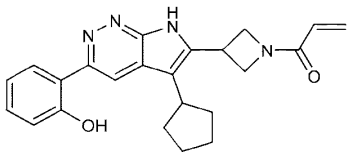
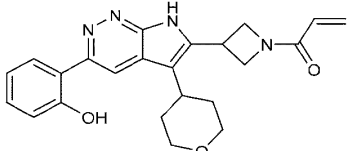
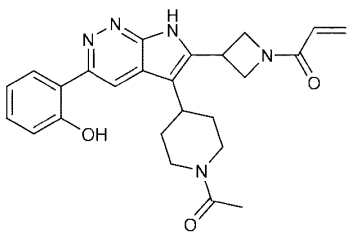
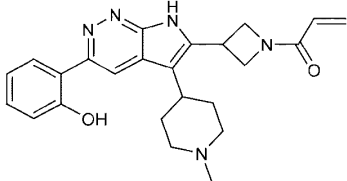
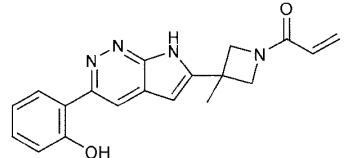
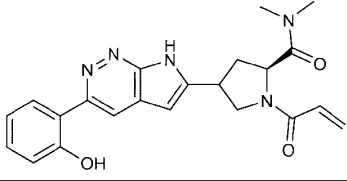
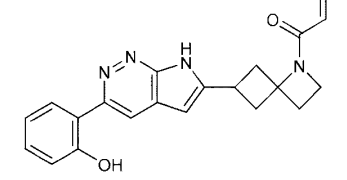
Ex.	Structure	Name
99		1-((1R,5R,6R)-6-([5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-3-azabicyclo[3.3.0]oct-3-yl)-2-propen-1-one
100		1-((3S)-4-[3-chloro-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-3-fluoro-1-pyrrolidinyl)-2-propen-1-one
101		1-([3-hydroxy-3-([5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-pyrrolidinyl)-2-propen-1-one
102		1-([3-[5-(o-hydroxyphenyl)-3-morpholino-1H-1,6,7-triazainden-2-yl]-1-azetidiny]-2-propen-1-one
103		1-([5-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-6-aza-spiro[2.5]octyl]-2-propen-1-one
104		1-((3-((S)-3-methyl-1-piperidyl)-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl)-1-azetidiny)-2-propen-1-one
105		1-([5-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1,2,3,4-tetrahydro-1-quinolyl]-2-propen-1-one
106		N-([3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-3-oxetanyl]acrylamide

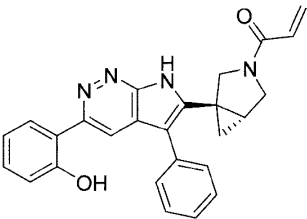
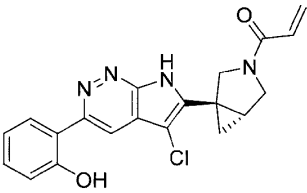
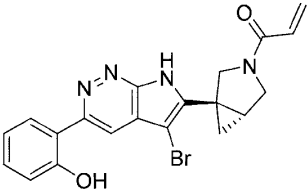
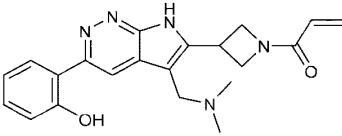
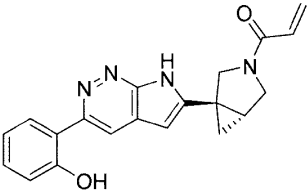
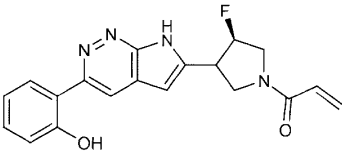
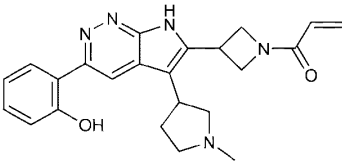
Ex.	Structure	Name
107	 2nd eluting isomer	1-{3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-4-morpholinyl}-2-propen-1-one
108	 1st eluting isomer	1-{3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-4-morpholinyl}-2-propen-1-one
109		1-{6-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-azabicyclo[2.2.1]hept-2-yl}-2-propen-1-one
110		1-{3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-azetidiny]-2-propen-1-one
111		1-(3-{5-(o-hydroxyphenyl)-3-[(tetrahydro-2H-pyran-4-yl)methyl]-1H-1,6,7-triazainden-2-yl}-1-azetidiny)-2-propen-1-one
112		1-{(4S)-4-fluoro-3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-piperidyl}-2-propen-1-one
113		1-{(3R)-4-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-3-methyl-1-pyrrolidiny]-2-propen-1-one
114		1-{3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-4-methyl-1-pyrrolidiny]-2-propen-1-one

Ex.	Structure	Name
115		1-((1S,4S,6S)-6-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-azabicyclo[2.2.1]hept-2-yl)-2-propen-1-one
116		1-((1R,4R)-6-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-azabicyclo[2.2.1]hept-2-yl)-2-propen-1-one
117		1-((3S)-4-[3-bromo-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-3-fluoro-1-pyrrolidinyl)-2-propen-1-one
118		1-((2R)-3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-methyl-1-pyrrolidinyl)-2-propen-1-one
119		1-((5S)-1-[3-bromo-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-3-azabicyclo[3.1.0]hex-3-yl)-2-propen-1-one
120		1-((5S)-1-[3-chloro-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-3-azabicyclo[3.1.0]hex-3-yl)-2-propen-1-one
121		1-([3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1,2,3,4-tetrahydro-2-isoquinolyl]-2-propen-1-one 2 nd eluting isomer

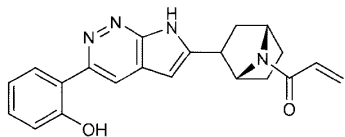
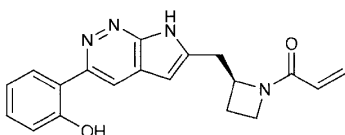
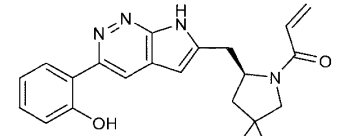
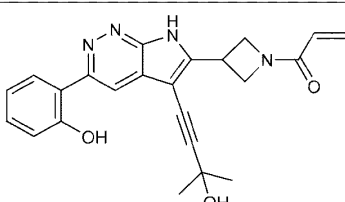
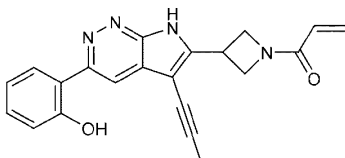
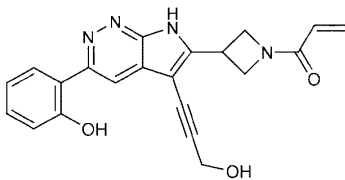
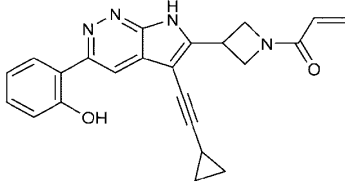
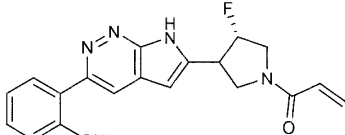
Ex.	Structure	Name
122	 1st eluting isomer	1-{3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1,2,3,4-tetrahydro-2-isoquinolyl}-2-propen-1-one
123		1-{3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-3-methyl-1-pyrrolidinyl}-2-propen-1-one
124		1-{(3S)-3-fluoro-4-[3-fluoro-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-pyrrolidinyl}-2-propen-1-one
125	 1st eluting isomer	1-{2-[3-bromo-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-piperidyl}-2-propen-1-one
126		1-{3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-4-morpholinyl}-2-propen-1-one
127		1-{3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1,2,3,4-tetrahydro-2-isoquinolyl}-2-propen-1-one
128		(E)-4-(dimethylamino)-1-{4-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-isoindolinyl}-2-buten-1-one

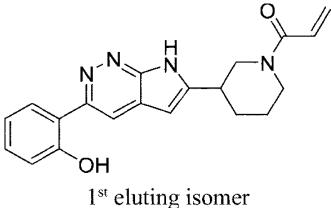
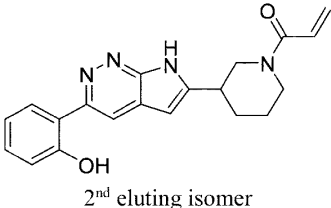
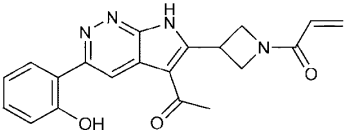
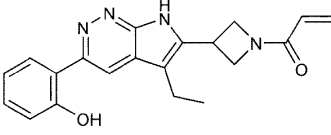
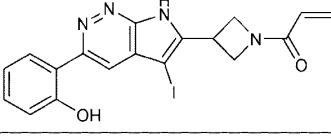
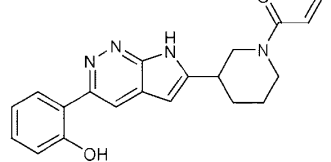
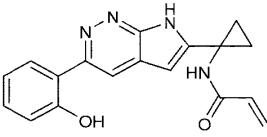
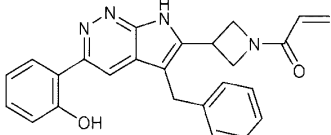
Ex.	Structure	Name
129		[2-(1-acryloyl-3-azetidiny)-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-3-yl]acetonitrile
130		1-[(3R)-4-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-3-methoxy-1-pyrrolidiny]-2-propen-1-one
131		1-[(3S)-4-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-3-methoxy-1-pyrrolidiny]-2-propen-1-one
132		1-[2-[5-(o-hydroxyphenyl)-3-phenyl-1H-1,6,7-triazainden-2-yl]-1-piperidyl]-2-propen-1-one
133		1-[6-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-3-azabicyclo[3.1.1]hept-3-yl]-2-propen-1-one
134		1-[7-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-5-oxa-2-aza-2-spiro[3.4]octyl]-2-propen-1-one
135		1-[6-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-aza-2-spiro[3.3]heptyl]-2-propen-1-one
136		1-[3-[5-(o-hydroxyphenyl)-3-isopropyl-1H-1,6,7-triazainden-2-yl]-1-azetidiny]-2-propen-1-one

Ex.	Structure	Name
137		1-{3-[3-cyclopentyl-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-azetidiny]-2-propen-1-one
138		1-{3-[5-(o-hydroxyphenyl)-3-(tetrahydro-2H-pyran-4-yl)-1H-1,6,7-triazainden-2-yl]-1-azetidiny]-2-propen-1-one
139		1-{3-[3-(1-acetyl-4-piperidyl)-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-azetidiny]-2-propen-1-one
140		1-{3-[5-(o-hydroxyphenyl)-3-(1-methyl-4-piperidyl)-1H-1,6,7-triazainden-2-yl]-1-azetidiny]-2-propen-1-one
141		1-{3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-3-methyl-1-azetidiny]-2-propen-1-one
142		N,N-dimethyl-(2S)-1-acryloyl-4-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-pyrrolidinecarboxamide
143		1-{6-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-aza-1-spiro[3.3]heptyl}-2-propen-1-one

Ex.	Structure	Name
144		1-((5R)-1-[5-(o-hydroxyphenyl)-3-phenyl-1H-1,6,7-triazainden-2-yl]-3-azabicyclo[3.1.0]hex-3-yl)-2-propen-1-one
145		1-((5R)-1-[3-chloro-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-3-azabicyclo[3.1.0]hex-3-yl)-2-propen-1-one
146		1-((5R)-1-[3-bromo-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-3-azabicyclo[3.1.0]hex-3-yl)-2-propen-1-one
147		1-(3-{3-[(dimethylamino)methyl]-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl}-1-azetidyl)-2-propen-1-one
148		1-((5R)-1-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-3-azabicyclo[3.1.0]hex-3-yl)-2-propen-1-one
149		1-((3R)-3-fluoro-4-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-pyrrolidinyl)-2-propen-1-one
150		1-(3-{5-(o-hydroxyphenyl)-3-(1-methyl-3-pyrrolidinyl)-1H-1,6,7-triazainden-2-yl}-1-azetidyl)-2-propen-1-one

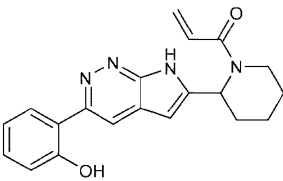
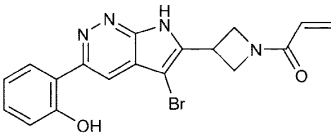
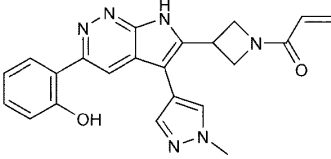
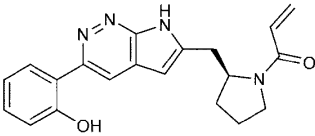
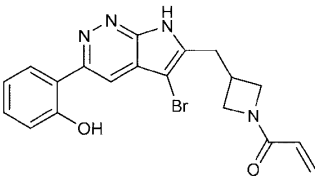
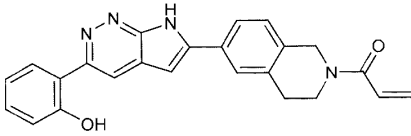
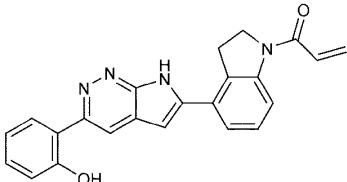
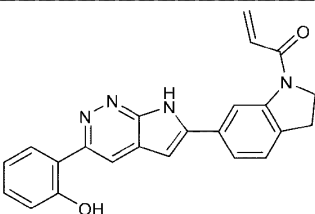
Ex.	Structure	Name
151		1-((R)-3-[5-(o-hydroxyphenyl)-3-methyl-1H-1,6,7-triazainden-2-yl]-1-pyrrolidinyl)-2-propen-1-one
152		1-{3-[3-(2-cyclopropylethyl)-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-azetidiny]-2-propen-1-one
153		1-{3-[5-(o-hydroxyphenyl)-3-(3-methoxypropyl)-1H-1,6,7-triazainden-2-yl]-1-azetidiny]-2-propen-1-one
154		1-((1S)-1-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-3-azabicyclo[3.1.0]hex-3-yl)-2-propen-1-one
155		1-((2S)-4-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-methyl-1-pyrrolidinyl)-2-propen-1-one
156		(1R)-4-[2-(1-acryloyl-3-azetidiny)-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-3-yl]cyclohexanecarboxamide
157		(1S)-4-[2-(1-acryloyl-3-azetidiny)-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-3-yl]cyclohexanecarboxamide

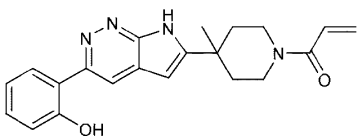
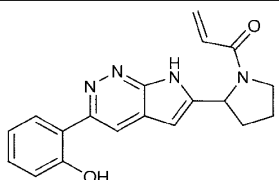
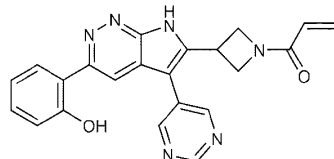
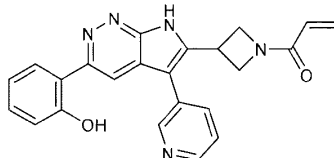
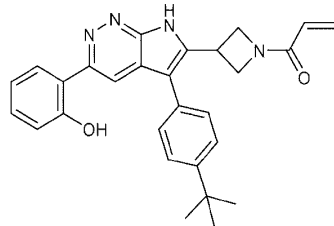
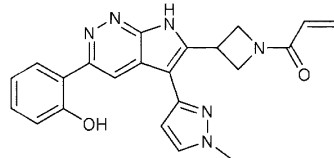
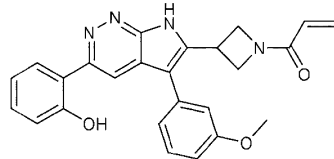
Ex.	Structure	Name
158		1-((1R,4S)-2-([5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-7-azabicyclo[2.2.1]hept-7-yl)-2-propen-1-one
159		1-[(S)-2-([5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]methyl)-1-azetidiny]-2-propen-1-one
160		1-[(S)-6-([5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]methyl)-5-aza-5-spiro[2.4]heptyl]-2-propen-1-one
161		1-{3-[3-(3-hydroxy-3-methyl-1-butynyl)-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-azetidiny]-2-propen-1-one
162		1-{3-[5-(o-hydroxyphenyl)-3-(1-propynyl)-1H-1,6,7-triazainden-2-yl]-1-azetidiny]-2-propen-1-one
163		1-{3-[5-(o-hydroxyphenyl)-3-(3-hydroxy-1-propynyl)-1H-1,6,7-triazainden-2-yl]-1-azetidiny]-2-propen-1-one
164		1-{3-[3-(2-cyclopropylethynyl)-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-azetidiny]-2-propen-1-one
165		1-[(3S)-3-fluoro-4-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-pyrrolidiny]-2-propen-1-one

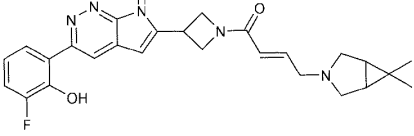
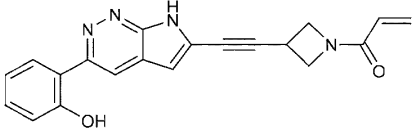
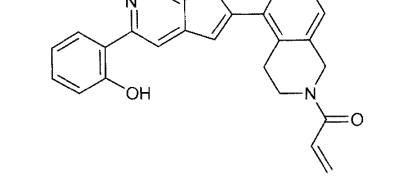
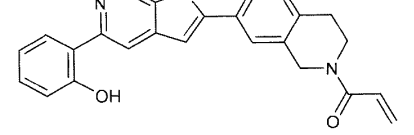
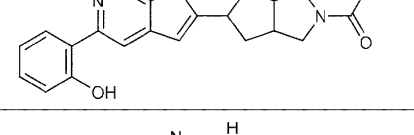
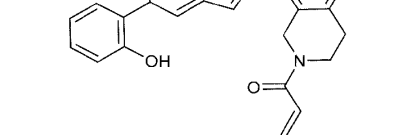
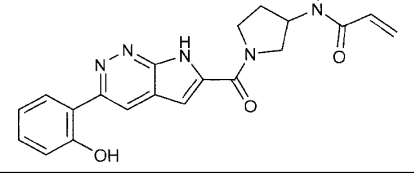
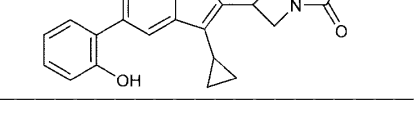
Ex.	Structure	Name
166	 1st eluting isomer	1-{3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-piperidyl}-2-propen-1-one
167	 2nd eluting isomer	1-{3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-piperidyl}-2-propen-1-one
168		1-{3-[3-acetyl-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-azetidyl}-2-propen-1-one
169		1-{3-[3-ethyl-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-azetidyl}-2-propen-1-one
170		1-{3-[5-(o-hydroxyphenyl)-3-iodo-1H-1,6,7-triazainden-2-yl]-1-azetidyl}-2-propen-1-one
171		1-{3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-piperidyl}-2-propen-1-one
172		N-{1-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]cyclopropyl}acrylamide
173		1-{3-[3-benzyl-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-azetidyl}-2-propen-1-one

Ex.	Structure	Name
174		1-[(R)-3-[5-(o-hydroxyphenyl)-3-phenyl-1H-1,6,7-triazainden-2-yl]-1-pyrrolidinyl]-2-propen-1-one
175		1-[(S)-3-[5-(o-hydroxyphenyl)-3-methyl-1H-1,6,7-triazainden-2-yl]-1-pyrrolidinyl]-2-propen-1-one
176		1-[3-[5-(o-hydroxyphenyl)-3-(3-pyrazolyl)-1H-1,6,7-triazainden-2-yl]-1-azetidiny]-2-propen-1-one
177		1-[(R)-2-[[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]methyl]-1-pyrrolidinyl]-2-propen-1-one
178		1-[3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2,2-dimethyl-1-azetidiny]-2-propen-1-one
179		1-[(S)-3-[5-(o-hydroxyphenyl)-3-phenyl-1H-1,6,7-triazainden-2-yl]-1-pyrrolidinyl]-2-propen-1-one
180		(E)-1-[(S)-3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-pyrrolidinyl]-4-(6,6-dimethyl-3-azabicyclo[3.1.0]hex-3-yl)-2-buten-1-one
181		(E)-1-[(R)-3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-pyrrolidinyl]-4-(6,6-dimethyl-3-azabicyclo[3.1.0]hex-3-yl)-2-buten-1-one

Ex.	Structure	Name
182		(E)-4-(3-azabicyclo[3.2.1]oct-3-yl)-1-{3-[5-(o-hydroxyphenyl)-3-phenyl-1H-1,6,7-triazainden-2-yl]-1-azetidiny}-2-buten-1-one
183		(E)-4-(diethylamino)-1-{3-[5-(o-hydroxyphenyl)-3-phenyl-1H-1,6,7-triazainden-2-yl]-1-azetidiny}-2-buten-1-one
184		2-fluoro-1-{3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-azetidiny}-2-propen-1-one
185		1-{3-[5-(3-fluoro-2-hydroxyphenyl)-3-phenyl-1H-1,6,7-triazainden-2-yl]-1-azetidiny}-2-propen-1-one
186		N-{3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]bicyclo[1.1.1]pent-1-yl}-N-methylacrylamide
187		1-{4-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-isoindolinyl}-2-propen-1-one
188		1-{2-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-7-aza-7-spiro[3.5]nonyl}-2-propen-1-one
189		1-{1-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-3-azabicyclo[3.1.0]hex-3-yl}-2-propen-1-one

Ex.	Structure	Name
190		1-{2-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-piperidyl}-2-propen-1-one
191		1-{3-[3-bromo-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-azetidyl}-2-propen-1-one
192		1-{3-[5-(o-hydroxyphenyl)-3-(1-methyl-4-pyrazolyl)-1H-1,6,7-triazainden-2-yl]-1-azetidyl}-2-propen-1-one
193		1-[(S)-2-{[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]methyl}-1-pyrrolidyl]-2-propen-1-one
194		1-(3-{[3-bromo-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]methyl}-1-azetidyl)-2-propen-1-one
195		1-{6-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1,2,3,4-tetrahydro-2-isoquinolyl}-2-propen-1-one
196		1-{4-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-indolyl}-2-propen-1-one
197		1-{6-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-indolyl}-2-propen-1-one

Ex.	Structure	Name
198		1-{4-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-4-methyl-1-piperidyl}-2-propen-1-one
199		1-{2-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-pyrrolidinyl}-2-propen-1-one
200		1-{3-[5-(o-hydroxyphenyl)-3-(5-pyrimidinyl)-1H-1,6,7-triazainden-2-yl]-1-azetidiny]-2-propen-1-one
201		1-{3-[5-(o-hydroxyphenyl)-3-(3-pyridyl)-1H-1,6,7-triazainden-2-yl]-1-azetidiny]-2-propen-1-one
202		1-(3-{3-[p-(tert-butyl)phenyl]-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-azetidiny)-2-propen-1-one
203		1-{3-[5-(o-hydroxyphenyl)-3-(1-methyl-3-pyrazolyl)-1H-1,6,7-triazainden-2-yl]-1-azetidiny]-2-propen-1-one
204		1-{3-[5-(o-hydroxyphenyl)-3-(m-methoxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-azetidiny]-2-propen-1-one

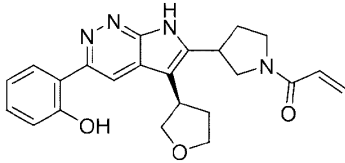
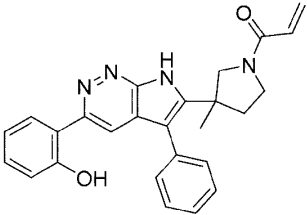
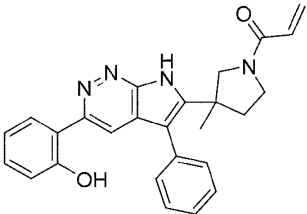
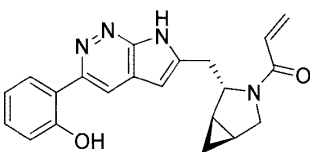
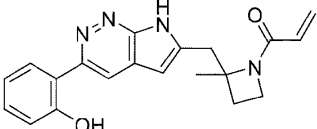
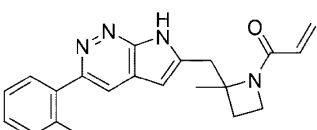
Ex.	Structure	Name
205		(E)-4-(6,6-dimethyl-3-azabicyclo[3.1.0]hex-3-yl)-1-{3-[5-(3-fluoro-2-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-azetidiny}-2-buten-1-one
206		1-(3-{2-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]ethynyl}-1-azetidiny)-2-propen-1-one
207		1-{5-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1,2,3,4-tetrahydro-2-isoquinolyl}-2-propen-1-one
208		1-{7-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1,2,3,4-tetrahydro-2-isoquinolyl}-2-propen-1-one
209		1-{7-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-3-azabicyclo[3.3.0]oct-3-yl}-2-propen-1-one
210		1-{8-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1,2,3,4-tetrahydro-2-isoquinolyl}-2-propen-1-one
211		N-(1-{[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]carbonyl}-3-pyrrolidiny)-N-methylacrylamide
212		1-{3-[3-cyclopropyl-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-azetidiny}-2-propen-1-one

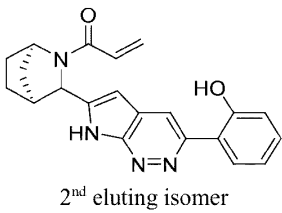
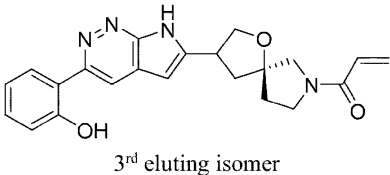
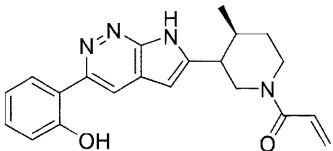
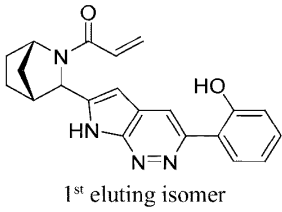
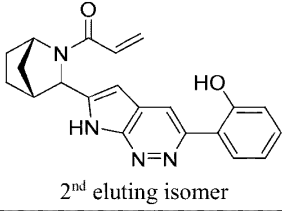
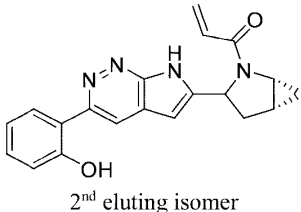
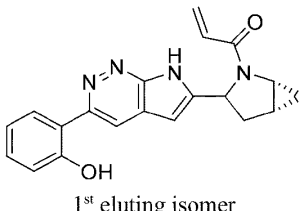
Ex.	Structure	Name
213		1-{3-[5-(o-hydroxyphenyl)-3-(4-pyridyl)-1H-1,6,7-triazainden-2-yl]-1-azetidiny]-2-propen-1-one
214		1-{3-[5-(o-hydroxyphenyl)-3-(p-methoxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-azetidiny]-2-propen-1-one
215		1-{3-[3-(p-chlorophenyl)-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-azetidiny]-2-propen-1-one
216		1-{3-[5-(o-hydroxyphenyl)-3-methyl-1H-1,6,7-triazainden-2-yl]-1-azetidiny]-2-propen-1-one
217		N-{3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]bicyclo[1.1.1]pent-1-yl}acrylamide
218		1-[(1R,6r)-6-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-3-azabicyclo[3.1.0]hex-3-yl]-2-propen-1-one
219		1-{3-[5-(o-hydroxyphenyl)-3-methyl-1H-1,6,7-triazainden-2-yl]-1-azepanyl}-2-propen-1-one
220		(E)-4,4,4-trifluoro-1-{3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-azetidiny]-2-buten-1-one

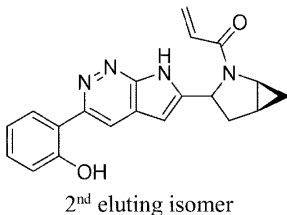
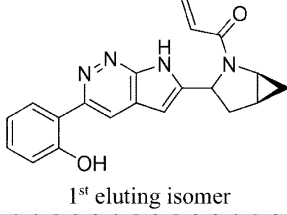
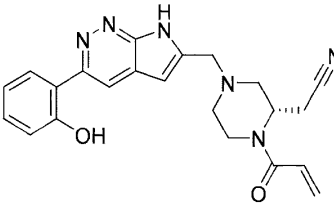
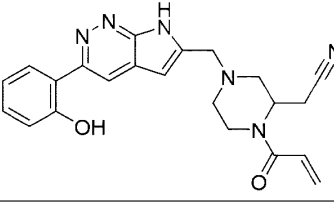
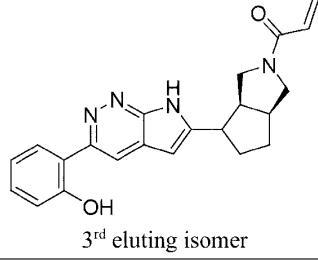
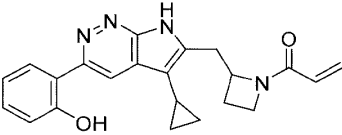
Ex.	Structure	Name
221		(E)-4-{3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-azetidynyl}-4-oxo-2-butenenitrile
222		1-{3-[3-chloro-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-azetidynyl}-2-propen-1-one
223		1-{3-[5-(o-hydroxyphenyl)-3-phenyl-1H-1,6,7-triazainden-2-yl]-1-azetidynyl}-2-propen-1-one
224		1-(3-{[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]methyl}-1-azetidynyl)-2-propen-1-one
225		(E)-4-(8-azabicyclo[3.2.1]oct-8-yl)-1-{3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-azetidynyl}-2-buten-1-one
226		(E)-1-{3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-azetidynyl}-4-(4-methyl-2-azabicyclo[2.1.1]hex-2-yl)-2-buten-1-one
227		(E)-4-(2-azabicyclo[2.1.1]hex-2-yl)-1-{3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-azetidynyl}-2-buten-1-one
228		(E)-4-(6,6-dimethyl-3-azabicyclo[3.1.0]hex-3-yl)-1-{3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-azetidynyl}-2-buten-1-one
229		(E)-4-(diethylamino)-1-{3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-azetidynyl}-2-buten-1-one

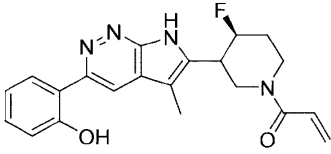
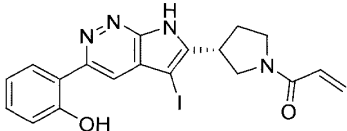
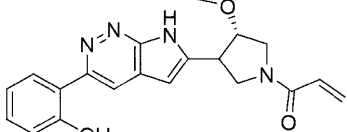
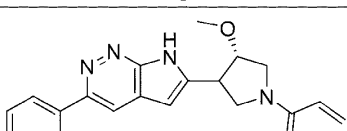
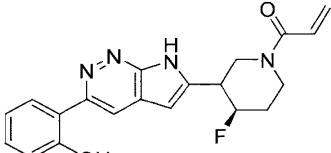
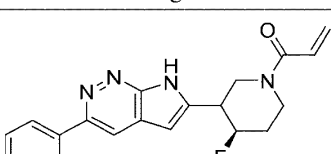
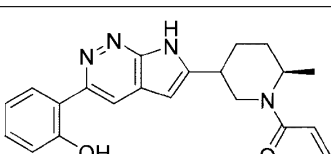
Ex.	Structure	Name
230		1-(4-{[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]methyl}-1-piperazinyl)-2-propen-1-one
231		1-((R)-3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-pyrrolidinyl)-2-propen-1-one
232		1-((S)-3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-pyrrolidinyl)-2-propen-1-one
233		1-{3-[5-(3-fluoro-2-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-azetidyl}-2-propen-1-one
234		1-(4-{[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]carbonyl}-1-piperazinyl)-2-propen-1-one
235		1-{4-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-piperidyl}-2-propen-1-one
236		1-{3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-pyrrolidinyl}-2-propen-1-one
237		1-((4S)-3-[3-bromo-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-4-fluoro-1-piperidyl)-2-propen-1-one 1 st eluting isomer

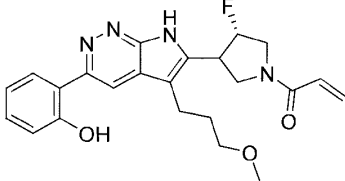
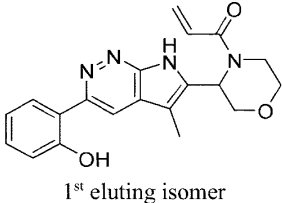
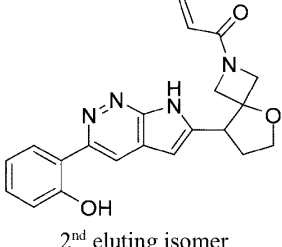
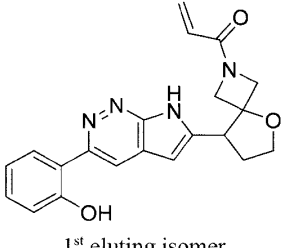
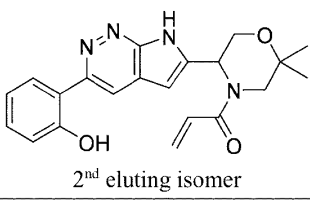
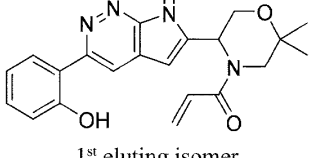
Ex.	Structure	Name
238		1-((1R,5R,6R)-6-[3-bromo-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-3-azabicyclo[3.3.0]oct-3-yl)-2-propen-1-one
239		1-(4-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-azabicyclo[2.2.1]hept-2-yl)-2-propen-1-one
240		1-((3S)-3-fluoro-4-[5-(o-hydroxyphenyl)-3-(4-pyridyl)-1H-1,6,7-triazainden-2-yl]-1-pyrrolidinyl)-2-propen-1-one
241		1-((3S)-3-fluoro-4-[5-(o-hydroxyphenyl)-3-phenyl-1H-1,6,7-triazainden-2-yl]-1-pyrrolidinyl)-2-propen-1-one
242		1-(3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-oxa-8-aza-8-spiro[4.5]decyl)-2-propen-1-one
243		1-(2-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-7-azabicyclo[2.2.1]hept-7-yl)-2-propen-1-one
244		1-(3-[3-((S)-tetrahydro-3-furyl)-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-pyrrolidinyl)-2-propen-1-one 2 nd eluting isomer

Ex.	Structure	Name
245	 1st eluting isomer	1-[3-{3-[(R)-tetrahydro-3-furyl]-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl}-1-pyrrolidinyl]-2-propen-1-one
246	 2nd eluting isomer	1-{3-[5-(o-hydroxyphenyl)-3-phenyl]-1H-1,6,7-triazainden-2-yl}-3-methyl-1-pyrrolidinyl]-2-propen-1-one
247	 1st eluting isomer	1-{3-[5-(o-hydroxyphenyl)-3-phenyl]-1H-1,6,7-triazainden-2-yl}-3-methyl-1-pyrrolidinyl]-2-propen-1-one
248		1-[(1R,2S,5S)-2-{[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]methyl}-3-azabicyclo[3.1.0]hex-3-yl]-2-propen-1-one
249	 2nd eluting isomer	1-[2-{[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]methyl}-2-methyl-1-azetidiny]-2-propen-1-one
250	 1st eluting isomer	1-[2-{[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]methyl}-2-methyl-1-azetidiny]-2-propen-1-one

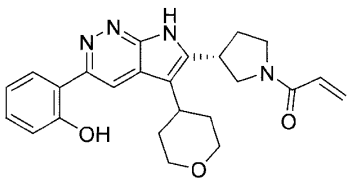
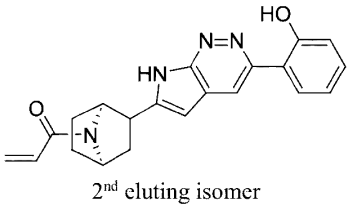
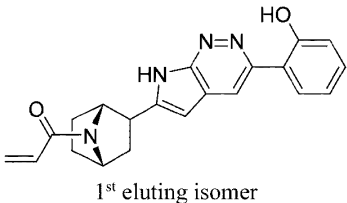
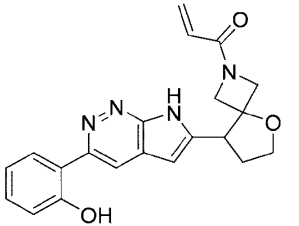
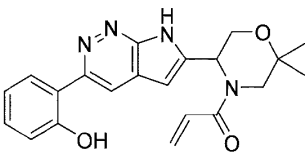
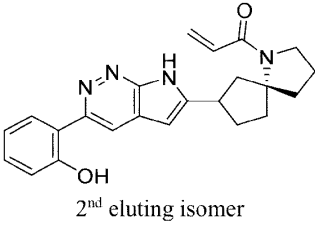
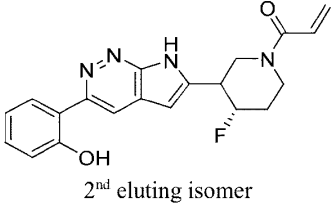
Ex.	Structure	Name
251	 2nd eluting isomer	1-((3R,4S)-3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-propen-1-one)azabicyclo[2.2.1]hept-2-yl]-2-propen-1-one
252	 3rd eluting isomer	1-((3S)-3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-oxa-7-aza-7-spiro[4.4]nonyl)-2-propen-1-one
253	 1st eluting isomer	1-((4S)-3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-4-methyl-1-piperidyl)-2-propen-1-one
254	 1st eluting isomer	1-((1S,4R)-3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-azabicyclo[2.2.1]hept-2-yl)-2-propen-1-one
255	 2nd eluting isomer	1-((1S,4R)-3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-azabicyclo[2.2.1]hept-2-yl)-2-propen-1-one
256	 2nd eluting isomer	1-((1R,5R)-3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-azabicyclo[3.1.0]hex-2-yl)-2-propen-1-one
257	 1st eluting isomer	1-((1R,5R)-3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-azabicyclo[3.1.0]hex-2-yl)-2-propen-1-one

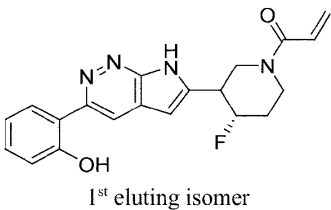
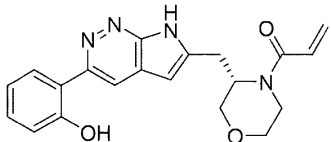
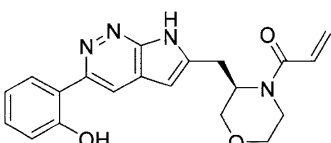
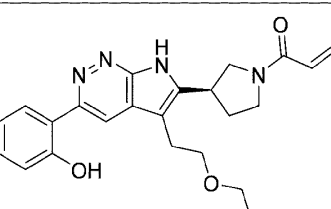
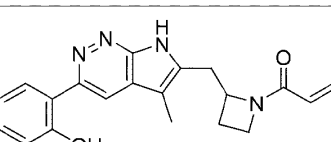
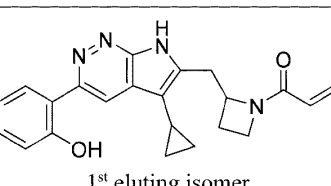
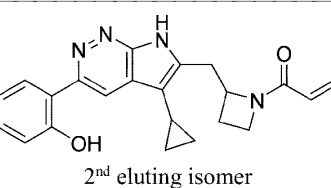
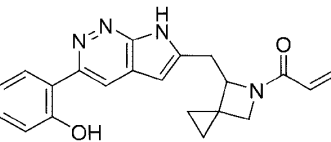
Ex.	Structure	Name
258	 2nd eluting isomer	1-((1S,5S)-3-(5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl)-2-azabicyclo[3.1.0]hex-2-yl)-2-propen-1-one
259	 1st eluting isomer	1-((1S,5S)-3-(5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl)-2-azabicyclo[3.1.0]hex-2-yl)-2-propen-1-one
260		[1-(acryloyl-4-((5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl)methyl)-2-piperazinyl]acetonitrile
261		[1-(acryloyl-4-((5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl)methyl)-2-piperazinyl]acetonitrile
262	 3rd eluting isomer	1-((1S,6R)-6-(5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl)-3-azabicyclo[3.3.0]oct-3-yl)-2-propen-1-one
263		1-(2-((3-cyclopropyl-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl)methyl)-1-azetidiny)-2-propen-1-one

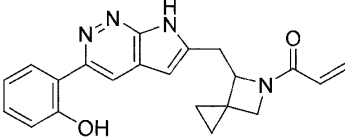
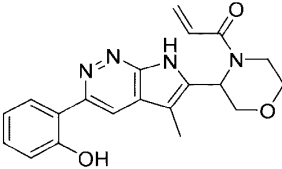
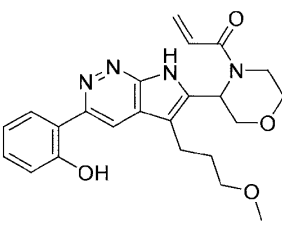
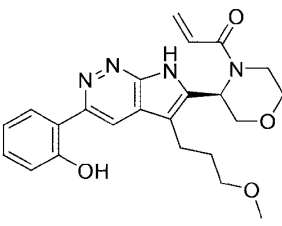
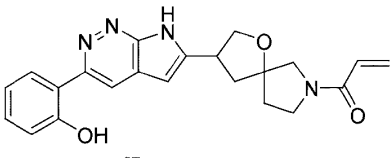
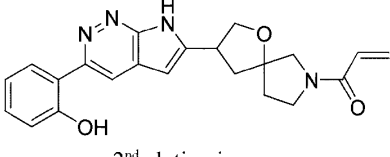
Ex.	Structure	Name
264	 1st eluting isomer	1-((4S)-4-fluoro-3-[5-(o-hydroxyphenyl)-3-methyl-1H-1,6,7-triazainden-2-yl]-1-piperidyl)-2-propen-1-one
265		1-((R)-3-[5-(o-hydroxyphenyl)-3-iodo-1H-1,6,7-triazainden-2-yl]-1-pyrrolidinyl)-2-propen-1-one
266	 2nd eluting isomer	1-((4S)-3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-4-methoxy-1-pyrrolidinyl)-2-propen-1-one
267	 1st eluting isomer	1-((4S)-3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-4-methoxy-1-pyrrolidinyl)-2-propen-1-one
268	 2nd eluting isomer	1-((4R)-4-fluoro-3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-piperidyl)-2-propen-1-one
269	 1st eluting isomer	1-((4R)-4-fluoro-3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-piperidyl)-2-propen-1-one
270	 2nd eluting isomer	1-((2R)-5-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-methyl-1-piperidyl)-2-propen-1-one

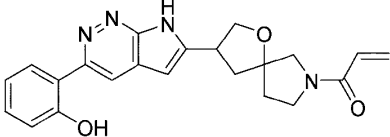
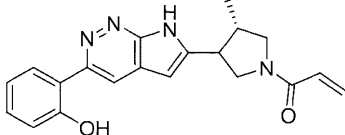
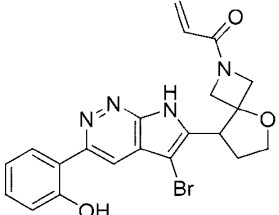
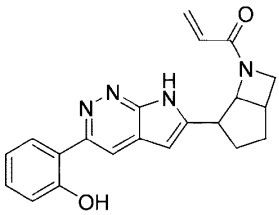
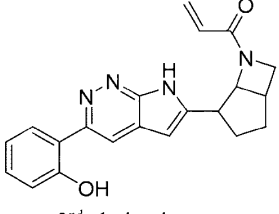
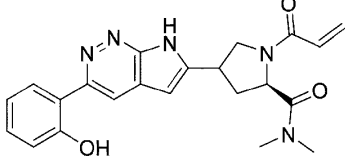
Ex.	Structure	Name
271		1-[(3S)-3-fluoro-4-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-pyrrolidinyl]-2-propen-1-one
272	 1 st eluting isomer	1-[3-[5-(o-hydroxyphenyl)-3-methyl-1H-1,6,7-triazainden-2-yl]-4-morpholinyl]-2-propen-1-one
273	 2 nd eluting isomer	1-[8-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-5-oxa-2-aza-2-spiro[3.4]octyl]-2-propen-1-one
274	 1 st eluting isomer	1-[8-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-5-oxa-2-aza-2-spiro[3.4]octyl]-2-propen-1-one
275	 2 nd eluting isomer	1-[5-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2,2-dimethyl-4-morpholinyl]-2-propen-1-one
276	 1 st eluting isomer	1-[5-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2,2-dimethyl-4-morpholinyl]-2-propen-1-one

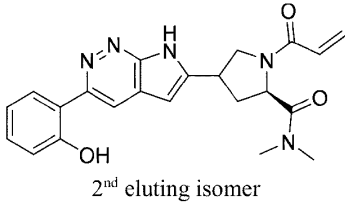
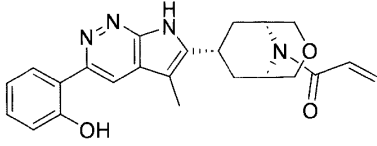
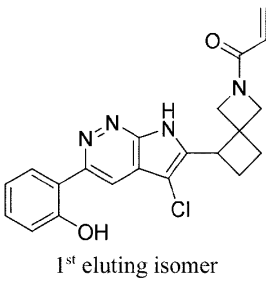
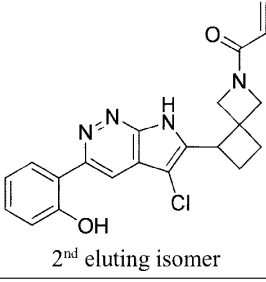
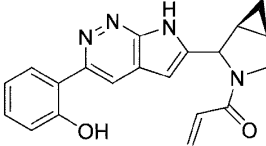
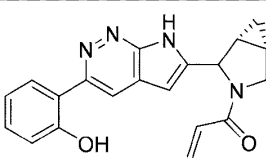
Ex.	Structure	Name
277		1-{3-[3-bromo-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-pyrrolidinyl}-2-propen-1-one
278		1-{3-[3-bromo-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-4-morpholinyl}-2-propen-1-one 2 nd eluting isomer
279		1-{3-[3-bromo-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-4-morpholinyl}-2-propen-1-one 1 st eluting isomer
280		N-{1-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]cyclopropyl}-N-methylacrylamide
281		1-[(3R)-3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2-methyl-4-morpholinyl]-2-propen-1-one 1 st eluting isomer
282		1-[(3S)-3-fluoro-4-[5-(o-hydroxyphenyl)-3-(1-methyl-4-pyrazolyl)-1H-1,6,7-triazainden-2-yl]-1-pyrrolidinyl]-2-propen-1-one
283		1-[(3S)-3-fluoro-4-[5-(o-hydroxyphenyl)-3-(3-methyl-4-pyrazolyl)-1H-1,6,7-triazainden-2-yl]-1-pyrrolidinyl]-2-propen-1-one

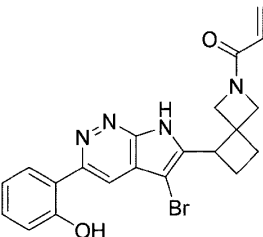
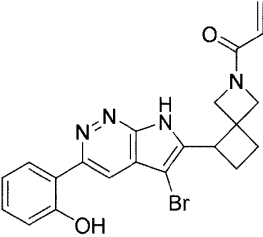
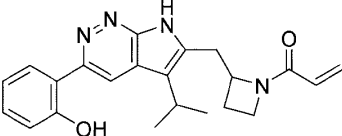
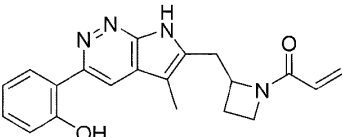
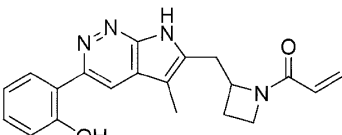
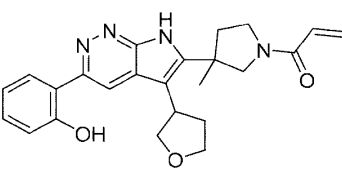
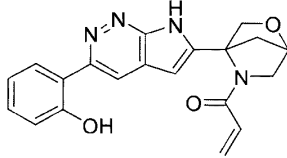
Ex.	Structure	Name
284		1-[(R)-3-[5-(o-hydroxyphenyl)-3-[(tetrahydro-2H-pyran-4-yl)-1H-1,6,7-triazainden-2-yl]-1-pyrrolidinyl]-2-propen-1-one
285	 2 nd eluting isomer	1-[(1S,4R)-2-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-7-azabicyclo[2.2.1]hept-7-yl]-2-propen-1-one
286	 1 st eluting isomer	1-[(1R,4S)-2-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-7-azabicyclo[2.2.1]hept-7-yl]-2-propen-1-one
287		1-[8-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-5-oxa-2-aza-2-spiro[3.4]octyl]-2-propen-1-one
288		1-[5-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-2,2-dimethyl-4-morpholinyl]-2-propen-1-one
289	 2 nd eluting isomer	1-[(5S)-7-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-aza-1-spiro[4.4]nonyl]-2-propen-1-one
290	 2 nd eluting isomer	1-[(4S)-4-fluoro-3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-piperidyl]-2-propen-1-one

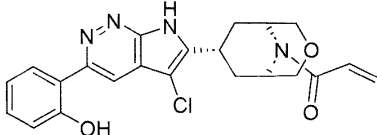
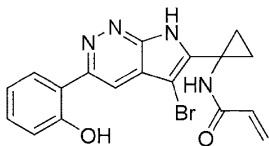
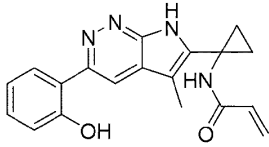
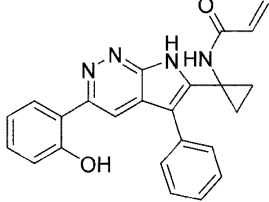
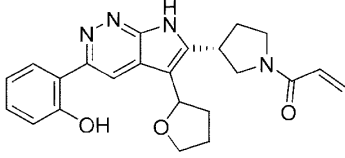
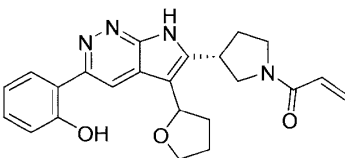
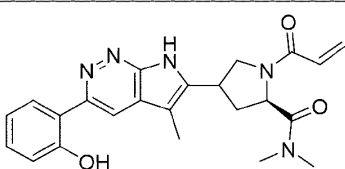
Ex.	Structure	Name
291	 1st eluting isomer	1-((4S)-4-fluoro-3-[5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-1-piperidyl)-2-propen-1-one
292		(S)-1-(3-((3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)morpholino)prop-2-en-1-one
293		(R)-1-(3-((3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)morpholino)prop-2-en-1-one
294		(R)-1-(3-(5-(2-ethoxyethyl)-3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)pyrrolidin-1-yl)prop-2-en-1-one
295		1-(2-((3-(2-hydroxyphenyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)azetidin-1-yl)prop-2-en-1-one
296	 1st eluting isomer	1-(2-((5-cyclopropyl-3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)azetidin-1-yl)prop-2-en-1-one
297	 2nd eluting isomer	1-(2-((5-cyclopropyl-3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)azetidin-1-yl)prop-2-en-1-one
298		1-(4-((3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)-5-azaspiro[2.3]hexan-5-yl)prop-2-en-1-one

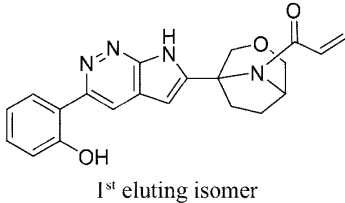
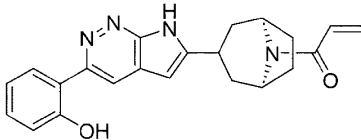
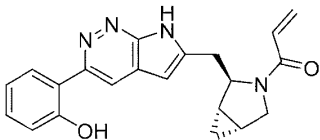
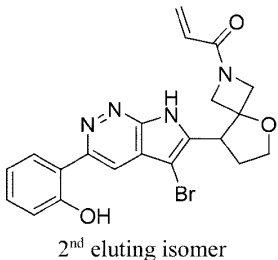
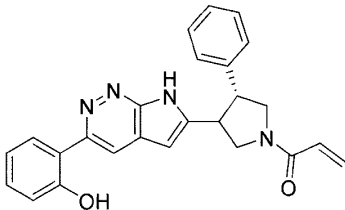
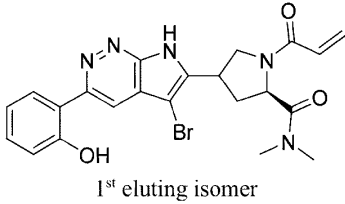
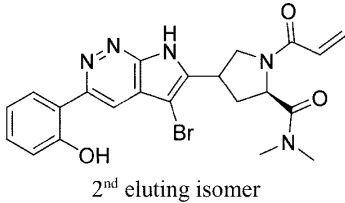
Ex.	Structure	Name
299	 2nd eluting isomer	1-(4-((3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)-5-azaspiro[2.3]hexan-5-yl)prop-2-en-1-one
300	 2nd eluting isomer	1-(3-(3-(2-hydroxyphenyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)morpholino)prop-2-en-1-one
301	 2nd eluting isomer	1-(3-(3-(2-hydroxyphenyl)-5-(3-methoxypropyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)morpholino)prop-2-en-1-one
302	 1st eluting isomer	1-(3-(3-(2-hydroxyphenyl)-5-(3-methoxypropyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)morpholino)prop-2-en-1-one
303	 1st eluting isomer	1-(3-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-1-oxa-7-azaspiro[4.4]nonan-7-yl)prop-2-en-1-one
304	 2nd eluting isomer	1-(3-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-1-oxa-7-azaspiro[4.4]nonan-7-yl)prop-2-en-1-one

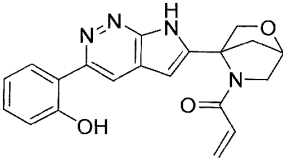
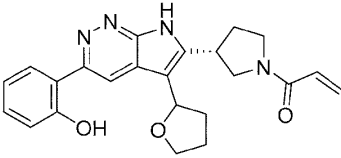
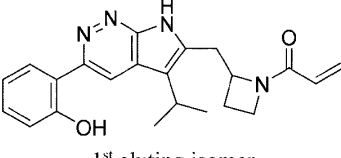
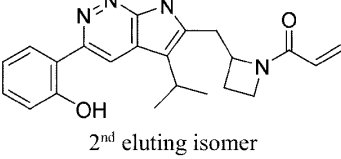
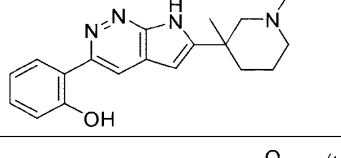
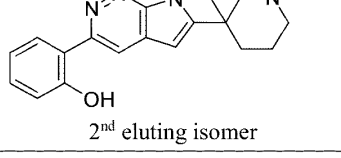
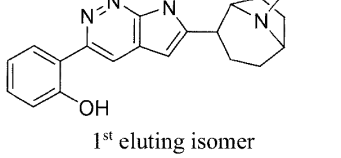
Ex.	Structure	Name
305	 4th eluting isomer	1-(3-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-1-oxa-7-azaspiro[4.4]nonan-7-yl)prop-2-en-1-one
306		1-((4S)-3-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-4-methylpyrrolidin-1-yl)prop-2-en-1-one
307	 1st eluting isomer	1-(8-(5-bromo-3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-5-oxa-2-azaspiro[3.4]octan-2-yl)prop-2-en-1-one
308	 1st eluting isomer	1-(4-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-6-azabicyclo[3.2.0]heptan-6-yl)prop-2-en-1-one
309	 2nd eluting isomer	1-(4-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-6-azabicyclo[3.2.0]heptan-6-yl)prop-2-en-1-one
310	 1st eluting isomer	(2R)-1-acryloyl-4-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-N,N-dimethylpyrrolidine-2-carboxamide

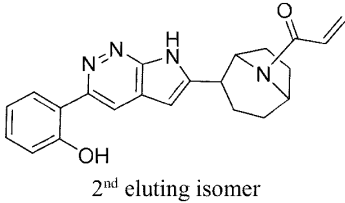
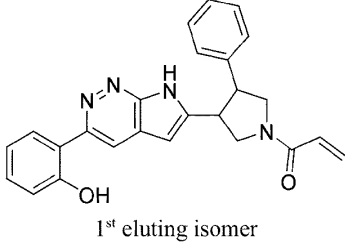
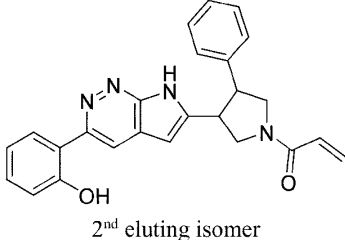
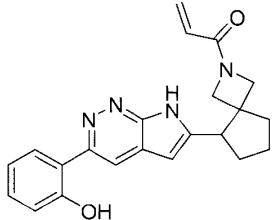
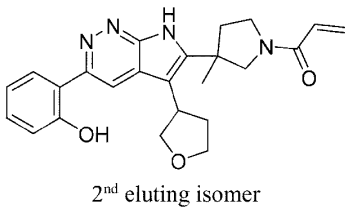
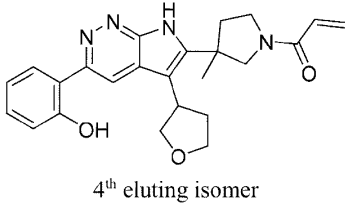
Ex.	Structure	Name
311	 2nd eluting isomer	(4S)-1-acryloyl-4-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-N,N-dimethylpyrrolidine-2-carboxamide
312		1-((1R,5S,7r)-7-(3-(2-hydroxyphenyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one
313	 1st eluting isomer	1-(5-(5-chloro-3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-2-azaspiro[3.3]heptan-2-yl)prop-2-en-1-one
314	 2nd eluting isomer	1-(5-(5-chloro-3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-2-azaspiro[3.3]heptan-2-yl)prop-2-en-1-one
315		1-((1S,5R)-2-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-azabicyclo[3.1.0]hexan-3-yl)prop-2-en-1-one
316		1-((1R,5S)-2-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-azabicyclo[3.1.0]hexan-3-yl)prop-2-en-1-one

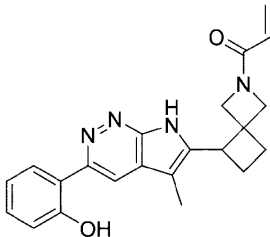
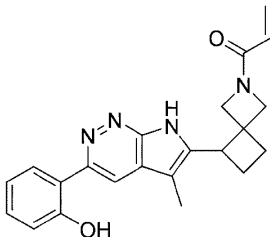
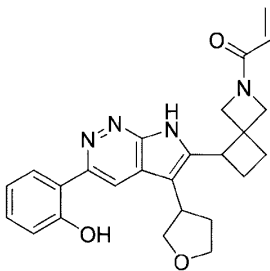
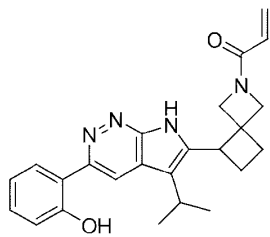
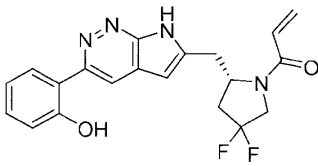
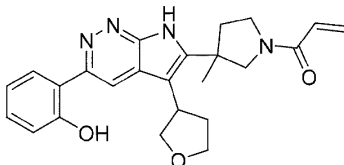
Ex.	Structure	Name
317	 1st eluting isomer	1-(5-(5-bromo-3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-2-azaspiro[3.3]heptan-2-yl)prop-2-en-1-one
318	 2nd eluting isomer	1-(5-(5-bromo-3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-2-azaspiro[3.3]heptan-2-yl)prop-2-en-1-one
319		1-(2-((3-(2-hydroxyphenyl)-5-isopropyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)azetidin-1-yl)prop-2-en-1-one
320	 1st eluting isomer	1-(2-((3-(2-hydroxyphenyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)azetidin-1-yl)prop-2-en-1-one
321	 2nd eluting isomer	1-(2-((3-(2-hydroxyphenyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)azetidin-1-yl)prop-2-en-1-one
322		1-(3-(3-(2-hydroxyphenyl)-5-(tetrahydrofuran-3-yl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-methylpyrrolidin-1-yl)prop-2-en-1-one
323		1-(4-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)prop-2-en-1-one

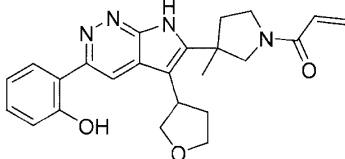
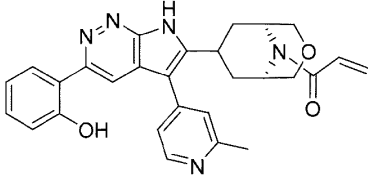
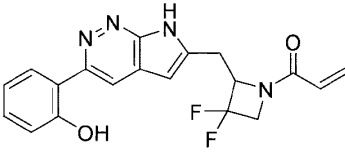
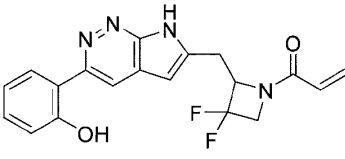
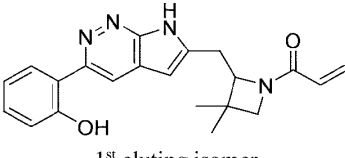
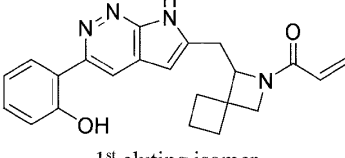
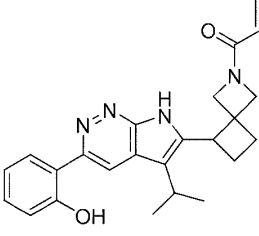
Ex.	Structure	Name
324		1-((1R,5S,7r)-7-(5-chloro-3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one
325		N-(1-(5-bromo-3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)cyclopropyl)acrylamide
326		N-(1-(3-(2-hydroxyphenyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)cyclopropyl)acrylamide
327		N-(1-(3-(2-hydroxyphenyl)-5-phenyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)cyclopropyl)acrylamide
328		1-((3R)-3-(3-(2-hydroxyphenyl)-5-(tetrahydrofuran-2-yl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)pyrrolidin-1-yl)prop-2-en-1-one
329	 1 st eluting isomer	1-((3R)-3-(3-(2-hydroxyphenyl)-5-(tetrahydrofuran-2-yl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)pyrrolidin-1-yl)prop-2-en-1-one
330		(2R)-1-acryloyl-4-(3-(2-hydroxyphenyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)-N,N-dimethylpyrrolidine-2-carboxamide

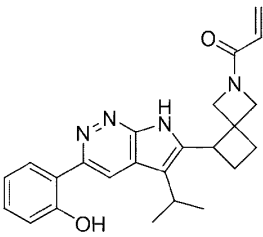
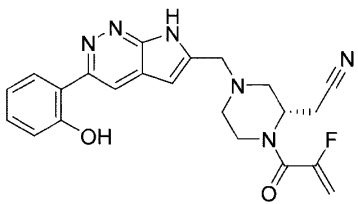
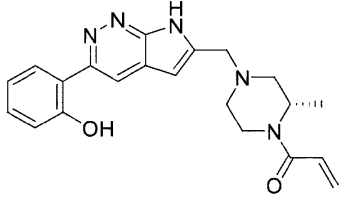
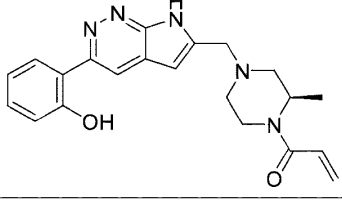
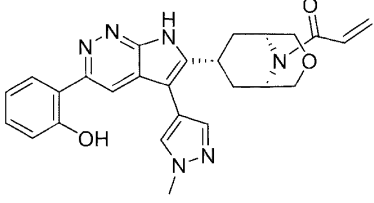
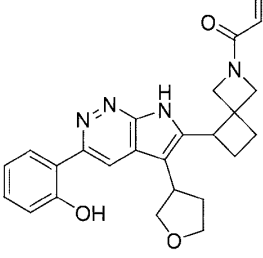
Ex.	Structure	Name
331	 1st eluting isomer	1-(1-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-8-azabicyclo[3.2.1]octan-8-yl)prop-2-en-1-one
332		1-((1R,5S)-3-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-8-azabicyclo[3.2.1]octan-8-yl)prop-2-en-1-one
333		1-((1S,2R,5R)-2-((3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)-3-azabicyclo[3.1.0]hexan-3-yl)prop-2-en-1-one
334	 2nd eluting isomer	1-(8-(5-bromo-3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-5-oxa-2-azaspiro[3.4]octan-2-yl)prop-2-en-1-one
335		1-((4R)-3-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-4-phenylpyrrolidin-1-yl)prop-2-en-1-one
336	 1st eluting isomer	(2R)-1-acryloyl-4-(5-bromo-3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-N,N-dimethylpyrrolidine-2-carboxamide
337	 2nd eluting isomer	(2R)-1-acryloyl-4-(5-bromo-3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-N,N-dimethylpyrrolidine-2-carboxamide

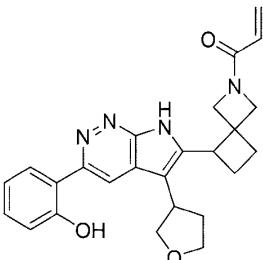
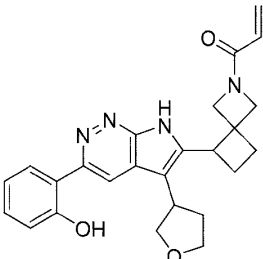
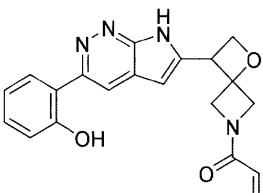
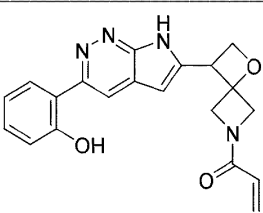
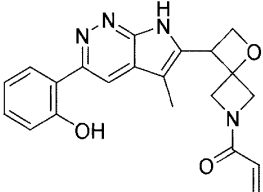
Ex.	Structure	Name
338	 1st eluting isomer	1-(4-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)prop-2-en-1-one
339	 2nd eluting isomer	1-((3R)-3-(3-(2-hydroxyphenyl)-5-(tetrahydrofuran-2-yl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)pyrrolidin-1-yl)prop-2-en-1-one
340	 1st eluting isomer	1-(2-((3-(2-hydroxyphenyl)-5-isopropyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)azetidin-1-yl)prop-2-en-1-one
341	 2nd eluting isomer	1-(2-((3-(2-hydroxyphenyl)-5-isopropyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)azetidin-1-yl)prop-2-en-1-one
342		1-(3-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-methylpiperidin-1-yl)prop-2-en-1-one
343	 2nd eluting isomer	1-(3-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-methylpiperidin-1-yl)prop-2-en-1-one
344	 1st eluting isomer	1-(2-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-8-azabicyclo[3.2.1]octan-8-yl)prop-2-en-1-one

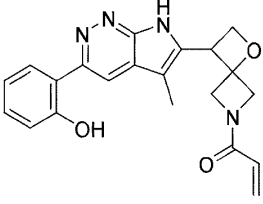
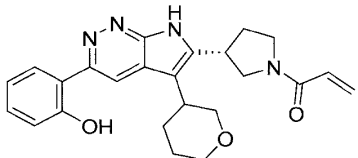
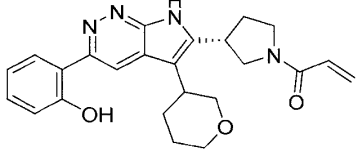
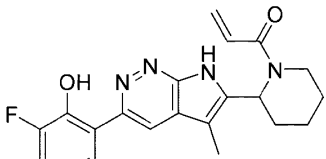
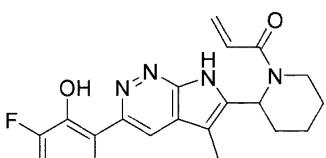
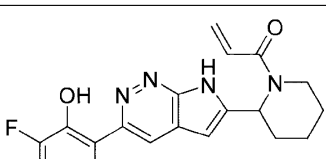
Ex.	Structure	Name
345	 2nd eluting isomer	1-(2-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-8-azabicyclo[3.2.1]octan-8-yl)prop-2-en-1-one
346	 1st eluting isomer	1-(3-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-4-phenylpyrrolidin-1-yl)prop-2-en-1-one
347	 2nd eluting isomer	1-(3-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-4-phenylpyrrolidin-1-yl)prop-2-en-1-one
348		1-(5-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-2-azaspiro[3.4]octan-2-yl)prop-2-en-1-one
349	 2nd eluting isomer	1-(3-(3-(2-hydroxyphenyl)-5-(tetrahydrofuran-3-yl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-methylpyrrolidin-1-yl)prop-2-en-1-one
350	 4th eluting isomer	1-(3-(3-(2-hydroxyphenyl)-5-(tetrahydrofuran-3-yl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-methylpyrrolidin-1-yl)prop-2-en-1-one

Ex.	Structure	Name
351	 1st eluting isomer	1-(5-(3-(2-hydroxyphenyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)-2-azaspiro[3.3]heptan-2-yl)prop-2-en-1-one
352	 2nd eluting isomer	1-(5-(3-(2-hydroxyphenyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)-2-azaspiro[3.3]heptan-2-yl)prop-2-en-1-one
353		1-(5-(3-(2-hydroxyphenyl)-5-(tetrahydrofuran-3-yl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-2-azaspiro[3.3]heptan-2-yl)prop-2-en-1-one
354		1-(5-(3-(2-hydroxyphenyl)-5-isopropyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)-2-azaspiro[3.3]heptan-2-yl)prop-2-en-1-one
355		(S)-1-(4,4-difluoro-2-((3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)pyrrolidin-1-yl)prop-2-en-1-one
356	 1st eluting isomer	1-(3-(3-(2-hydroxyphenyl)-5-(tetrahydrofuran-3-yl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-methylpyrrolidin-1-yl)prop-2-en-1-one

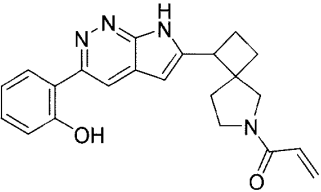
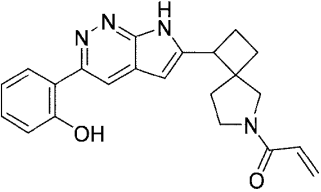
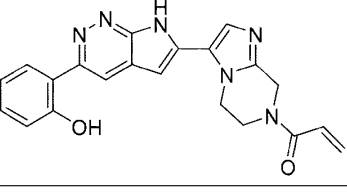
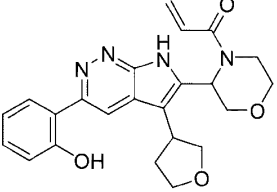
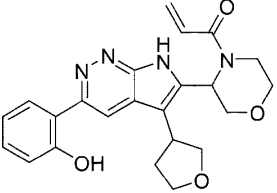
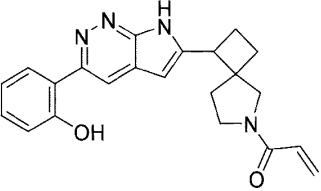
Ex.	Structure	Name
357	 3rd eluting isomer	1-(3-(3-(2-hydroxyphenyl)-5-(tetrahydrofuran-3-yl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-methylpyrrolidin-1-yl)prop-2-en-1-one
358		1-((1R,5S)-7-(3-(2-hydroxyphenyl)-5-(2-methylpyridin-4-yl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one
359	 1st eluting isomer	1-(3,3-difluoro-2-((3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)azetidin-1-yl)prop-2-en-1-one
360	 2nd eluting isomer	1-(3,3-difluoro-2-((3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)azetidin-1-yl)prop-2-en-1-one
361	 1st eluting isomer	1-(2-((3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)-3,3-dimethylazetidin-1-yl)prop-2-en-1-one
362	 1st eluting isomer	1-(1-((3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)-2-azaspiro[3.3]heptan-2-yl)prop-2-en-1-one
363	 1st eluting isomer	1-(5-(3-(2-hydroxyphenyl)-5-isopropyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)-2-azaspiro[3.3]heptan-2-yl)prop-2-en-1-one

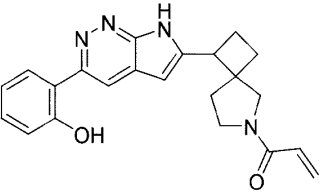
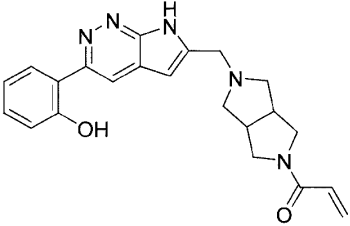
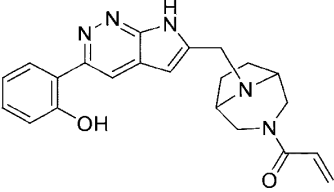
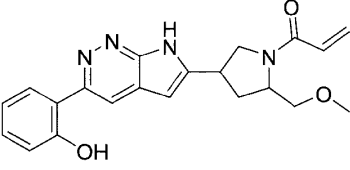
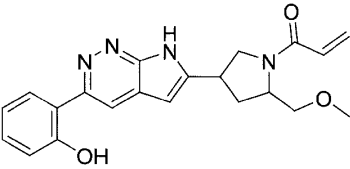
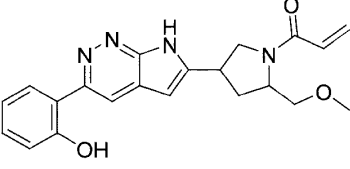
Ex.	Structure	Name
364	 2nd eluting isomer	1-(5-(3-(2-hydroxyphenyl)-5-isopropyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)-2-azaspiro[3.3]heptan-2-yl)prop-2-en-1-one
365		(S)-2-(1-(2-fluoroacryloyl)-4-((3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)piperazin-2-yl)acetonitrile
366		(S)-1-(4-((3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)-2-methylpiperazin-1-yl)prop-2-en-1-one
367		(R)-1-(4-((3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)-2-methylpiperazin-1-yl)prop-2-en-1-one
368		1-((1R,5S,7r)-7-(3-(2-hydroxyphenyl)-5-(1-methyl-1H-pyrazol-4-yl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one
369	 2nd eluting isomer	1-(5-(3-(2-hydroxyphenyl)-5-(tetrahydrofuran-3-yl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-2-azaspiro[3.3]heptan-2-yl)prop-2-en-1-one

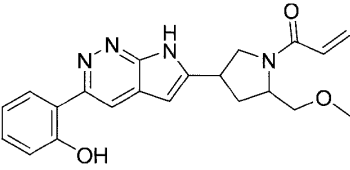
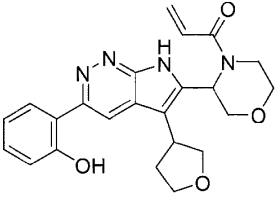
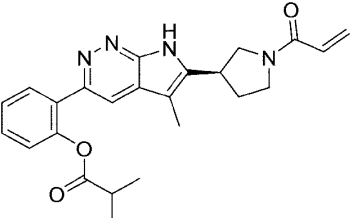
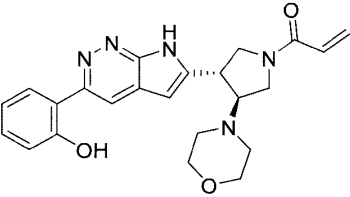
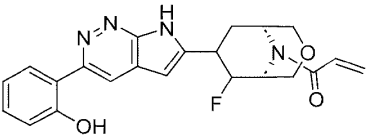
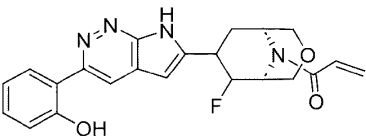
Ex.	Structure	Name
370	 4th eluting isomer	1-(5-(3-(2-hydroxyphenyl)-5-(tetrahydrofuran-3-yl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-2-azaspiro[3.3]heptan-2-yl)prop-2-en-1-one
371	 1st eluting isomer	1-(5-(3-(2-hydroxyphenyl)-5-(tetrahydrofuran-3-yl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-2-azaspiro[3.3]heptan-2-yl)prop-2-en-1-one
372	 1st eluting isomer	1-(3-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-1-oxa-6-azaspiro[3.3]heptan-6-yl)prop-2-en-1-one
373	 2nd eluting isomer	1-(3-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-1-oxa-6-azaspiro[3.3]heptan-6-yl)prop-2-en-1-one
374	 1st eluting isomer	1-(3-(3-(2-hydroxyphenyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)-1-oxa-6-azaspiro[3.3]heptan-6-yl)prop-2-en-1-one

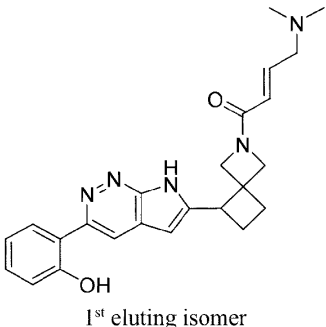
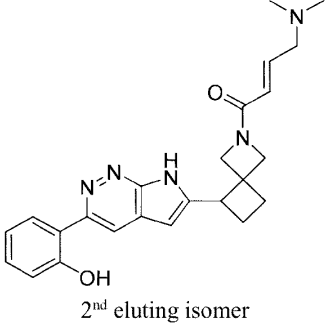
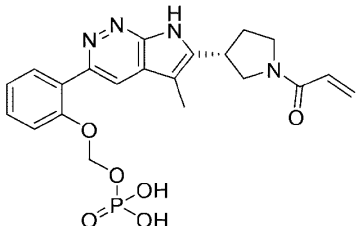
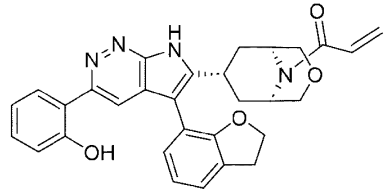
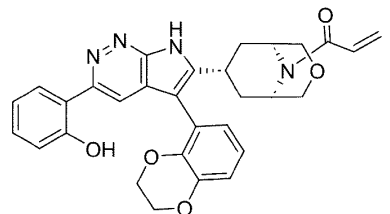
Ex.	Structure	Name
375	 2nd eluting isomer	1-(3-(3-(2-hydroxyphenyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)-1-oxa-6-azaspiro[3.3]heptan-6-yl)prop-2-en-1-one
376	 1st eluting isomer	1-((3R)-3-(3-(2-hydroxyphenyl)-5-(tetrahydro-2H-pyran-3-yl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)pyrrolidin-1-yl)prop-2-en-1-one
377	 2nd eluting isomer	1-((3R)-3-(3-(2-hydroxyphenyl)-5-(tetrahydro-2H-pyran-3-yl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)pyrrolidin-1-yl)prop-2-en-1-one
378	 1st eluting isomer	1-(2-(3-(3-fluoro-2-hydroxyphenyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)piperidin-1-yl)prop-2-en-1-one
379	 2nd eluting isomer	1-(2-(3-(3-fluoro-2-hydroxyphenyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)piperidin-1-yl)prop-2-en-1-one
380	 1st eluting isomer	1-(2-(3-(3-fluoro-2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)piperidin-1-yl)prop-2-en-1-one

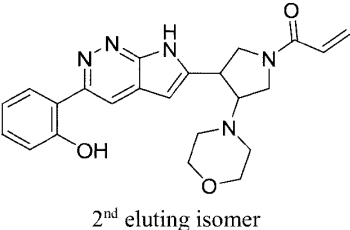
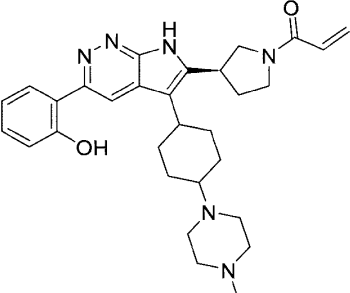
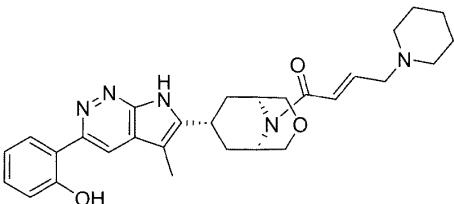
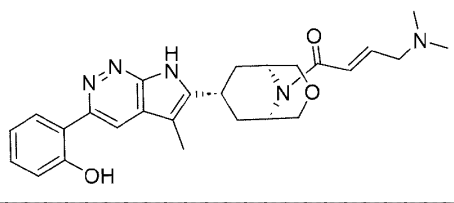
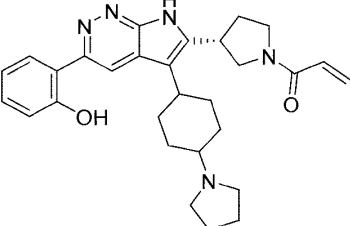
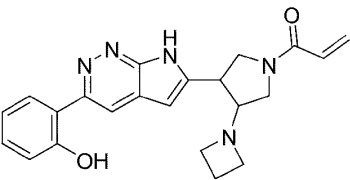
Ex.	Structure	Name
381		1-(6-((3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)-2,6-diazaspiro[3.3]heptan-2-yl)prop-2-en-1-one
382		(R)-1-(3-(3-(2-hydroxyphenyl)-5-(4-morpholinocyclohexyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)pyrrolidin-1-yl)prop-2-en-1-one
383		1-(5-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-2-azaspiro[3.4]octan-2-yl)prop-2-en-1-one 2 nd eluting isomer
384		1-((1S,5S)-6-fluoro-7-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one
385		(R,E)-3-cyclopropyl-2-(3-(3-(2-hydroxyphenyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)pyrrolidine-1-carbonyl)acrylonitrile
386		1-(3-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)-3,8-diazabicyclo[3.2.1]octan-8-yl)prop-2-en-1-one

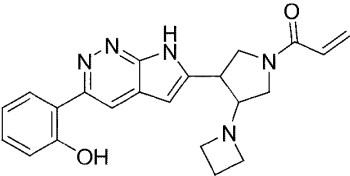
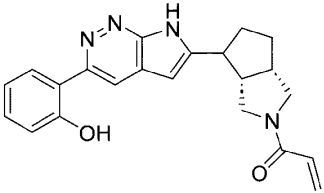
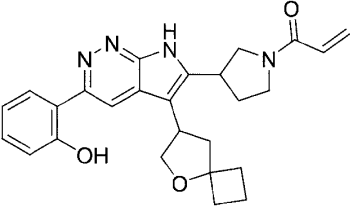
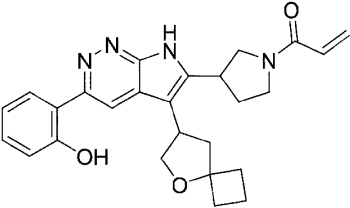
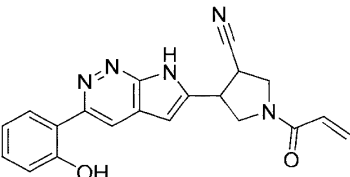
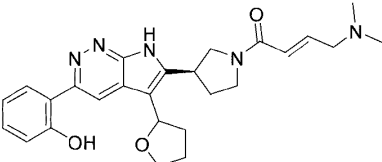
Ex.	Structure	Name
387	 3rd eluting isomer	1-(1-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-6-azaspiro[3.4]octan-6-yl)prop-2-en-1-one
388	 4th eluting isomer	1-(1-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-6-azaspiro[3.4]octan-6-yl)prop-2-en-1-one
389		1-(3-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-5,6-dihydroimidazo[1,2-a]pyrazin-7(8H)-yl)prop-2-en-1-one
390	 1st eluting isomer	1-(3-(3-(2-hydroxyphenyl)-5-(tetrahydrofuran-3-yl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)morpholino)prop-2-en-1-one
391	 2nd eluting isomer	1-(3-(3-(2-hydroxyphenyl)-5-(tetrahydrofuran-3-yl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)morpholino)prop-2-en-1-one
392	 4th eluting isomer	1-(1-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-6-azaspiro[3.4]octan-6-yl)prop-2-en-1-one

Ex.	Structure	Name
393	 3rd eluting isomer	1-(1-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-6-azaspiro[3.4]octan-6-yl)prop-2-en-1-one
394		1-(5-((3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)prop-2-en-1-one
395		1-(8-((3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)prop-2-en-1-one
397	 1st eluting isomer	1-(4-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-2-(methoxymethyl)pyrrolidin-1-yl)prop-2-en-1-one
398	 2nd eluting isomer	1-(4-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-2-(methoxymethyl)pyrrolidin-1-yl)prop-2-en-1-one
399	 3rd eluting isomer	1-(4-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-2-(methoxymethyl)pyrrolidin-1-yl)prop-2-en-1-one

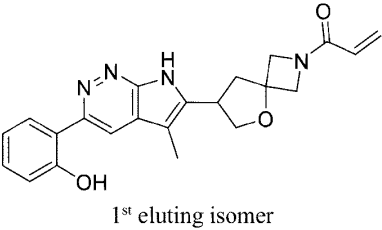
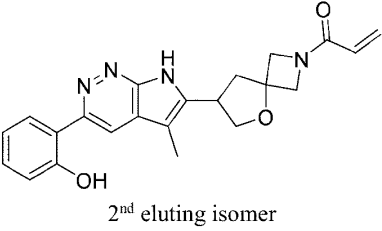
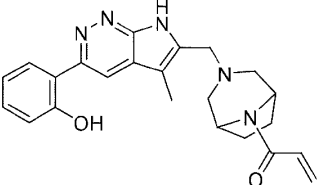
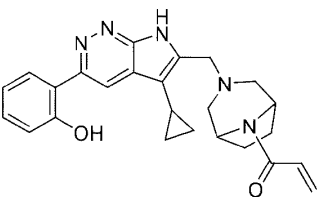
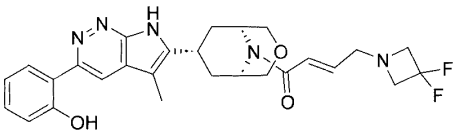
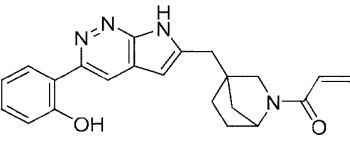
Ex.	Structure	Name
400	 4th eluting isomer	1-(4-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-2-(methoxymethyl)pyrrolidin-1-yl)prop-2-en-1-one
401	 1st eluting isomer	1-(3-(3-(2-hydroxyphenyl)-5-(tetrahydrofuran-3-yl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)morpholino)prop-2-en-1-one
402		(R)-2-(6-(1-acryloylpyrrolidin-3-yl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-3-yl)phenyl isobutyrate
403		1-((3R,4S)-3-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-4-morpholinopyrrolidin-1-yl)prop-2-en-1-one
404	 1st eluting isomer	1-((1S,5S)-6-fluoro-7-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one
405	 2nd eluting isomer	1-((1S,5S)-6-fluoro-7-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one

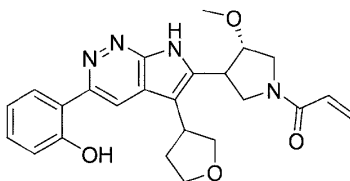
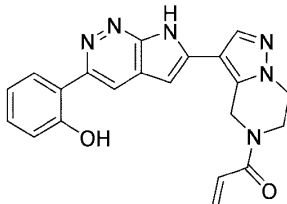
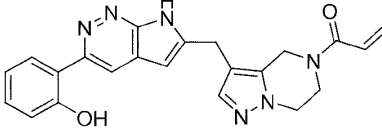
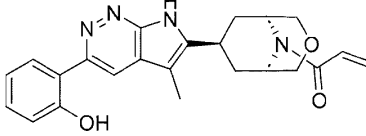
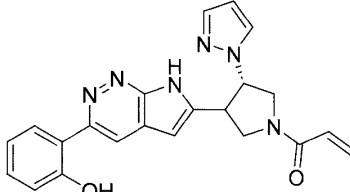
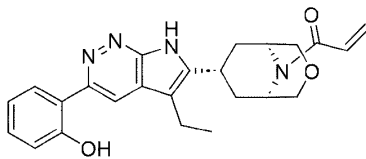
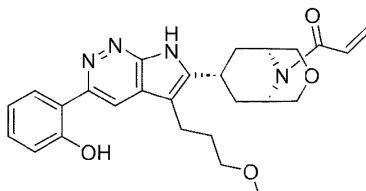
Ex.	Structure	Name
406	 1st eluting isomer	(E)-4-(dimethylamino)-1-(5-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-2-azaspiro[3.3]heptan-2-yl)but-2-en-1-one
407	 2nd eluting isomer	(E)-4-(dimethylamino)-1-(5-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-2-azaspiro[3.3]heptan-2-yl)but-2-en-1-one
408		(R)-(2-(6-(1-acryloylpyrrolidin-3-yl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-3-yl)phenoxy)methyl dihydrogen phosphate
409		1-((1R,5S,7r)-7-(5-(2,3-dihydrobenzofuran-7-yl)-3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one
410		1-((1R,5S,7r)-7-(5-(2,3-dihydrobenzo[b][1,4]dioxin-5-yl)-3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one

Ex.	Structure	Name
411	 2nd eluting isomer	1-(3-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-4-morpholinopyrrolidin-1-yl)prop-2-en-1-one
412		(R)-1-(3-(3-(2-hydroxyphenyl)-5-(4-(4-methylpiperazin-1-yl)cyclohexyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)pyrrolidin-1-yl)prop-2-en-1-one
413		(E)-1-((1R,5S,7r)-7-(3-(2-hydroxyphenyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)-4-(piperidin-1-yl)but-2-en-1-one
414		(E)-4-(dimethylamino)-1-((1R,5S,7r)-7-(3-(2-hydroxyphenyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)but-2-en-1-one
415		(R)-1-(3-(3-(2-hydroxyphenyl)-5-(4-(pyrrolidin-1-yl)cyclohexyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)pyrrolidin-1-yl)prop-2-en-1-one
416	 1st eluting isomer	1-(3-(azetidin-1-yl)-4-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)pyrrolidin-1-yl)prop-2-en-1-one

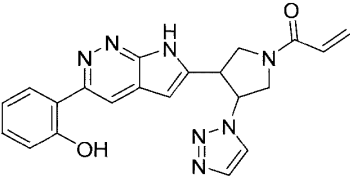
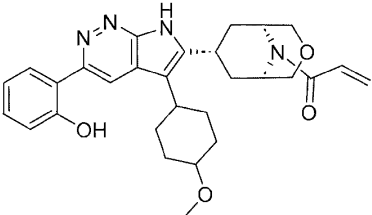
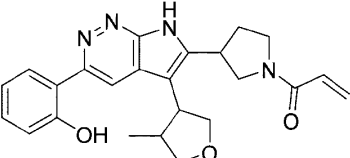
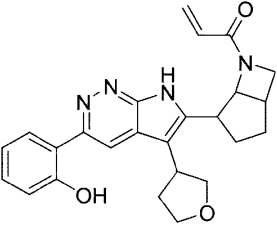
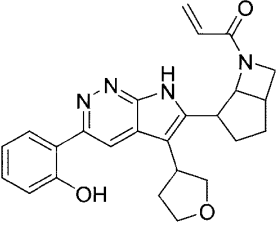
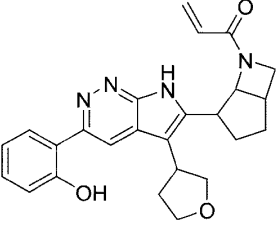
Ex.	Structure	Name
417	 2nd eluting isomer	1-(3-(azetidin-1-yl)-4-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)pyrrolidin-1-yl)prop-2-en-1-one
418	 2nd eluting isomer	1-((3aS,6aS)-4-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)hexahydrocyclopenta[c]pyrrol-2(1H)-yl)prop-2-en-1-one
419	 1st eluting isomer	1-(3-(3-(2-hydroxyphenyl)-5-(5-oxaspiro[3.4]octan-7-yl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)pyrrolidin-1-yl)prop-2-en-1-one
420	 2nd eluting isomer	1-(3-(3-(2-hydroxyphenyl)-5-(5-oxaspiro[3.4]octan-7-yl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)pyrrolidin-1-yl)prop-2-en-1-one
421	 1st eluting isomer	1-acryloyl-4-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)pyrrolidine-3-carbonitrile
422		(E)-4-(dimethylamino)-1-((3R)-3-(3-(2-hydroxyphenyl)-5-(tetrahydrofuran-2-yl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)pyrrolidin-1-yl)but-2-en-1-one

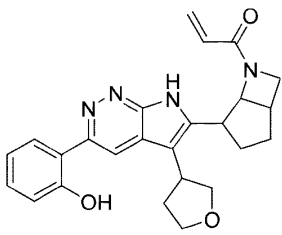
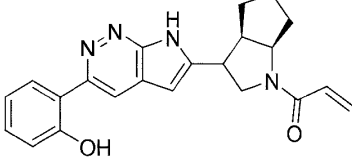
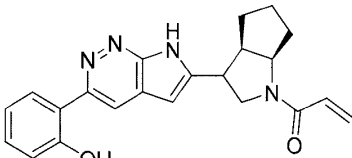
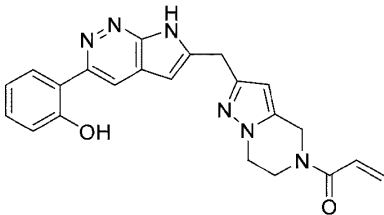
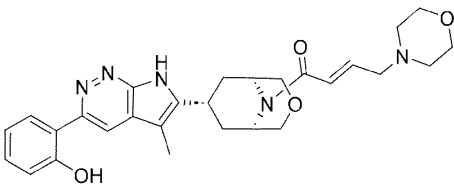
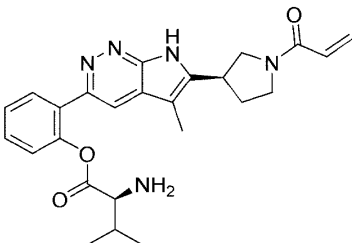
Ex.	Structure	Name
423		1-((1R,5S,7r)-7-(3-(2-hydroxyphenyl)-5-iodo-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one
424		1-((1R,5S,7r)-7-(3-(2-hydroxyphenyl)-5-phenyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one
425		1-((4S)-3-(3-(2-hydroxyphenyl)-5-(tetrahydrofuran-3-yl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-4-methoxypyrrolidin-1-yl)prop-2-en-1-one
426		1-((4S)-3-(3-(2-hydroxyphenyl)-5-(tetrahydrofuran-3-yl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-4-methoxypyrrolidin-1-yl)prop-2-en-1-one
427		1-(2-((3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)ethynyl)azetidin-1-yl)prop-2-en-1-one
428		1-(2-((3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)ethynyl)azetidin-1-yl)prop-2-en-1-one
429		1-(3-((3-(2-hydroxyphenyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)ethynyl)azetidin-1-yl)prop-2-en-1-one

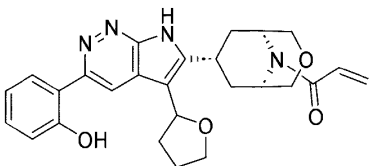
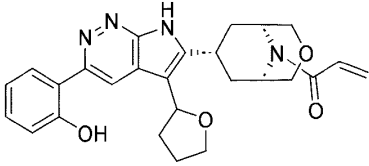
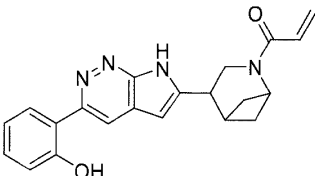
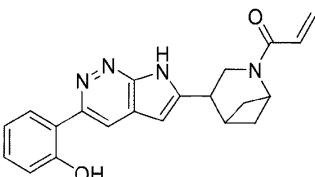
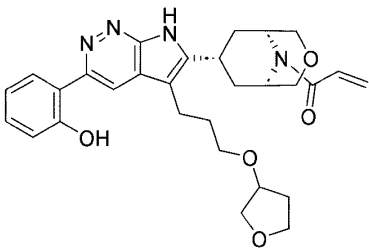
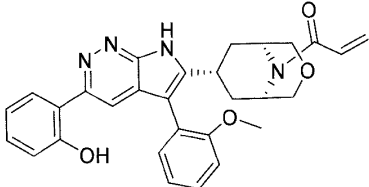
Ex.	Structure	Name
430	 1st eluting isomer	1-(7-(3-(2-hydroxyphenyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)-5-oxa-2-azaspiro[3.4]octan-2-yl)prop-2-en-1-one
431	 2nd eluting isomer	1-(7-(3-(2-hydroxyphenyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)-5-oxa-2-azaspiro[3.4]octan-2-yl)prop-2-en-1-one
432		1-(3-((3-(2-hydroxyphenyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)-3,8-diazabicyclo[3.2.1]octan-8-yl)prop-2-en-1-one
433		1-(3-((5-cyclopropyl-3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)-3,8-diazabicyclo[3.2.1]octan-8-yl)prop-2-en-1-one
434		(E)-4-(3,3-difluoroazetidin-1-yl)-1-((1R,5S,7r)-7-(3-(2-hydroxyphenyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)but-2-en-1-one
435	 1st eluting isomer	1-(4-((3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)-2-azabicyclo[2.2.1]heptan-2-yl)prop-2-en-1-one

Ex.	Structure	Name
436	 4th eluting isomer	1-((4S)-3-(3-(2-hydroxyphenyl)-5-(tetrahydrofuran-3-yl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-4-methoxypyrrolidin-1-yl)prop-2-en-1-one
437		1-(3-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-6,7-dihydropyrazolo[1,5-a]pyrazin-5(4H)-yl)prop-2-en-1-one
438		1-(3-((3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)-6,7-dihydropyrazolo[1,5-a]pyrazin-5(4H)-yl)prop-2-en-1-one
439		1-((1R,5S,7s)-7-(3-(2-hydroxyphenyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one
440	 1st eluting isomer	1-((4S)-3-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-4-(1H-pyrazol-1-yl)pyrrolidin-1-yl)prop-2-en-1-one
441		1-((1R,5S,7r)-7-(5-ethyl-3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one
442		1-((1R,5S,7r)-7-(3-(2-hydroxyphenyl)-5-(3-methoxypropyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one

Ex.	Structure	Name
443		1-(4-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-2-azaspiro[4.4]nonan-2-yl)prop-2-en-1-one
444		1-((E)-4-((1R,5S,7r)-7-(3-(2-hydroxyphenyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)-4-oxobut-2-en-1-yl)pyrrolidin-2-one
445		1-(4-(3-(2-hydroxyphenyl)-5-isopropyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)-6-azabicyclo[3.2.0]heptan-6-yl)prop-2-en-1-one
446		1-(4-(3-(2-hydroxyphenyl)-5-isopropyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)-6-azabicyclo[3.2.0]heptan-6-yl)prop-2-en-1-one
447		1-(4-(3-(2-hydroxyphenyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)-6-azabicyclo[3.2.0]heptan-6-yl)prop-2-en-1-one
448		1-(4-(3-(2-hydroxyphenyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)-6-azabicyclo[3.2.0]heptan-6-yl)prop-2-en-1-one

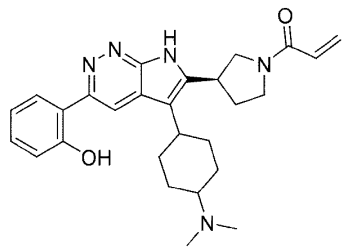
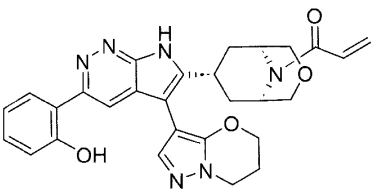
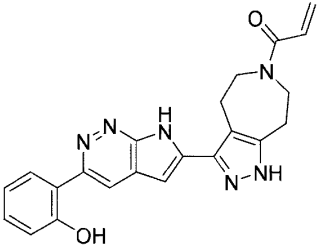
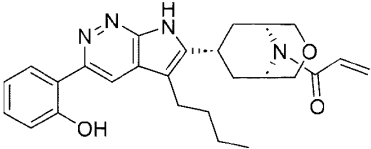
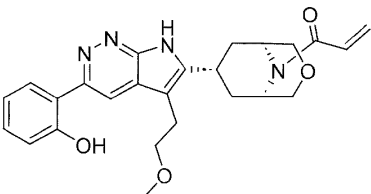
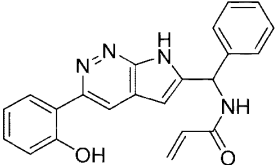
Ex.	Structure	Name
449	 2nd eluting isomer	1-(3-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-4-(1H-1,2,3-triazol-1-yl)pyrrolidin-1-yl)prop-2-en-1-one
450		1-((1R,5S,7r)-7-(3-(2-hydroxyphenyl)-5-(4-methoxycyclohexyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one
451		1-(3-(3-(2-hydroxyphenyl)-5-(4-methyltetrahydrofuran-3-yl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)pyrrolidin-1-yl)prop-2-en-1-one
452	 1st eluting isomer	1-(4-(3-(2-hydroxyphenyl)-5-(tetrahydrofuran-3-yl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-6-azabicyclo[3.2.0]heptan-6-yl)prop-2-en-1-one
453	 2nd eluting isomer	1-(4-(3-(2-hydroxyphenyl)-5-(tetrahydrofuran-3-yl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-6-azabicyclo[3.2.0]heptan-6-yl)prop-2-en-1-one
454	 3rd eluting isomer	1-(4-(3-(2-hydroxyphenyl)-5-(tetrahydrofuran-3-yl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-6-azabicyclo[3.2.0]heptan-6-yl)prop-2-en-1-one

Ex.	Structure	Name
455	 4th eluting isomer	1-(4-(3-(2-hydroxyphenyl)-5-(tetrahydrofuran-3-yl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-6-azabicyclo[3.2.0]heptan-6-yl)prop-2-en-1-one
456	 1st eluting isomer	1-((3aR,6aR)-3-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)hexahydrocyclopenta[b]pyrrol-1(2H)-yl)prop-2-en-1-one
457	 2nd eluting isomer	1-((3aR,6aR)-3-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)hexahydrocyclopenta[b]pyrrol-1(2H)-yl)prop-2-en-1-one
458		1-(2-((3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)-6,7-dihydropyrazolo[1,5-a]pyrazin-5(4H)-yl)prop-2-en-1-one
459		(E)-1-((1R,5S,7r)-7-(3-(2-hydroxyphenyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)-4-morpholinobut-2-en-1-one
460		2-(6-((R)-1-acryloylpyrrolidin-3-yl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-3-yl)phenyl L-valinate

Ex.	Structure	Name
461	 1st eluting isomer	1-((1R,5S,7r)-7-(3-(2-hydroxyphenyl)-5-(tetrahydrofuran-2-yl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one
462	 2nd eluting isomer	1-((1R,5S,7r)-7-(3-(2-hydroxyphenyl)-5-(tetrahydrofuran-2-yl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one
463	 1st eluting isomer	1-(4-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-2-azabicyclo[3.1.1]heptan-2-yl)prop-2-en-1-one
464	 2nd eluting isomer	1-(4-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-2-azabicyclo[3.1.1]heptan-2-yl)prop-2-en-1-one
465		1-((1R,5S,7r)-7-(3-(2-hydroxyphenyl)-5-(3-((tetrahydrofuran-3-yl)oxy)propyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one
466		1-((1R,5S,7r)-7-(3-(2-hydroxyphenyl)-5-(2-methoxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one

Ex.	Structure	Name
467		(R)-1-(3-(3-(2-hydroxyphenyl)-5-(2-oxaspiro[3.3]heptan-6-yl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)pyrrolidin-1-yl)prop-2-en-1-one
468		1-((2R)-4-(3-(2-hydroxyphenyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)-2-(methoxymethyl)pyrrolidin-1-yl)prop-2-en-1-one 1 st eluting isomer
469		1-((2R)-4-(3-(2-hydroxyphenyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)-2-(methoxymethyl)pyrrolidin-1-yl)prop-2-en-1-one 2 nd eluting isomer
470		1-((1R,5S,7r)-7-(3-(2-hydroxyphenyl)-5-isopropyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one
471		1-((1R,5S,7r)-7-(3-(2-hydroxyphenyl)-5-(4-morpholinocyclohexyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one
472		1-(5-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-2-azabicyclo[2.2.1]heptan-2-yl)prop-2-en-1-one 1 st eluting isomer
473		1-(5-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-2-azabicyclo[2.2.1]heptan-2-yl)prop-2-en-1-one 2 nd eluting isomer

Ex.	Structure	Name
474		1-((1R,5S,7r)-7-(5-(sec-butyl)-3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one
475		1-((1R,5S,7r)-7-(5-(cyclopropyl)-3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one
476		1-((1R,5S,7r)-7-(3-(2-hydroxyphenyl)-5-(3-methoxypyridin-4-yl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one
477		1-((1R,5S,7r)-7-(5-(5-fluoro-3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one
478		1-((1R,5S,7r)-7-(3-(2-hydroxyphenyl)-5-(methoxymethyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one
479		1-((1R,5S,7r)-7-(5-(1,4-dioxan-2-yl)-3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one

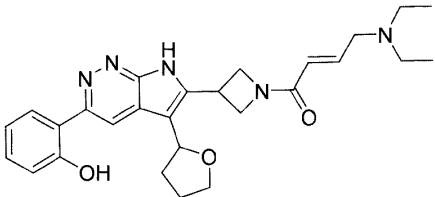
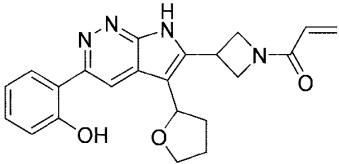
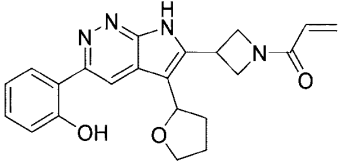
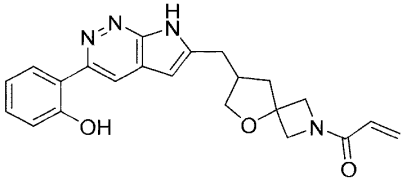
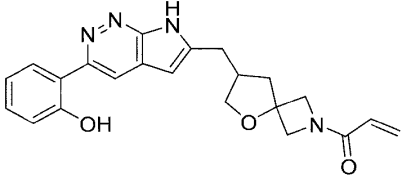
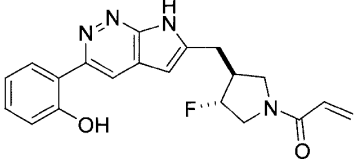
Ex.	Structure	Name
480		(R)-1-(3-(5-(4-(dimethylamino)cyclohexyl)-3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)pyrrolidin-1-yl)prop-2-en-1-one
481		1-((1R,5S,7r)-7-(5-(6,7-dihydro-5H-pyrazolo[5,1-b][1,3]oxazin-3-yl)-3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one
482		1-(3-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-4,5,7,8-tetrahydropyrazolo[3,4-d]azepin-6(1H)-yl)prop-2-en-1-one
483		1-((1R,5S,7r)-7-(5-butyl-3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one
484		1-((1R,5S,7r)-7-(3-(2-hydroxyphenyl)-5-(2-methoxyethyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one
485		N-((3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)(phenyl)methyl)acrylamide

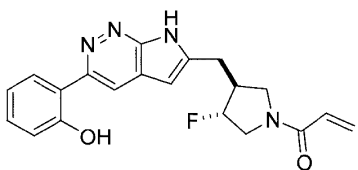
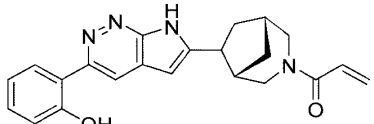
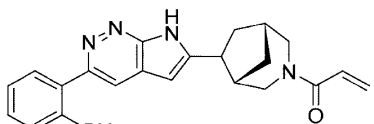
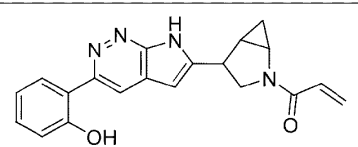
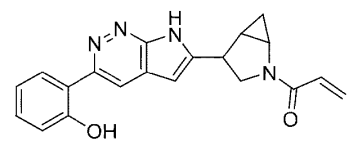
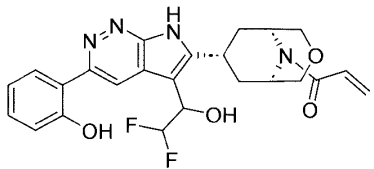
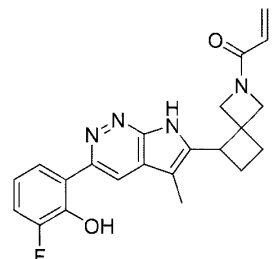
Ex.	Structure	Name
486		N-((4-((3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)oxazol-5-yl)methyl)acrylamide
487		1-(3-(3-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)cyclobutyl)azetidin-1-yl)prop-2-en-1-one
488		(S)-1-(3-(3-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)azetidin-1-yl)pyrrolidin-1-yl)prop-2-en-1-one
489		N-(2,2,2-trifluoro-1-(3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)ethyl)acrylamide
490		N-((5-bromo-3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)acrylamide
491		
492		

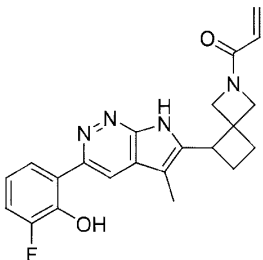
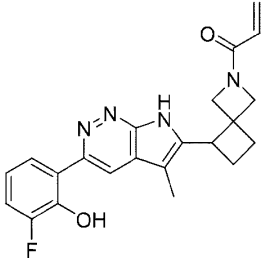
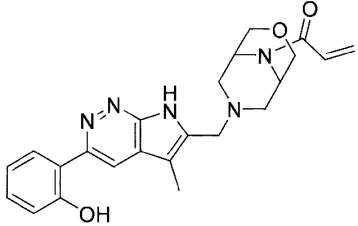
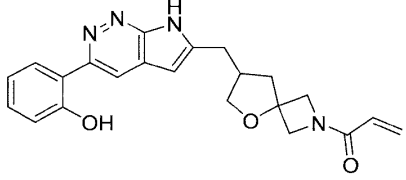
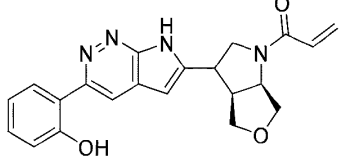
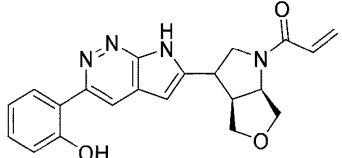
Ex.	Structure	Name
493		
494		
495	 2 nd eluting isomer	
496	 1 st eluting isomer	
497		
498		
499		
500	 2 nd eluting isomer	

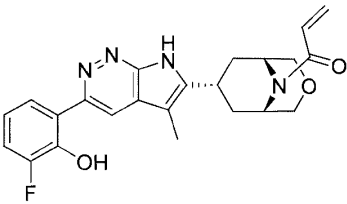
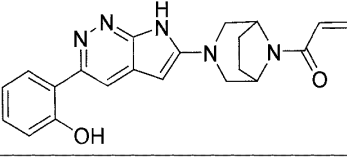
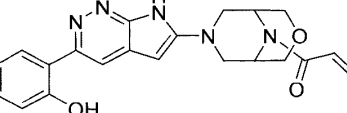
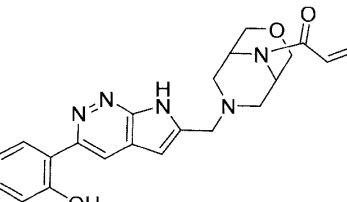
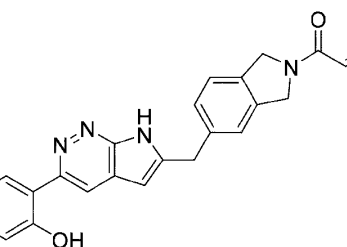
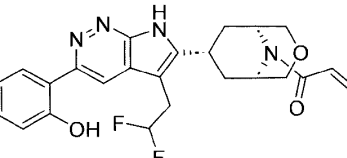
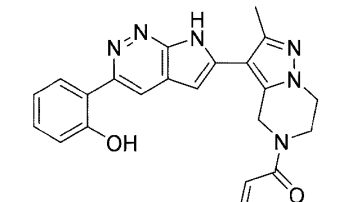
Ex.	Structure	Name
501	1st eluting isomer	
502	2nd eluting isomer	
503	1st eluting isomer	
504		
505		
506	2nd eluting isomer	

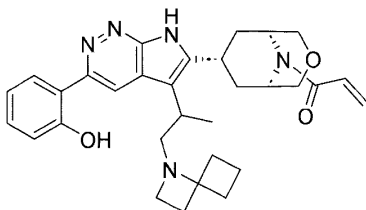
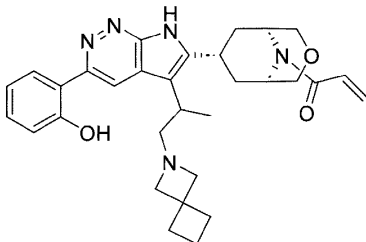
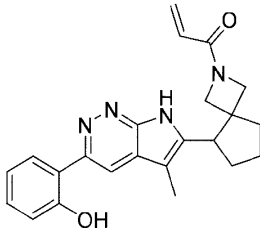
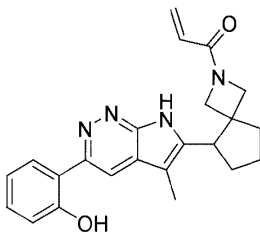
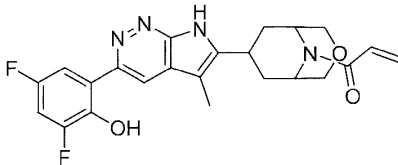
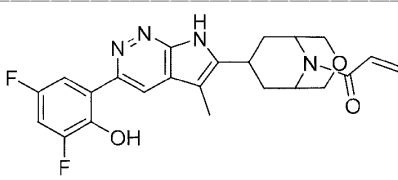
Ex.	Structure	Name
507	1st eluting isomer	
508	2nd eluting isomer	
509	1st eluting isomer	
510	2nd eluting isomer(s)	
511	1st eluting isomer(s)	
512	2nd eluting isomer	

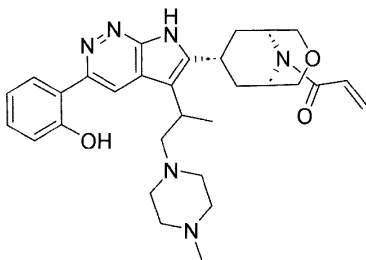
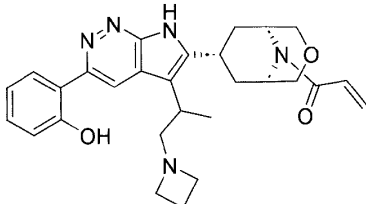
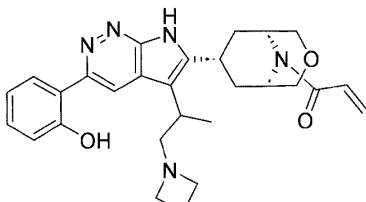
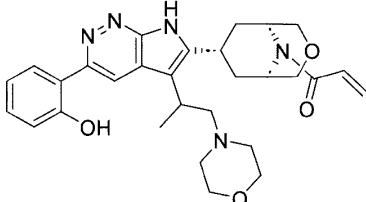
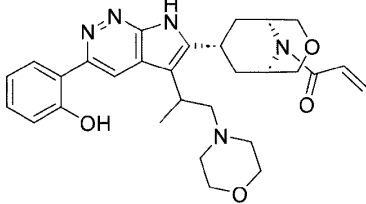
Ex.	Structure	Name
513	 1st eluting isomer	
514	 2nd eluting isomer	
515	 1st eluting isomer	
516	 2nd eluting isomer	
517	 1st eluting isomer	
518	 2nd eluting isomer	

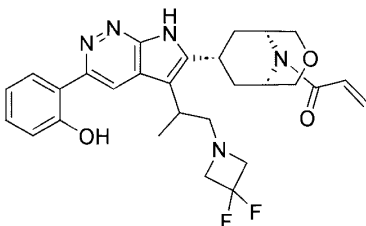
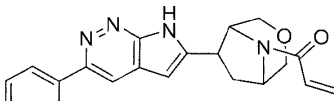
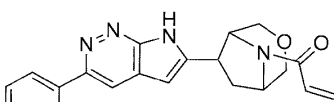
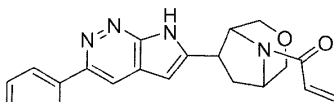
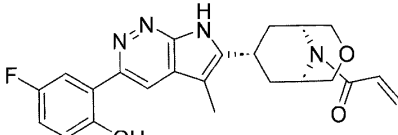
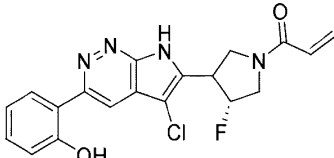
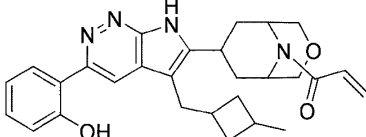
Ex.	Structure	Name
519	 1st eluting isomer	
520	 2nd eluting	
521	 1st eluting	
522	 2nd eluting isomer(s)	
523	 1st eluting isomer(s)	
524		
525	 2nd eluting isomer	

Ex.	Structure	Name
526	 1 st eluting isomer	
527		
528		
529		
530	 2 nd eluting isomer	
531	 1 st eluting isomer	

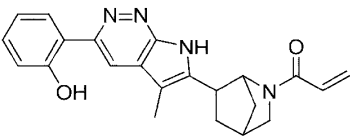
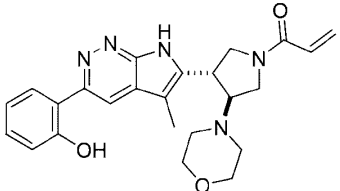
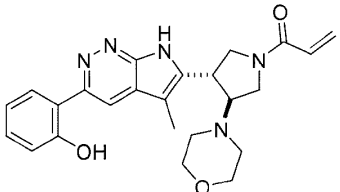
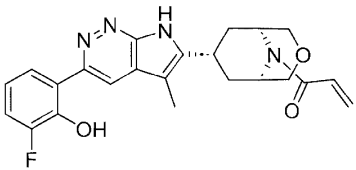
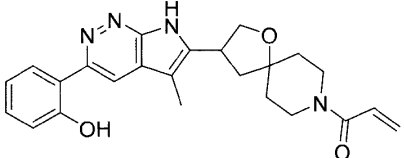
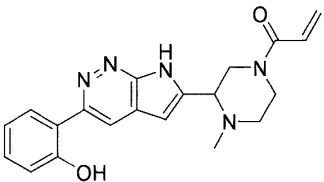
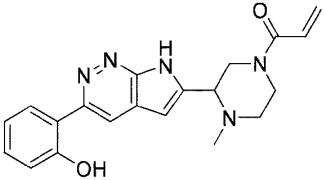
Ex.	Structure	Name
532		
533		
534		
535		
536		
537		
538		

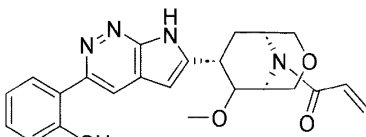
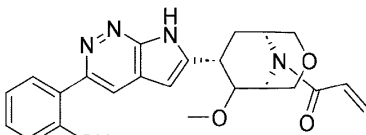
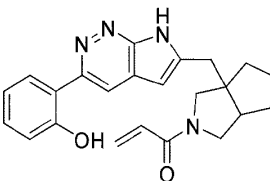
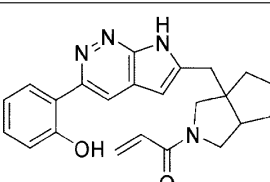
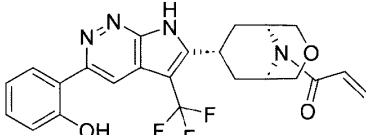
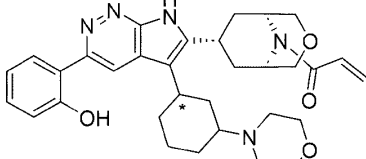
Ex.	Structure	Name
539		
540		
541	 2 nd eluting isomer	
542	 1 st eluting isomer	
543	 2 nd eluting isomer	
544	 1 st eluting isomer	

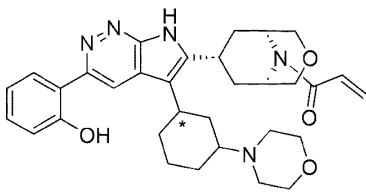
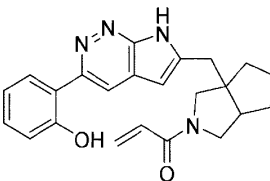
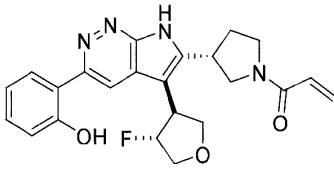
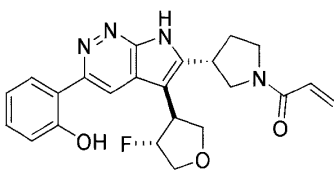
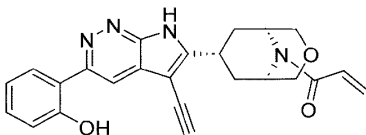
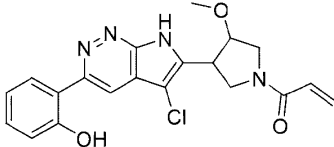
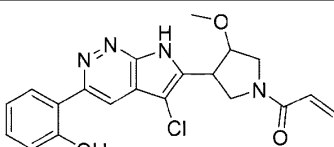
Ex.	Structure	Name
545		
546	 2 nd eluting isomer	
547	 1 st eluting isomer	
548	 2 nd eluting isomer	
549	 1 st eluting isomer	

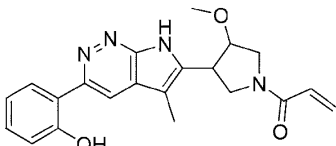
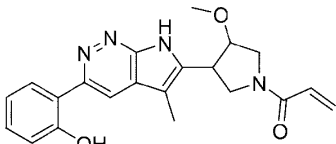
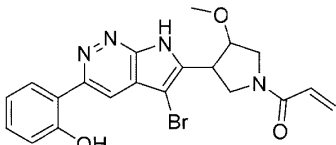
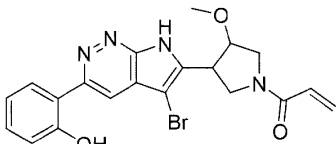
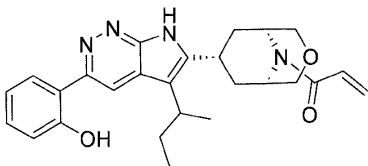
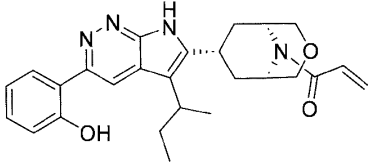
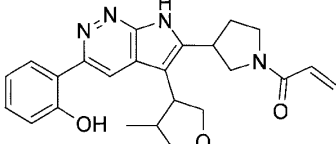
Ex.	Structure	Name
550		
551	 2 nd eluting isomer(s)	
552	 1 st eluting isomer(s)	
553		
554		
555		
556	 2 nd eluting isomer	

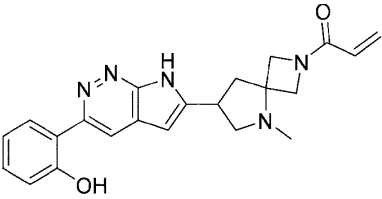
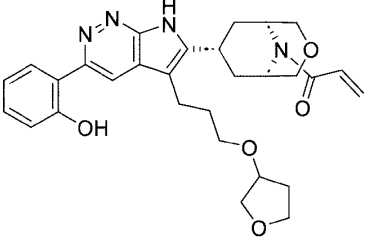
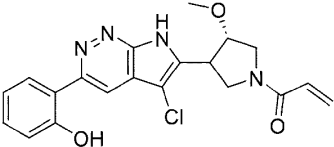
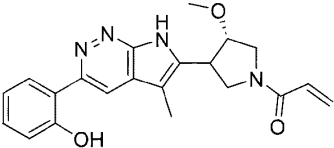
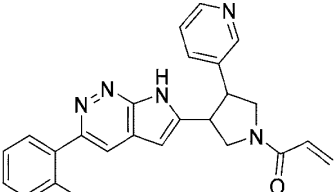
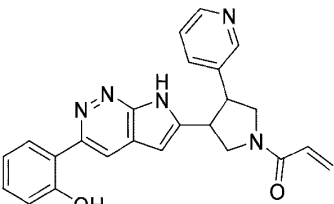
Ex.	Structure	Name
557	1st eluting isomer	
558	2nd eluting isomer	
559	1st eluting isomer	
560	2nd eluting isomer(s)	
561	1st eluting isomer(s)	
562	2nd eluting isomer	
563	1st eluting isomer	

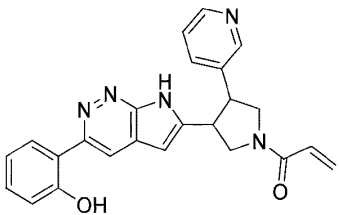
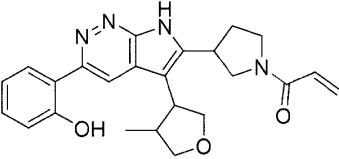
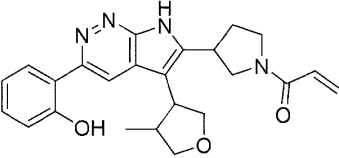
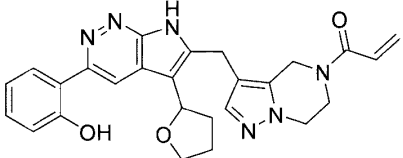
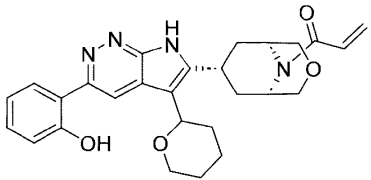
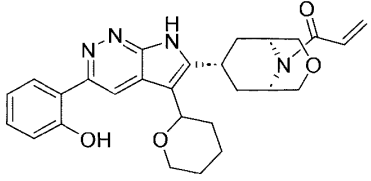
Ex.	Structure	Name
564		
565	 2 nd eluting isomer	
566	 1 st eluting isomer	
567		
568		
569	 2 nd eluting isomer	
570	 1 st eluting isomer	

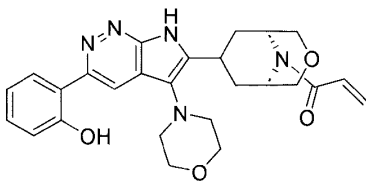
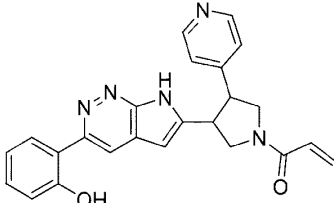
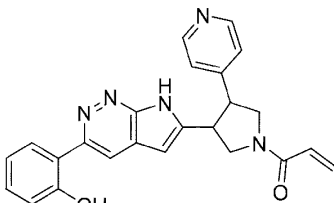
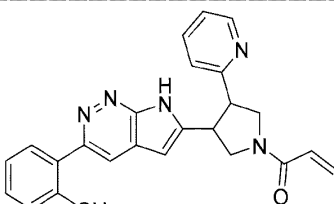
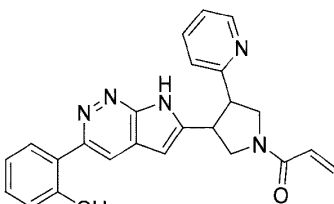
Ex.	Structure	Name
571	 2 nd eluting isomer	
572	 1 st eluting isomer	
573	 2 nd eluting isomer	
574	 1 st eluting isomer	
575	 2 nd eluting isomer(s)	
576	 2 nd eluting isomer(s)	

Ex.	Structure	Name
577	 1 st eluting isomer(s)	
578		
579	 2 nd eluting isomer	
580	 1 st eluting isomer	
581		
582	 mixture of enantiomers, 2 nd eluting	
583	 mixture of enantiomers, 1 st eluting	

Ex.	Structure	Name
584	 mixture of enantiomers, 2 nd eluting	
585	 mixture of enantiomers, 1 st eluting	
586	 mixture of enantiomers, 2 nd eluting	
587	 mixture of enantiomers, 1 st eluting	
588	 2 nd eluting isomer	
589	 1 st eluting isomer	
590	 3 rd eluting isomer	

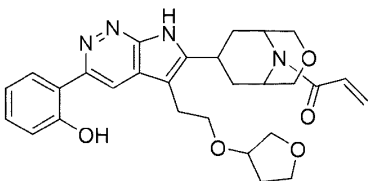
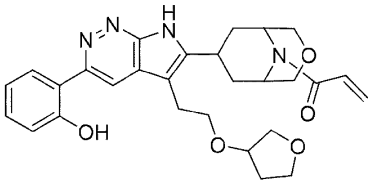
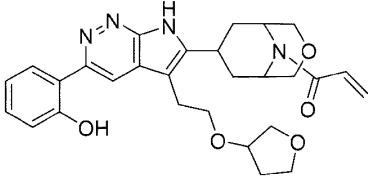
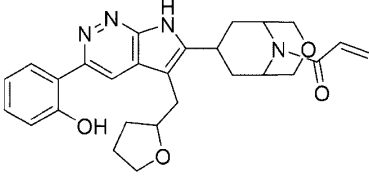
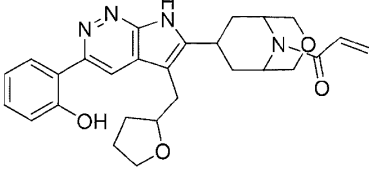
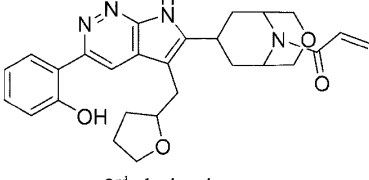
Ex.	Structure	Name
591		
592	 2 nd eluting isomer	
593		
594		
595	 Diastereomer 2, 2 nd eluting isomer	
596	 Diastereomer 2, 1 st eluting isomer	

Ex.	Structure	Name
597	 Diastereomer 1, 1st eluting isomer	
598	 2nd eluting isomer	
599	 1st eluting isomer	
600		
601	 2nd eluting isomer	
602	 1st eluting isomer	

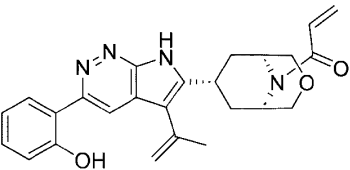
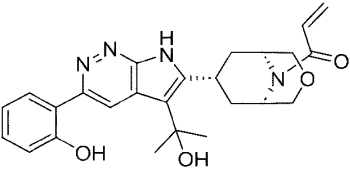
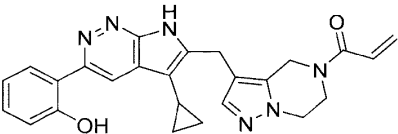
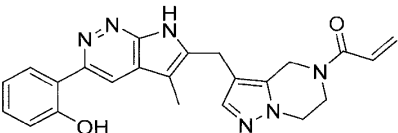
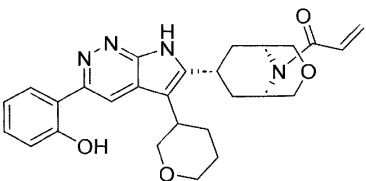
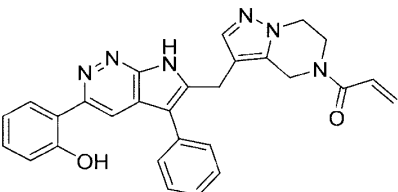
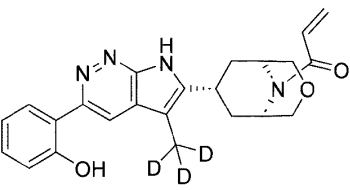
Ex.	Structure	Name
603		
604	 4 th eluting isomer	
605	 3 rd eluting isomer	
606	 mixture of enantiomers, single unknown diastereomer	
607	 mixture of enantiomers, single unknown diastereomer	

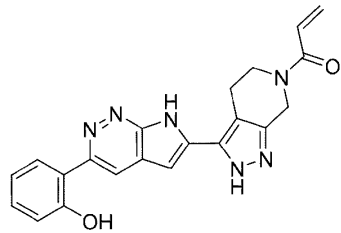
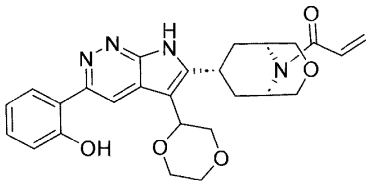
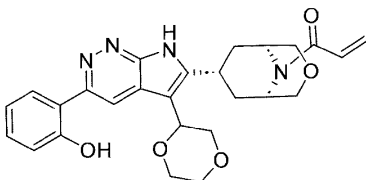
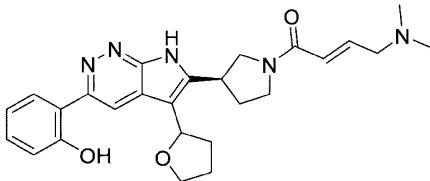
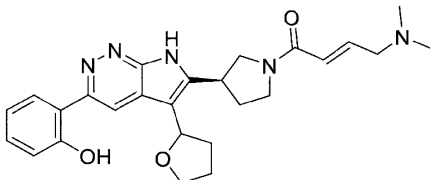
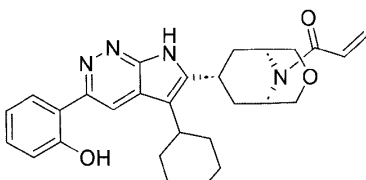
Ex.	Structure	Name
608	2nd eluting isomer	
609	1st eluting isomer	
610	2nd eluting isomer	
611	1st eluting isomer	
612	2nd eluting isomer	
613	1st eluting isomer	

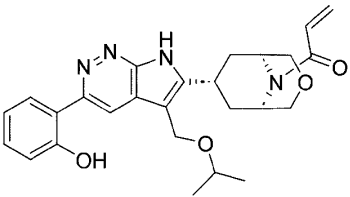
Ex.	Structure	Name
614	2nd eluting isomer	
615	1st eluting isomer	
616	2nd eluting isomer	
617	1st eluting isomer	
618	2nd eluting isomer	
619	1st eluting isomer	

Ex.	Structure	Name
620	 3rd eluting isomer	
621	 2nd eluting isomer	
622	 1st eluting isomer	
623	 2nd eluting isomer	
624	 4th eluting isomer	
625	 3rd eluting isomer	

Ex.	Structure	Name
626	1st eluting isomer	
627		
628	2nd eluting isomer	
629	1st eluting isomer	
630		
631		

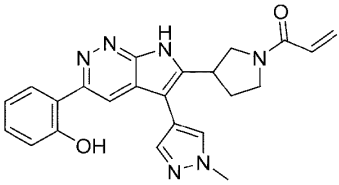
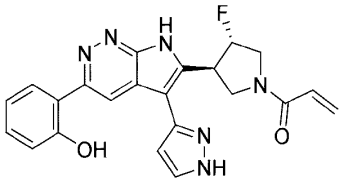
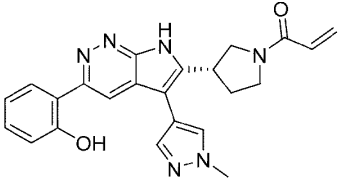
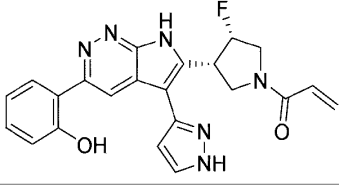
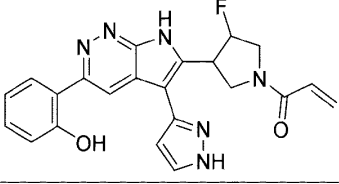
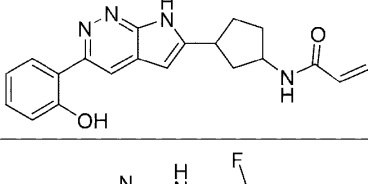
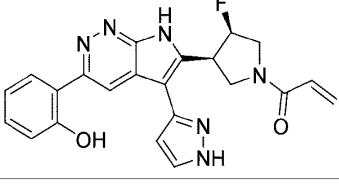
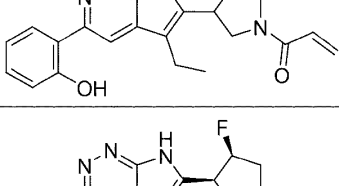
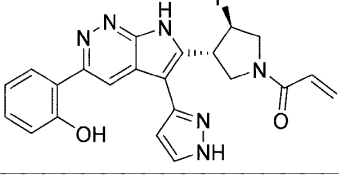
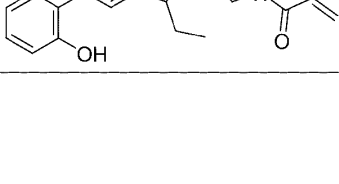
Ex.	Structure	Name
632		
633		
634		
635		
636		
637		
638		

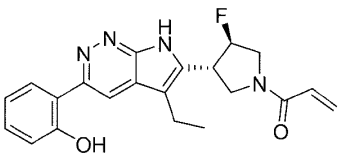
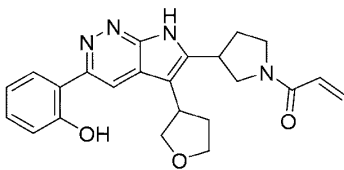
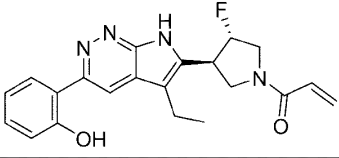
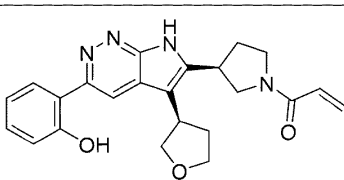
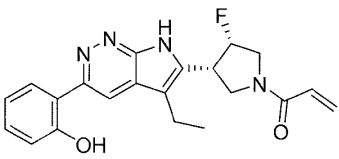
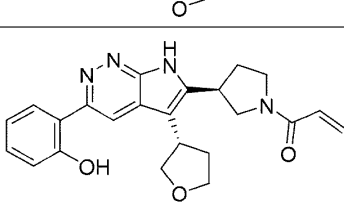
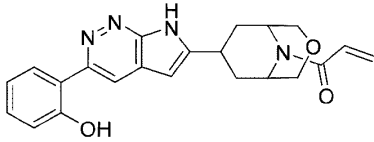
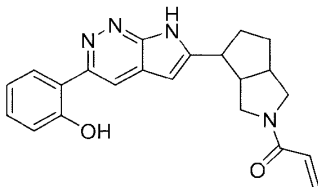
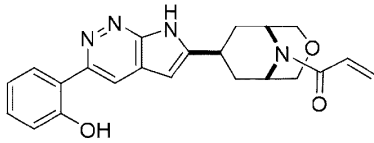
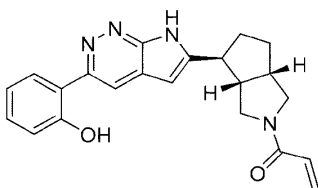
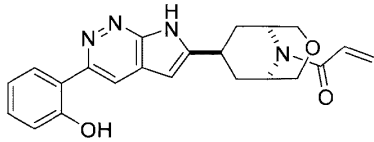
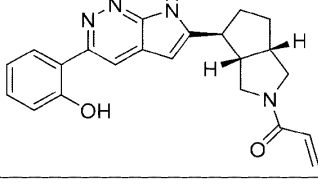
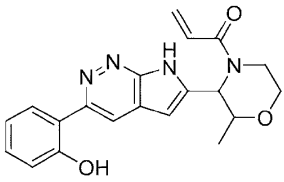
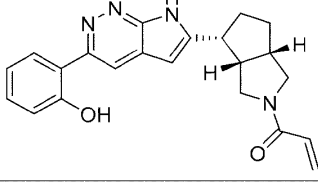
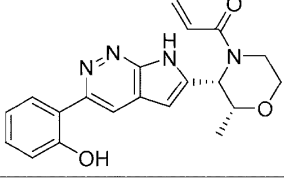
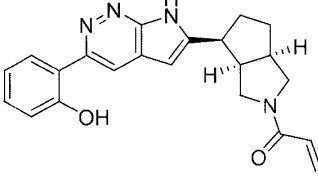
Ex.	Structure	Name
639		
640	 2 nd eluting isomer	
641	 1 st eluting isomer	
642	 2 nd eluting isomer	
643	 1 st eluting isomer	
644		

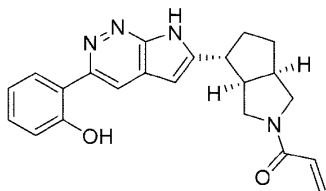
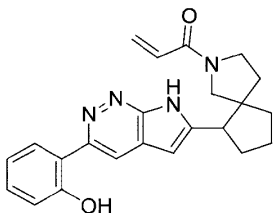
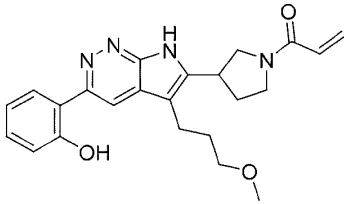
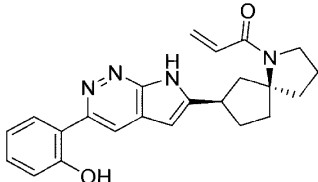
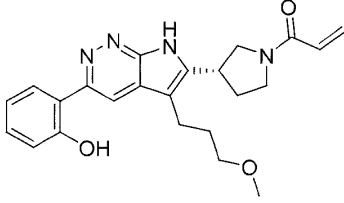
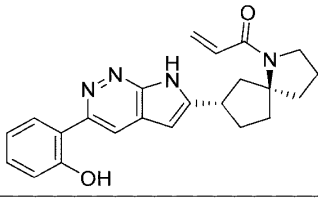
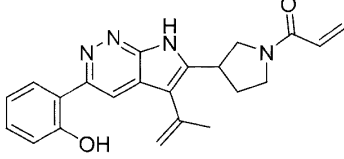
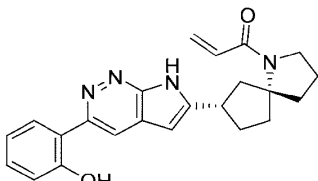
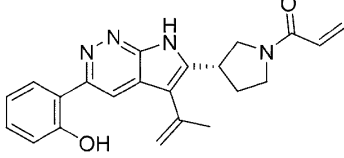
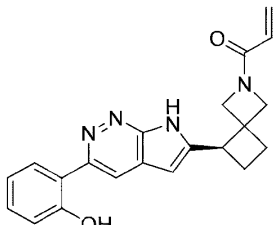
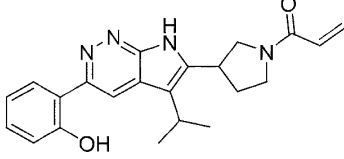
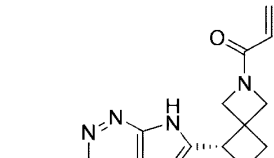
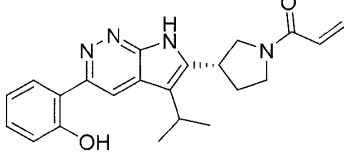
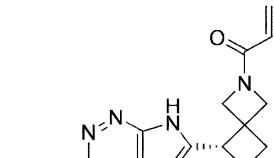
Ex.	Structure	Name
645		

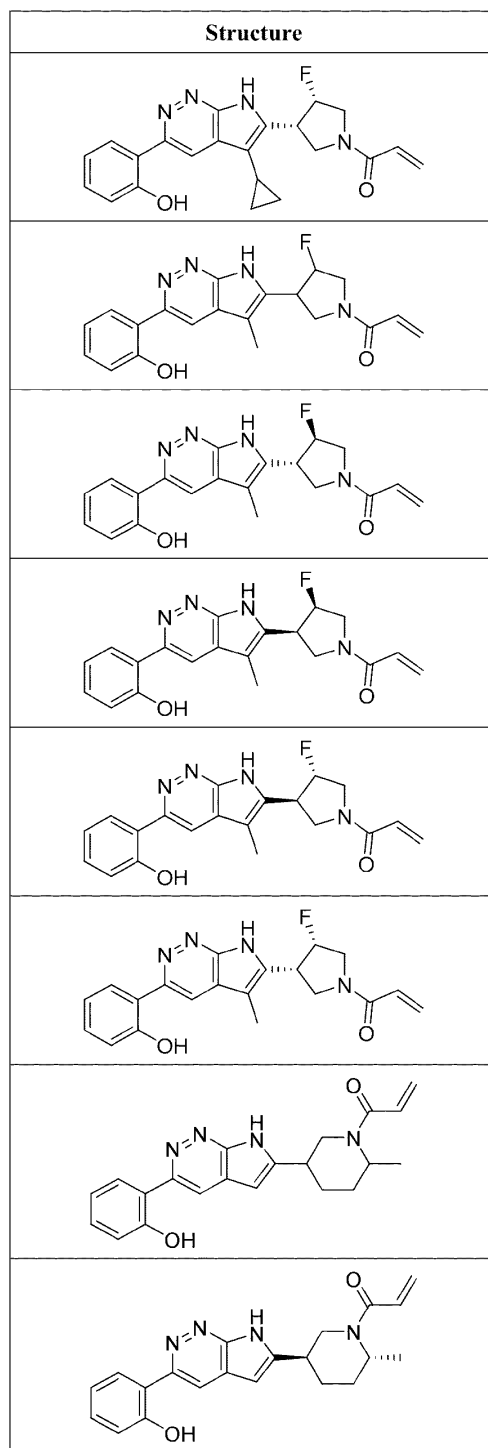
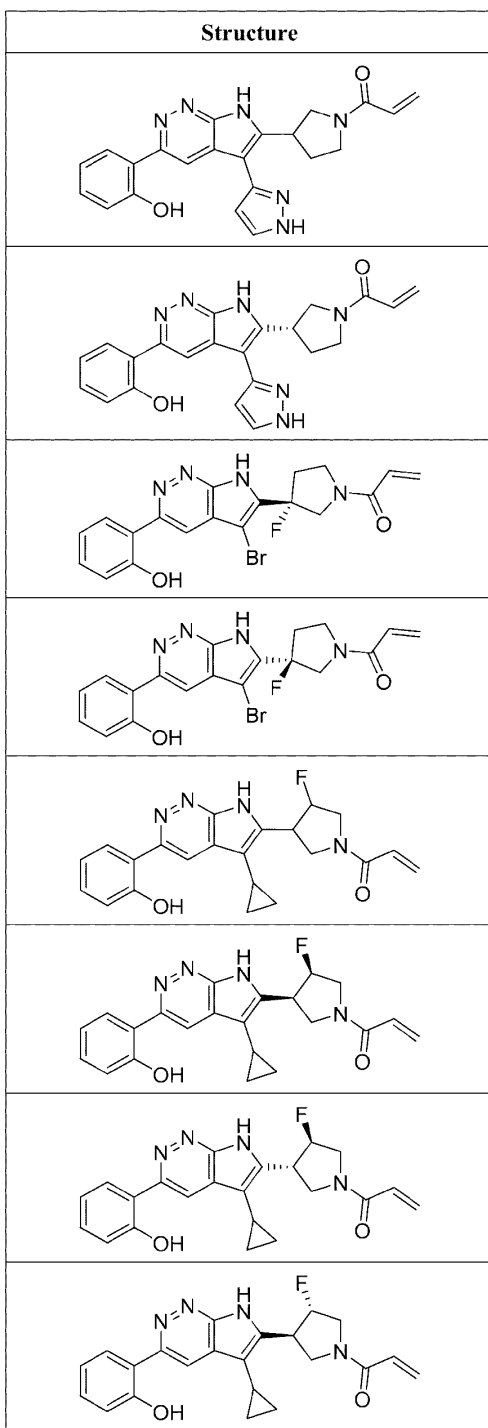
[0245] In one embodiment, provided is a compound, or a pharmaceutically acceptable salt, solvate, isotopically enriched analog, or tautomer thereof, selected from Table 2.

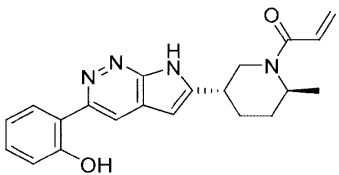
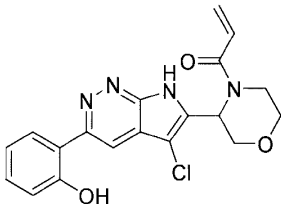
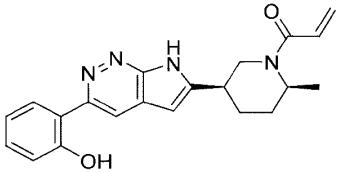
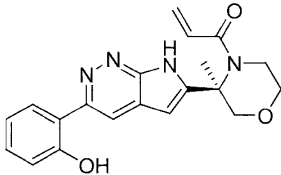
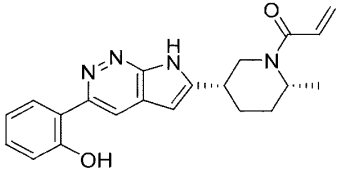
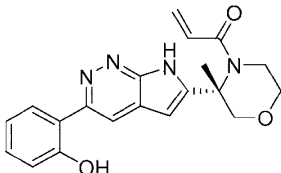
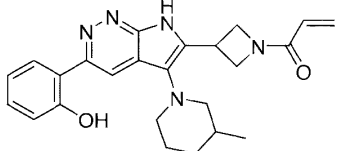
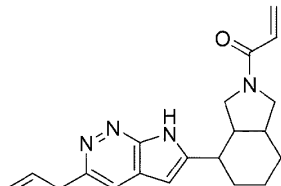
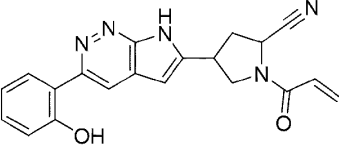
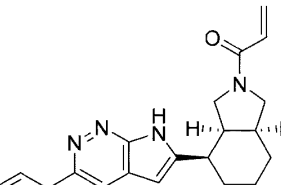
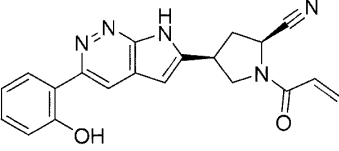
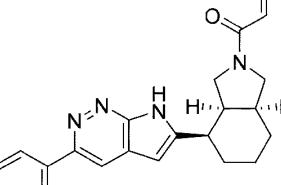
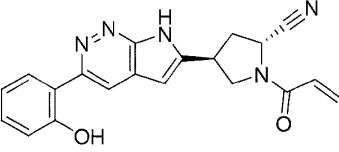
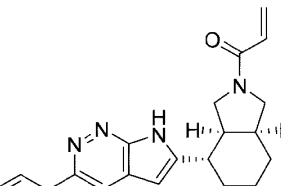
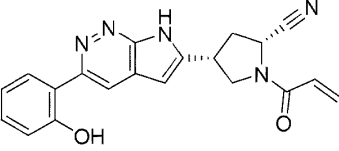
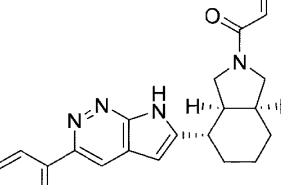
Table 2

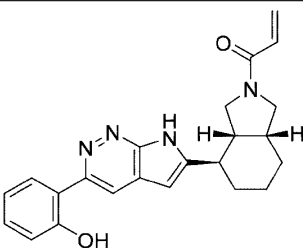
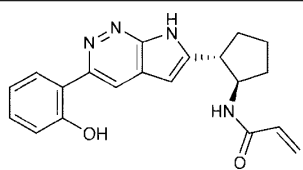
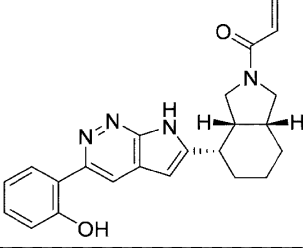
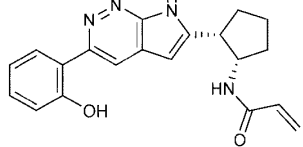
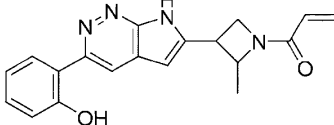
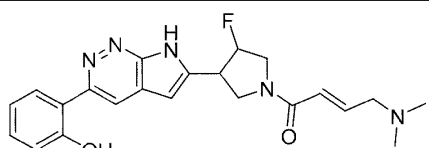
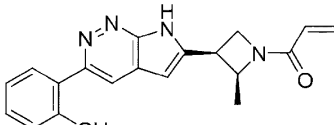
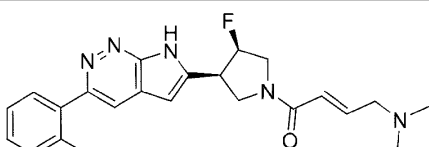
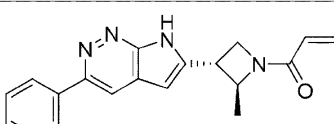
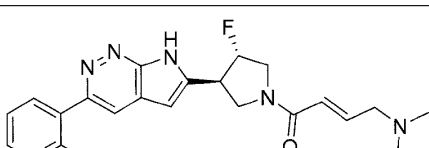
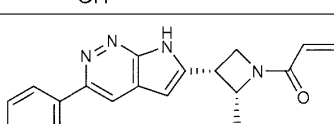
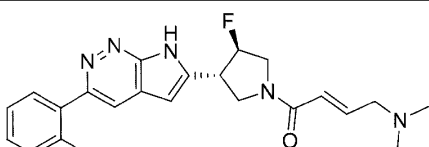
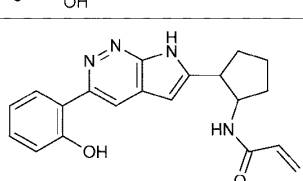
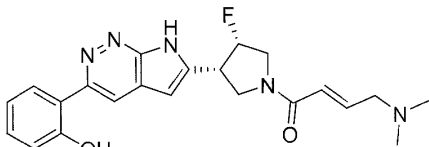
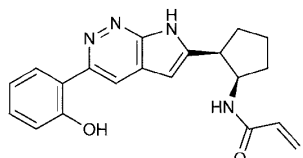
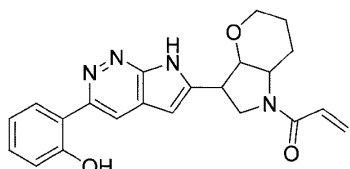
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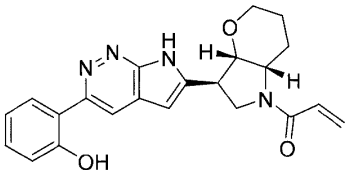
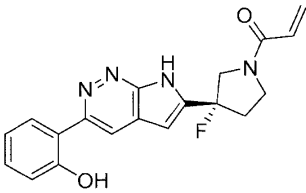
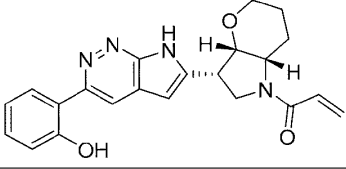
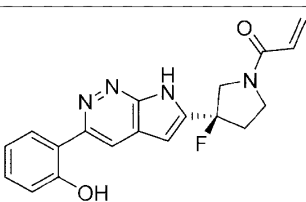
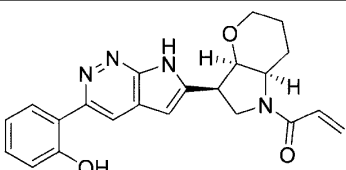
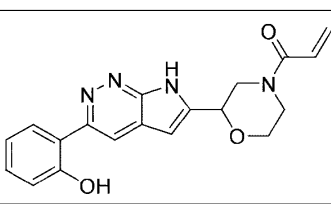
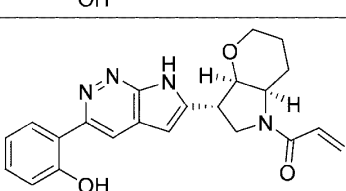
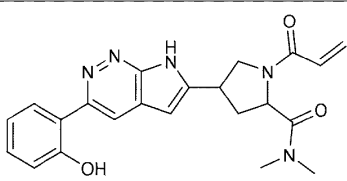
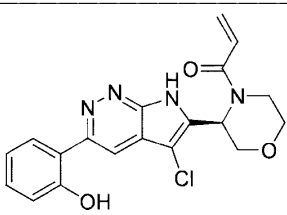
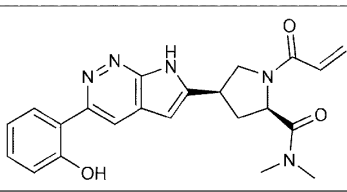
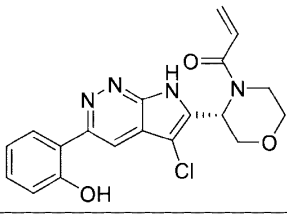
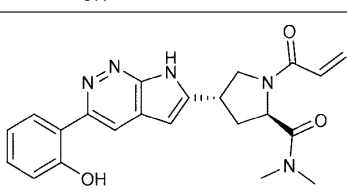
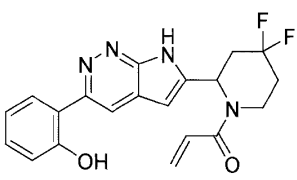
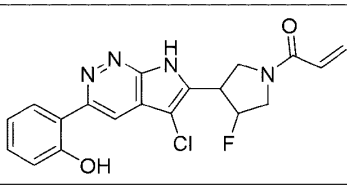
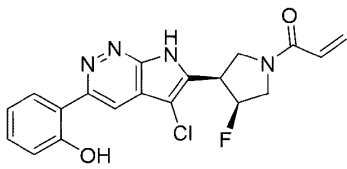
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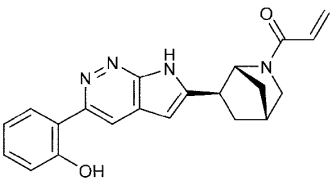
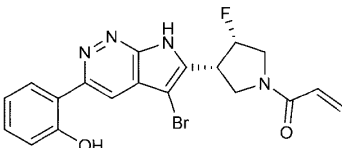
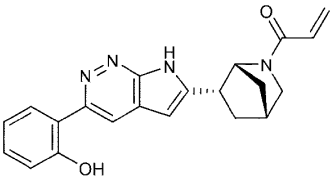
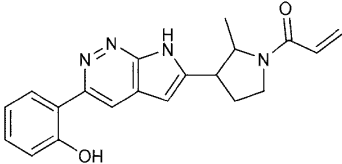
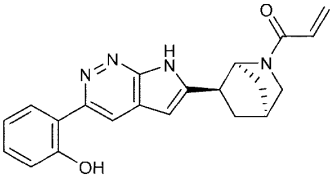
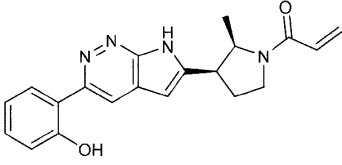
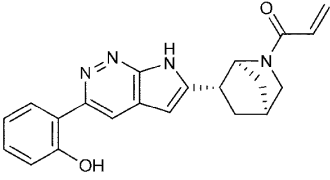
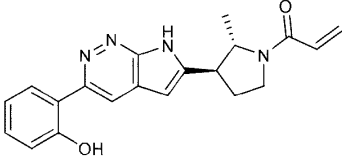
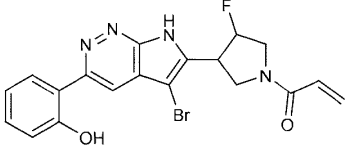
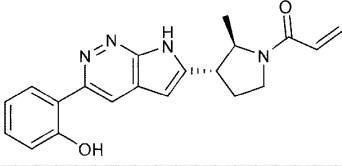
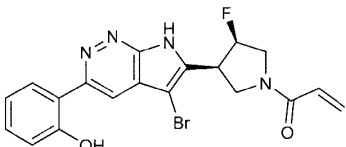
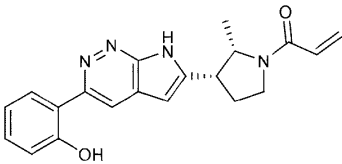
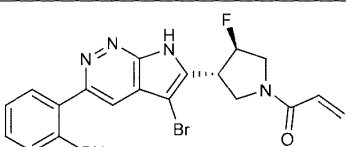
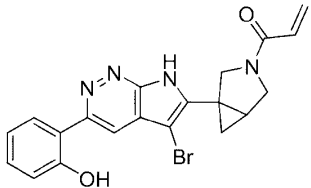
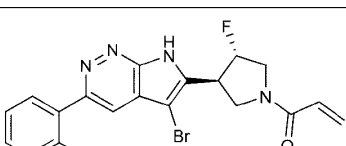
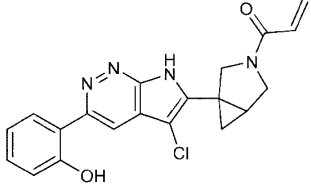


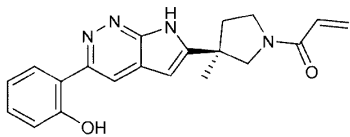
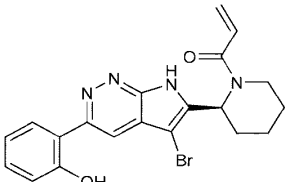
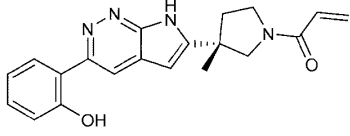
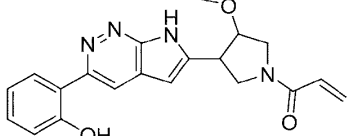
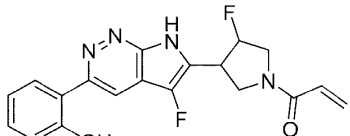
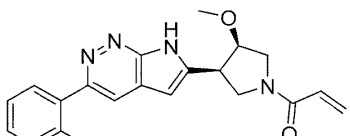
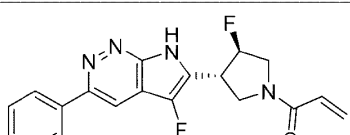
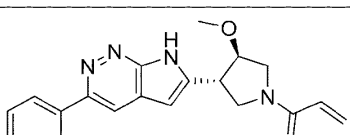
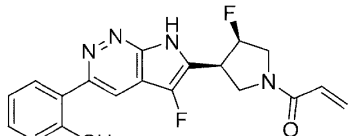
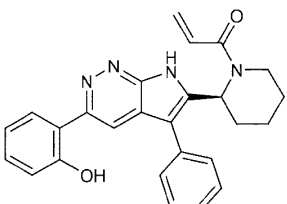
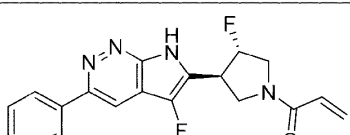
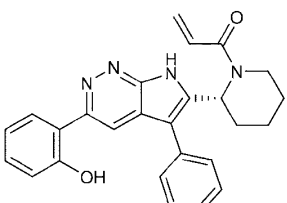
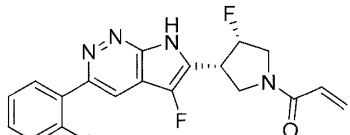
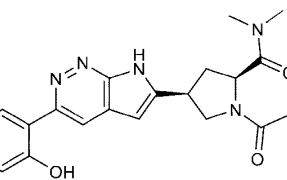
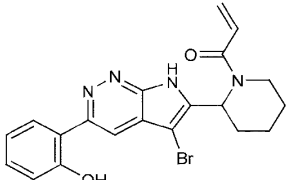
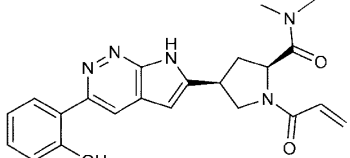
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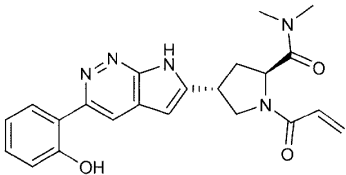
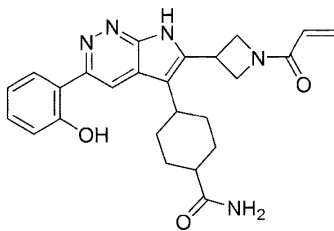
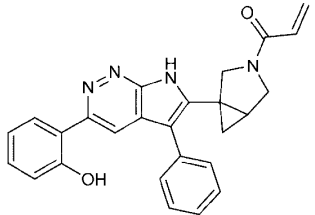
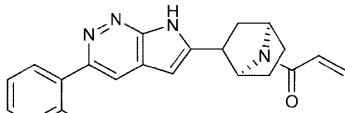
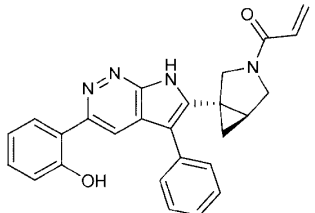
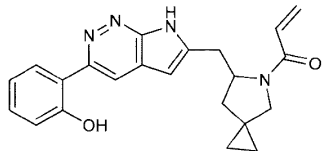
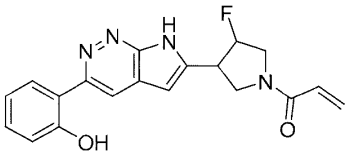
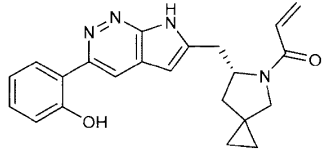
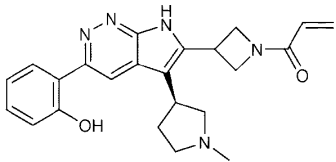
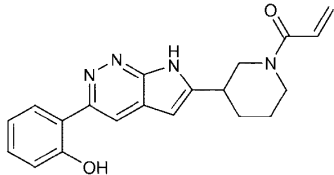
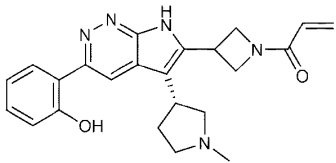
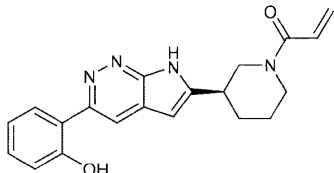
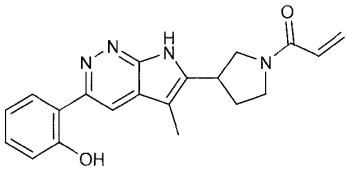
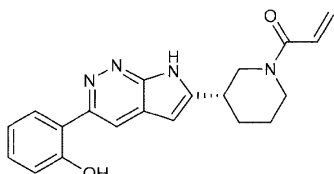
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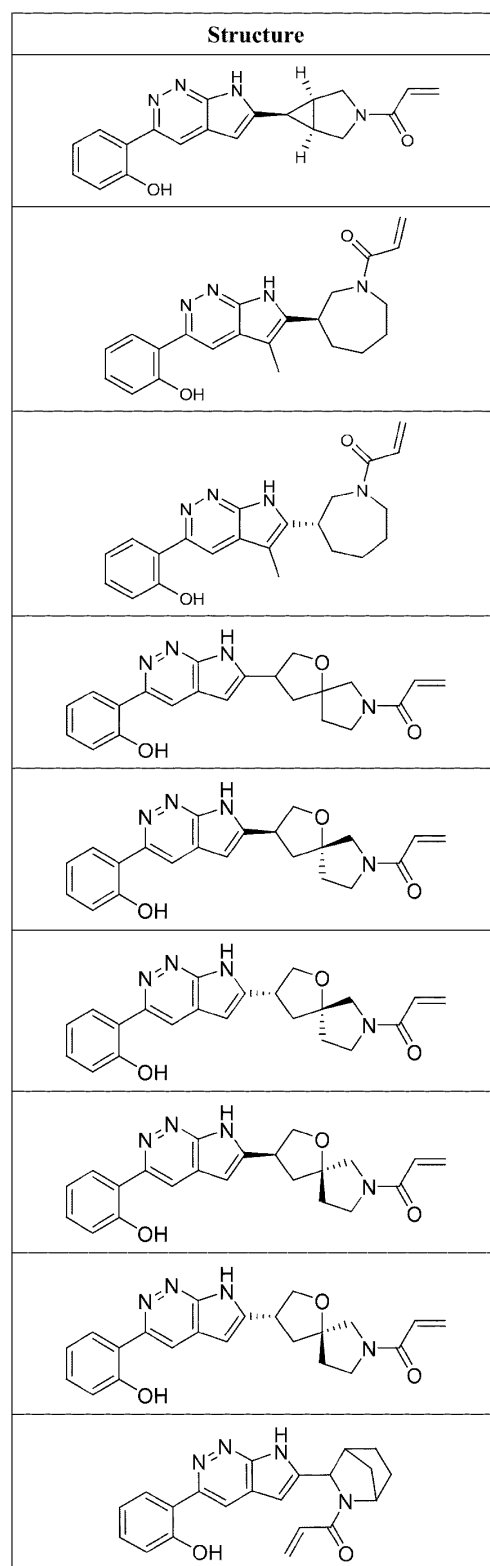
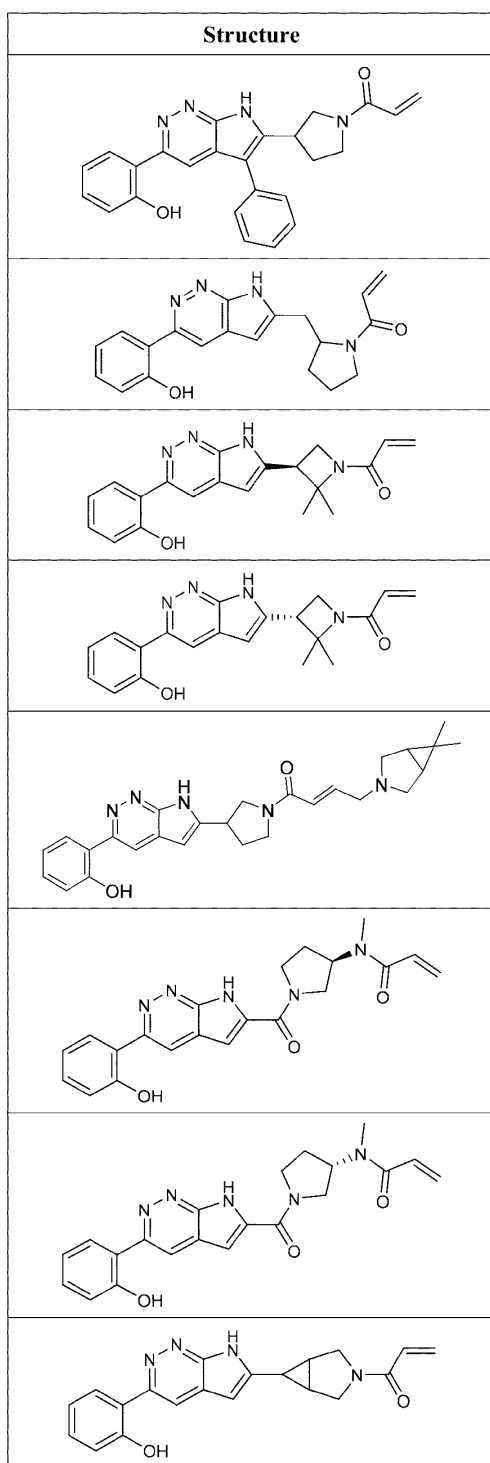
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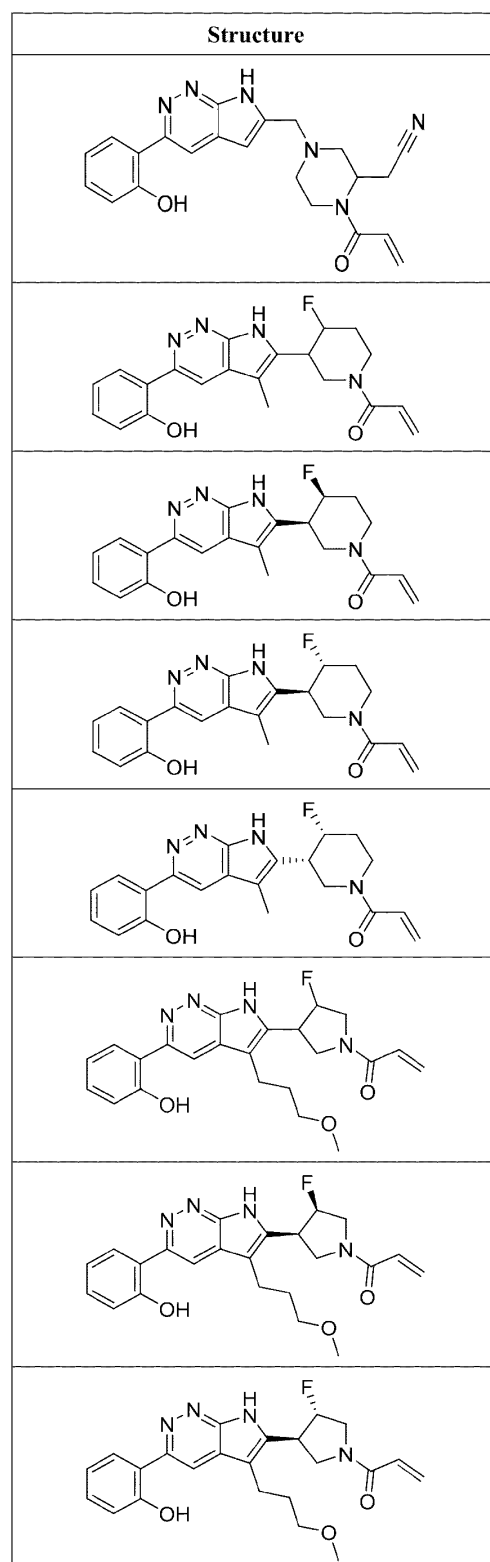
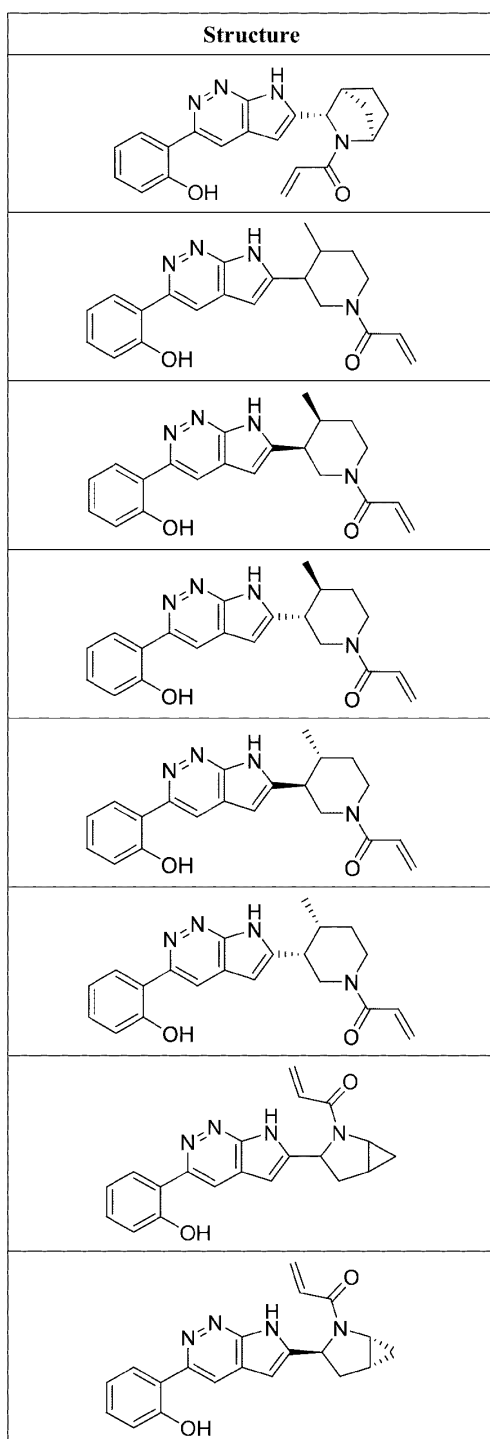
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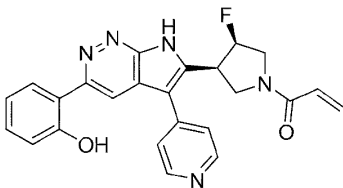
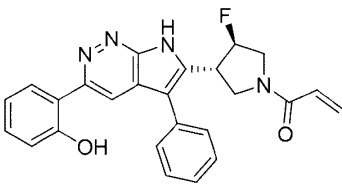
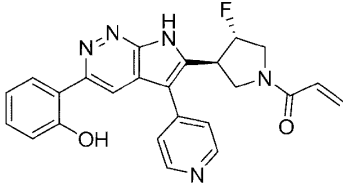
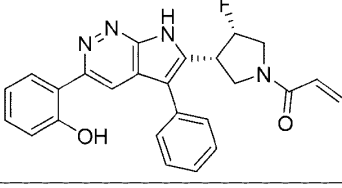
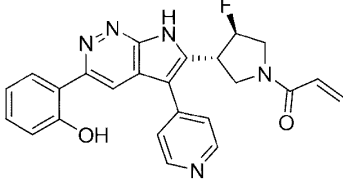
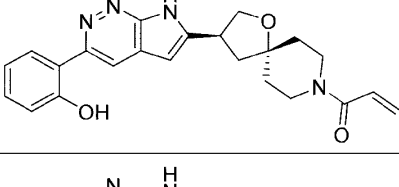
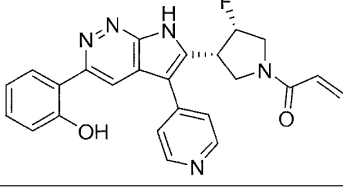
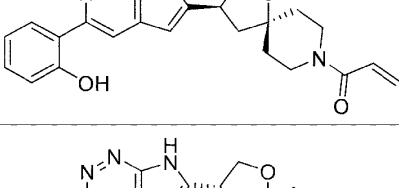
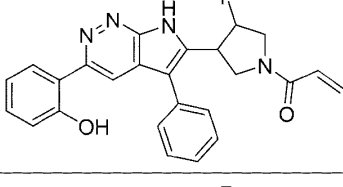
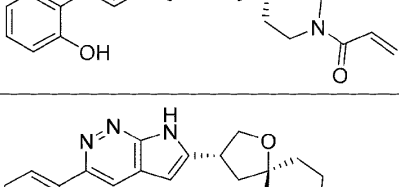
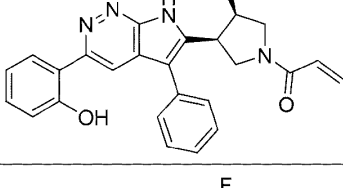
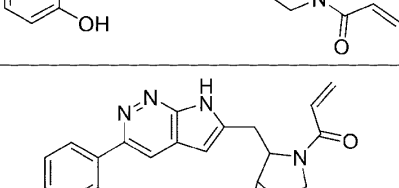
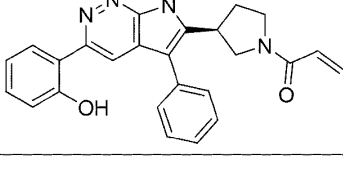
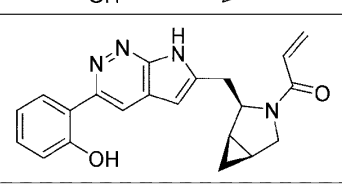
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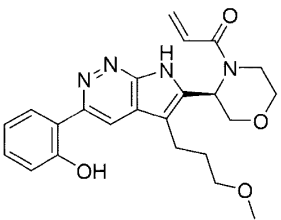
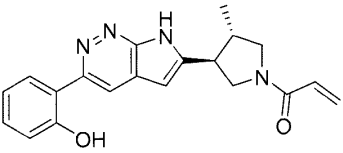
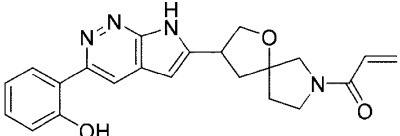
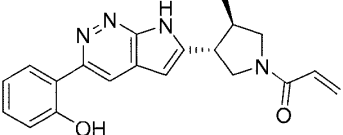
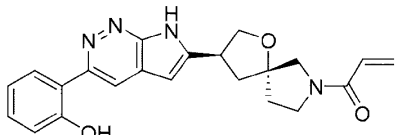
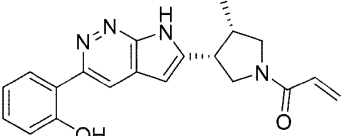
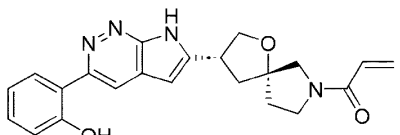
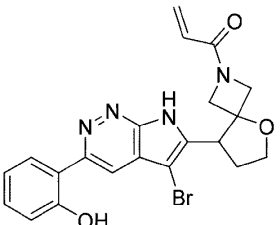
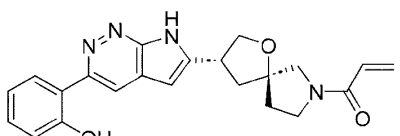
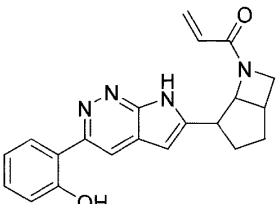
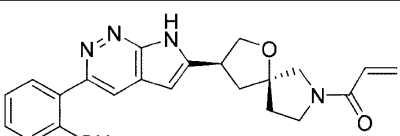
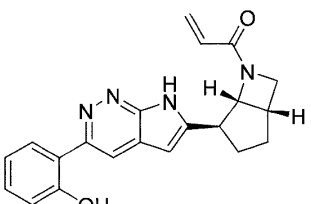
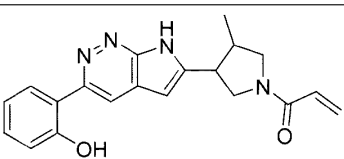
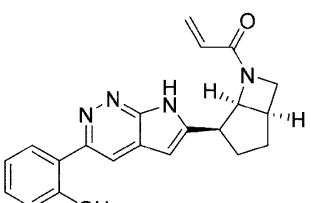
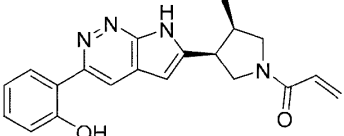
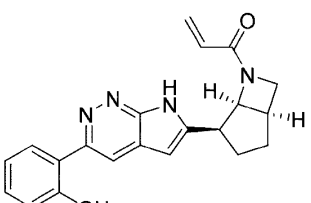


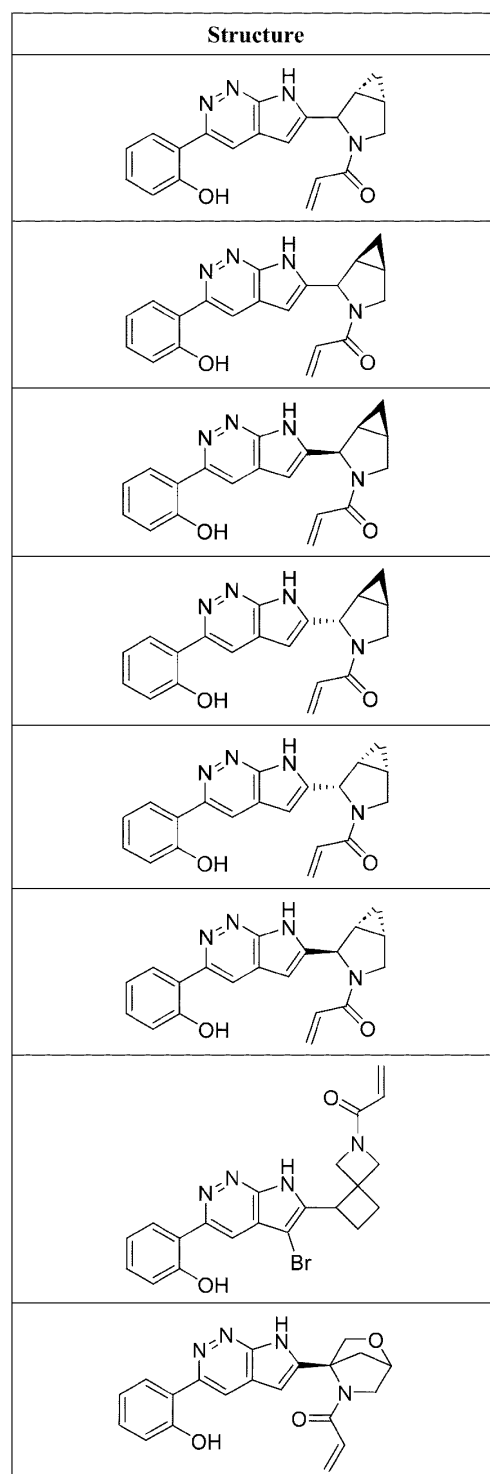
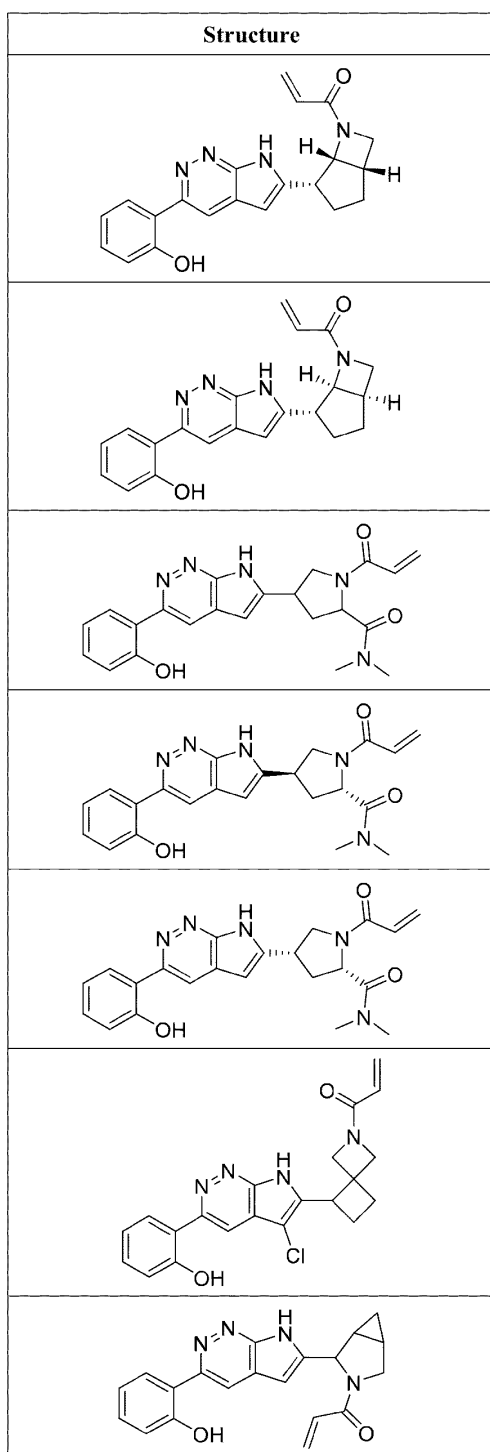
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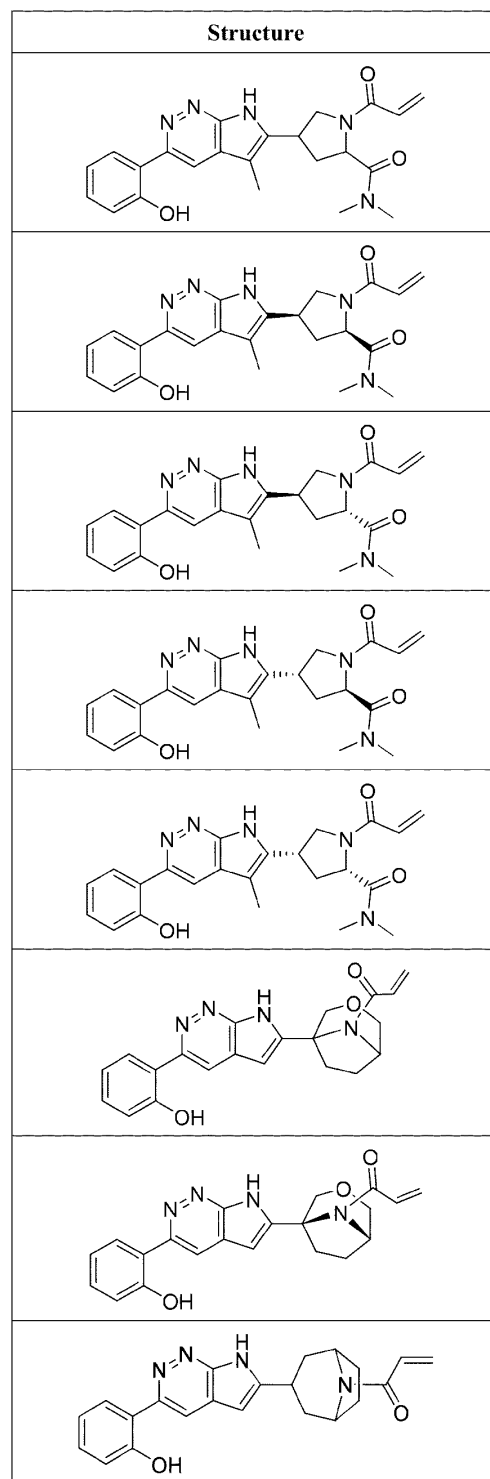
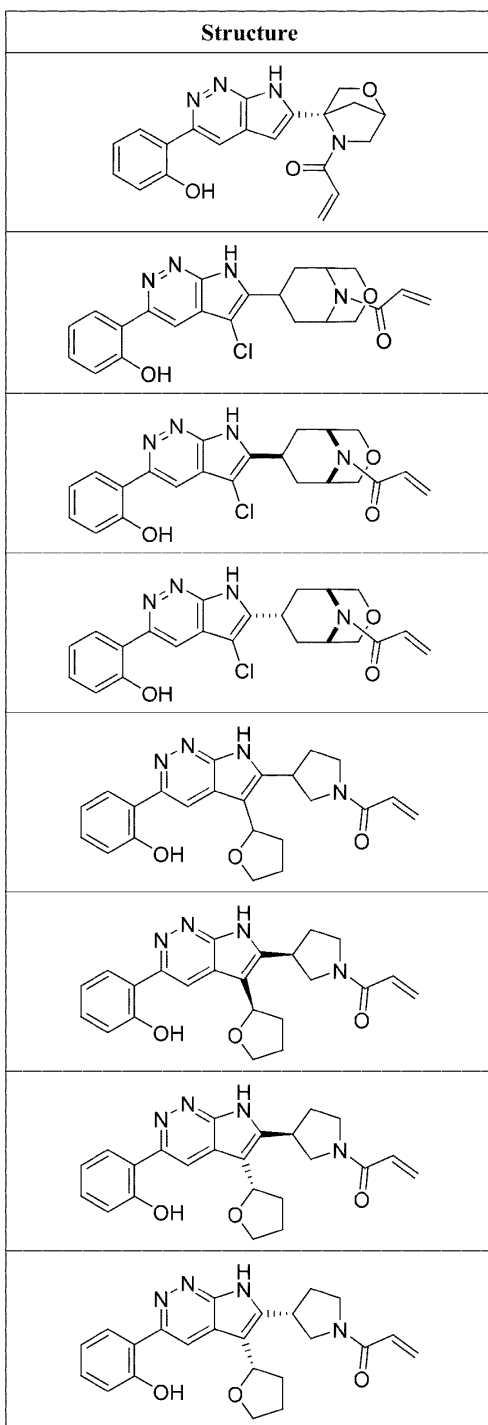
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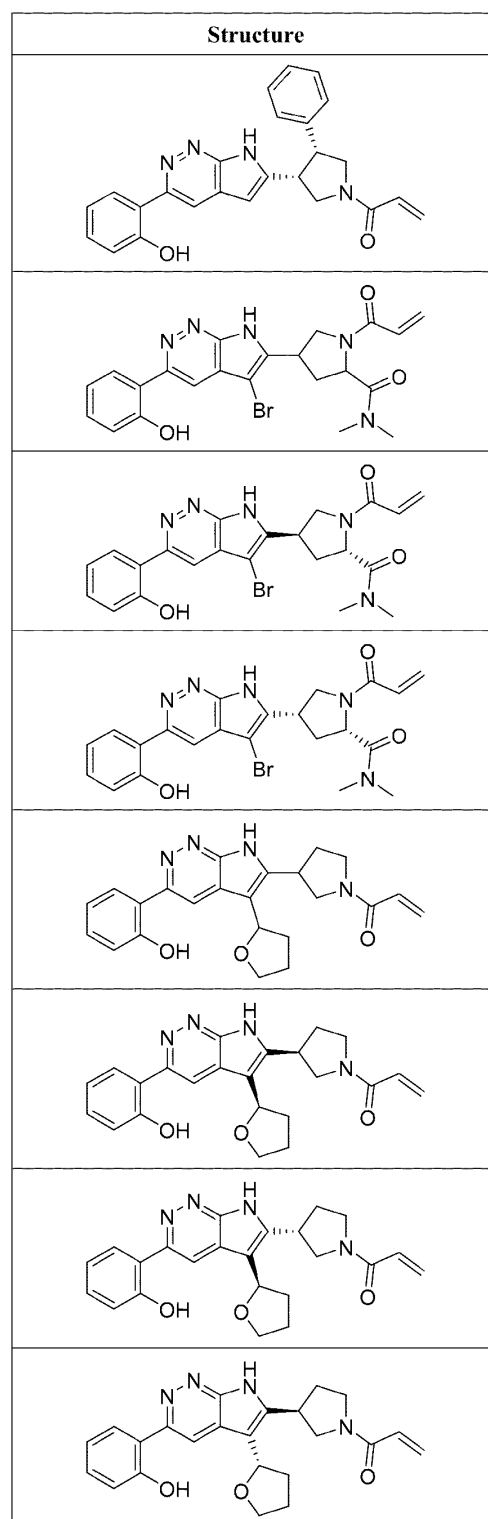
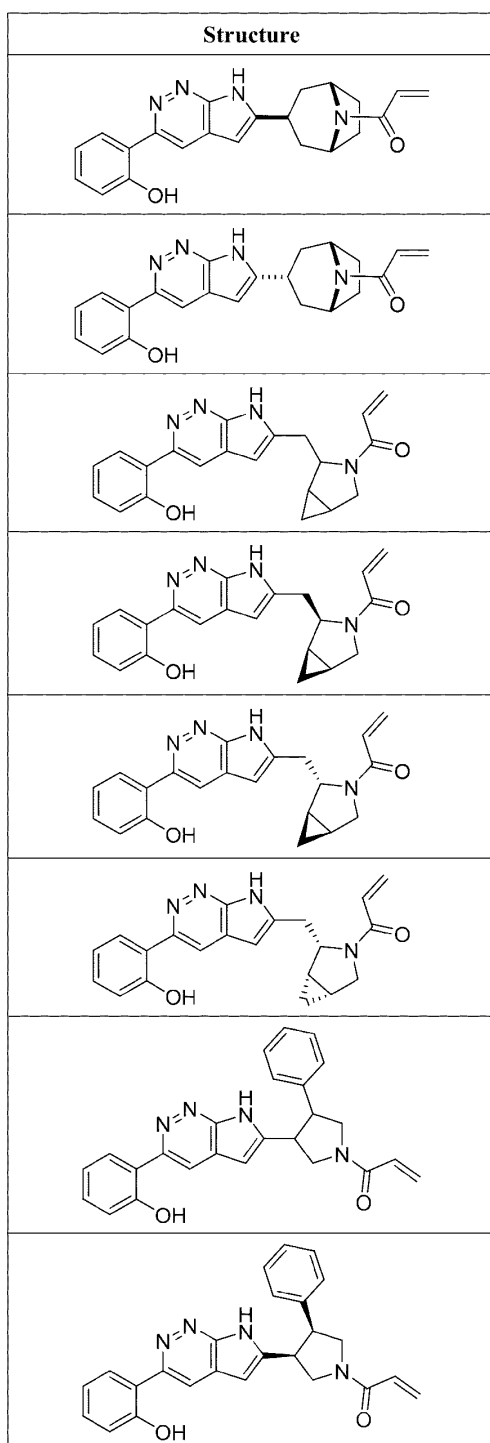
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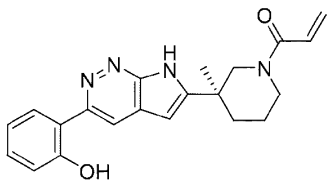
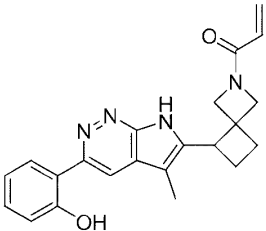
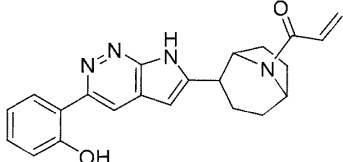
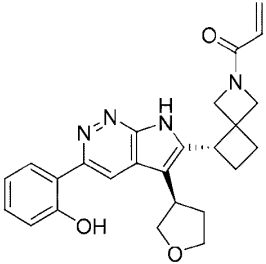
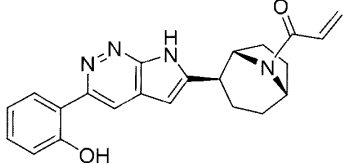
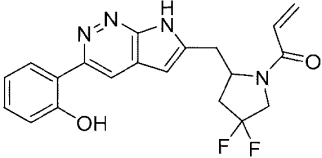
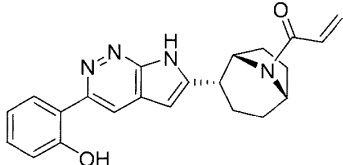
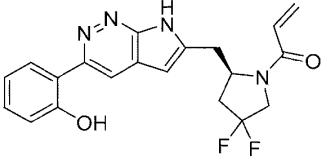
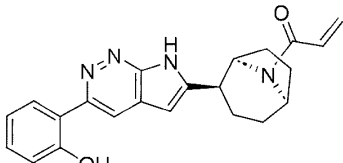
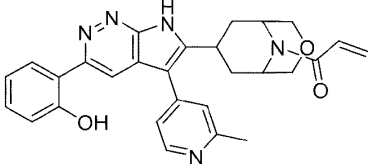
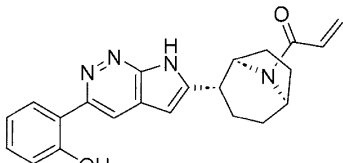
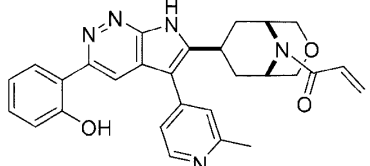
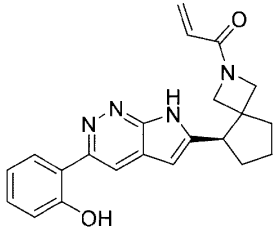
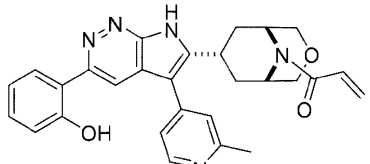
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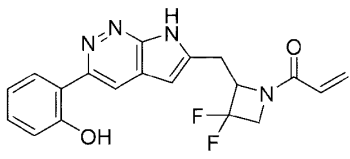
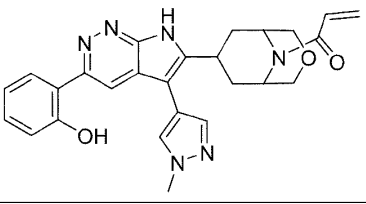
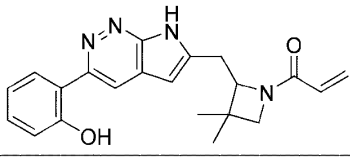
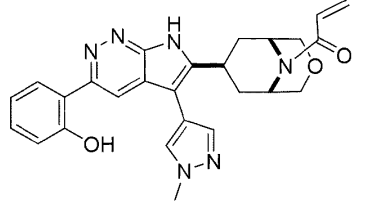
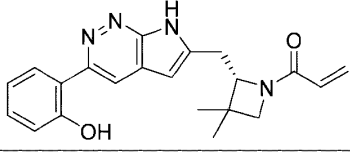
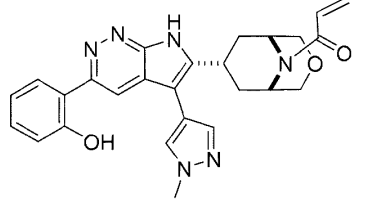
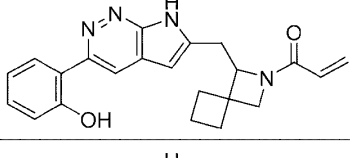
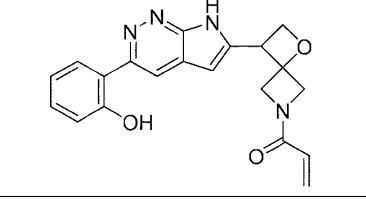
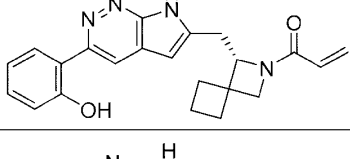
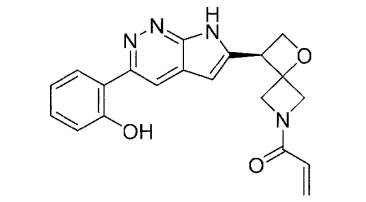
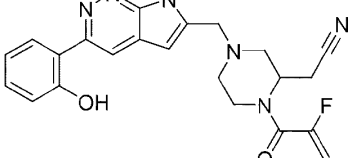
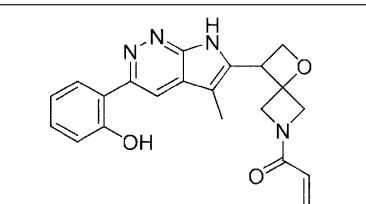
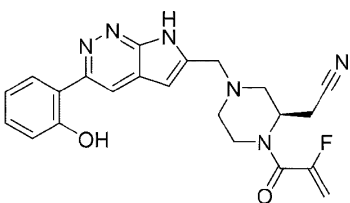
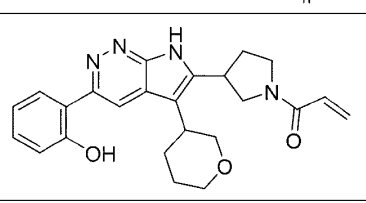
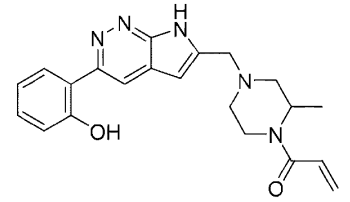
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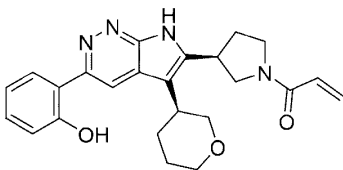
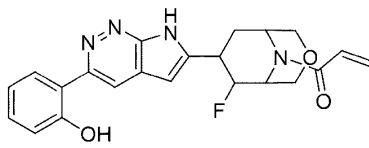
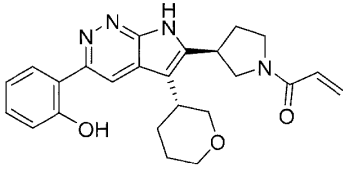
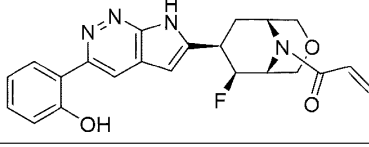
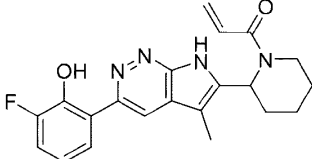
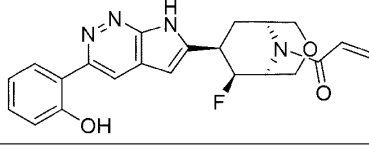
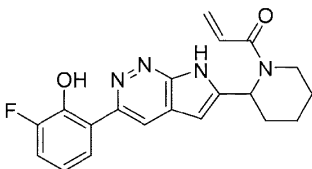
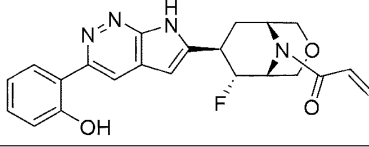
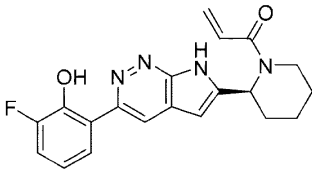
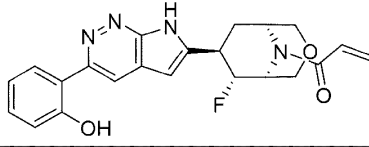
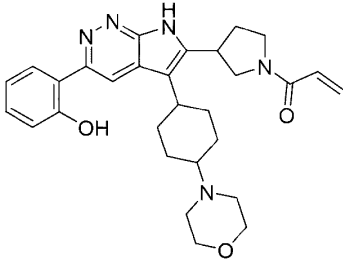
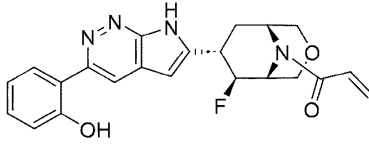
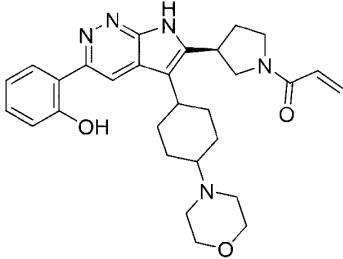
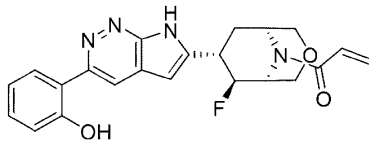
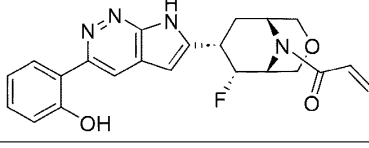
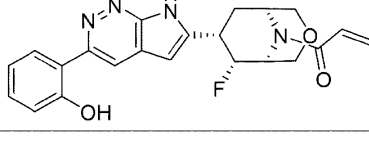


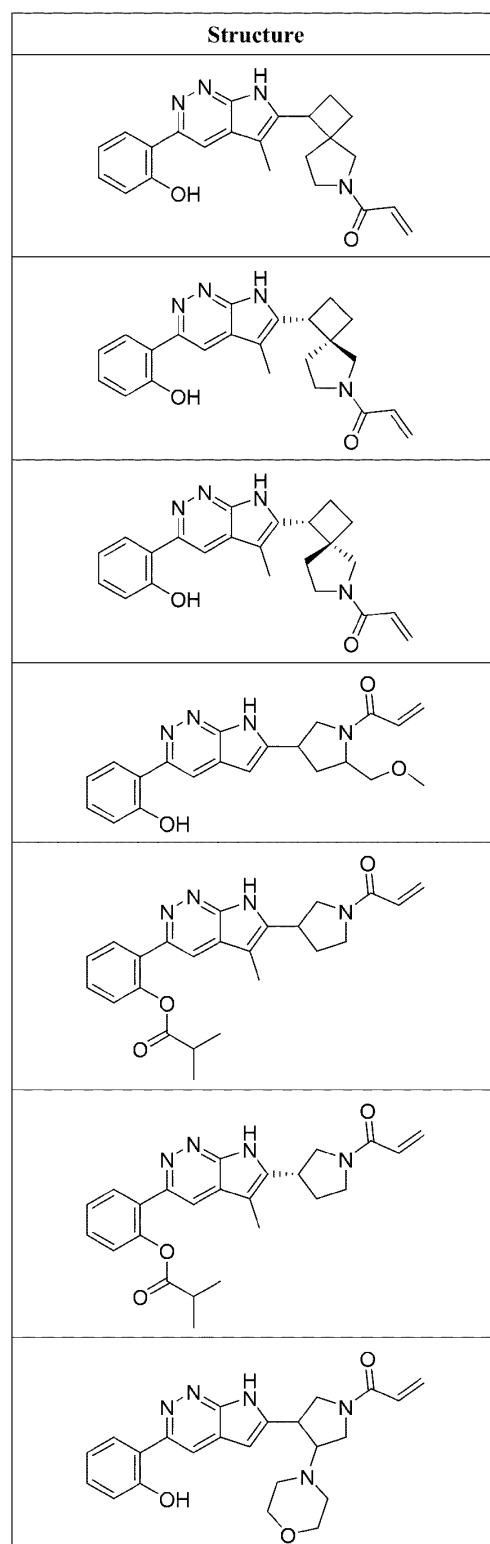
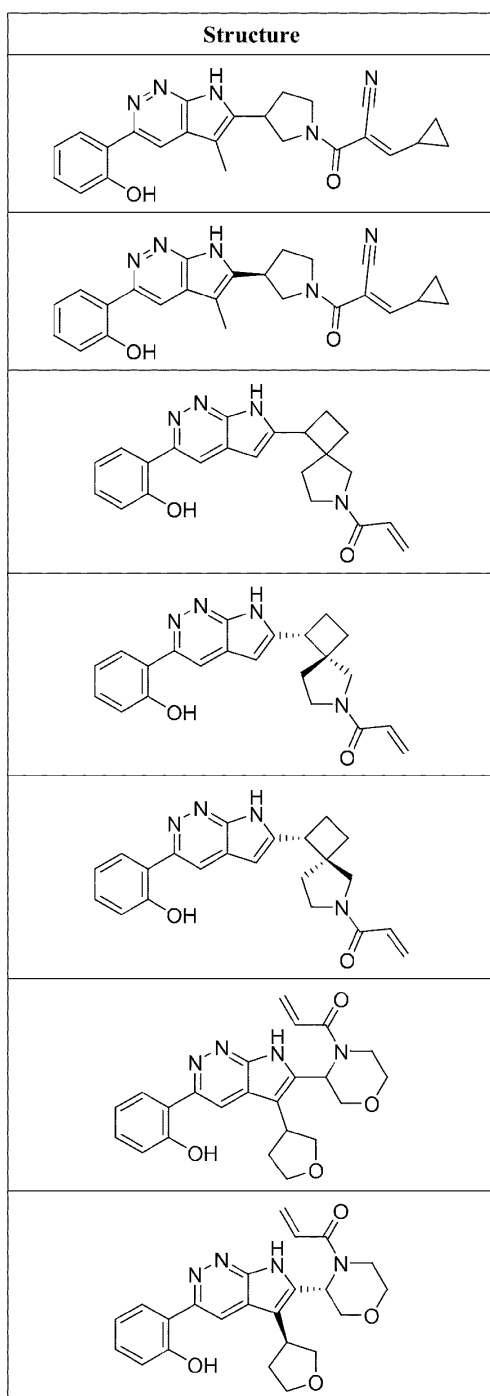


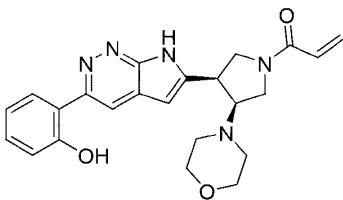
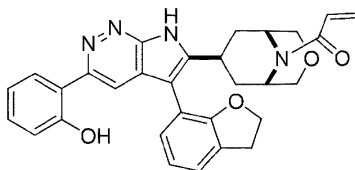
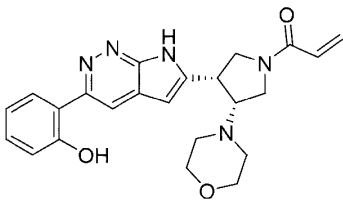
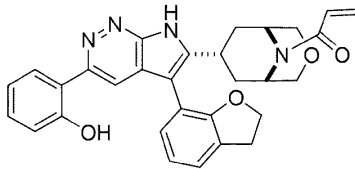
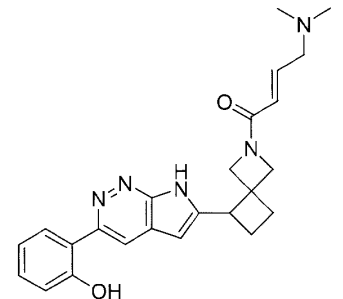
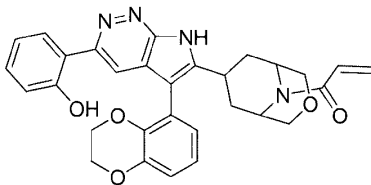
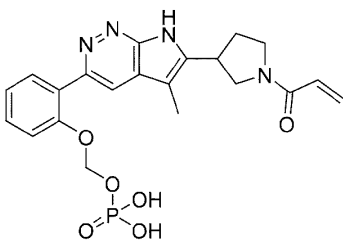
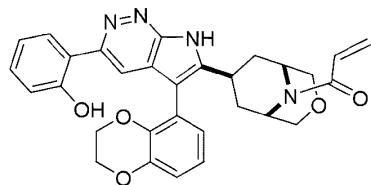
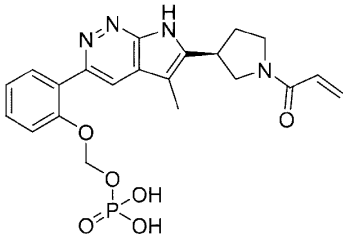
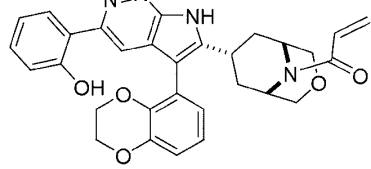
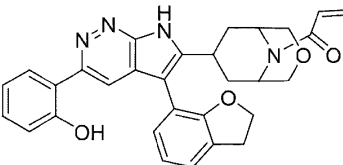
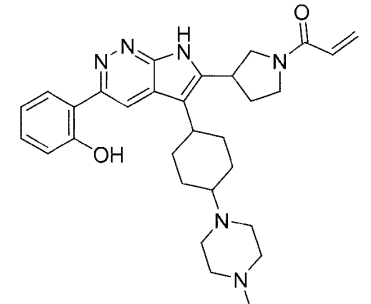


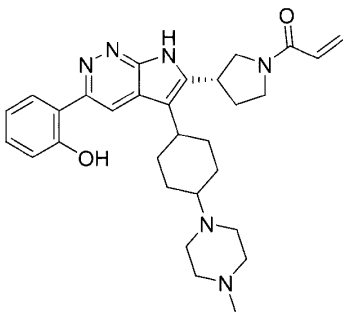
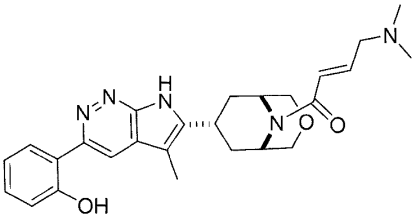
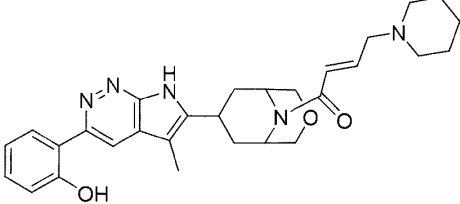
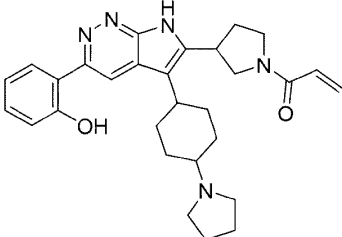
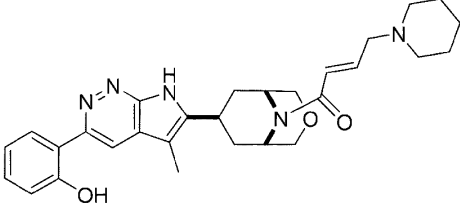
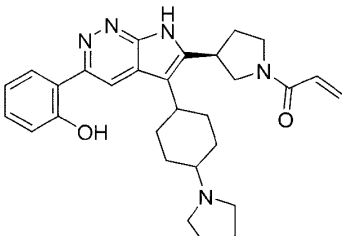
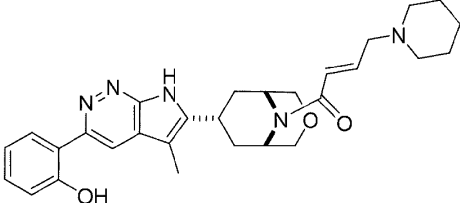
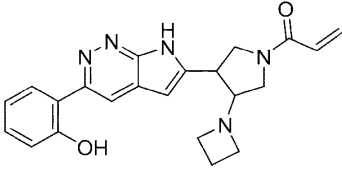
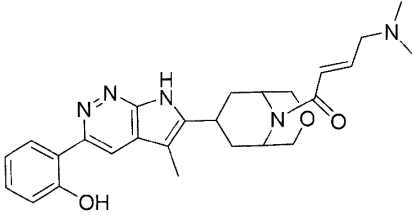
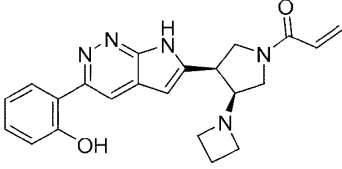
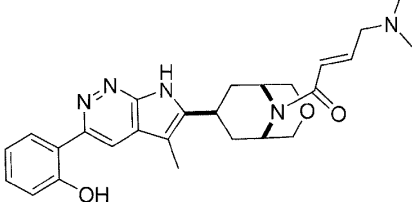
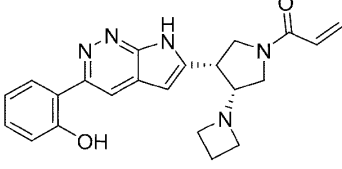
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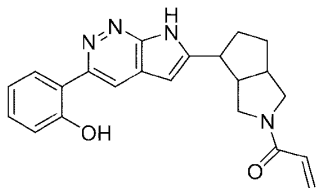
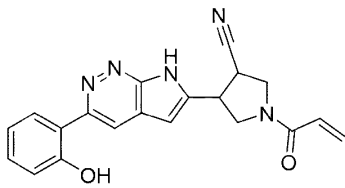
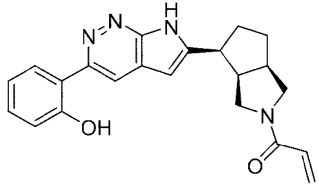
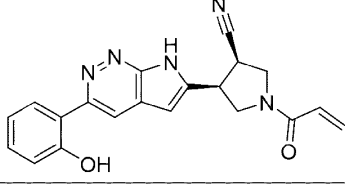
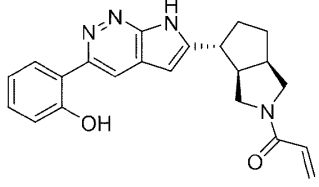
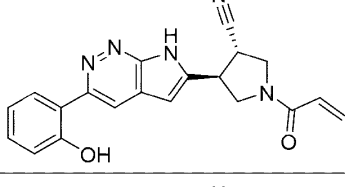
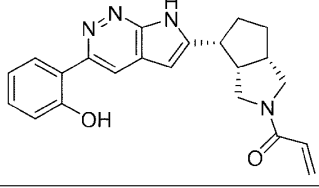
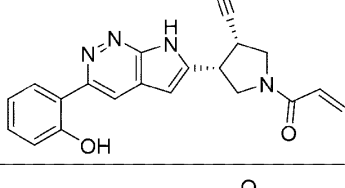
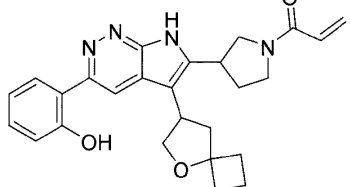
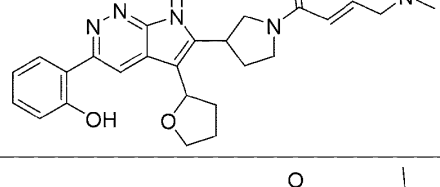
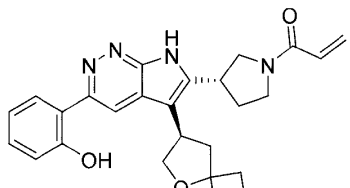
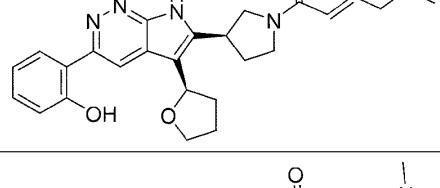
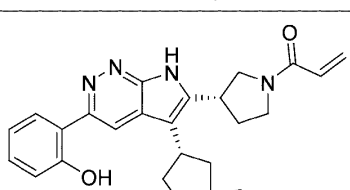
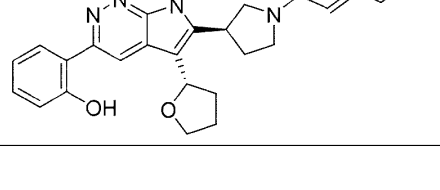
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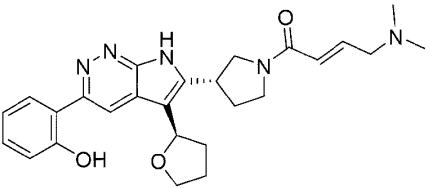
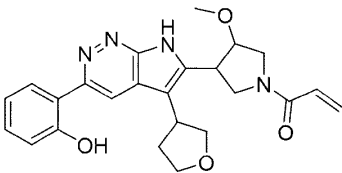
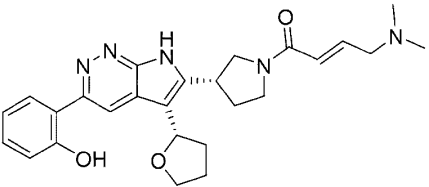
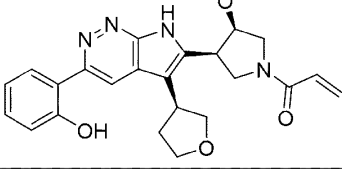
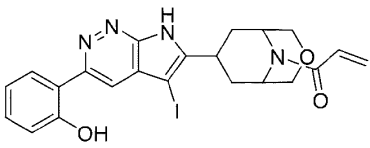
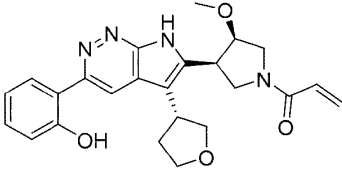
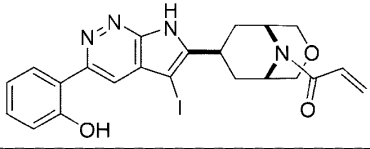
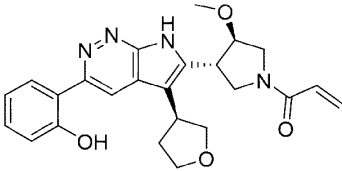
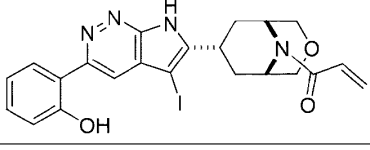
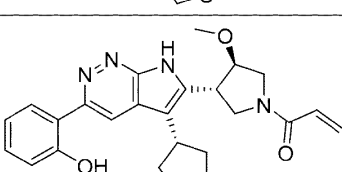
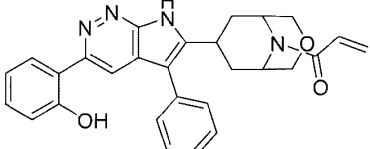
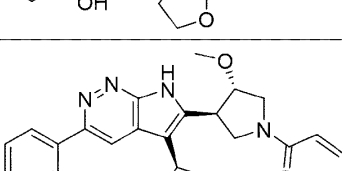
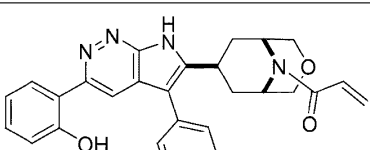
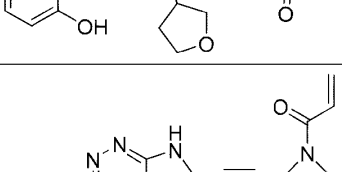
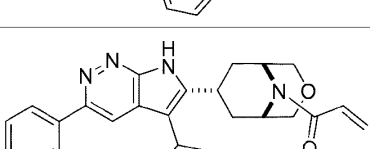
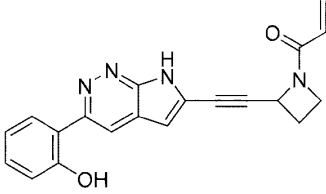
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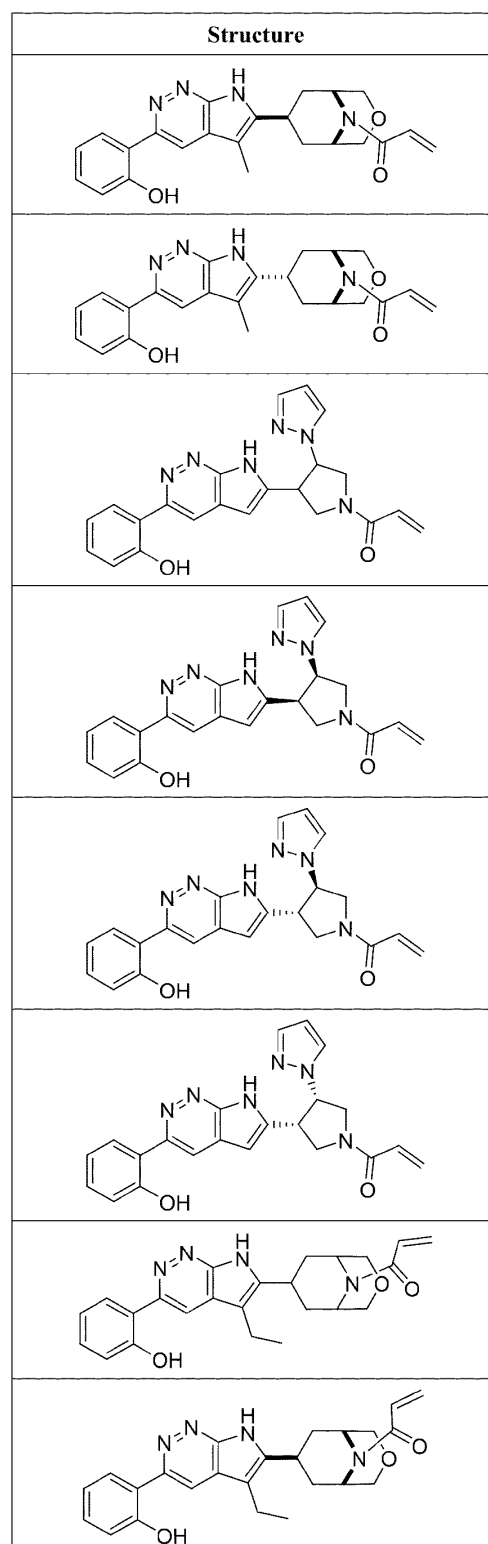
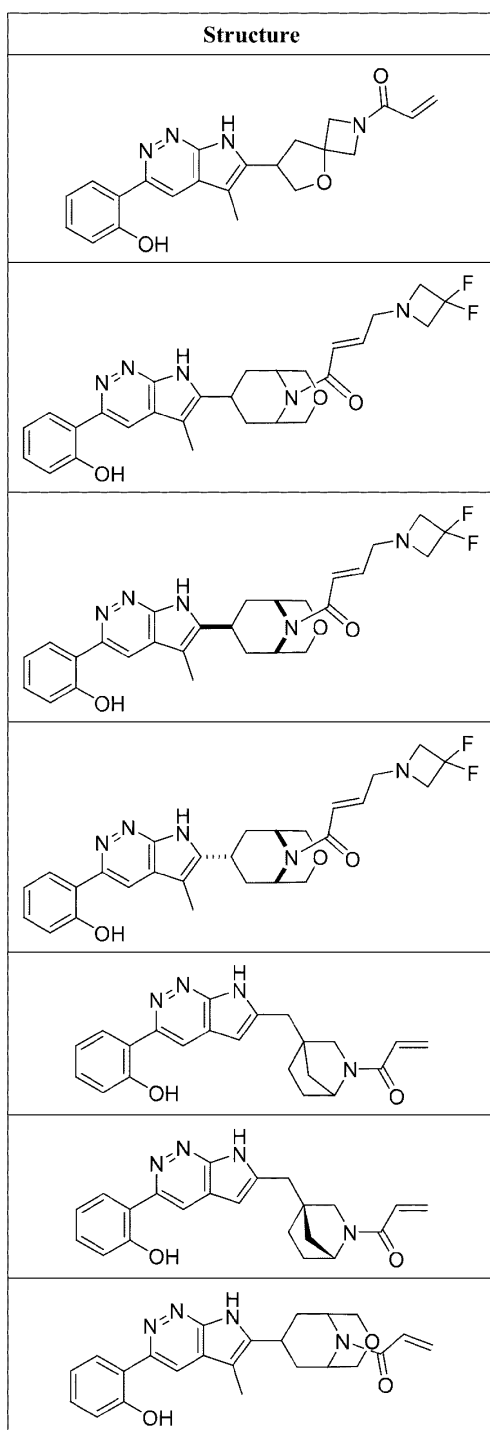


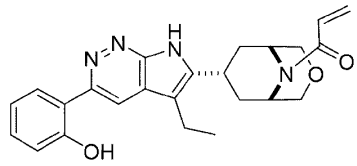
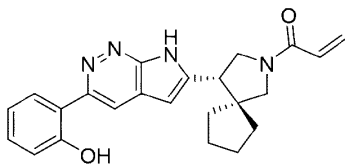
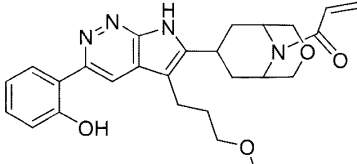
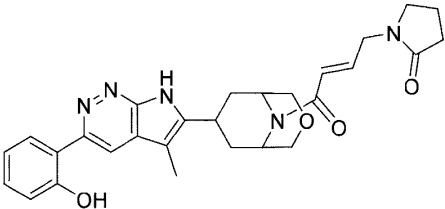
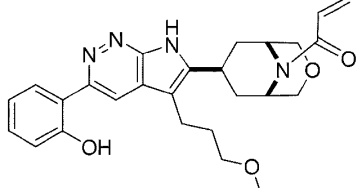
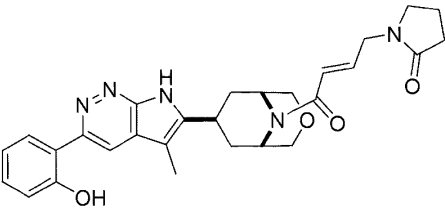
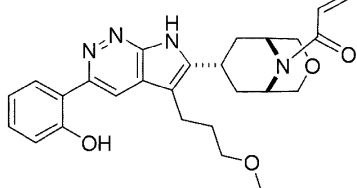
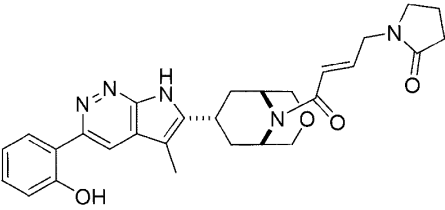
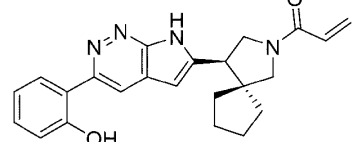
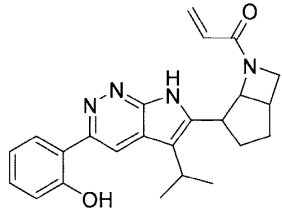
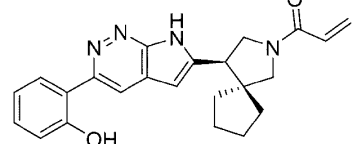
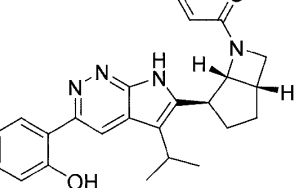
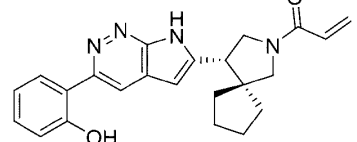
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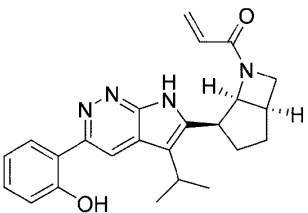
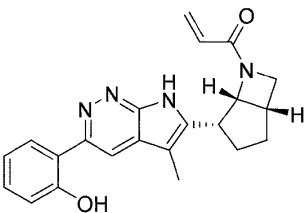
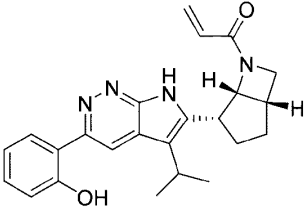
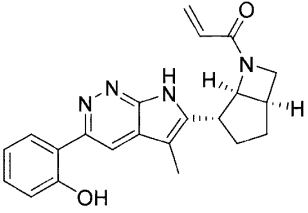
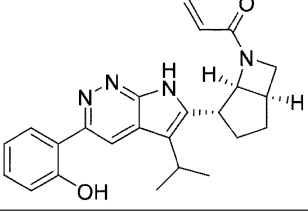
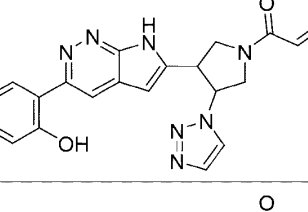
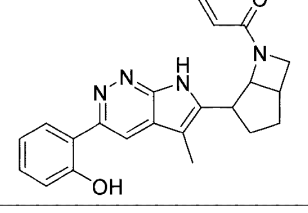
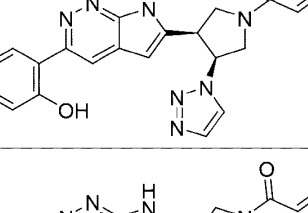
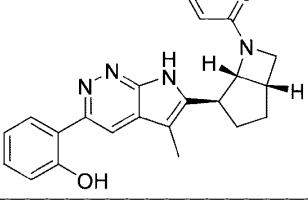
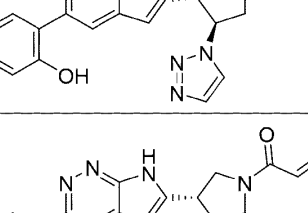
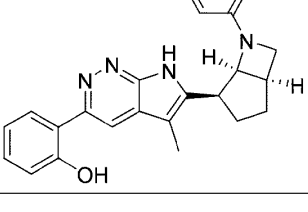
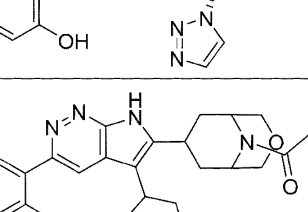
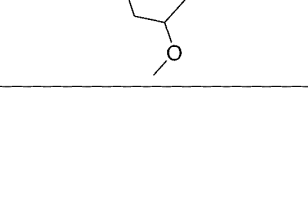
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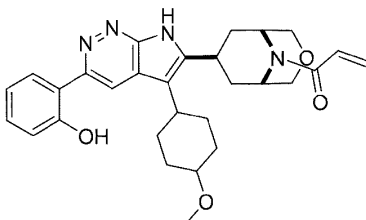
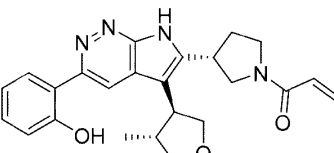
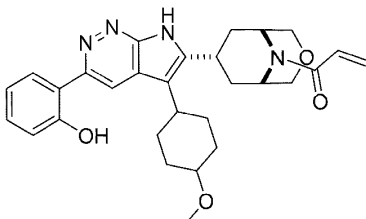
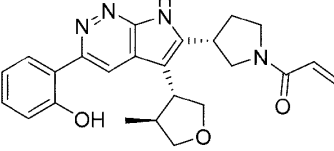
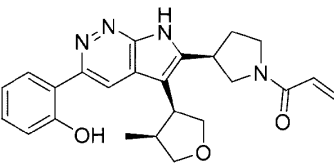
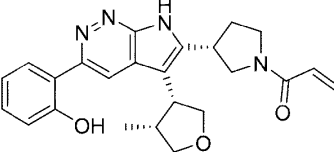
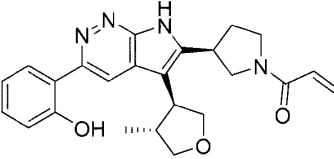
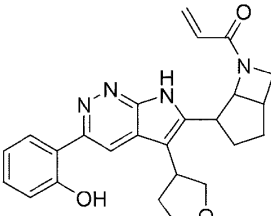
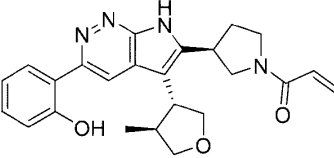
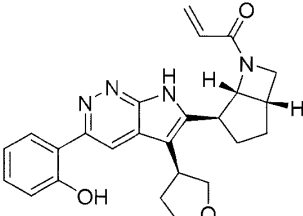
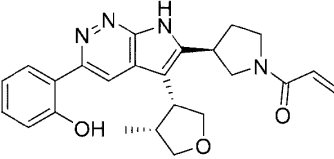
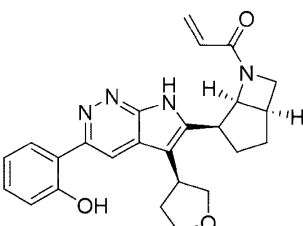
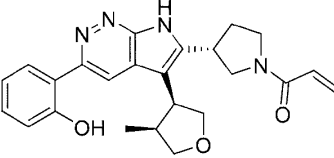
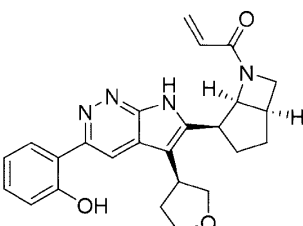
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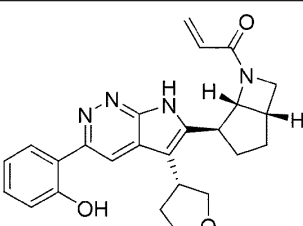
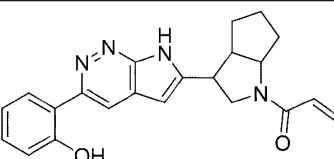
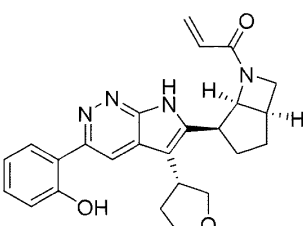
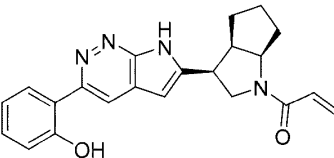
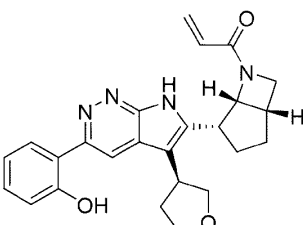
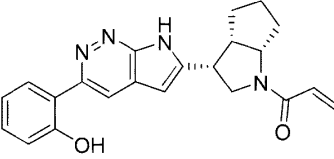
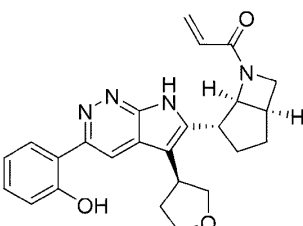
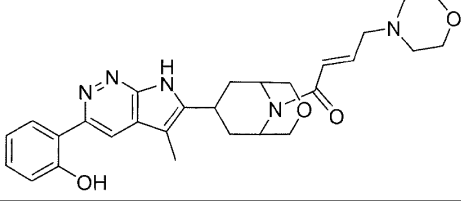
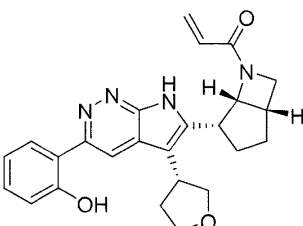
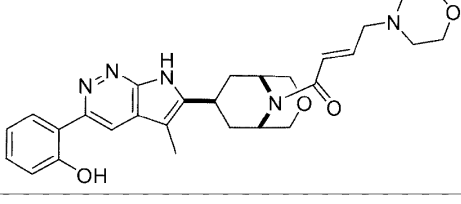
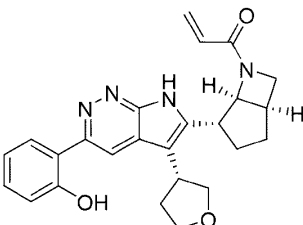
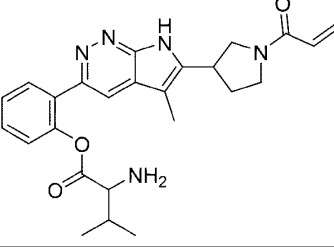
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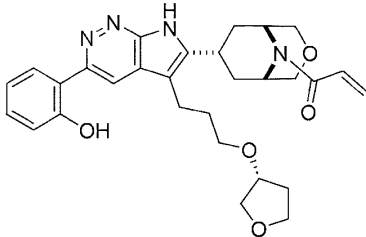
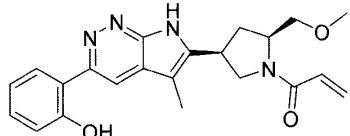
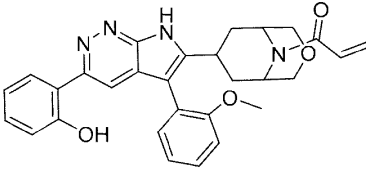
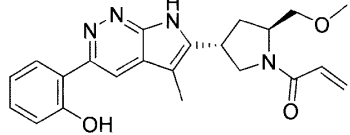
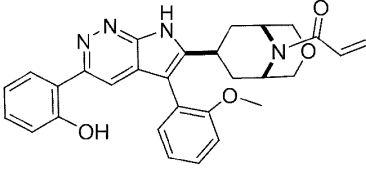
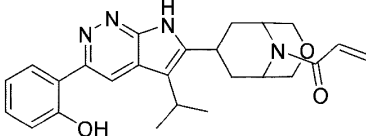
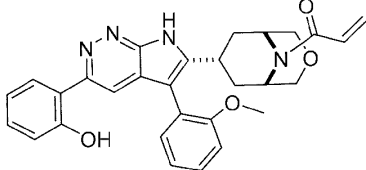
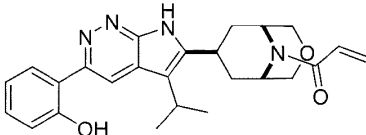
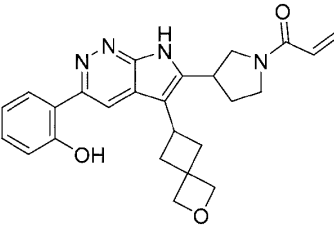
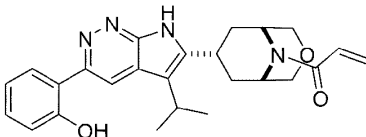
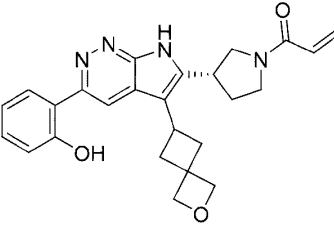
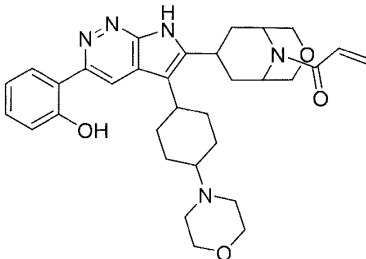
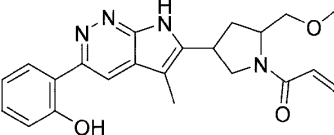
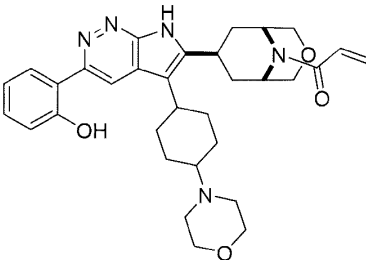
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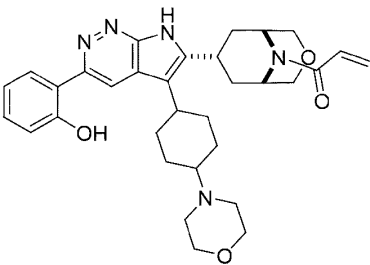
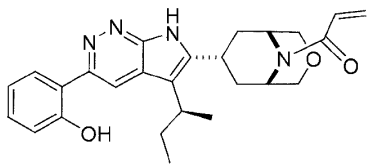
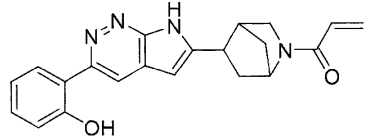
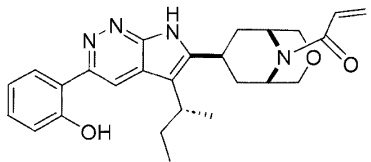
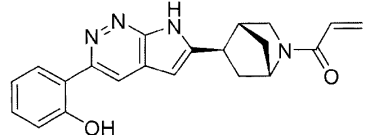
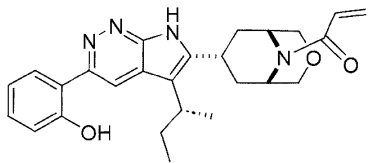
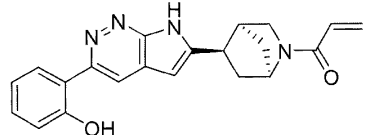
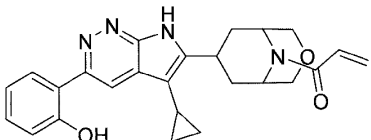
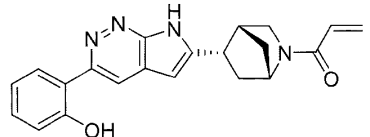
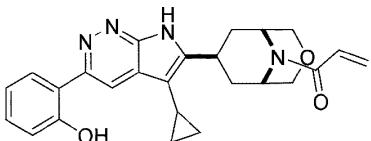
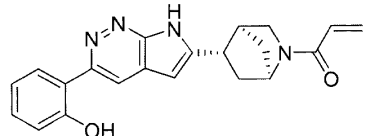
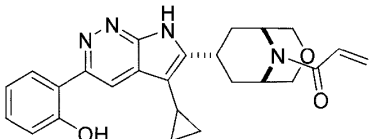
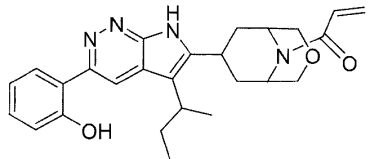
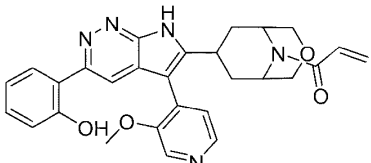
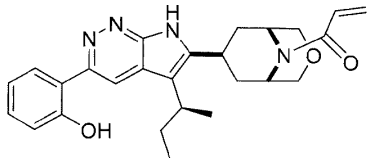
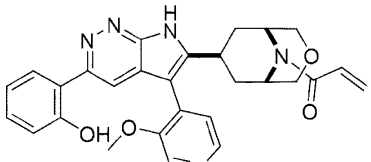
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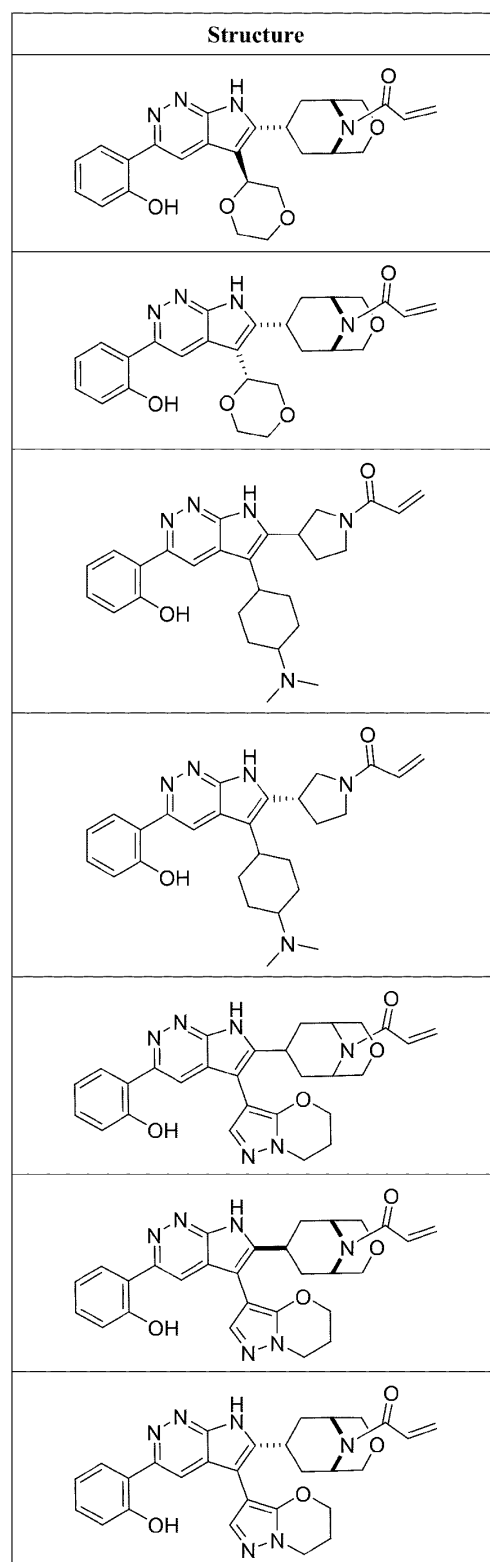
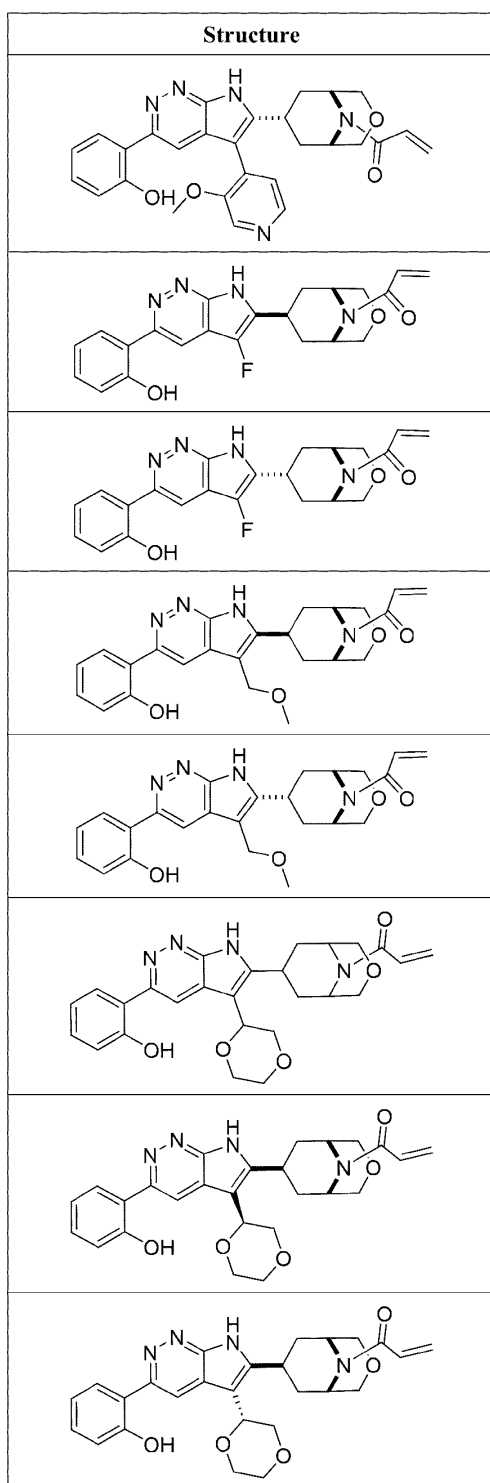
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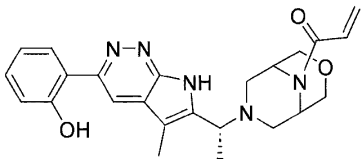
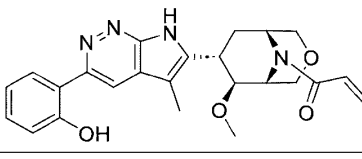
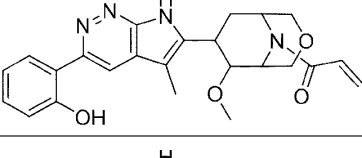
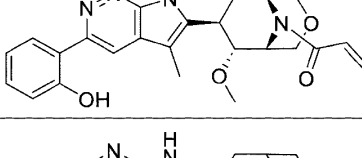
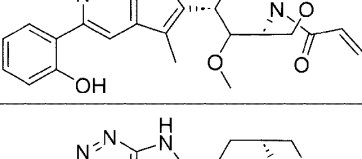
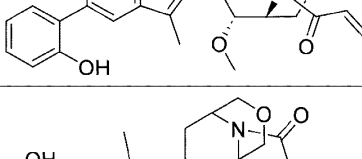
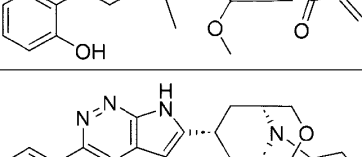
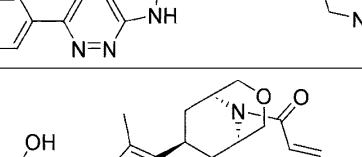
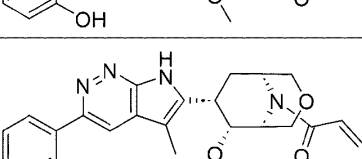
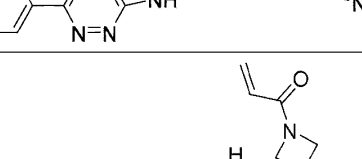
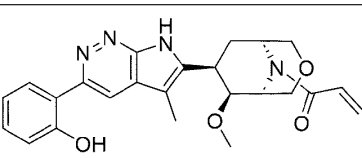
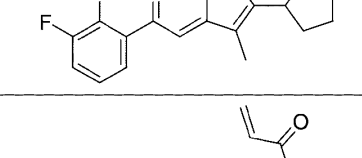
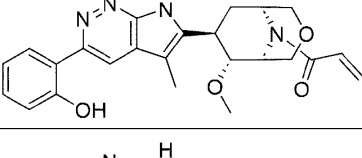
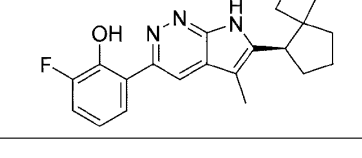
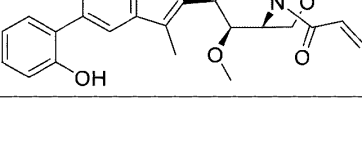
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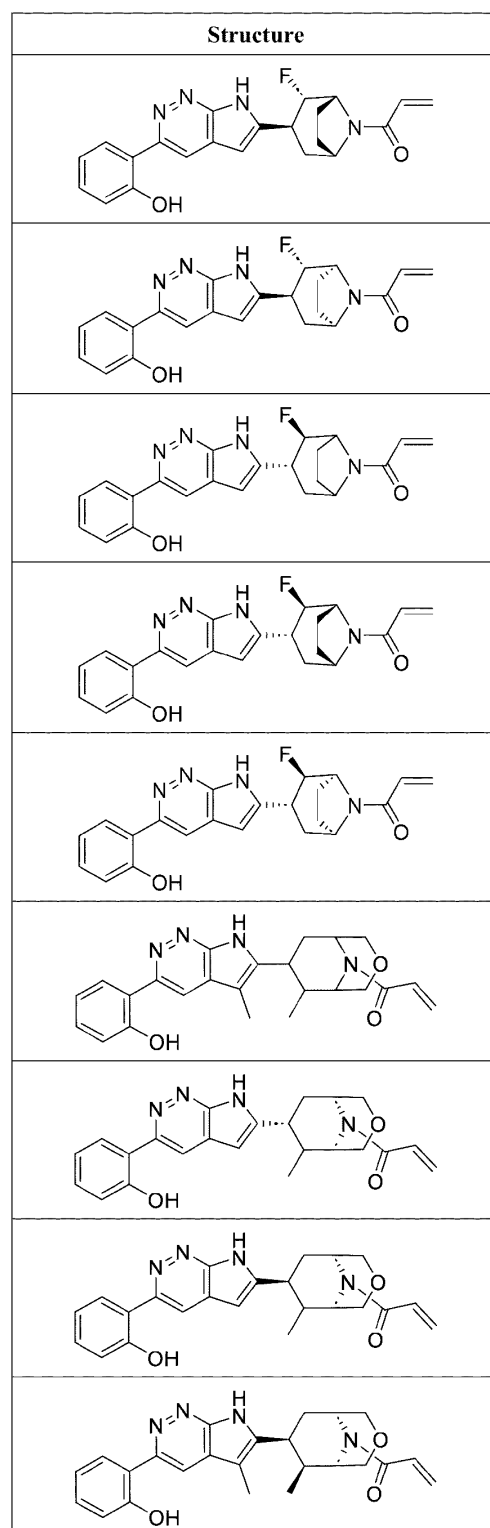
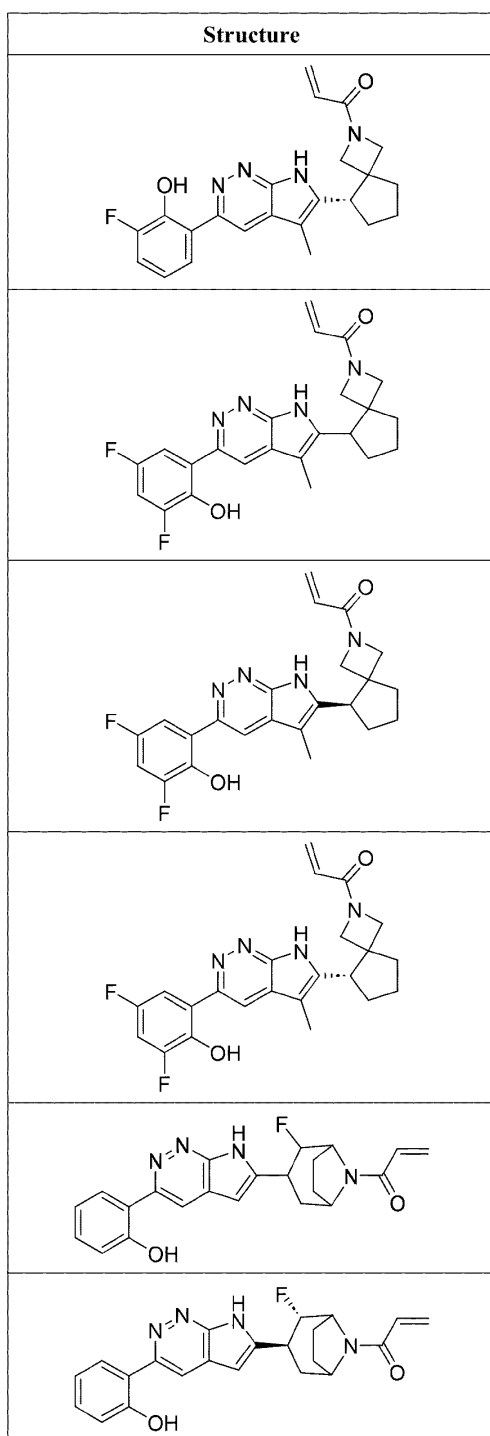
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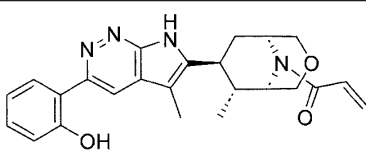
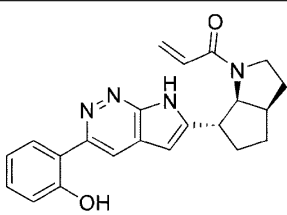
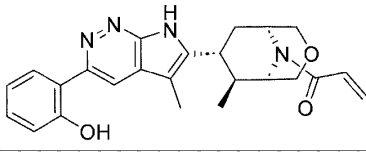
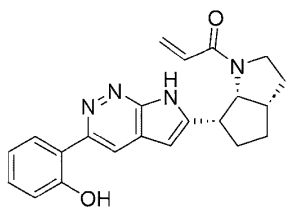
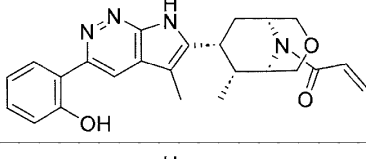
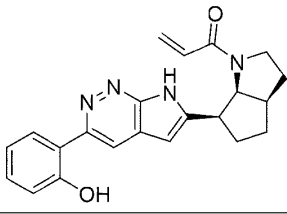
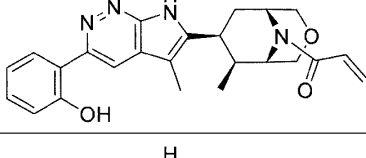
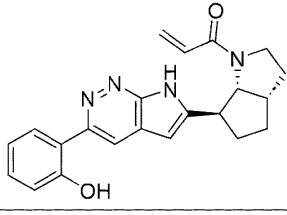
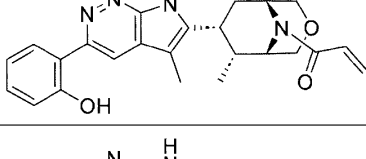
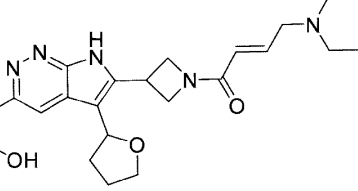
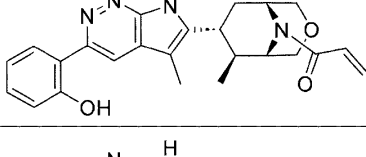
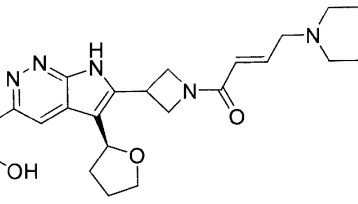
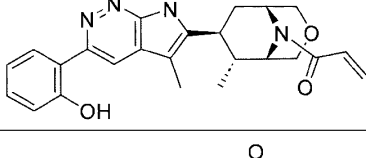
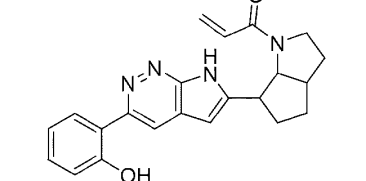
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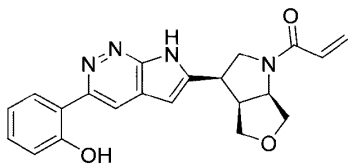
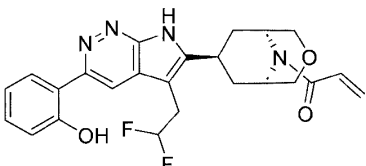
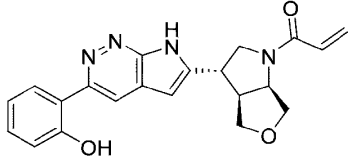
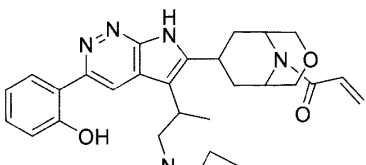
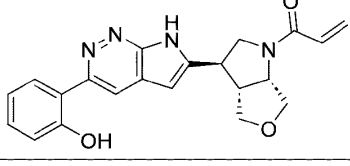
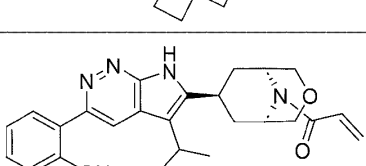
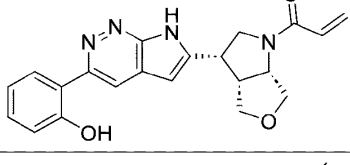
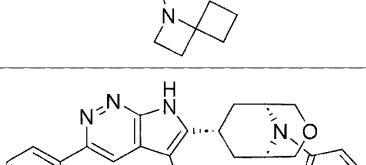
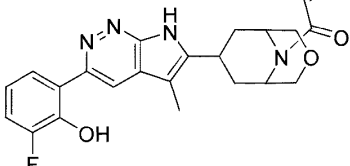
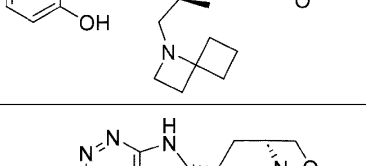
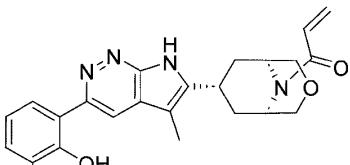
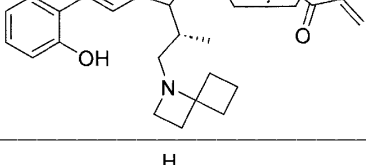
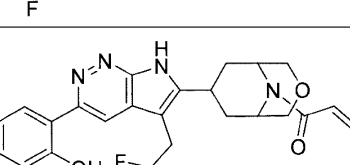
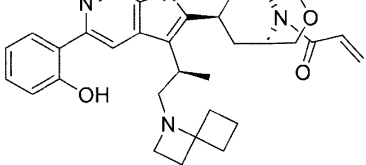
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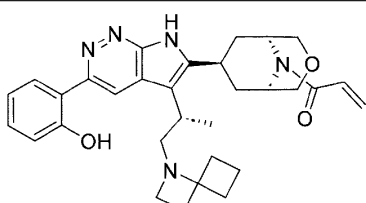
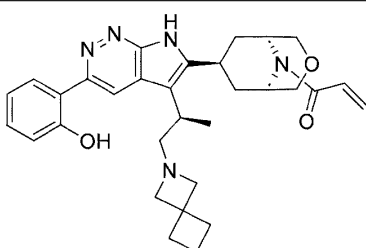
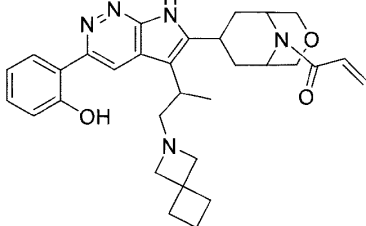
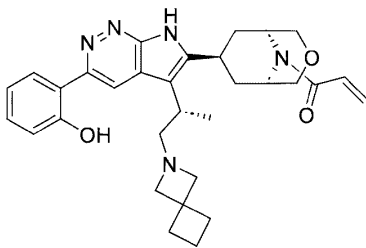
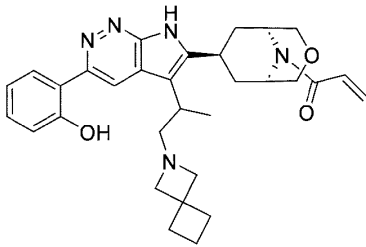
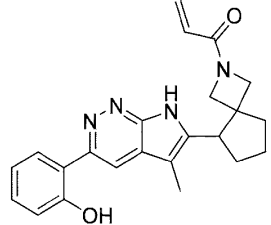
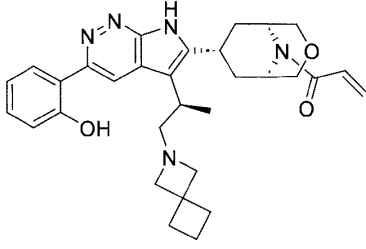
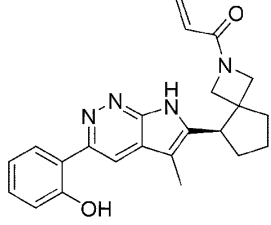
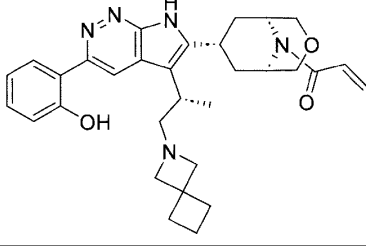
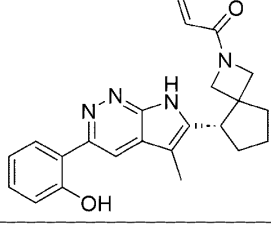
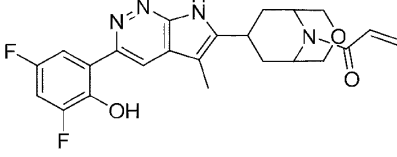


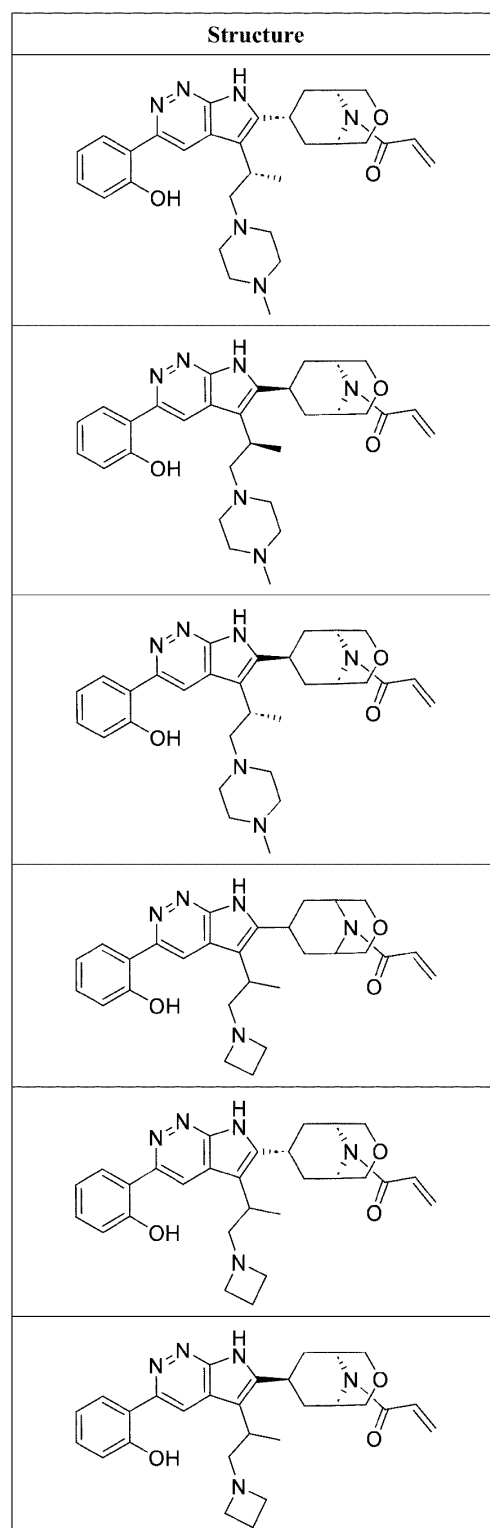
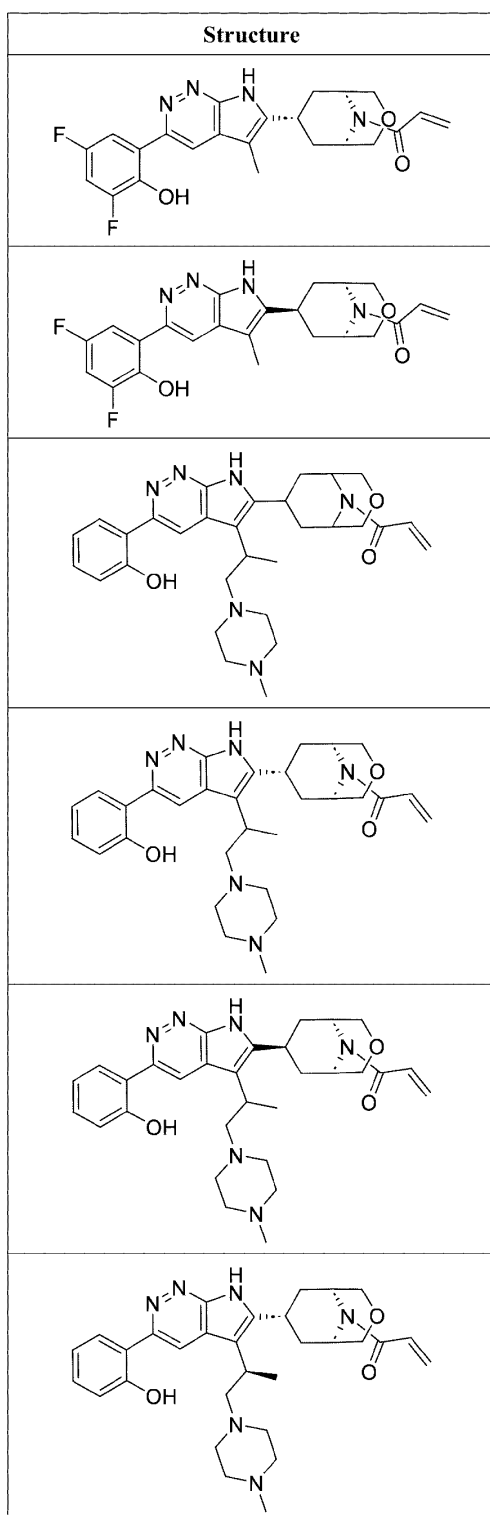
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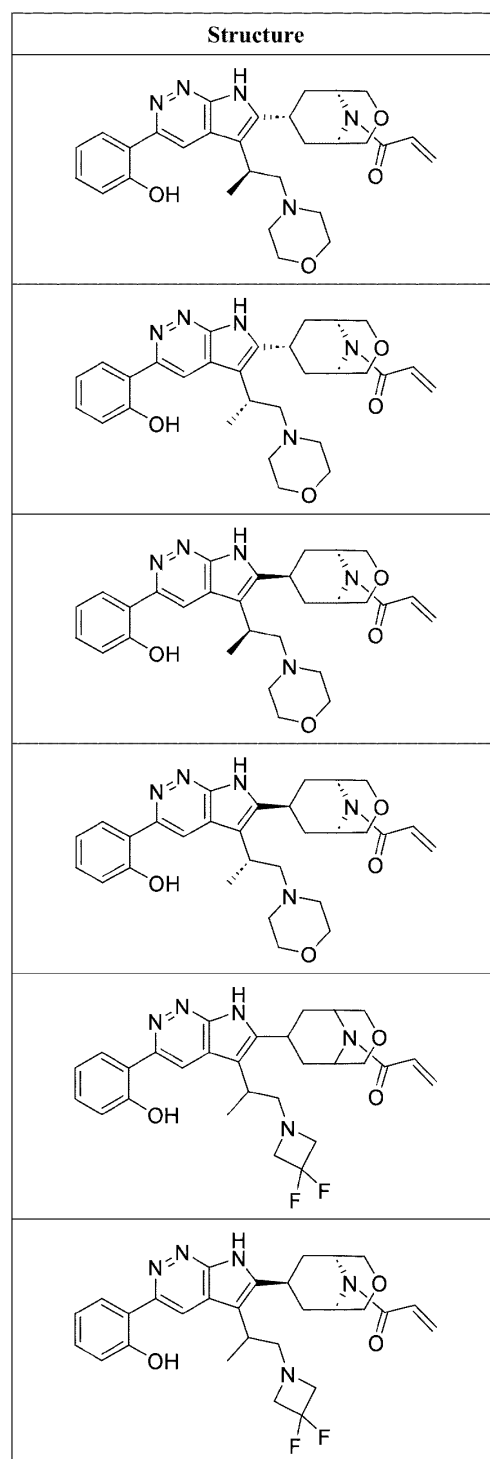
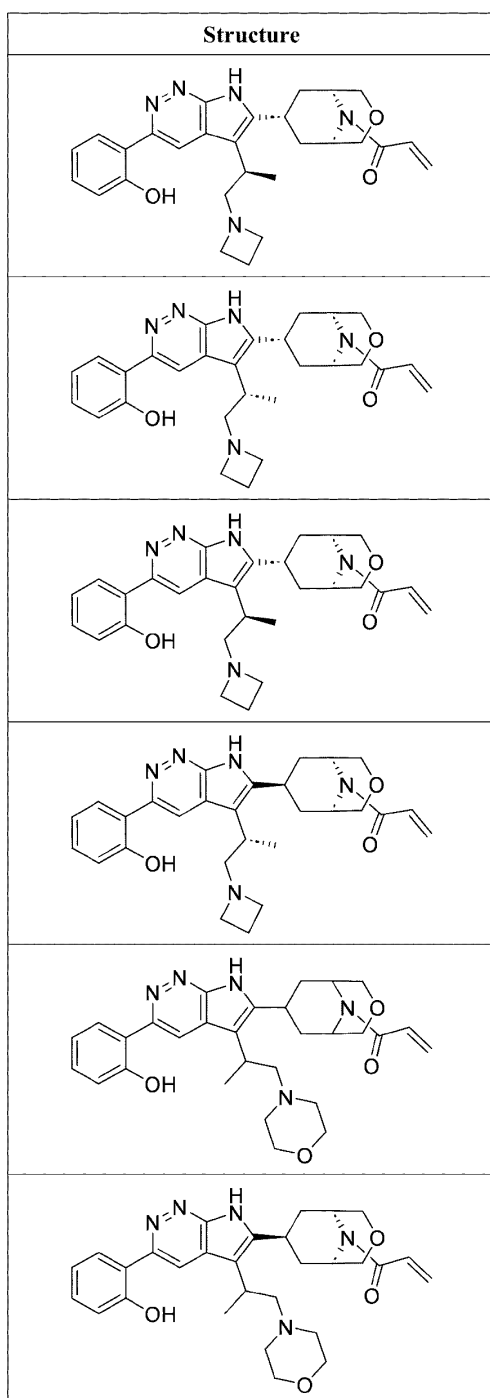
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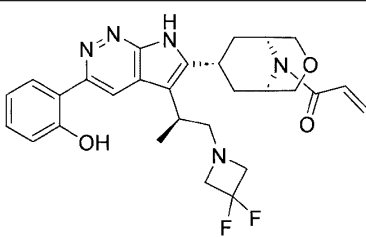
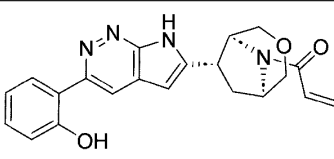
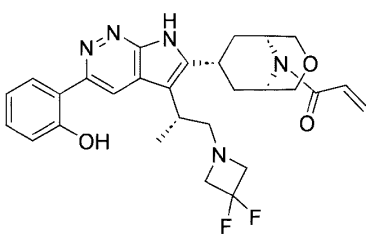
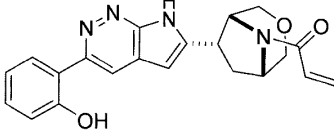
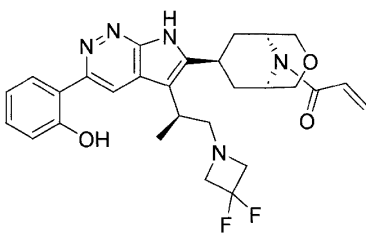
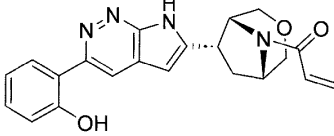
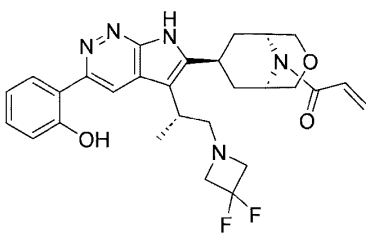
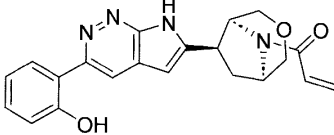
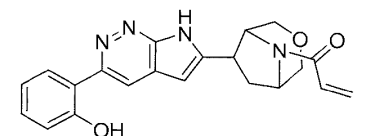
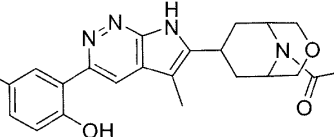
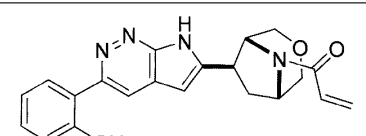
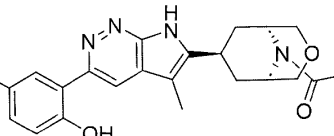
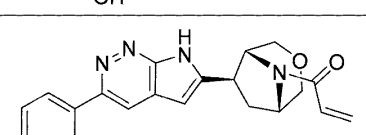
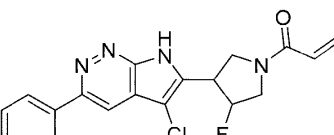
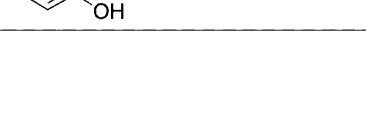
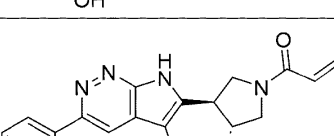
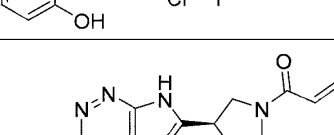
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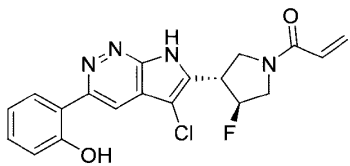
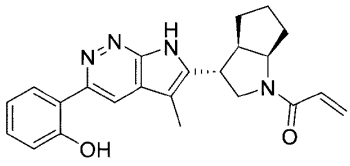
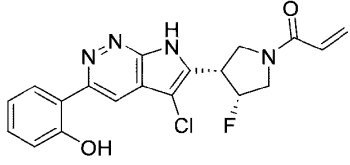
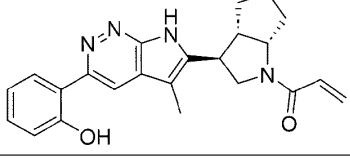
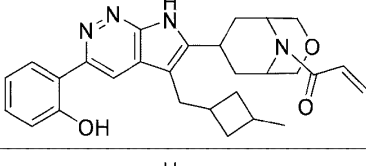
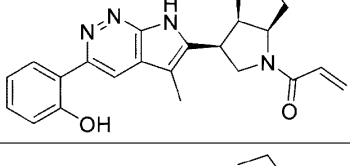
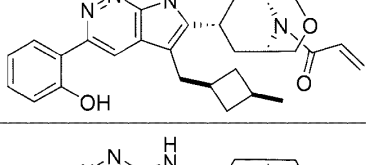
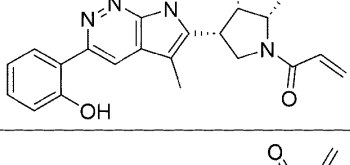
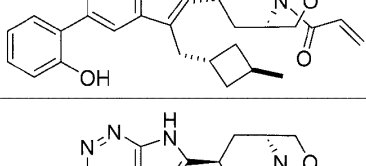
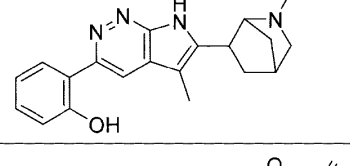
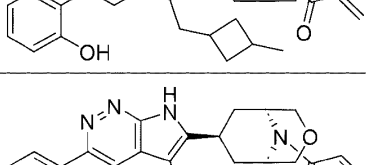
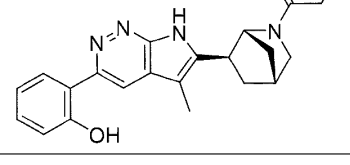
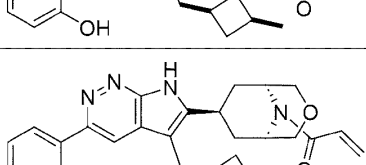
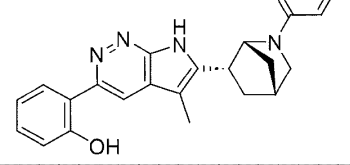
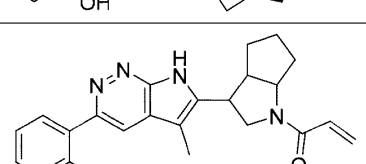
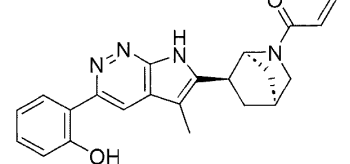
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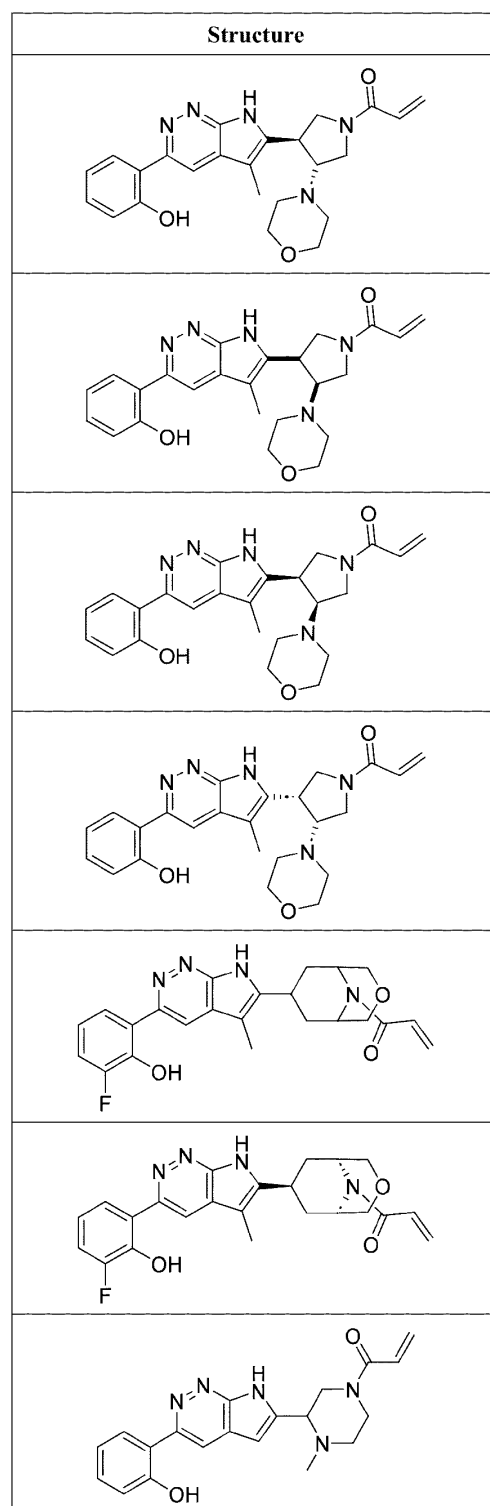
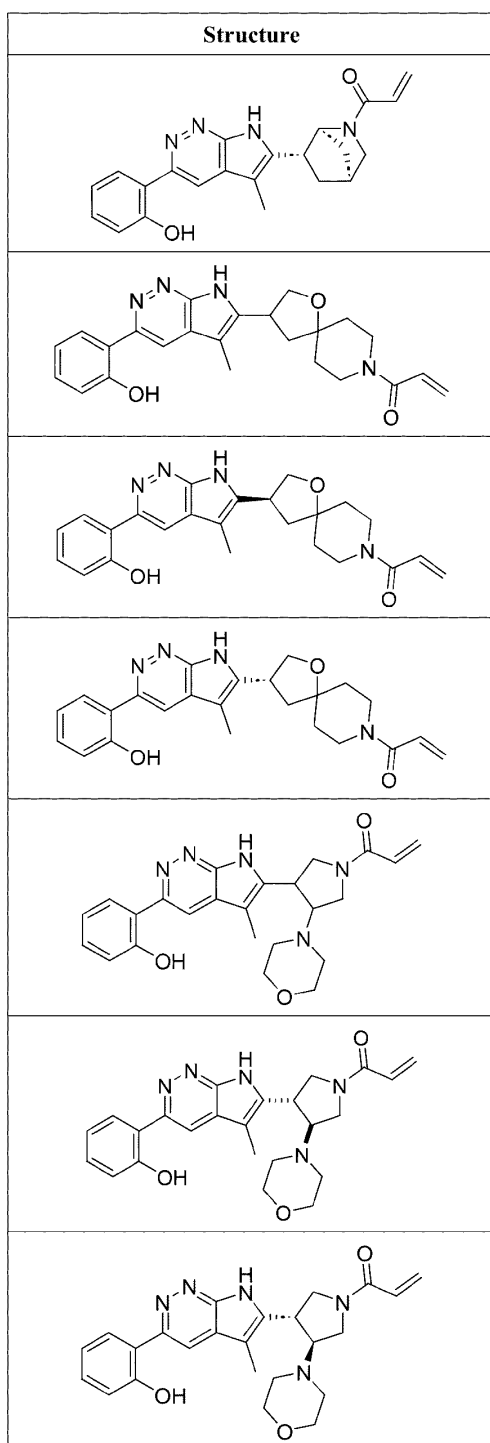
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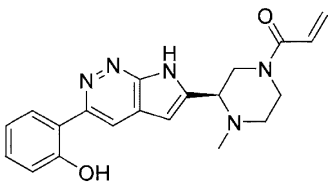
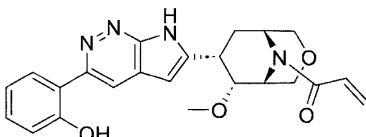
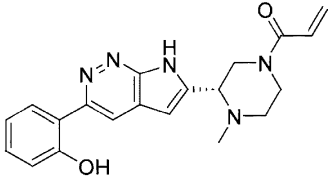
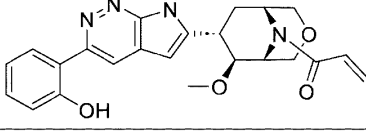
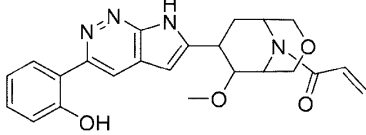
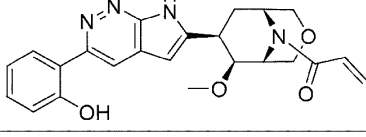
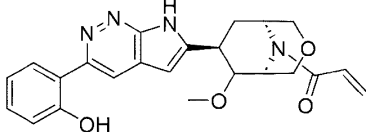
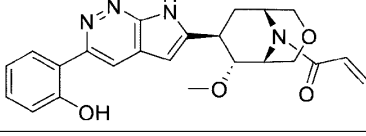
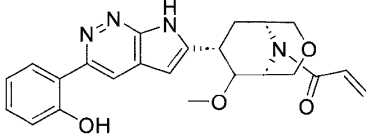
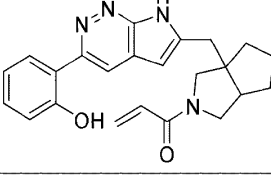
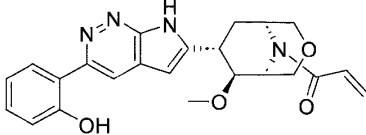
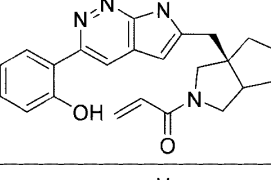
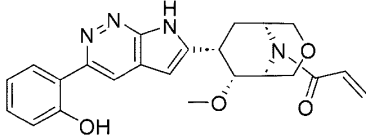
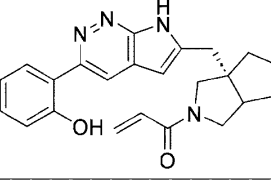
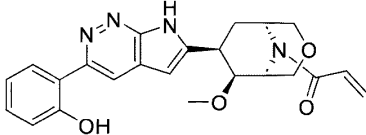
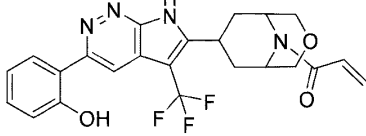
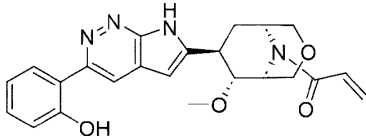


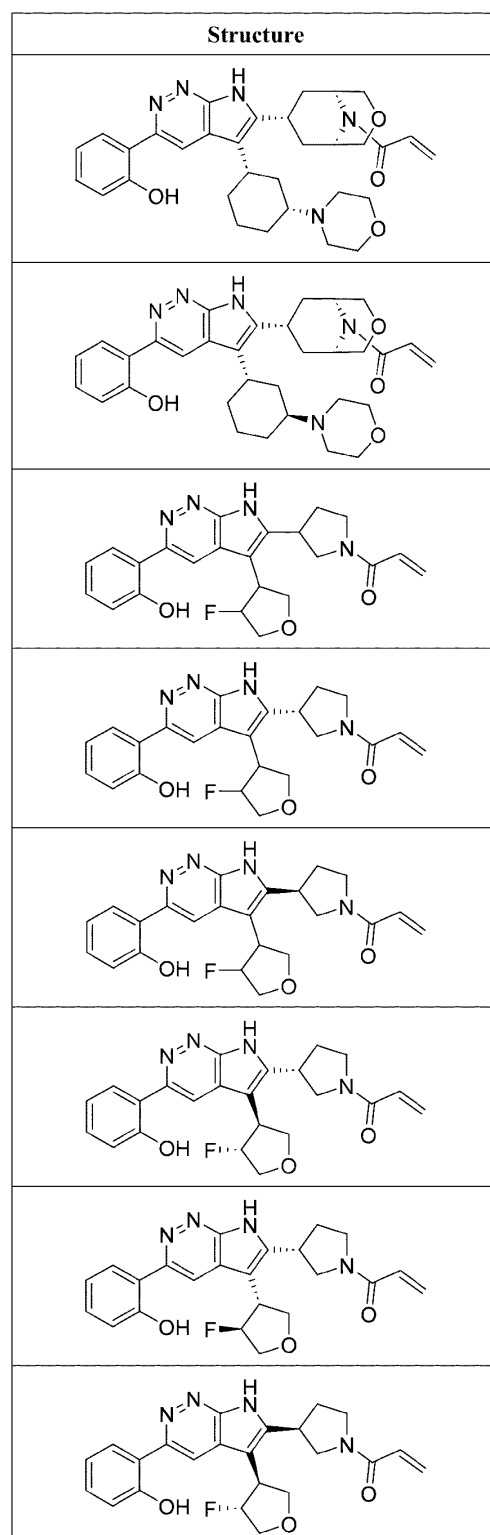
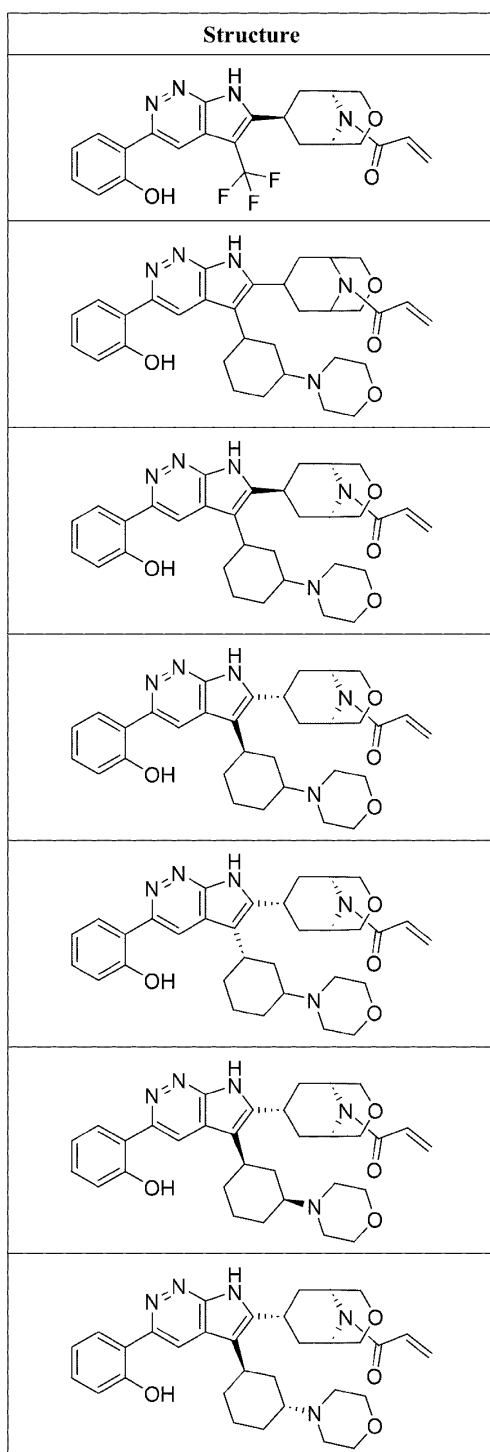


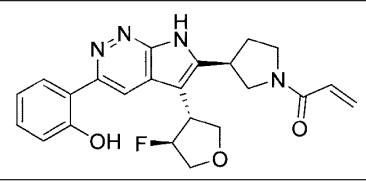
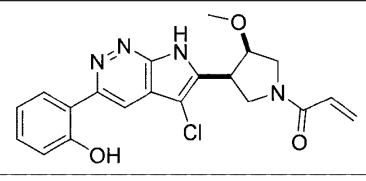
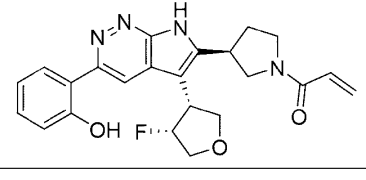
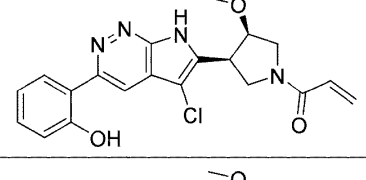
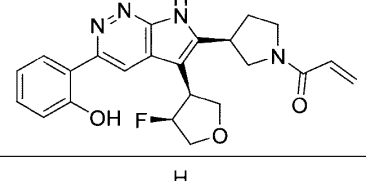
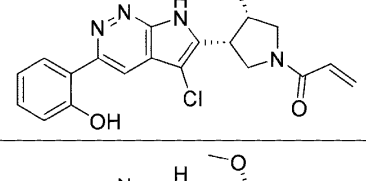
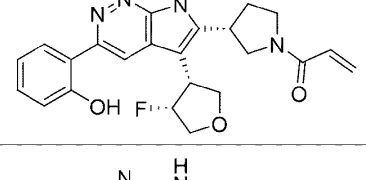
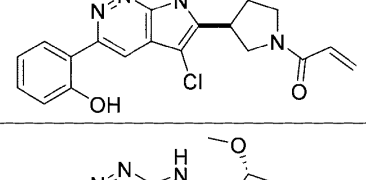
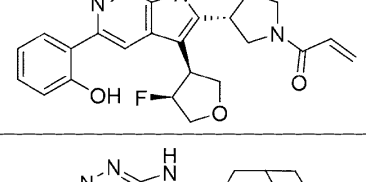
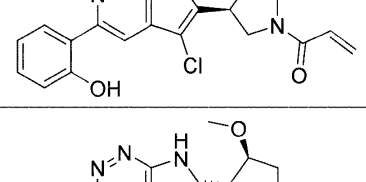
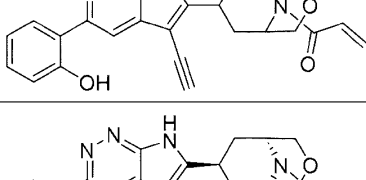
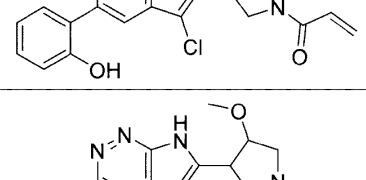
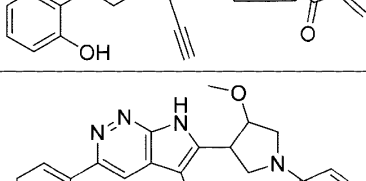
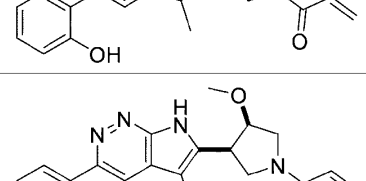
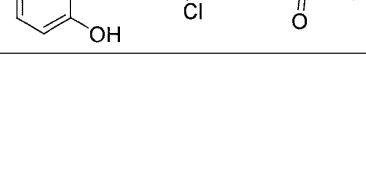
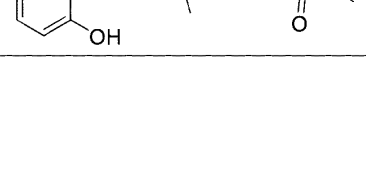
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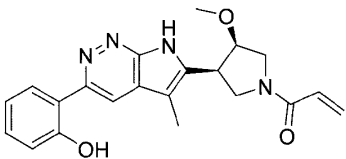
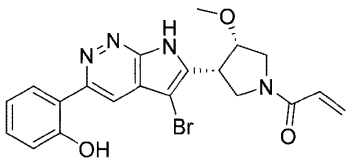
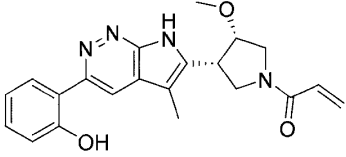
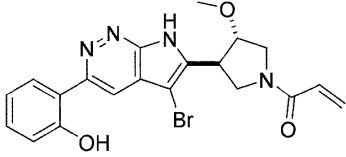
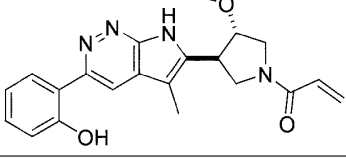
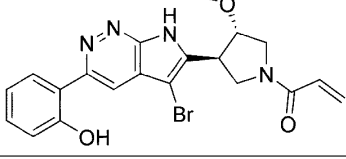
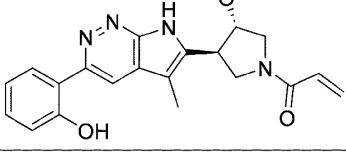
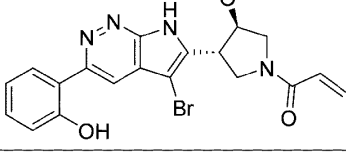
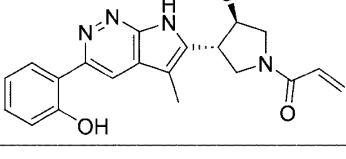
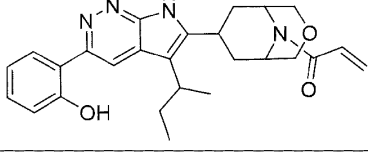
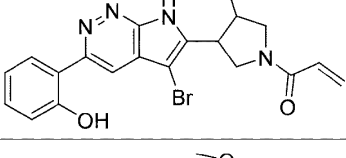
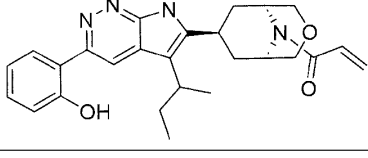
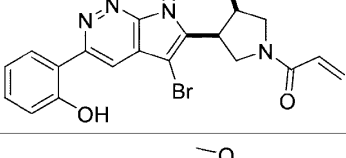
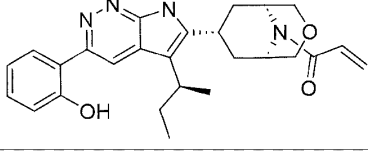
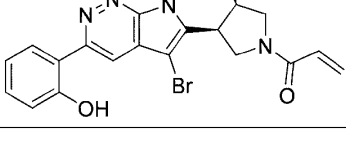
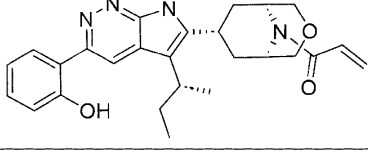
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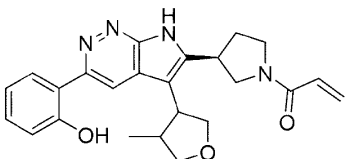
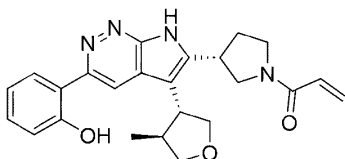
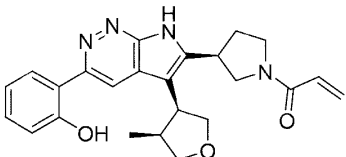
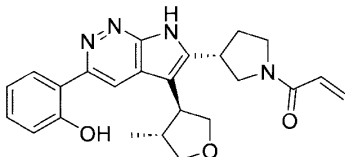
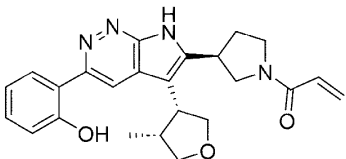
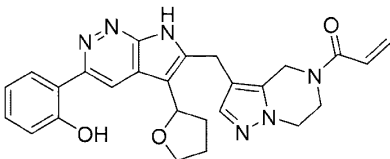
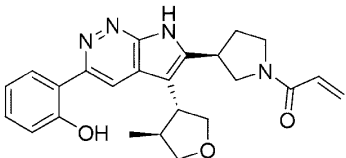
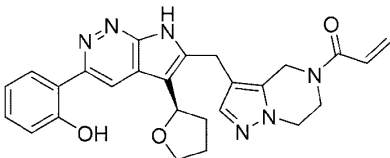
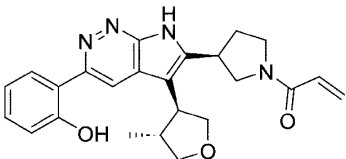
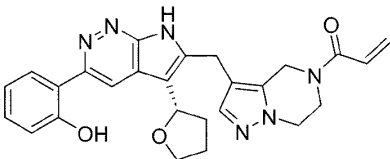
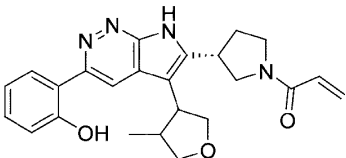
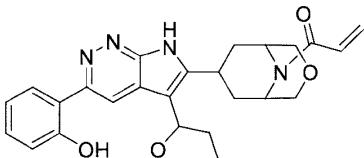
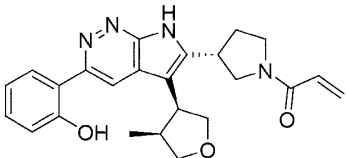
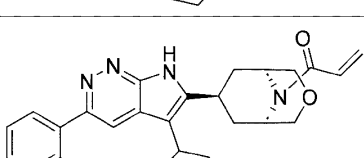
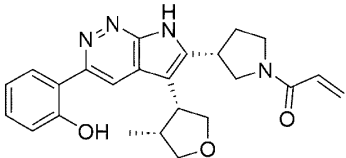
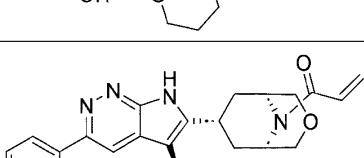
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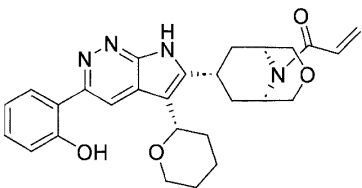
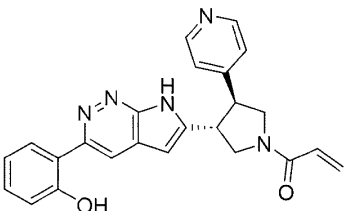
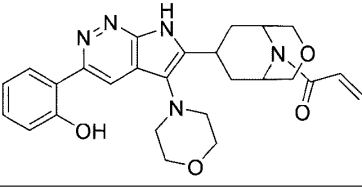
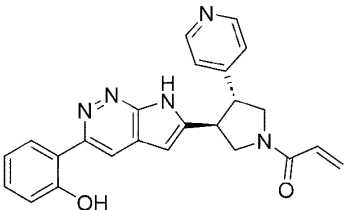
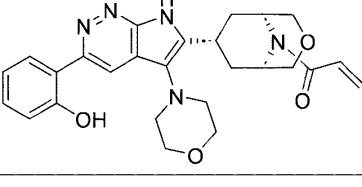
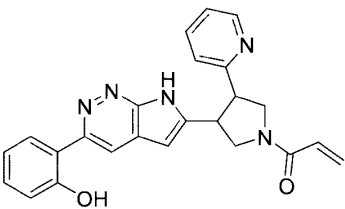
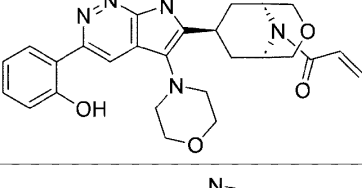
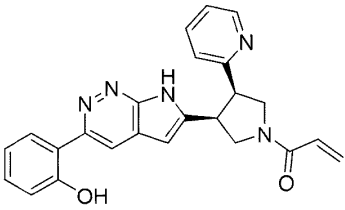
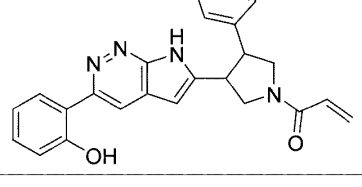
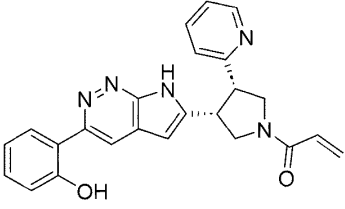
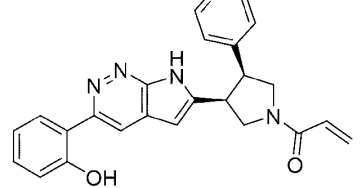
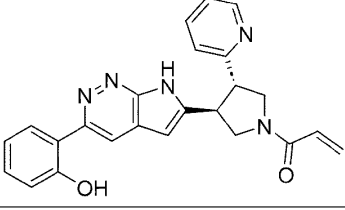
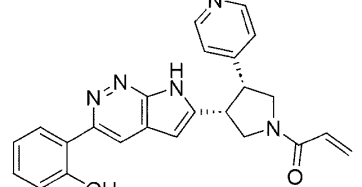


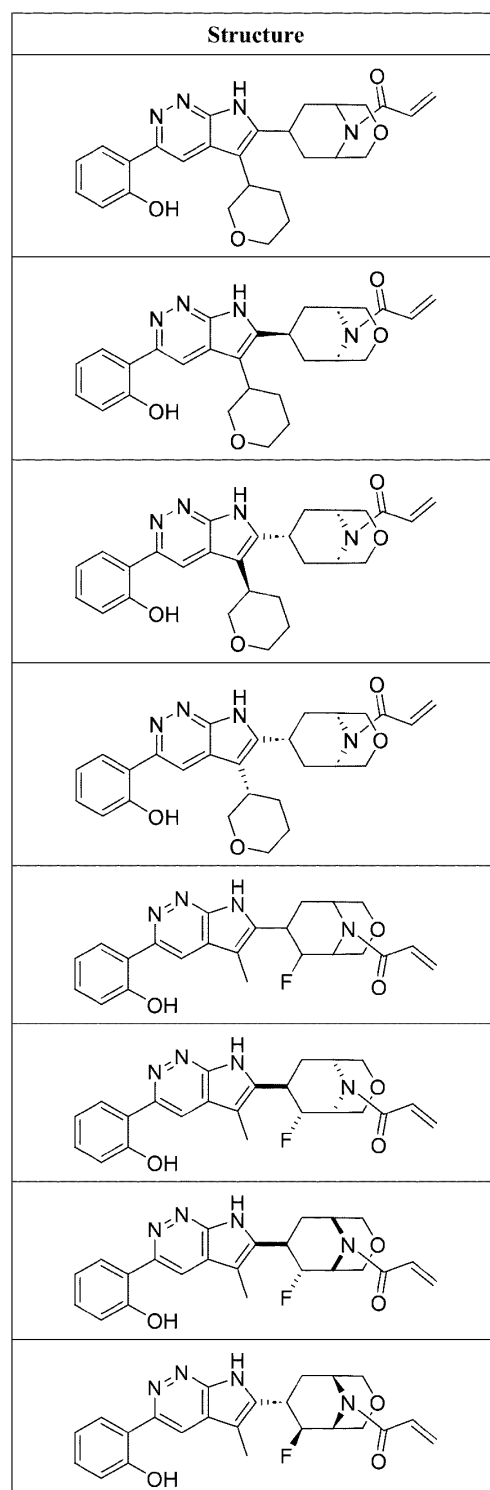
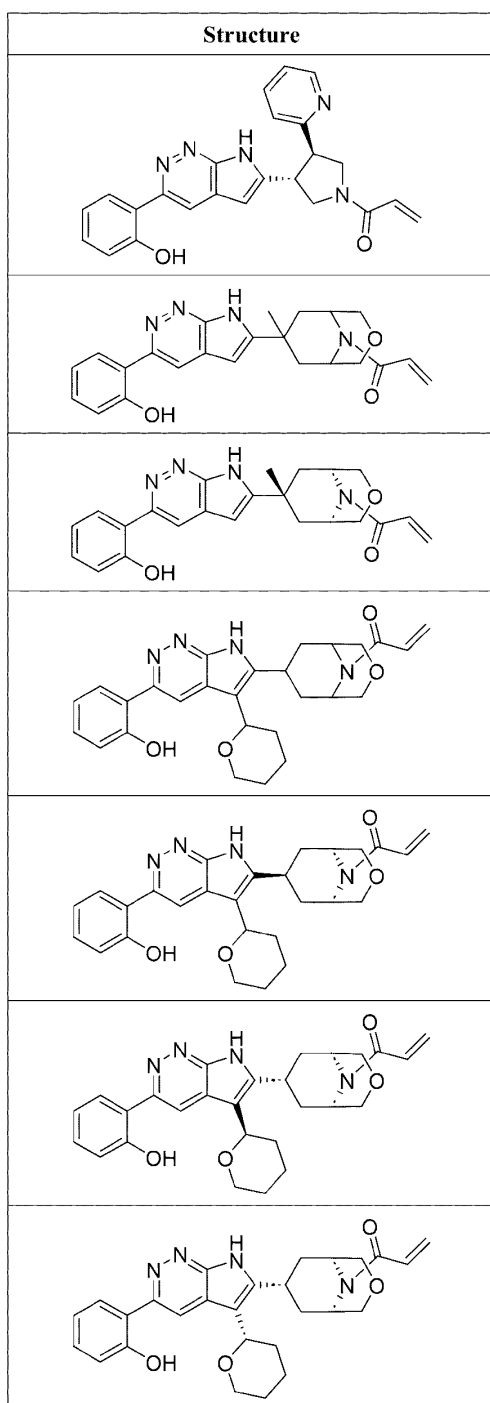
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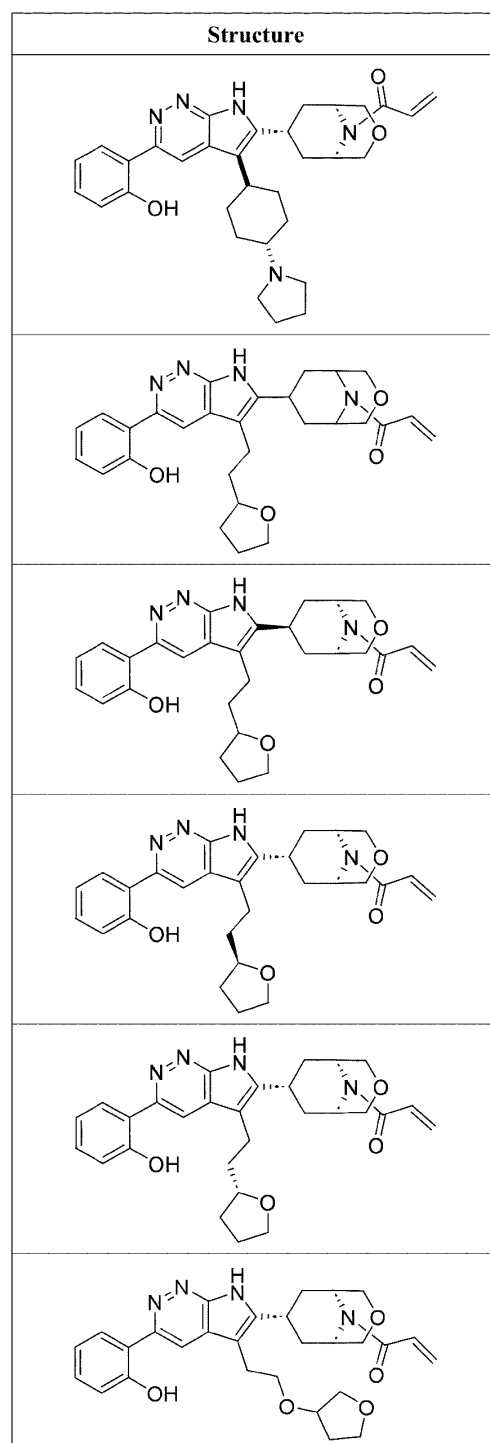
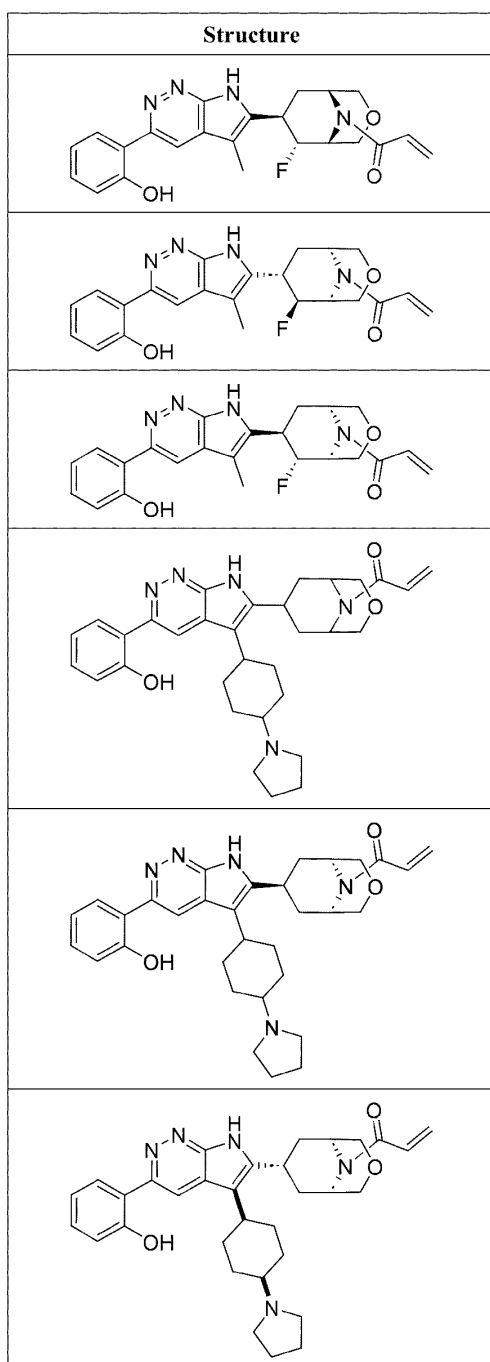
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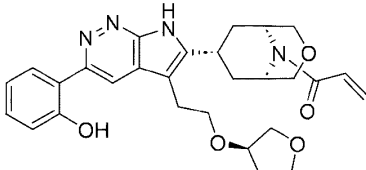
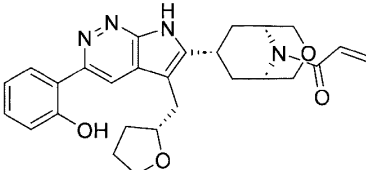
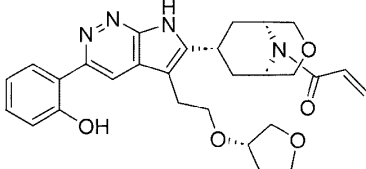
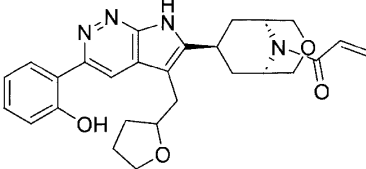
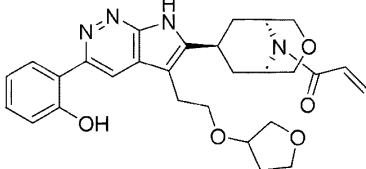
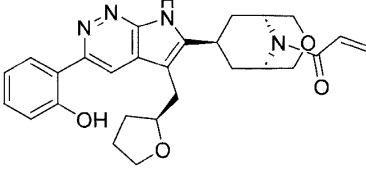
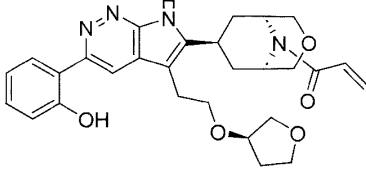
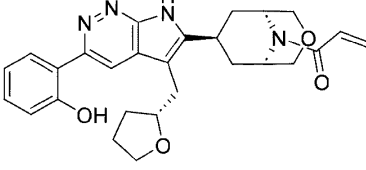
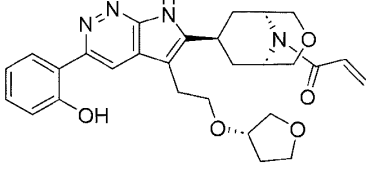
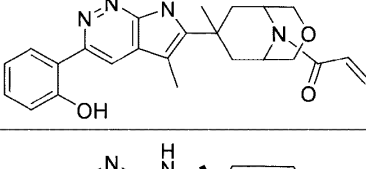
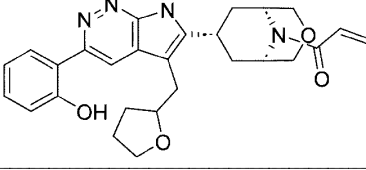
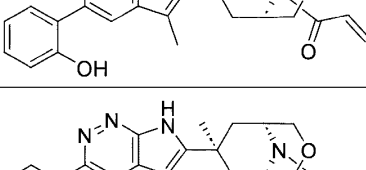
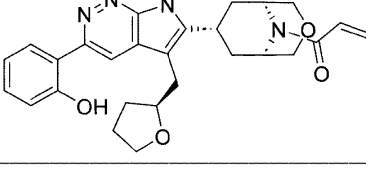
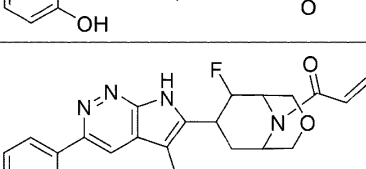
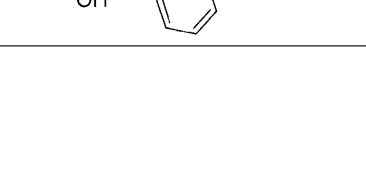
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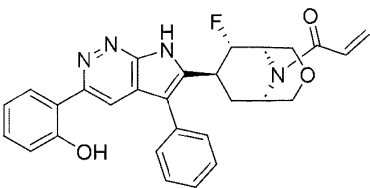
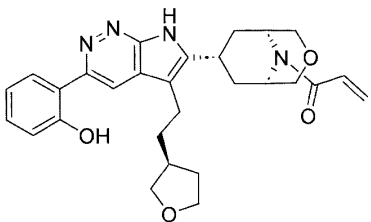
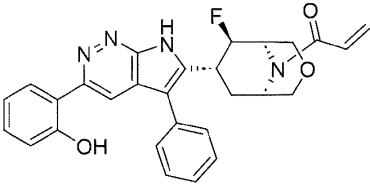
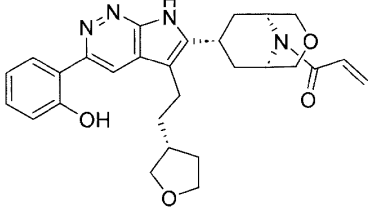
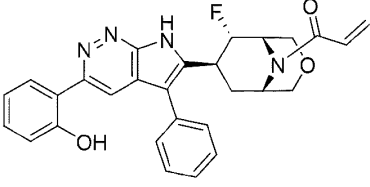
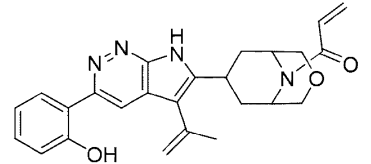
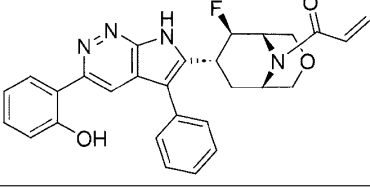
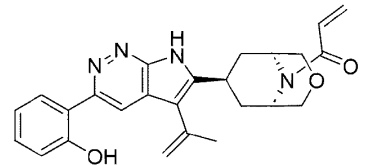
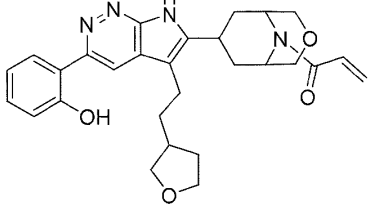
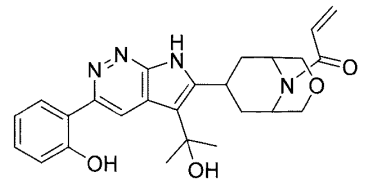
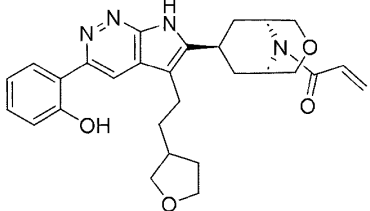
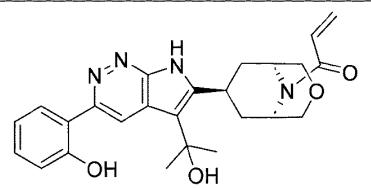
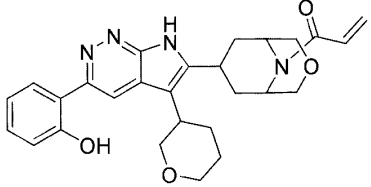
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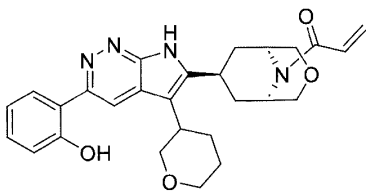
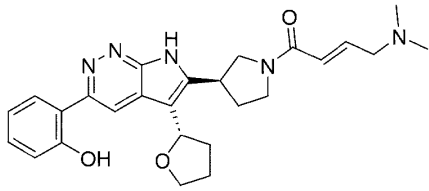
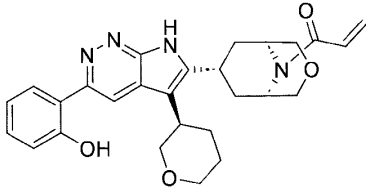
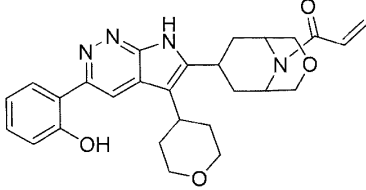
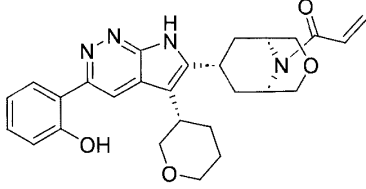
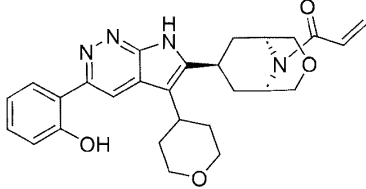
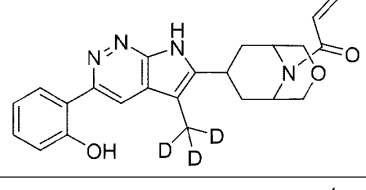
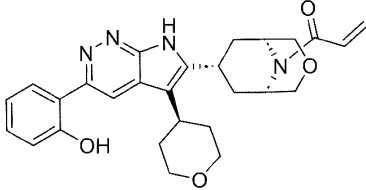
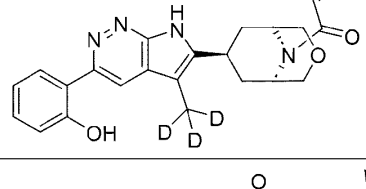
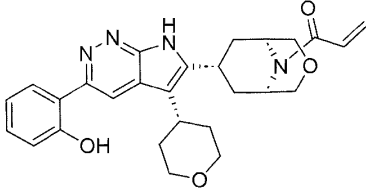
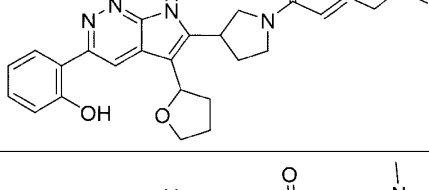
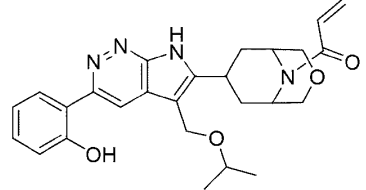
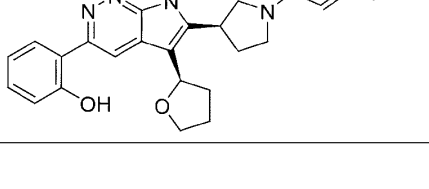
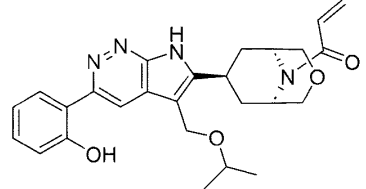
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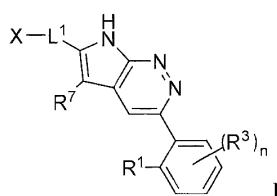
[0246] For the compounds having a meso substituent, e.g., a 3-oxa-9-azabicyclo[3.3.1]nonane, the diastereomers may be depicted in Table 2 with straight or wedged bonds to show the relative stereochemistry.

Methods

[0247] In one embodiment, the compounds and compositions described herein are useful in methods for treating a SMARCA2 dependent disease or disorder or a disease or disorder that is mediated, at least in part by, SMARCA2. The methods comprise administering to a subject suffering from a SMARCA2 dependent disease or disorder an effective amount of a compound, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof or a pharmaceutical composition comprising said compound, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof as described herein.

[0248] In one embodiment, there is provided a compound, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof or a pharmaceutical composition comprising said compound, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof as described herein for use in treating an SMARCA2 dependent disease or disorder.

[0249] In one embodiment, provided are methods of treating a SMARCA2 dependent disease or disorder or a disease or disorder that is mediated, at least in part by, SMARCA2, comprising administering to a subject suffering from a SMARCA2 dependent disease or disorder an effective amount of a compound of Formula I:



or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein:

n is 0, 1, or 2;

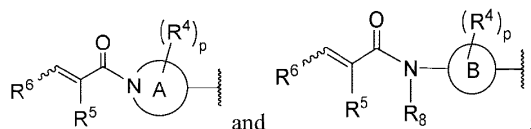
R¹ is hydroxy, halo, cyano, C₁₋₄ alkoxy, or N(R²)₂;

R² is independently hydrogen, C₁₋₄ alkyl, or C₃₋₆ cycloalkyl, wherein each alkyl or cycloalkyl is unsubstituted or substituted with one to three Z¹;

each R³ is independently halo, cyano, C₁₋₆ alkyl, or C₁₋₃ haloalkyl;

L¹ is a bond, C₁₋₄ alkylene, -C₁₋₄ alkylene-heteroaryl-, C₂₋₃ alkenylene, C₂₋₃ alkynylene, or -C(O)-;

X is selected from:



p is 0, 1, or 2;

Ring A is a monocyclic, spirocyclic, fused bicyclic, or bridged bicyclic 4-10 membered heterocyclyl or a monocyclic or fused bicyclic 5-10 membered heteroaryl;

Ring B is a monocyclic, spirocyclic, fused bicyclic, or bridged bicyclic 3-10 membered cycloalkyl, a monocyclic, spirocyclic, fused bicyclic, or bridged bicyclic 4-10 membered heterocyclyl, or a monocyclic or fused bicyclic 5-10 membered heteroaryl; wherein the nitrogen atom and L¹ may be attached anywhere on Ring B, including on the same carbon;

each R⁴ is independently oxo, halo, cyano, -NO₂, -SF₅, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, -C(O)R¹¹, -C(O)OR¹¹, -S(O)₀₋₂R¹¹, -NR¹¹S(O)₀₋₂R¹¹, -S(O)₀₋₂N(R¹¹)₂, -NR¹¹S(O)₀₋₂N(R¹¹)₂, -NR¹¹C(O)N(R¹¹)₂, -C(O)N(R¹¹)₂, -NR¹¹C(O)R¹¹, -OC(O)N(R¹¹)₂, or -NR¹¹C(O)OR¹¹; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z¹;

R⁵ is hydrogen, halo, cyano, or C₁₋₆ alkyl optionally substituted with one to three Z¹;

R⁶ is hydrogen, halo, cyano, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, -C(O)R¹¹, -C(O)OR¹¹, -S(O)₀₋₂R¹¹, -NR¹¹S(O)₀₋₂R¹¹, -S(O)₀₋₂N(R¹¹)₂, -NR¹¹S(O)₀₋₂N(R¹¹)₂, -NR¹¹C(O)N(R¹¹)₂, -C(O)N(R¹¹)₂, -NR¹¹C(O)R¹¹, -OC(O)N(R¹¹)₂, or -NR¹¹C(O)OR¹¹; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z¹;

R⁷ is hydrogen, halo, cyano, -NO₂, -SF₅, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, -C(O)R¹¹, -C(O)OR¹¹, -S(O)₀₋₂R¹¹, -NR¹¹S(O)₀₋₂R¹¹, -S(O)₀₋₂N(R¹¹)₂, -NR¹¹S(O)₀₋₂N(R¹¹)₂, -NR¹¹C(O)N(R¹¹)₂, -C(O)N(R¹¹)₂, -NR¹¹C(O)R¹¹, -OC(O)N(R¹¹)₂, or -NR¹¹C(O)OR¹¹; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z¹;

R⁸ is hydrogen or C₁₋₆ alkyl optionally substituted with one to three Z¹;

each Z¹ is independently halo, cyano, -NO₂, -SF₅, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, -C(O)R¹¹, -C(O)OR¹¹, -S(O)₀₋₂R¹¹, -NR¹¹S(O)₀₋₂R¹¹, -S(O)₀₋₂N(R¹¹)₂, -NR¹¹S(O)₀₋₂N(R¹¹)₂, -NR¹¹C(O)N(R¹¹)₂, -C(O)N(R¹¹)₂, -NR¹¹C(O)R¹¹, -OC(O)N(R¹¹)₂, or -NR¹¹C(O)OR¹¹; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1a};

each R¹¹ is independently hydrogen, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1a};

each Z^{1a} is independently hydroxy, halo, cyano, -NO₂, -SF₅, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹³)₂, -OR¹³, -C(O)R¹³, -C(O)OR¹³, -S(O)₀₋₂R¹³, -NR¹³S(O)₀₋₂R¹³, -S(O)₀₋₂N(R¹³)₂, -NR¹³S(O)₀₋₂N(R¹³)₂, -NR¹³C(O)N(R¹³)₂, -C(O)N(R¹³)₂, -NR¹³C(O)R¹³,

-OC(O)N(R¹³)₂, or -NR¹³C(O)OR¹³; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1b};

each R¹³ is independently hydrogen, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1b};

each Z^{1b} is independently halo, cyano, hydroxy, -SH, -NH₂, -NO₂, -SF₅, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -L-C₁₋₆ alkyl, -L-C₂₋₆ alkenyl, -L-C₂₋₆ alkynyl, -L-C₁₋₆ haloalkyl, -L-C₃₋₁₀ cycloalkyl, -L-heterocyclyl, -L-aryl, or -L-heteroaryl; and

each L is independently -O-, -NH-, -S-, -S(O)-, -S(O)₂-, -N(C₁₋₆ alkyl)-, -N(C₂₋₆ alkenyl)-, -N(C₂₋₆ alkynyl)-, -N(C₁₋₆ haloalkyl)-, -N(C₃₋₁₀ cycloalkyl)-, -N(heterocyclyl)-, -N(aryl)-, -N(heteroaryl)-, -C(O)-, -C(O)O-, -C(O)NH-, -C(O)N(C₁₋₆ alkyl)-, -C(O)N(C₂₋₆ alkenyl)-, -C(O)N(C₂₋₆ alkynyl)-, -C(O)N(C₁₋₆ haloalkyl)-, -C(O)N(C₃₋₁₀ cycloalkyl)-, -C(O)N(heterocyclyl)-, -C(O)N(aryl)-, -C(O)N(heteroaryl)-, -NHC(O)-, -NHC(O)O-, -NHC(O)NH-, -NHS(O)-, or -S(O)₂NH-;

wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, and heteroaryl of Z^{1b} and L is further independently optionally substituted with one to five hydroxy, halo, cyano, hydroxy, -SH, -NH₂, -NO₂, -SF₅, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkoxy, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl.

[0250] In some embodiments, this disclosure provides for a method for modulating or degrading protein which is expressed from the SMARCA2 gene, which method comprises contacting the protein with an effective amount of a compound of Formula I, II, III, IV, or any subformula thereof, under conditions wherein the protein which is expressed from the SMARCA2 gene is modulated or degraded.

[0251] In some embodiments, this disclosure provides for a method for modulating or degrading protein which is expressed from the SMARCA4 gene, which method comprises contacting the protein with an effective amount of a compound of Formula I, II, III, IV, or any subformula thereof, under conditions wherein the protein which is expressed from the SMARCA4 gene is modulated or degraded.

[0252] In some embodiments, there is provided a method to modulate or degrade protein which is expressed from the SMARCA2 gene in a subject, which method comprises administering to said subject an effective amount of a compound of Formula I, II, III, IV, or any subformula thereof, or a pharmaceutical composition comprising an effective amount of a compound of Formula I, or any subformula thereof, and a pharmaceutically acceptable excipient.

[0253] In some embodiments, there is provided a method to modulate or degrade protein which is expressed from the SMARCA4 gene in a subject, which method comprises administering to said subject an effective amount of a compound of Formula I, II, III, IV, or any subformula thereof, or a pharmaceutical composition comprising an effective amount of a compound of Formula I, II, III, IV, or any subformula thereof, and a pharmaceutically acceptable excipient.

[0254] In some embodiments, there is provided a method for treating cancer in a subject in need thereof, which method comprises selecting a subject whose cancer is mediated at least in part by SMARCA2 and

administering to said subject an effective amount of a compound of Formula I, II, III, IV, or any subformula thereof, or an effective amount of a pharmaceutical composition comprising a pharmaceutically acceptable excipient and an effective amount of a compound of Formula I, II, III, IV, or any subformula thereof.

[0255] In some embodiments, there is provided a method for treating cancer in a subject in need thereof, which method comprises selecting a subject whose cancer is mediated at least in part by SMARCA4 and administering to said subject an effective amount of a compound of Formula I, II, III, IV, or any subformula thereof, or an effective amount of a pharmaceutical composition comprising a pharmaceutically acceptable excipient and an effective amount of a compound of Formula I, II, III, IV, or any subformula thereof.

[0256] In some embodiments, there is provided a method for treating hyperplasia in a subject in need thereof, which method comprises administering to said subject an effective amount of a compound of Formula I, II, III, IV, or any subformula thereof, or an effective amount of a pharmaceutical composition comprising a pharmaceutically acceptable excipient and an effective amount of a compound of Formula I, II, III, IV, or any subformula thereof.

[0257] In one embodiment, the method relates to a compound, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof or a pharmaceutical composition comprising said compound, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof as described herein for use in manufacture of a medicament for reducing levels of protein which is expressed from the SMARCA2 gene, where reduction of such protein levels treats or ameliorates the diseases or disorder.

[0258] In one embodiment, the methods described herein comprise use of a prodrug of the compounds described herein. Prodrugs may be prepared by modifying functional groups present in the compounds in such a way that the modifications are cleaved, either in routine manipulation or *in vivo*, to the parent compounds. Prodrugs include compounds described herein wherein a hydroxy, amino, carboxyl, or sulfhydryl group in a compound described herein is bonded to any group that may be cleaved *in vivo* to regenerate the free hydroxy, amino, or sulfhydryl group, respectively. Examples of prodrugs include, but are not limited to esters (e.g., acetate, formate, and benzoate derivatives), amides, guanidines, carbamates (e.g., N,N-dimethylaminocarbonyl) of hydroxy functional groups in compounds described herein, and the like.

[0259] In one embodiment, the method relates to a compound, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof or a pharmaceutical composition comprising said compound, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof as described herein for use as described herein, wherein the degradation of protein which is expressed from the SMARCA2 gene at 1 μ M concentration of the compounds described herein is in the range of about 25%-99%. The degradation of the protein which is expressed from the SMARCA2 gene is measured by the assay described in the biological example. In some embodiments, the degradation of the protein which is expressed from the SMARCA2 gene is from

about 25% to about 50%, from about 45% to about 70%, from about 65% to about 90% or from about 75% to about 99%. In some embodiments, the degradation of the protein which is expressed from the SMARCA2 gene is from about 25% to about 35%, from about 35% to about 45%, from about 45% to about 55%, from about 55% to about 65%, from about 65% to about 75%, from about 75% to about 85%, from about 85% to about 99%. In some embodiments, the degradation of the protein which is expressed from the SMARCA2 gene is more than 60%. In some embodiments, the degradation of the protein which is expressed from the SMARCA2 gene is more than 70%. In some embodiments, the degradation of the protein which is expressed from the SMARCA2 gene is more than 80%. In some embodiments, the degradation of the protein which is expressed from the SMARCA2 gene is more than 90%.

[0260] The compounds and compositions described herein are useful in treating SMARCA2 dependent diseases or disorders such as, e.g., liposarcoma, glioblastoma, bladder cancer, adrenocortical cancer, multiple myeloma, colorectal cancer, non-small cell lung cancer, Human Papilloma Virus-associated cervical, oropharyngeal, penis, anal, thyroid, or vaginal cancer or Epstein-Barr Virus-associated nasopharyngeal carcinoma, gastric cancer, rectal cancer, thyroid cancer, Hodgkin lymphoma or diffuse large B-cell lymphoma. The cancer also may be selected from prostate cancer, breast carcinoma, lymphomas, leukemia, myeloma, bladder carcinoma, colon cancer, cutaneous melanoma, hepatocellular carcinoma, endometrial cancer, ovarian cancer, cervical cancer, lung cancer, renal cancer, glioblastoma multiform, glioma, thyroid cancer, parathyroid tumor, nasopharyngeal cancer, tongue cancer, pancreatic cancer, esophageal cancer, cholangiocarcinoma, gastric cancer, soft tissue sarcomas, rhabdomyosarcoma (RMS), synovial sarcoma, osteosarcoma, rhabdoid cancers, cancer for which the immune response is deficient, an immunogenic cancer, and Ewing's sarcoma. In one embodiment, the SMARCA2-dependent disease or disorder is a disease or disorder is selected from non-small cell lung cancer (NSCLC), melanoma, triple-negative breast cancer (TNBC), nasopharyngeal cancer (NPC), microsatellite stable colorectal cancer (mssCRC), thymoma, carcinoid, and gastrointestinal stromal tumor (GIST). In another embodiment, the cancer is selected from non-small cell lung cancer (NSCLC), melanoma, triple-negative breast cancer (TNBC), nasopharyngeal cancer (NPC), microsatellite stable colorectal cancer (mssCRC), thymoma, carcinoid, acute myelogenous leukemia, and gastrointestinal stromal tumor (GIST). In another embodiment, the SMARCA2-dependent disease or disorder is a disease or disorder is selected from non-small cell lung cancer (NSCLC), melanoma, triple-negative breast cancer (TNBC), nasopharyngeal cancer (NPC), and microsatellite stable colorectal cancer (mssCRC).

[0261] The compounds of the disclosure can be administered in effective amounts to treat or prevent a disorder and/or prevent the development thereof in subjects.

[0262] In certain embodiments, compounds as described herein are useful in the treatment of proliferative disorders (e.g., cancer, benign neoplasms, inflammatory disease, and autoimmune diseases). In certain embodiments, according to the methods of treatment of the present application, levels of cell proteins of interest, e.g., pathogenic and oncogenic proteins are modulated, or their growth is inhibited or the proteins are degraded by contacting said cells with a compound or composition, as described herein. In other embodiments, the compounds are useful in treating cancer.

[0263] Thus, in another aspect of the application, methods for the treatment of cancer are provided comprising administering a therapeutically effective amount of compound or composition, as described herein, to a subject in need thereof. In certain embodiments, a method for the treatment of cancer is provided comprising administering a therapeutically effective amount of a compound, or a pharmaceutical composition comprising a compound as described herein to a subject in need thereof, in such amounts and for such time as is necessary to achieve the desired result. In some embodiments, the compounds of present application are administered orally or intravenously. In certain embodiments of the present application a “therapeutically effective amount” of the compound or pharmaceutical composition is that amount effective for killing or inhibiting the growth of tumor cells. The compounds and compositions, according to the method of the present application, may be administered using any amount and any route of administration effective for killing or inhibiting the growth of tumor cells. Thus, the expression “amount effective to kill or inhibit the growth of tumor cells,” as used herein, refers to a sufficient amount of agent to kill or inhibit the growth of tumor cells. The exact amount required will vary from subject to subject, depending on the species, age, and general condition of the subject, the severity of the disease, the particular anticancer agent, its mode of administration, and the like. In certain embodiments of the present application a “therapeutically effective amount” of the compound or pharmaceutical composition described herein is that amount effective for reducing the levels of target proteins. In certain embodiments of the present application a “therapeutically effective amount” of the compound or pharmaceutical composition is that amount effective to kill or inhibit the growth of skin cells.

[0264] In certain embodiments, the method involves the administration of a therapeutically effective amount of the compound or a pharmaceutically acceptable derivative thereof to a subject (including, but not limited to a human or other mammal in need of it. In certain embodiments, the compounds or compositions described herein are useful for the treatment of cancer (including, but not limited to, glioblastoma, retinoblastoma, breast cancer, cervical cancer, colon and rectal cancer, leukemia, lymphoma, lung cancer (including, but not limited to small cell lung cancer), melanoma and/or skin cancer, multiple myeloma, non-Hodgkin's lymphoma, ovarian cancer, pancreatic cancer, prostate cancer and gastric cancer, bladder cancer, uterine cancer, kidney cancer, testicular cancer, stomach cancer, brain cancer, liver cancer, or esophageal cancer).

[0265] In certain embodiments, the compounds or compositions described herein are useful in the treatment of cancers and other proliferative disorders, including, but not limited to breast cancer, cervical cancer, colon and rectal cancer, leukemia, lung cancer, melanoma, multiple myeloma, non-Hodgkin's lymphoma, ovarian cancer, pancreatic cancer, prostate cancer, and gastric cancer. In certain embodiments, compounds or compositions described herein are active against solid tumors.

[0266] Another aspect of the application relates to a method of treating or lessening the severity of a disease or condition associated with a proliferation disorder in a patient, said method comprising a step of administering to said patient, a compound of Formula I or a composition comprising said compound.

[0267] It will be appreciated that the compounds and compositions, according to the method of the present application, may be administered using any amount and any route of administration effective for the treatment of cancer and/or disorders associated with cell hyperproliferation. For example, when using the compounds for the treatment of cancer, the expression “effective amount” as used herein, refers to a sufficient amount of agent to inhibit proliferation, or refers to a sufficient amount to reduce the effects of cancer. The exact amount required will vary from subject to subject, depending on the species, age, and general condition of the subject, the severity of the diseases, the particular anticancer agent, its mode of administration, and the like.

[0268] The present application provides methods for the treatment of a proliferative disorder in a subject in need thereof by administering to a subject in need of such treatment, a therapeutically effective amount of a compound of the present application, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof. The proliferative disorder can be cancer or a precancerous condition. The present application further provides the use of a compound of the present application, or a pharmaceutically acceptable salt, salt, solvate, stereoisomer, or tautomer thereof, for the preparation of a medicament useful for the treatment of a proliferative disorder.

[0269] The present application also provides methods of protecting against a proliferative disorder in a subject in need thereof by administering a therapeutically effective amount of compound of the present application, or a pharmaceutically acceptable salt, salt, solvate, stereoisomer, or tautomer thereof, to a subject in need of such treatment. The proliferative disorder can be cancer or a precancerous condition. The present application also provides the use of compound of the present application, or a pharmaceutically acceptable salt, salt, solvate, stereoisomer, or tautomer thereof, for the preparation of a medicament useful for the prevention of a proliferative disorder.

[0270] As used herein, the term “proliferative disorder” refers to conditions in which unregulated or abnormal growth, or both, of cells can lead to the development of an unwanted condition or disease, which may or may not be cancerous. Exemplary proliferative disorders of the application encompass a variety of conditions wherein cell division is deregulated. Exemplary proliferative disorder include, but are not limited to, neoplasms, benign tumors, malignant tumors, pre-cancerous conditions, in situ tumors, encapsulated tumors, metastatic tumors, liquid tumors, solid tumors, immunological tumors, hematological tumors, cancers, carcinomas, leukemias, lymphomas, sarcomas, and rapidly dividing cells. The term “rapidly dividing cell” as used herein is defined as any cell that divides at a rate that exceeds or is greater than what is expected or observed among neighboring or juxtaposed cells within the same tissue. A proliferative disorder includes a precancer or a precancerous condition. A proliferative disorder includes cancer. The methods provided herein are used to treat or alleviate a symptom of cancer. The term “cancer” includes solid tumors, as well as, hematologic tumors and/or malignancies. A “precancer cell” or “precancerous cell” is a cell manifesting a proliferative disorder that is a precancer or a precancerous condition. A “cancer cell” or “cancerous cell” is a cell manifesting a proliferative disorder that is a cancer. Any reproducible means of measurement may be used to identify cancer cells or precancerous cells. Cancer cells or precancerous cells can be identified by histological typing or grading

of a tissue sample (e.g., a biopsy sample). Cancer cells or precancerous cells can be identified through the use of appropriate molecular markers.

[0271] Exemplary non-cancerous conditions or disorders which may be treatable by the compounds described herein include, but are not limited to, rheumatoid arthritis; inflammation; autoimmune disease; lymphoproliferative conditions; acromegaly; rheumatoid spondylitis; osteoarthritis; gout, other arthritic conditions; sepsis; septic shock; endotoxic shock; gram-negative sepsis; toxic shock syndrome; asthma; adult respiratory distress syndrome; chronic obstructive pulmonary disease; chronic pulmonary inflammation; inflammatory bowel disease; Crohn's disease; psoriasis; eczema; ulcerative colitis; pancreatic fibrosis; hepatic fibrosis; acute and chronic renal disease; irritable bowel syndrome; pyresis; restenosis; cerebral malaria; stroke and ischemic injury; neural trauma; Alzheimer's disease; Huntington's disease; Parkinson's disease; acute and chronic pain; allergic rhinitis; allergic conjunctivitis; chronic heart failure; acute coronary syndrome; cachexia; malaria; leprosy; leishmaniasis; Lyme disease; Reiter's syndrome; acute synovitis; muscle degeneration, bursitis; tendonitis; tenosynovitis; herniated, ruptures, or prolapsed intervertebral disk syndrome; osteopetrosis; thrombosis; restenosis; silicosis; pulmonary sarcoidosis; bone resorption diseases, such as osteoporosis; graft-versus-host reaction; Multiple Sclerosis; lupus; fibromyalgia; AIDS and other viral diseases such as Herpes Zoster, Herpes Simplex I or II, influenza virus and cytomegalovirus; and diabetes mellitus.

[0272] Exemplary cancers include, but are not limited to, adrenocortical carcinoma, AIDS-related cancers, AIDS-related lymphoma, anal cancer, anorectal cancer, cancer of the anal canal, appendix cancer, childhood cerebellar astrocytoma, childhood cerebral astrocytoma, basal cell carcinoma, skin cancer (non-melanoma), biliary cancer, extrahepatic bile duct cancer, intrahepatic bile duct cancer, bladder cancer, urinary bladder cancer, bone and joint cancer, osteosarcoma and malignant fibrous histiocytoma, brain cancer, brain tumor, brain stem glioma, cerebellar astrocytoma, cerebral astrocytoma/malignant glioma, ependymoma, medulloblastoma, supratentorial primitive neuroectodermal tumors, visual pathway and hypothalamic glioma, breast cancer, bronchial adenomas/carcinoids, carcinoid tumor, gastrointestinal, nervous system cancer, nervous system lymphoma, central nervous system cancer, central nervous system lymphoma, cervical cancer, childhood cancers, chronic lymphocytic leukemia, chronic myelogenous leukemia, chronic myeloproliferative disorders, colon cancer, colorectal cancer, cutaneous T-cell lymphoma, lymphoid neoplasm, mycosis fungoides, Sezary Syndrome, endometrial cancer, esophageal cancer, extracranial germ cell tumor, extragonadal germ cell tumor, extrahepatic bile duct cancer, eye cancer, intraocular melanoma, retinoblastoma, gallbladder cancer, gastric (stomach) cancer, gastrointestinal carcinoid tumor, gastrointestinal stromal tumor (GIST), germ cell tumor, ovarian germ cell tumor, gestational trophoblastic tumor glioma, head and neck cancer, hepatocellular (liver) cancer, Hodgkin lymphoma, hypopharyngeal cancer, intraocular melanoma, ocular cancer, islet cell tumors (endocrine pancreas), Kaposi Sarcoma, kidney cancer, renal cancer, kidney cancer, laryngeal cancer, acute lymphoblastic leukemia, acute myeloid leukemia, chronic lymphocytic leukemia, chronic myelogenous leukemia, hairy cell leukemia, lip and oral cavity cancer, liver cancer, lung cancer, non-small cell lung cancer, small cell lung cancer, AIDS-related lymphoma, non-Hodgkin

lymphoma, primary central nervous system lymphoma, Waldenstrom macroglobulinemia, medulloblastoma, melanoma, intraocular (eye) melanoma, Merkel cell carcinoma, mesothelioma malignant, mesothelioma, metastatic squamous neck cancer, mouth cancer, cancer of the tongue, multiple endocrine neoplasia syndrome, mycosis fungoides, myelodysplastic syndromes, myelodysplastic/myeloproliferative diseases, chronic myelogenous leukemia, acute myeloid leukemia, multiple myeloma, chronic myeloproliferative disorders, nasopharyngeal cancer, neuroblastoma, oral cancer, oral cavity cancer, oropharyngeal cancer, ovarian cancer, ovarian epithelial cancer, ovarian low malignant potential tumor, pancreatic cancer, islet cell pancreatic cancer, paranasal sinus and nasal cavity cancer, parathyroid cancer, penile cancer, pharyngeal cancer, pheochromocytoma, pineoblastoma and supratentorial primitive neuroectodermal tumors, pituitary tumor, plasma cell neoplasm/multiple myeloma, pleuropulmonary blastoma, prostate cancer, rectal cancer, renal pelvis and ureter, transitional cell cancer, retinoblastoma, rhabdomyosarcoma, salivary gland cancer, Ewing family of sarcoma tumors, Kaposi Sarcoma, soft tissue sarcoma, uterine cancer, uterine sarcoma, skin cancer (non-melanoma), skin cancer (melanoma), Merkel cell skin carcinoma, small intestine cancer, soft tissue sarcoma, squamous cell carcinoma, stomach (gastric) cancer, supratentorial primitive neuroectodermal tumors, testicular cancer, throat cancer, thymoma, thymoma and thymic carcinoma, thyroid cancer, transitional cell cancer of the renal pelvis and ureter and other urinary organs, gestational trophoblastic tumor, urethral cancer, endometrial uterine cancer, uterine sarcoma, uterine corpus cancer, vaginal cancer, vulvar cancer, and Wilms' Tumor.

[0273] A “proliferative disorder of the hematologic system” is a proliferative disorder involving cells of the hematologic system. A proliferative disorder of the hematologic system can include lymphoma, leukemia, myeloid neoplasms, mast cell neoplasms, myelodysplasia, benign monoclonal gammopathy, lymphomatoid granulomatosis, lymphomatoid papulosis, polycythemia vera, chronic myelocytic leukemia, agnogenic myeloid metaplasia, and essential thrombocythemia. A proliferative disorder of the hematologic system can include hyperplasia, dysplasia, and metaplasia of cells of the hematologic system. The compositions of the present application may be used to treat a cancer selected from the group consisting of a hematologic cancer of the present application or a hematologic proliferative disorder of the present application. A hematologic cancer of the present application can include multiple myeloma, lymphoma (including Hodgkin's lymphoma, non-Hodgkin's lymphoma, childhood lymphomas, and lymphomas of lymphocytic and cutaneous origin), leukemia (including childhood leukemia, hairy-cell leukemia, acute lymphocytic leukemia, acute myelocytic leukemia, chronic lymphocytic leukemia, chronic myelocytic leukemia, chronic myelogenous leukemia, and mast cell leukemia), myeloid neoplasms and mast cell neoplasms.

[0274] A “proliferative disorder of the lung” is a proliferative disorder involving cells of the lung. Proliferative disorders of the lung can include all forms of proliferative disorders affecting lung cells. Proliferative disorders of the lung can include lung cancer, a precancer or precancerous condition of the lung, benign growths or lesions of the lung, and malignant growths or lesions of the lung, and metastatic lesions in tissue and organs in the body other than the lung. Compositions of the present application may

be used to treat lung cancer or proliferative disorders of the lung. Lung cancer can include all forms of cancer of the lung. Lung cancer can include malignant lung neoplasms, carcinoma in situ, typical carcinoid tumors, and atypical carcinoid tumors. Lung cancer can include small cell lung cancer ("SCLC"), non-small cell lung cancer ("NSCLC"), squamous cell carcinoma, adenocarcinoma, small cell carcinoma, large cell carcinoma, adenosquamous cell carcinoma, and mesothelioma. Lung cancer can include "scar carcinoma", bronchioalveolar carcinoma, giant cell carcinoma, spindle cell carcinoma, and large cell neuroendocrine carcinoma. Lung cancer can include lung neoplasms having histologic and ultrastructural heterogeneity (e.g., mixed cell types).

[0275] Proliferative disorders of the lung can include all forms of proliferative disorders affecting lung cells. Proliferative disorders of the lung can include lung cancer, precancerous conditions of the lung. Proliferative disorders of the lung can include hyperplasia, metaplasia, and dysplasia of the lung. Proliferative disorders of the lung can include asbestos-induced hyperplasia, squamous metaplasia, and benign reactive mesothelial metaplasia. Proliferative disorders of the lung can include replacement of columnar epithelium with stratified squamous epithelium, and mucosal dysplasia. Individuals exposed to inhaled injurious environmental agents such as cigarette smoke and asbestos may be at increased risk for developing proliferative disorders of the lung. Prior lung diseases that may predispose individuals to development of proliferative disorders of the lung can include chronic interstitial lung disease, necrotizing pulmonary disease, scleroderma, rheumatoid disease, sarcoidosis, interstitial pneumonitis, tuberculosis, repeated pneumonias, idiopathic pulmonary fibrosis, granulomata, asbestosis, fibrosing alveolitis, and Hodgkin's disease.

[0276] A "proliferative disorder of the colon" is a proliferative disorder involving cells of the colon. In one embodiment, the proliferative disorder of the colon is colon cancer. In one embodiment, compositions of the present application may be used to treat colon cancer or proliferative disorders of the colon. Colon cancer can include all forms of cancer of the colon. Colon cancer can include sporadic and hereditary colon cancers. Colon cancer can include malignant colon neoplasms, carcinoma in situ, typical carcinoid tumors, and atypical carcinoid tumors. Colon cancer can include adenocarcinoma, squamous cell carcinoma, and adenosquamous cell carcinoma. Colon cancer can be associated with a hereditary syndrome selected from the group consisting of hereditary nonpolyposis colorectal cancer, familial adenomatous polyposis, Gardner's syndrome, Peutz-Jeghers syndrome, Turcot's syndrome and juvenile polyposis. Colon cancer can be caused by a hereditary syndrome selected from the group consisting of hereditary nonpolyposis colorectal cancer, familial adenomatous polyposis, Gardner's syndrome, Peutz-Jeghers syndrome, Turcot's syndrome and juvenile polyposis.

[0277] Proliferative disorders of the colon can include all forms of proliferative disorders affecting colon cells. Proliferative disorders of the colon can include colon cancer, precancerous conditions of the colon, adenomatous polyps of the colon and metachronous lesions of the colon. A proliferative disorder of the colon can include adenoma. Proliferative disorders of the colon can be characterized by hyperplasia, metaplasia, and dysplasia of the colon. Prior colon diseases that may predispose individuals to development of proliferative disorders of the colon can include prior colon cancer. Current disease that

may predispose individuals to development of proliferative disorders of the colon can include Crohn's disease and ulcerative colitis. A proliferative disorder of the colon can be associated with a mutation in a gene selected from the group consisting of p53, ras, FAP and DCC. An individual can have an elevated risk of developing a proliferative disorder of the colon due to the presence of a mutation in a gene selected from the group consisting of p53, ras, FAP and DCC.

[0278] A “proliferative disorder of the pancreas” is a proliferative disorder involving cells of the pancreas. Proliferative disorders of the pancreas can include all forms of proliferative disorders affecting pancreatic cells. Proliferative disorders of the pancreas can include pancreas cancer, a precancer or precancerous condition of the pancreas, hyperplasia of the pancreas, and dysplasia of the pancreas, benign growths or lesions of the pancreas, and malignant growths or lesions of the pancreas, and metastatic lesions in tissue and organs in the body other than the pancreas. Pancreatic cancer includes all forms of cancer of the pancreas. Pancreatic cancer can include ductal adenocarcinoma, adenosquamous carcinoma, pleomorphic giant cell carcinoma, mucinous adenocarcinoma, osteoclast-like giant cell carcinoma, mucinous cystadenocarcinoma, acinar carcinoma, unclassified large cell carcinoma, small cell carcinoma, pancreatoblastoma, papillary neoplasm, mucinous cystadenoma, papillary cystic neoplasm, and serous cystadenoma. Pancreatic cancer can also include pancreatic neoplasms having histologic and ultrastructural heterogeneity (e.g., mixed cell types).

[0279] A “proliferative disorder of the prostate” is a proliferative disorder involving cells of the prostate. Proliferative disorders of the prostate can include all forms of proliferative disorders affecting prostate cells. Proliferative disorders of the prostate can include prostate cancer, a precancer or precancerous condition of the prostate, benign growths or lesions of the prostate, and malignant growths or lesions of the prostate, and metastatic lesions in tissue and organs in the body other than the prostate. Proliferative disorders of the prostate can include hyperplasia, metaplasia, and dysplasia of the prostate.

[0280] A “proliferative disorder of the skin” is a proliferative disorder involving cells of the skin. Proliferative disorders of the skin can include all forms of proliferative disorders affecting skin cells. Proliferative disorders of the skin can include a precancer or precancerous condition of the skin, benign growths or lesions of the skin, melanoma, malignant melanoma and other malignant growths or lesions of the skin, and metastatic lesions in tissue and organs in the body other than the skin. Proliferative disorders of the skin can include hyperplasia, metaplasia, and dysplasia of the skin.

[0281] A “proliferative disorder of the ovary” is a proliferative disorder involving cells of the ovary. Proliferative disorders of the ovary can include all forms of proliferative disorders affecting cells of the ovary. Proliferative disorders of the ovary can include a precancer or precancerous condition of the ovary, benign growths or lesions of the ovary, ovarian cancer, malignant growths or lesions of the ovary, and metastatic lesions in tissue and organs in the body other than the ovary. Proliferative disorders of the skin can include hyperplasia, metaplasia, and dysplasia of cells of the ovary.

[0282] A “proliferative disorder of the breast” is a proliferative disorder involving cells of the breast. Proliferative disorders of the breast can include all forms of proliferative disorders affecting breast cells. Proliferative disorders of the breast can include breast cancer, a precancer or precancerous condition of

the breast, benign growths or lesions of the breast, and malignant growths or lesions of the breast, and metastatic lesions in tissue and organs in the body other than the breast. Proliferative disorders of the breast can include hyperplasia, metaplasia, and dysplasia of the breast.

[0283] A cancer that is to be treated can be staged according to the American Joint Committee on Cancer (AJCC) TNM classification system, where the tumor (T) has been assigned a stage of TX, T1, T1mic, T1a, T1b, T1c, T2, T3, T4, T4a, T4b, T4c, or T4d; and where the regional lymph nodes (N) have been assigned a stage of NX, N0, N1, N2, N2a, N2b, N3, N3a, N3b, or N3c; and where distant metastasis (M) can be assigned a stage of MX, M0, or M1. A cancer that is to be treated can be staged according to an American Joint Committee on Cancer (AJCC) classification as Stage I, Stage IIA, Stage IIB, Stage IIIA, Stage IIIB, Stage IIIC, or Stage IV. A cancer that is to be treated can be assigned a grade according to an AJCC classification as Grade GX (e.g., grade cannot be assessed), Grade 1, Grade 2, Grade 3 or Grade 4. A cancer that is to be treated can be staged according to an AJCC pathologic classification (pN) of pNX, pN0, pN0 (I-), pN0 (I+), pN0 (mol-), pN0 (mol+), pN1, pN1(mi), pN1a, pN1b, pN1c, pN2, pN2a, pN2b, pN3, pN3a, pN3b, or pN3c.

[0284] A cancer that is to be treated can include a tumor that has been determined to be less than or equal to about 2 centimeters in diameter. A cancer that is to be treated can include a tumor that has been determined to be from about 2 to about 5 centimeters in diameter. A cancer that is to be treated can include a tumor that has been determined to be greater than or equal to about 3 centimeters in diameter. A cancer that is to be treated can include a tumor that has been determined to be greater than 5 centimeters in diameter. A cancer that is to be treated can be classified by microscopic appearance as well differentiated, moderately differentiated, poorly differentiated, or undifferentiated. A cancer that is to be treated can be classified by microscopic appearance with respect to mitosis count (e.g., amount of cell division) or nuclear pleiomorphism (e.g., change in cells). A cancer that is to be treated can be classified by microscopic appearance as being associated with areas of necrosis (e.g., areas of dying or degenerating cells). A cancer that is to be treated can be classified as having an abnormal karyotype, having an abnormal number of chromosomes, or having one or more chromosomes that are abnormal in appearance. A cancer that is to be treated can be classified as being aneuploid, triploid, tetraploid, or as having an altered ploidy. A cancer that is to be treated can be classified as having a chromosomal translocation, or a deletion or duplication of an entire chromosome, or a region of deletion, duplication or amplification of a portion of a chromosome.

[0285] A cancer that is to be treated can be evaluated by DNA cytometry, flow cytometry, or image cytometry. A cancer that is to be treated can be typed as having 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, or 90% of cells in the synthesis stage of cell division (e.g., in S phase of cell division). A cancer that is to be treated can be typed as having a low S-phase fraction or a high S-phase fraction.

[0286] As used herein, a “normal cell” is a cell that cannot be classified as part of a “proliferative disorder”. A normal cell lacks unregulated or abnormal growth, or both, that can lead to the development of an unwanted condition or disease. In one embodiment, a normal cell possesses normally functioning cell cycle checkpoint control mechanisms.

[0287] One skilled in the art may refer to general reference texts for detailed descriptions of known techniques discussed herein or equivalent techniques. These texts include Ausubel et al., *Current Protocols in Molecular Biology*, John Wiley and Sons, Inc. (2005); Sambrook et al., *Molecular Cloning, A Laboratory Manual* (3rd edition), Cold Spring Harbor Press, Cold Spring Harbor, N.Y. (2000); Coligan et al., *Current Protocols in Immunology*, John Wiley & Sons, N.Y.; Erma et al., *Current Protocols in Pharmacology*, John Wiley & Sons, N.Y.; Fingl et al., *The Pharmacological Basis of Therapeutics* (1975), Remington's *Pharmaceutical Sciences*, Mack Publishing Co., Easton, Pa., 18th edition (1990). These texts can, of course, also be referred to in making or using an aspect of the application.

[0288] In certain embodiments, compounds of the application are useful in the treatment of proliferative disorders (e.g., cancer, benign neoplasms, inflammatory disease, and autoimmune diseases). In certain embodiments, according to the methods of treatment of the present application, levels of cell proteins of interest, e.g., pathogenic and oncogenic proteins are modulated, or their growth is inhibited by contacting said cells with a compound or composition, as described herein. In other embodiments, the compounds are useful in treating cancer.

[0289] In certain embodiments, the method involves the administration of a therapeutically effective amount of the compound or a pharmaceutically acceptable derivative thereof to a subject (including, but not limited to a human or animal) in need of it. In certain embodiments, the compounds are useful for the treatment of cancer (including, but not limited to, glioblastoma, retinoblastoma, breast cancer, cervical cancer, colon and rectal cancer, leukemia, lymphoma, lung cancer (including, but not limited to small cell lung cancer), melanoma and/or skin cancer, multiple myeloma, non-Hodgkin's lymphoma, ovarian cancer, pancreatic cancer, prostate cancer and gastric cancer, bladder cancer, uterine cancer, kidney cancer, testicular cancer, stomach cancer, brain cancer, liver cancer, or esophageal cancer).

[0290] In certain embodiments, the anticancer agents are useful in the treatment of cancers and other proliferative disorders, including, but not limited to breast cancer, cervical cancer, colon and rectal cancer, leukemia, lung cancer, melanoma, multiple myeloma, non-Hodgkin's lymphoma, ovarian cancer, pancreatic cancer, prostate cancer, and gastric cancer. In certain embodiments, the anticancer agents are active against solid tumors.

[0291] Additionally, the present application provides pharmaceutically acceptable derivatives of the compounds, and methods of treating a subject using these compounds, pharmaceutical compositions thereof, or either of these in combination with one or more additional therapeutic agents.

[0292] For example, other therapies or anticancer agents that may be used in combination with the compounds disclosed herein including surgery, radiotherapy, endocrine therapy, biologic response modifiers (interferons, interleukins, and tumor necrosis factor (TNF), to name a few), hyperthermia and cryotherapy, agents to attenuate any adverse effects (e.g., antiemetics), and other approved chemotherapeutic drugs, including, but not limited to, alkylating drugs (mechlorethamine, chlorambucil, cyclophosphamide, melphalan, ifosfamide), antimetabolites (methotrexate), purine antagonists and pyrimidine antagonists (6-mercaptopurine, 5-fluorouracil, cytarabine, gemcitabine), spindle poisons (vinblastine, vincristine, vinorelbine, paclitaxel), podophyllotoxins (etoposide, irinotecan, topotecan),

antibiotics (doxorubicin, bleomycin, mitomycin), nitrosoureas (carmustine, lomustine), inorganic ions (cisplatin, carboplatin), enzymes (asparaginase), and hormones (tamoxifen, leuprolide, flutamide, and megestrol), to name a few. For a more comprehensive discussion of overview of cancer therapy see The Merck Manual, Twentieth Ed. 2020, the entire contents of which are hereby incorporated by reference. See also the National Cancer Institute (NCI) website (www.nci.nih.gov) and the Food and Drug Administration (FDA) website for a list of the FDA approved oncology drugs (www.fda.gov/cder/cancer/druglistframe).

[0293] In certain embodiments, the pharmaceutical compositions comprising the compounds disclosed herein further comprise one or more additional therapeutically active ingredients (e.g., chemotherapeutic and/or palliative). For purposes of the application, the term “palliative” refers to treatment that is focused on the relief of symptoms of a disease and/or side effects of a therapeutic regimen, but is not curative. For example, palliative treatment encompasses painkillers, anti-nausea medications and anti-sickness drugs. In addition, chemotherapy, radiotherapy and surgery can all be used palliatively (that is, to reduce symptoms without going for cure; e.g., for shrinking tumors and reducing pressure, bleeding, pain and other symptoms of cancer).

Administration, Pharmaceutical Compositions

[0294] Administration of the disclosed compounds and pharmaceutical compositions can be accomplished via any mode of administration for therapeutic agents. These modes include systemic or local administration such as oral, nasal, parenteral, transdermal, subcutaneous, vaginal, buccal, rectal or topical administration modes.

[0295] Depending on the intended mode of administration, the disclosed compositions can be in solid, semi-solid or liquid dosage form, such as, for example, injectables, tablets, suppositories, pills, time-release capsules, elixirs, tinctures, emulsions, syrups, powders, liquids, suspensions, or the like, sometimes in unit dosages and consistent with conventional pharmaceutical practices. Likewise, they can also be administered in intravenous (both bolus and infusion), intraperitoneal, subcutaneous or intramuscular form, and all using forms well known to those skilled in the pharmaceutical arts.

[0296] Illustrative pharmaceutical compositions are tablets and gelatin capsules comprising a compound of the disclosure and a pharmaceutically acceptable carrier, such as a) a diluent, e.g., purified water, triglyceride oils, such as hydrogenated or partially hydrogenated vegetable oil, or mixtures thereof, corn oil, olive oil, sunflower oil, safflower oil, fish oils, such as EPA or DHA, or their esters or triglycerides or mixtures thereof, omega-3 fatty acids or derivatives thereof, lactose, dextrose, sucrose, mannitol, sorbitol, cellulose, sodium, saccharin, glucose and/or glycine; b) a lubricant, e.g., silica, talcum, stearic acid, its magnesium or calcium salt, sodium oleate, sodium stearate, magnesium stearate, sodium benzoate, sodium acetate, sodium chloride, and/or polyethylene glycol; for tablets also; c) a binder, e.g., magnesium aluminum silicate, starch paste, gelatin, tragacanth, methylcellulose, sodium carboxymethylcellulose, magnesium carbonate, natural sugars such as glucose or beta-lactose, corn sweeteners, natural and synthetic gums such as acacia, tragacanth or sodium alginate, waxes, and/or polyvinylpyrrolidone, if desired; d) a disintegrant, e.g., starches, agar, methyl cellulose, bentonite,

xanthan gum, alginic acid or its sodium salt, or effervescent mixtures; e) absorbent, colorant, flavorant and sweetener; f) an emulsifier or dispersing agent, such as Tween 80, Labrasol, HPMC, DOSS, caproyl 909, labrafac, labrafil, peceol, transcutoil, capmul MCM, capmul PG-12, captex 355, gelucire, vitamin E TGPS or other acceptable emulsifier; and/or g) an agent that enhances absorption of the compound such as cyclodextrin, hydroxypropyl-cyclodextrin, PEG400, PEG200.

[0297] Liquid, particularly injectable, compositions can, for example, be prepared by dissolution, dispersion, etc. For example, the disclosed compound is dissolved in or mixed with a pharmaceutically acceptable solvent such as, for example, water, saline, aqueous dextrose, glycerol, ethanol, and the like, to thereby form an injectable isotonic solution or suspension. Proteins such as albumin, chylomicron particles, or serum proteins can be used to solubilize the disclosed compounds.

[0298] The disclosed compounds can be also formulated as a suppository that can be prepared from fatty emulsions or suspensions; using polyalkylene glycols such as propylene glycol, as the carrier.

[0299] The disclosed compounds can also be administered in the form of liposome delivery systems, such as small unilamellar vesicles, large unilamellar vesicles, and multilamellar vesicles. Liposomes can be formed from a variety of phospholipids, containing cholesterol, stearylamine or phosphatidylcholines.

[0300] In some embodiments, a film of lipid components is hydrated with an aqueous solution of drug to form a lipid layer encapsulating the drug, as described in U.S. Pat. No. 5,262,564, which is hereby incorporated by reference in its entirety.

[0301] Disclosed compounds can also be delivered by the use of monoclonal antibodies as individual carriers to which the disclosed compounds are coupled. The disclosed compounds can also be coupled with soluble polymers as targetable drug carriers. Such polymers can include polyvinylpyrrolidone, pyran copolymer, polyhydroxypropylmethacrylamide-phenol, polyhydroxyethylaspanamidephenol, or polyethyleneoxidepolylysine substituted with palmitoyl residues. Furthermore, the disclosed compounds can be coupled to a class of biodegradable polymers useful in achieving controlled release of a drug, for example, polylactic acid, polyepsilon caprolactone, polyhydroxy butyric acid, polyorthoesters, polyacetals, polydihydropyrans, polycyanoacrylates, and cross-linked or amphipathic block copolymers of hydrogels. In one embodiment, disclosed compounds are not covalently bound to a polymer, e.g., a polycarboxylic acid polymer, or a polyacrylate.

[0302] Parental injectable administration is generally used for subcutaneous, intramuscular or intravenous injections and infusions. Injectables can be prepared in conventional forms, either as liquid solutions or suspensions or solid forms suitable for dissolving in liquid prior to injection.

[0303] Another aspect of the disclosure is directed to pharmaceutical compositions comprising a compound of Formula I, and a pharmaceutically acceptable carrier. The pharmaceutically acceptable carrier may further include an excipient, diluent, or surfactant.

[0304] Compositions can be prepared according to conventional mixing, granulating or coating methods, respectively, and the present pharmaceutical compositions can contain from about 0.1% to about 99%, from about 5% to about 90%, or from about 1% to about 20% of the disclosed compound by weight or volume.

[0305] In one embodiment, the disclosure provides a kit comprising two or more separate pharmaceutical compositions, at least one of which contains a compound of the present disclosure. In one embodiment, the kit comprises means for separately retaining said compositions, such as a container, divided bottle, or divided foil packet. An example of such a kit is a blister pack, as typically used for the packaging of tablets, capsules and the like.

[0306] The kit of the disclosure may be used for administering different dosage forms, for example, oral and parenteral, for administering the separate compositions at different dosage intervals, or for titrating the separate compositions against one another. To assist compliance, the kit of the disclosure typically comprises directions for administration.

[0307] Pharmaceutical dosage forms of a compound of this disclosure may be manufactured by any of the methods well-known in the art, such as, for example, by conventional mixing, sieving, dissolving, melting, granulating, dragee-making, tableting, suspending, extruding, spray-drying, levigating, emulsifying, (nano-/micro-) encapsulating, entrapping, or lyophilization processes. As noted above, the compositions of this disclosure can include one or more physiologically acceptable inactive ingredients that facilitate processing of active molecules into preparations for pharmaceutical use.

[0308] As noted above, the compositions are comprised of, in general, a compound of this disclosure in combination with at least one pharmaceutically acceptable excipient. Acceptable excipients are non-toxic, aid administration, and do not adversely affect the therapeutic benefit of the claimed compounds. Such excipient may be any solid, liquid, semi-solid or, in the case of an aerosol composition, gaseous excipient that is generally available to one of skill in the art.

[0309] Solid pharmaceutical excipients include starch, cellulose, talc, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, magnesium stearate, sodium stearate, glycerol monostearate, sodium chloride, dried skim milk and the like. Liquid and semi-solid excipients may be selected from glycerol, propylene glycol, water, ethanol and various oils, including those of petroleum, animal, vegetable or synthetic origin, e.g., peanut oil, soybean oil, mineral oil, sesame oil, etc. In some embodiments, liquid carriers, particularly for injectable solutions, include water, saline, aqueous dextrose, and glycols.

[0310] Compressed gases may be used to disperse a compound of this disclosure in an aerosol form. Inert gases suitable for this purpose are nitrogen, carbon dioxide, etc. Other suitable pharmaceutical excipients and their formulations are described in Remington's Pharmaceutical Sciences, edited by E. W. Martin (Mack Publishing Company, 18th ed., 1990).

[0311] The compositions of this disclosure may, if desired, be presented in a pack or dispenser device containing one or more unit dosage forms containing the active ingredient. Such a pack or device may, for example, comprise metal or plastic foil, such as a blister pack, or glass, and rubber stoppers such as in vials. The pack or dispenser device may be accompanied by instructions for administration.

Compositions comprising a compound of this disclosure that can be formulated in a compatible pharmaceutical carrier may also be prepared, placed in an appropriate container, and labeled for treatment of an indicated condition.

[0312] The amount of the compound in a formulation can vary within the full range employed by those skilled in the art. Typically, the formulation will contain, on a weight percent (wt %) basis, from about 0.01-99.99 wt % of a compound of this disclosure based on the total formulation, with the balance being one or more suitable pharmaceutical excipients. In one embodiment, the compound is present at a level of about 1-80 wt %. Representative pharmaceutical formulations are described below.

Dosing

[0313] The dosage regimen utilizing the disclosed compound is selected in accordance with a variety of factors including type, species, age, weight, sex, and medical condition of the patient; the severity of the condition to be treated; the route of administration; the renal or hepatic function of the patient; and the particular disclosed compound employed. A physician or veterinarian of ordinary skill in the art can readily determine and prescribe the effective amount of the drug required to prevent, counter or arrest the progress of the condition.

[0314] Effective dosage amounts of the compounds, when used for the indicated effects, range from about 0.5 mg to about 5000 mg of the disclosed compound as needed to treat the condition.

Formulation Examples

[0315] The following are representative pharmaceutical formulations containing a compound of this disclosure.

Formulation Example 1 -- Tablet formulation

[0316] The following ingredients are mixed intimately and pressed into single scored tablets.

Ingredient	Quantity per tablet, mg
compound of this disclosure	400
Cornstarch	50
croscarmellose sodium	25
Lactose	120
magnesium stearate	5

Formulation Example 2 -- Capsule formulation

[0317] The following ingredients are mixed intimately and loaded into a hard-shell gelatin capsule.

Ingredient	Quantity per capsule, mg
compound of this disclosure	200
lactose, spray-dried	148
magnesium stearate	2

Formulation Example 3 -- Suspension formulation

[0318] The following ingredients are mixed to form a suspension for oral administration.

Ingredient	Amount
compound of this disclosure	1.0 g
fumaric acid	0.5 g
sodium chloride	2.0 g
methyl paraben	0.15 g
propyl paraben	0.05 g
granulated sugar	25.0 g
sorbitol (70% solution)	13.00 g
Veegum K (Vanderbilt Co.)	1.0 g
Flavoring	0.035 mL
Colorings	0.5 mg
distilled water	q.s. to 100 mL

Formulation Example 4 -- Injectable formulation

[0319] The following ingredients are mixed to form an injectable formulation.

Ingredient	Amount
compound of this disclosure	0.2 mg-20 mg
sodium acetate buffer solution, 0.4 M	2.0 mL
HCl (1N) or NaOH (1N)	q.s. to suitable pH
water (distilled, sterile)	q.s. to 20 mL

Formulation Example 5 -- Suppository Formulation

[0320] A suppository of total weight 2.5 g is prepared by mixing the compound of this disclosure with Witepsol® H-15 (triglycerides of saturated vegetable fatty acid; Riches-Nelson, Inc., New York), and has the following composition:

Ingredient	Amount
Compound of this disclosure	500 mg
Witepsol® H-15	balance

General Synthetic Methods

[0321] The compounds described herein can be prepared from readily available starting materials using the following general methods and procedures. It will be appreciated that where typical process conditions (i.e., reaction temperatures, times, mole ratios of reactants, solvents, pressures, etc.) are given, other process conditions can also be used unless otherwise stated. Optimum reaction conditions may vary with the particular reactants or solvent used, but such conditions can be determined by one skilled in the art by routine optimization procedures.

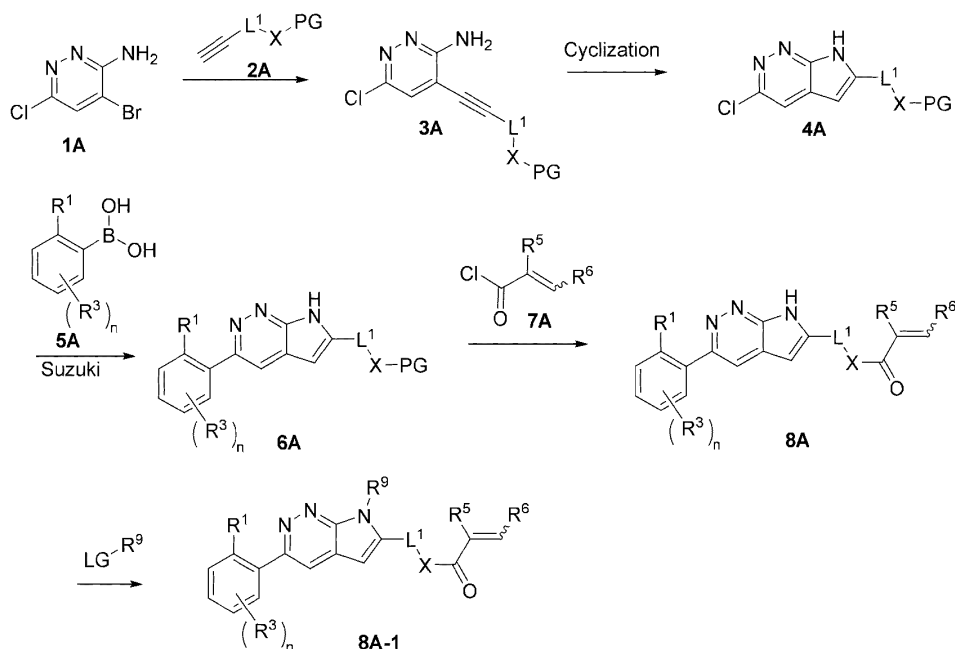
[0322] Additionally, as will be apparent to those skilled in the art, conventional protecting groups may be necessary to prevent certain functional groups from undergoing undesired reactions. Suitable

protecting groups for various functional groups as well as suitable conditions for protecting and deprotecting particular functional groups are well known in the art. For example, numerous protecting groups are described in T. W. Greene and P. G. M. Wuts, *Protecting Groups in Organic Synthesis*, Third Edition, Wiley, New York, 1999, and references cited therein.

[0323] The starting materials for the following reactions are generally known compounds or can be prepared by known procedures or obvious modifications thereof. For example, many of the starting materials are available from commercial suppliers such as Sigma Aldrich (St. Louis, Missouri, USA), Bachem (Torrance, California, USA), Emka-Chemce (St. Louis, Missouri, USA). Others may be prepared by procedures, or obvious modifications thereof, described in standard reference texts such as *Fieser and Fieser's Reagents for Organic Synthesis*, Volumes 1-15 (John Wiley, and Sons, 2016), *Rodd's Chemistry of Carbon Compounds*, Volumes 1-5, and *Supplementals* (Elsevier Science Publishers, 2001), *Organic Reactions*, Volumes 1-40 (John Wiley, and Sons, 2019), *March's Advanced Organic Chemistry*, (John Wiley, and Sons, 8th Edition, 2019), and *Larock's Comprehensive Organic Transformations* (VCH Publishers Inc., 1989).

Synthesis of Representative Compounds

[0324] The general synthesis of the compounds described herein is set forth in the reaction schemes below. Schemes 1-8 illustrate general methods for preparing compounds of Formula I. In Schemes 1-8, substituents L^1 , R^1 , R^3 , R^5 , R^6 , R^7 , R^9 , and n are each independently as defined throughout the specification, where X is depicted with the $-C(O)CR^5=R^6$ moiety. PG is a protecting group (including, but not limited to, Boc and the like). The -Cl in 1A, 3A, and 4A may be replaced by a suitable leaving group (such as halo, mesylate, tosylate, or -OH).



Scheme 1

[0325] In some embodiments, compounds of Formula I and sub-formulae thereof are prepared as shown in Scheme 1. In Scheme 1, the first step is a conventional Sonogashira coupling reaction wherein at least a stoichiometric amount of a suitable alkyne, compound **2A**, is combined with compound **1A** under conventional reaction conditions well known in the art including the use of palladium (II) bis(triphenylphosphine) dichloride and copper (I) iodide as catalysts typically in the presence of a suitable base such as diisopropylethylamine, triethylamine, pyridine, cesium carbonate and the like. The reaction is typically conducted in an inert solvent such as toluene, N,N-dimethylformamide, and the like. The reaction is typically conducted at from about 25 °C to about 110 °C for a period of time sufficient for substantial completion of the reaction as evidenced by e.g., thin layer chromatography. Upon reaction completion, conventional workup of the reaction solution can be followed by isolation / purification processes such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like to provide for compound **3A**.

[0326] In the next step, a cyclization reaction is performed, wherein at least a stoichiometric amount of compound **3A** in an inert diluent, such as tetrahydrofuran, dioxane, toluene, dimethoxyethane, and the like, typically in the presence of a suitable base such as TBAF, DeShong's salt, or the like. The reaction is typically maintained at from 80 °C to 100 °C until it is substantially complete. Conventional workup of the reaction solution can be followed by isolation / purification processes such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like to provide for compound **4A**.

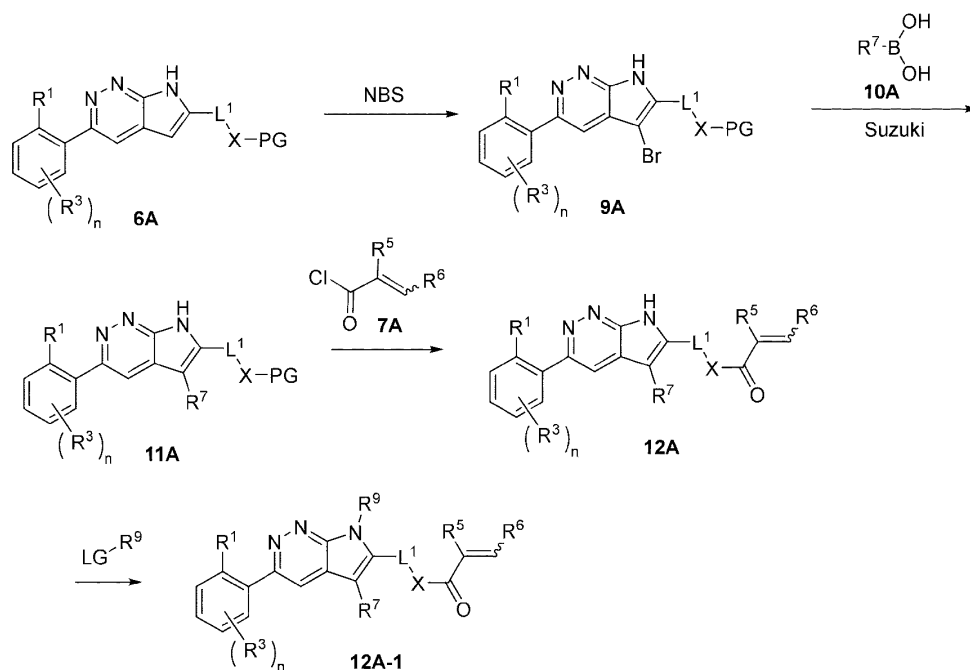
[0327] In the next step, a conventional Suzuki coupling reaction wherein at least a stoichiometric equivalent of a suitable boronic acid, compound **5A**, or an ester thereof, is combined with compound **4A**, in an inert diluent such as tetrahydrofuran, dioxane, toluene, dimethoxyethane, and the like, typically in the presence of a palladium catalyst (e.g., palladium diacetate) and a suitable base such as diisopropylethylamine, triethylamine, pyridine, potassium carbonate, and the like. The reaction is typically maintained at from 10 °C to 65 °C until it is substantially complete. Conventional workup of the reaction solution can be followed by isolation / purification processes such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like to provide for compound **6A**.

[0328] In the next step, the t-butoxycarbonyl (t-BOC) protecting group is removed by conventional conditions. The t-BOC group is illustrative only and other conventional amino blocking groups such as benzyl, 9-fluorenylmethoxycarbonyl (Fmoc), benzyloxycarbonyl (Cbz), p-nitrobenzyloxycarbonyl and the like. Upon reaction completion, conventional workup of the reaction solution can be followed by isolation / purification processes such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like.

[0329] In the final step, at least a stoichiometric amount of a suitable acid chloride, compound **7A**, is combined with compound from the previous step in an inert diluent such as DMF, DCM, MeCN and the like in the presence of a suitable base such as potassium carbonate, pyridine, triethylamine and the like. The reaction is typically maintained at from 0 °C to 50 °C until it is substantially complete. Conventional

workup of the reaction solution can be followed by isolation/purification processes such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like to provide for compound **8A**.

[0330] Additionally, compound **8A** may be further reacted to functionalize the amine. Suitable alkylating reagents such as dibenzyl(chloromethyl) phosphate or di(tert-butyl)chloromethyl phosphate may be used in the presence of a base to alkylate the amine, followed by acidic or reductive deprotection.



Scheme 2

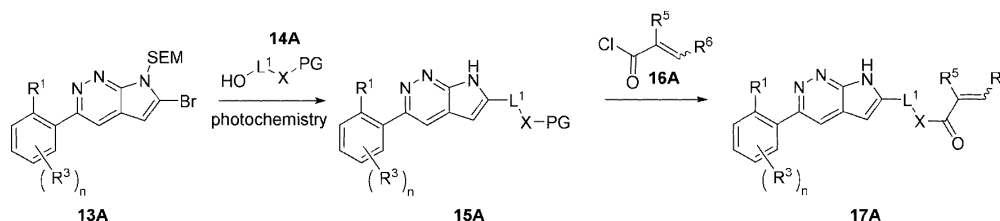
[0331] As to the reaction in Scheme 2, the first step is an aryl bromination reaction, wherein at least a stoichiometric equivalent of a suitable 7H-pyrrolo[2,3-c]pyridazine, compound **6A**, is combined with NBS, in an inert diluent such as tetrahydrofuran, DMF and the like. The reaction is typically maintained at from 0 °C to 40 °C until it is substantially complete. Conventional workup of the reaction solution can be followed by isolation / purification processes, such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like to provide for compound **9A**.

[0332] In the next step, a conventional Suzuki coupling reaction wherein at least a stoichiometric equivalent of a suitable boronic acid, compound **9A**, is combined with compound **10A**, in an inert diluent such as tetrahydrofuran, dioxane, toluene, dimethoxyethane, and the like, typically in the presence of a palladium catalyst (e.g., palladium diacetate) and a suitable base such as diisopropylethylamine, triethylamine, pyridine, potassium carbonate, and the like. The reaction is typically maintained at from 10 °C to 65 °C until it is substantially complete. Conventional workup of the reaction solution can be followed by isolation / purification processes such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like to provide for compound **11A**.

[0333] In the next step, the t-butoxycarbonyl (t-BOC) protecting group is removed by conventional conditions. The t-BOC group is illustrative only and other conventional amino blocking groups such as benzyl, 9-fluorenylmethoxycarbonyl (Fmoc), benzyloxycarbonyl (Cbz), p-nitrobenzyloxycarbonyl and the like. Upon reaction completion, conventional workup of the reaction solution can be followed by isolation / purification processes such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like.

[0334] In the final step, at least a stoichiometric amount of a suitable acid chloride, compound **7A**, is combined with compound from the previous step in an inert diluent such as DMF, DCM, MeCN and the like in the presence of a suitable base such as potassium carbonate, pyridine, triethylamine and the like. The reaction is typically maintained at from 0 °C to 50 °C until it is substantially complete.

[0335] Conventional workup of the reaction solution can be followed by isolation/purification processes such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like to provide for compound **12A**. Compound **12A** may additional further undergo reaction to provide an amine-functionalized compound **12A-1** via a similar protocol as shown above for compound **8A-1**.



Scheme 3

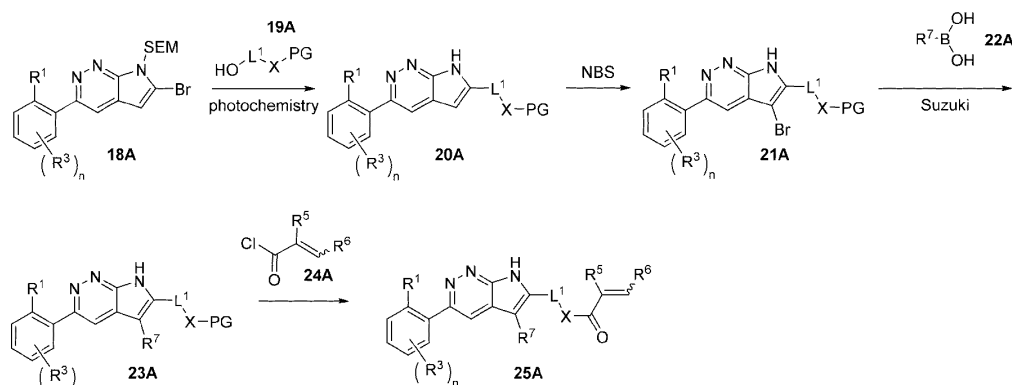
[0336] In Scheme 3, the first step is a metallaphotoredox-enabled deoxygenative arylation of an alcohol (Nature volume 598, pages 451–456 (2021)) wherein alcohol **14A** is first activated by reacting with a benzoxazolium salt (NHC-1) to form an NHC–alcohol adduct. Excitation of an Iridium-based photocatalyst in a presence of a base (quincludine) will then produce a deoxygenated alkyl radical which can further react with an aryl Ni(ii) species generated from the reaction of a nickel catalyst and an aryl bromide derivative **13A**. The reaction is typically maintained between 20 °C and 40 °C until it is substantially complete. Conventional workup of the reaction solution can be followed by isolation / purification processes, such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like to provide for compound **15A**.

[0337] In the next step, the t-butoxycarbonyl (t-BOC) protecting group is removed by conventional conditions. The t-BOC group is illustrative only and other conventional amino blocking groups such as benzyl, 9-fluorenylmethoxycarbonyl (Fmoc), benzyloxycarbonyl (Cbz), p-nitrobenzyloxycarbonyl and the like. Upon reaction completion, conventional workup of the reaction solution can be followed by isolation / purification processes such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like.

[0338] In the final step, at least a stoichiometric amount of a suitable acid chloride, compound **16A**, is combined with compound from the previous step in an inert diluent such as DMF, DCM, MeCN and the

like in the presence of a suitable base such as potassium carbonate, pyridine, triethylamine and the like. The reaction is typically maintained at from 0 °C to 50 °C until it is substantially complete.

[0339] Conventional workup of the reaction solution can be followed by isolation/purification processes such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like to provide for compound **17A**.



Scheme 4

[0340] In Scheme 4, the first step is a metallaphotoredox-enabled deoxygenative arylation of an alcohol (Nature volume 598, pages 451–456 (2021)) wherein alcohol **19A** is first activated by reacting with a benzoxazolium salt (NHC-1) to form an NHC–alcohol adduct. Excitation of an Iridium-based photocatalyst in a presence of a base (quinuclidine) will then produce a deoxygenated alkyl radical which can further react with an aryl Ni(ii) species generated from the reaction of a nickel catalyst and an aryl bromide derivative **18A**. The reaction is typically maintained between 20 °C and 40 °C until it is substantially complete. Conventional workup of the reaction solution can be followed by isolation / purification processes, such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like to provide for compound **20A**.

[0341] The second step is an aryl bromination reaction, wherein at least a stoichiometric equivalent of a suitable 7H-pyrrolo[2,3-c]pyridazine, compound **20A**, is combined with NBS, in an inert diluent such as tetrahydrofuran, DMF and the like. The reaction is typically maintained at from 0 °C to 40 °C until it is substantially complete. Conventional workup of the reaction solution can be followed by isolation / purification processes, such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like to provide for compound **21A**.

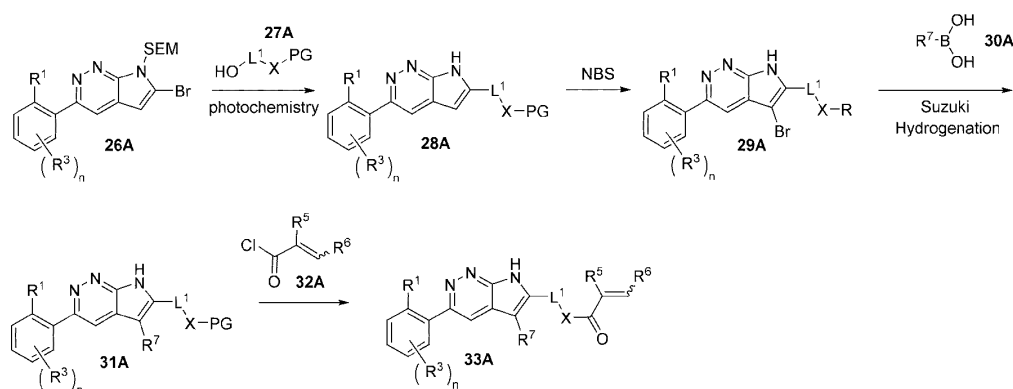
[0342] In the next step, a conventional Suzuki coupling reaction wherein at least a stoichiometric equivalent of a suitable boronic acid, compound **22A**, or an ester thereof, is combined with compound **21A**, in an inert diluent such as tetrahydrofuran, dioxane, toluene, dimethoxyethane, and the like, typically in the presence of a palladium catalyst (e.g., palladium diacetate) and a suitable base such as diisopropylethylamine, triethylamine, pyridine, potassium carbonate, and the like. The reaction is typically maintained at from 10 °C to 65 °C until it is substantially complete. Conventional workup of the reaction solution can be followed by isolation / purification processes such as crystallization,

chromatography, high performance liquid chromatography (HPLC), and the like to provide for compound **23A**.

[0343] In the next step, the t-butoxycarbonyl (t-BOC) protecting group is removed by conventional conditions. The t-BOC group is illustrative only and other conventional amino blocking groups such as benzyl, 9-fluorenylmethoxycarbonyl (Fmoc), benzyloxycarbonyl (Cbz), p-nitrobenzyloxycarbonyl and the like. Upon reaction completion, conventional workup of the reaction solution can be followed by isolation / purification processes such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like.

[0344] In the final step, at least a stoichiometric amount of a suitable acid chloride, compound **24A**, is combined with compound from the previous step in an inert diluent such as DMF, DCM, MeCN and the like in the presence of a suitable base such as potassium carbonate, pyridine, triethylamine and the like. The reaction is typically maintained at from 0 °C to 50 °C until it is substantially complete.

[0345] Conventional workup of the reaction solution can be followed by isolation/purification processes such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like to provide for compound **25A**.



Scheme 5

[0346] In Scheme 5, the first step is a metallaphotoredox-enabled deoxygenative arylation of an alcohol (Nature volume 598, pages 451–456 (2021)) wherein alcohol **27A** is first activated by reacting with a benzoxazolium salt (NHC-1) to form an NHC–alcohol adduct. Excitation of an Iridium-based photocatalyst in a presence of a base (quinuclidine) will then produce a deoxygenated alkyl radical which can further react with an aryl Ni(ii) species generated from the reaction of a nickel catalyst and an aryl bromide derivative **26A**. The reaction is typically maintained between 20 °C and 40 °C until it is substantially complete. Conventional workup of the reaction solution can be followed by isolation / purification processes, such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like to provide for compound **28A**.

[0347] The second step is an aryl bromination reaction, wherein at least a stoichiometric equivalent of a suitable 7H-pyrrolo[2,3-c]pyridazine, compound **28A**, is combined with NBS, in an inert diluent such as tetrahydrofuran, DMF and the like. The reaction is typically maintained at from 0 °C to 40 °C until it is

substantially complete. Conventional workup of the reaction solution can be followed by isolation / purification processes, such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like to provide for compound **29A**.

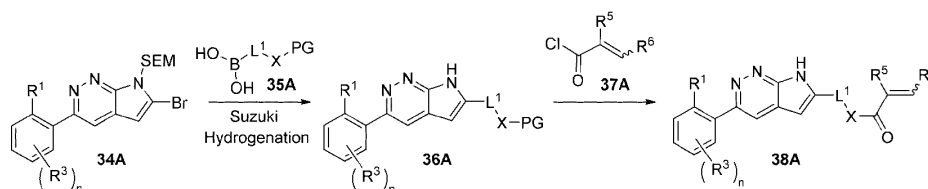
[0348] In the next step, a conventional Suzuki coupling reaction wherein at least a stoichiometric equivalent of a suitable boronic acid, compound **30A**, or an ester thereof, is combined with compound **29A**, in an inert diluent such as tetrahydrofuran, dioxane, toluene, dimethoxyethane, and the like, typically in the presence of a palladium catalyst (e.g., palladium diacetate) and a suitable base such as diisopropylethylamine, triethylamine, pyridine, potassium carbonate, and the like. The reaction is typically maintained at from 10 °C to 65 °C until it is substantially complete. Conventional workup of the reaction solution can be followed by isolation / purification processes such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like to provide for compound **31A**.

[0349] The Suzuki step is generally followed by an hydrogenation reaction to reduce the alkene group from the molecule. The reaction is carried out in the presence of hydrogen, palladium on carbon and the compound from the previous step dissolved in various solvents such as ethyl acetate, tetrahydrofuran, methanol and ethanol. Upon reaction completion, conventional workup of the reaction solution can be followed by isolation / purification processes such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like to provide for compound **31A**.

[0350] In the next step, the t-butoxycarbonyl (t-BOC) protecting group is removed by conventional conditions. The t-BOC group is illustrative only and other conventional amino blocking groups such as benzyl, 9-fluorenylmethoxycarbonyl (Fmoc), benzyloxycarbonyl (Cbz), p-nitrobenzyloxycarbonyl and the like. Upon reaction completion, conventional workup of the reaction solution can be followed by isolation / purification processes such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like.

[0351] In the final step, at least a stoichiometric amount of a suitable acid chloride, compound **32A**, is combined with compound from the previous step in an inert diluent such as DMF, DCM, MeCN and the like in the presence of a suitable base such as potassium carbonate, pyridine, triethylamine and the like. The reaction is typically maintained at from 0 °C to 50 °C until it is substantially complete.

[0352] Conventional workup of the reaction solution can be followed by isolation/purification processes such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like to provide for compound **33A**.



Scheme 6

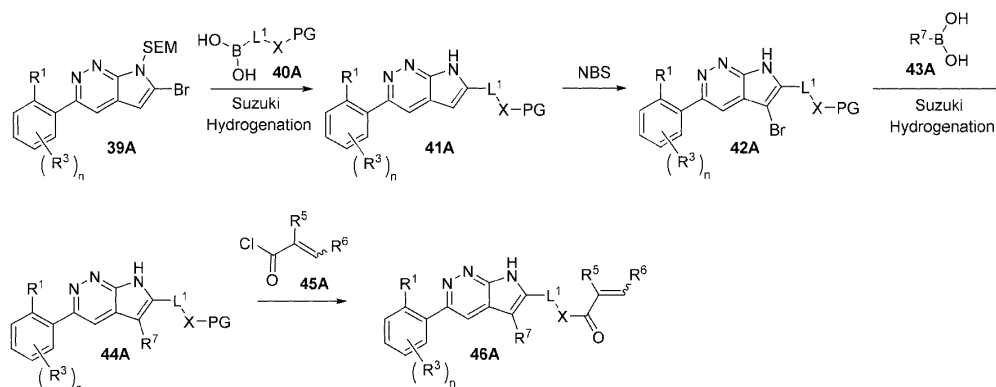
[0353] In the first step, a conventional Suzuki coupling reaction wherein at least a stoichiometric equivalent of a suitable boronic acid, compound **35A**, or an ester thereof, is combined with compound **34A**, in an inert diluent such as tetrahydrofuran, dioxane, toluene, dimethoxyethane, and the like, typically in the presence of a palladium catalyst (e.g., palladium diacetate) and a suitable base such as diisopropylethylamine, triethylamine, pyridine, potassium carbonate, and the like. The reaction is typically maintained at from 10 °C to 65 °C until it is substantially complete. Conventional workup of the reaction solution can be followed by isolation / purification processes such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like to provide the desired product.

[0354] The Suzuki reaction above is followed by an hydrogenation reaction to reduce the alkene group from the molecule. The reaction is carried out in the presence of hydrogen, palladium on carbon and the compound from the previous step dissolved in various solvents such as ethyl acetate, tetrahydrofuran, methanol and ethanol. Upon reaction completion, conventional workup of the reaction solution can be followed by isolation / purification processes such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like to provide for compound **36A**.

[0355] In the next step, the t-butoxycarbonyl (t-BOC) protecting group is removed by conventional conditions. The t-BOC group is illustrative only and other conventional amino blocking groups such as benzyl, 9-fluorenylmethoxycarbonyl (Fmoc), benzyloxycarbonyl (Cbz), p-nitrobenzyloxycarbonyl and the like. Upon reaction completion, conventional workup of the reaction solution can be followed by isolation / purification processes such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like.

[0356] In the final step, at least a stoichiometric amount of a suitable acid chloride, compound **37A**, is combined with compound from the previous step in an inert diluent such as DMF, DCM, MeCN and the like in the presence of a suitable base such as potassium carbonate, pyridine, triethylamine and the like. The reaction is typically maintained at from 0 °C to 50 °C until it is substantially complete.

[0357] Conventional workup of the reaction solution can be followed by isolation/purification processes such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like to provide for compound **38A**.



Scheme 7

[0358] In the first step, a conventional Suzuki coupling reaction wherein at least a stoichiometric equivalent of a suitable boronic acid, compound **40A**, or an ester thereof, is combined with compound **39A**, in an inert diluent such as tetrahydrofuran, dioxane, toluene, dimethoxyethane, and the like, typically in the presence of a palladium catalyst (e.g., palladium diacetate) and a suitable base such as diisopropylethylamine, triethylamine, pyridine, potassium carbonate, and the like. The reaction is typically maintained at from 10 °C to 65 °C until it is substantially complete. Conventional workup of the reaction solution can be followed by isolation / purification processes such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like to provide compound **41A**.

[0359] The second step is an aryl bromination reaction, wherein at least a stoichiometric equivalent of a suitable 7H-pyrrolo[2,3-c]pyridazine, compound **41A**, is combined with NBS, in an inert diluent such as tetrahydrofuran, DMF and the like. The reaction is typically maintained at from 0 °C to 40 °C until it is substantially complete. Conventional workup of the reaction solution can be followed by isolation / purification processes, such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like to provide for compound **42A**.

[0360] In the next step, a conventional Suzuki coupling reaction wherein at least a stoichiometric equivalent of a suitable boronic acid, compound **43A**, is combined with compound **42A**, in an inert diluent such as tetrahydrofuran, dioxane, toluene, dimethoxyethane, and the like, typically in the presence of a palladium catalyst (e.g., palladium diacetate) and a suitable base such as diisopropylethylamine, triethylamine, pyridine, potassium carbonate, and the like. The reaction is typically maintained at from 10 °C to 65 °C until it is substantially complete. Conventional workup of the reaction solution can be followed by isolation / purification processes such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like to provide for the desired compound.

[0361] The Suzuki reaction above is followed by an hydrogenation reaction to reduce alkene groups from the molecule. The reaction is carried out in the presence of hydrogen, palladium on carbon and the compound from the previous step dissolved in various solvents such as ethyl acetate, tetrahydrofuran, methanol and ethanol. Upon reaction completion, conventional workup of the reaction solution can be followed by isolation / purification processes such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like to provide for compound **44A**.

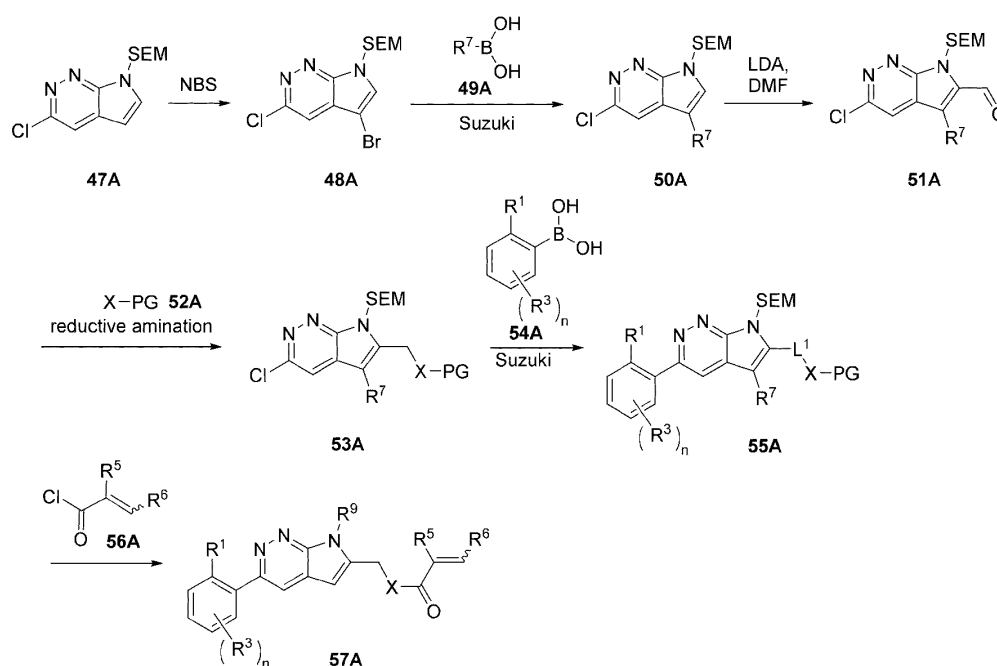
[0362] In the next step, the t-butoxycarbonyl (t-BOC) protecting group is removed by conventional conditions. The t-BOC group is illustrative only and other conventional amino blocking groups such as benzyl, 9-fluorenylmethoxycarbonyl (Fmoc), benzyloxycarbonyl (Cbz), p-nitrobenzyloxycarbonyl and the like. Upon reaction completion, conventional workup of the reaction solution can be followed by isolation / purification processes such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like.

[0363] The Suzuki reaction above is followed by an hydrogenation reaction to reduce the alkene group from. The reaction is carried out in the presence hydrogen, palladium on carbon and the compound from

the previous step dissolved in various solvents such as ethyl acetate, tetrahydrofuran, methanol and ethanol. Upon reaction completion, conventional workup of the reaction solution can be followed by isolation / purification processes such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like.

[0364] In the final step, at least a stoichiometric amount of a suitable acid chloride, compound **45A**, is combined with compound from the previous step in an inert diluent such as DMF, DCM, MeCN and the like in the presence of a suitable base such as potassium carbonate, pyridine, triethylamine and the like. The reaction is typically maintained at from 0 °C to 50 °C until it is substantially complete.

[0365] Conventional workup of the reaction solution can be followed by isolation/purification processes such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like to provide for compound **46A**.



Scheme 8

[0366] The first step is an aryl bromination reaction, wherein at least a stoichiometric equivalent of 3-chloro-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazine, compound **47A**, is combined with NBS, in an inert diluent such as tetrahydrofuran, DMF and the like. The reaction is typically maintained at from 0 °C to 40 °C until it is substantially complete. Conventional workup of the reaction solution can be followed by isolation / purification processes, such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like to provide for compound **48A**.

[0367] The second step is a conventional Suzuki coupling reaction wherein at least a stoichiometric equivalent of a suitable boronic acid, compound **49A**, or an ester thereof, is combined with compound **48A**, in an inert diluent such as tetrahydrofuran, dioxane, toluene, dimethoxyethane, and the like, typically in the presence of a palladium catalyst (e.g. palladium diacetate) and a suitable base such as

diisopropylethylamine, triethylamine, pyridine, potassium carbonate, and the like. The reaction is typically maintained at from 10 °C to 65 °C until it is substantially complete. Conventional workup of the reaction solution can be followed by isolation / purification processes such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like to provide compound **50A**.

[0368] The next step is a formylation reaction wherein at least a stoichiometric equivalent of compound **50A** dissolved in an inert diluent such as tetrahydrofuran, is sequentially reacted with a strong base (e.g. n-BuLi, s-BuLi, or t-BuLi, LDA), and then dimethylformamide. The reaction is typically maintained at -78 °C until it is substantially complete. Conventional workup of the reaction solution can be followed by isolation / purification processes, such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like to provide for compound **51A**.

[0369] In the next step, a conventional reductive amination is conducted wherein at least a stoichiometric equivalent of compound **51A** is combined with a primary or secondary amine **52A**, in an inert diluent such as tetrahydrofuran, dioxane, dimethylformamide and the like, in the presence of a reducing agent (e.g. sodium cyanoborohydride, Sodium triacetoxyborohydride). The reaction is typically maintained at from 20°C to 40 °C until it is substantially complete. Conventional workup of the reaction solution can be followed by isolation / purification processes, such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like to provide for compound **53A**.

[0370] The fifth step is a conventional Suzuki coupling reaction wherein at least a stoichiometric equivalent of a suitable boronic acid, compound **54A**, or an ester thereof, is combined with compound **53A**, in an inert diluent such as tetrahydrofuran, dioxane, toluene, dimethoxyethane, and the like, typically in the presence of a palladium catalyst (e.g. palladium diacetate) and a suitable base such as diisopropylethylamine, triethylamine, pyridine, potassium carbonate, and the like. The reaction is typically maintained at from 10 °C to 65 °C until it is substantially complete. Conventional workup of the reaction solution can be followed by isolation / purification processes such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like to provide compound **55A**.

[0371] In the next step, the t-butoxycarbonyl (t-BOC) protecting group is removed by conventional conditions. The t-BOC group is illustrative only and other conventional amino blocking groups such as benzyl, 9-fluorenylmethoxycarbonyl (Fmoc), benzyloxycarbonyl (Cbz), p-nitrobenzyloxycarbonyl and the like. Upon reaction completion, conventional workup of the reaction solution can be followed by isolation / purification processes such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like.

[0372] In the final step, at least a stoichiometric amount of a suitable acid chloride, compound **56A**, is combined with compound from the previous step in an inert diluent such as DMF, DCM, MeCN and the like in the presence of a suitable base such as potassium carbonate, pyridine, triethylamine and the like. The reaction is typically maintained at from 0 °C to 50 °C until it is substantially complete.

[0373] Conventional workup of the reaction solution can be followed by isolation/purification processes such as crystallization, chromatography, high performance liquid chromatography (HPLC), and the like to provide for compound **57A**.

[0374] Other starting materials used herein are either well known in the art, commercially available, or can be prepared by conventional synthetic methods.

EXAMPLES

[0375] This disclosure is further understood by reference to the following examples, which are intended to be purely exemplary of this disclosure. This disclosure is not limited in scope by the exemplified embodiments, which are intended as illustrations of single aspects of this disclosure only. Any methods that are functionally equivalent are within the scope of this disclosure. Various modifications of this disclosure in addition to those described herein will become apparent to those skilled in the art from the foregoing description and accompanying figures. Such modifications fall within the scope of the appended claims.

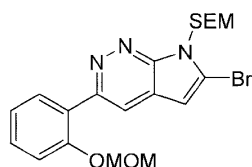
[0376] In the specification and in the examples below, all temperatures are in degrees Celsius. In addition, the following abbreviations have the following meanings. If not defined, these abbreviations have their art recognized meaning.

Abbreviation	Meaning
δ	chemical shift (ppm)
ACN or MeCN	Acetonitrile
Ar	Argon
Boc	tert -butoxycarbonyl
BOP	benzotriazole-1-yl-oxy-tris-(dimethylamino)-phosphonium hexafluorophosphate
BRET	Bioluminescence Resonance Energy Transfer
cataCXiumA-Pd-G2	chloro[(di(1-adamantyl)-N-butylphosphine)-2-(2-aminobiphenyl)]palladium(II)
Cbz	benzyloxycarbonyl
CbzCl	benzyloxycarbonyl chloride
DC ₅₀	corresponding to half maximal degradation
DCM	dichloromethane
DIEA or DIPEA	diisopropylethylamine
DMA	dimethylacetamide
DMAP	4-dimethylaminopyridine
DMF	N,N-dimethylformamide
DMSO	Dimethylsulfoxide
DMP	Dess–Martin periodinane
d ₆ -DMSO	deuterated dimethylsulfoxide
DSC	N,N'-disuccinimidyl carbonate

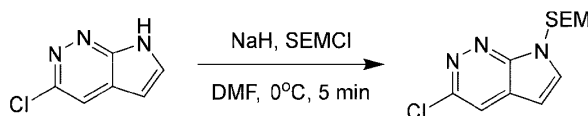
d ₄ -MeOH	deuterated methanol
dtbbpy	4,4'-di-tert-butyl-2,2'-dipyridyl
EDCI	1-ethyl-3-(3-dimethylaminopropyl)carbodiimide
eq.	equivalent(s)
ESI	electrospray ionization
EtOAc or EA	ethyl acetate
EtOH	Ethanol
FBS	Fetal Bovine Serum
FITC	fluorescein isothiocyanate
Fmoc	fluorenylmethyloxycarbonyl
¹ H NMR	proton nuclear magnetic resonance spectroscopy
HPLC	high performance liquid chromatography
IPA	isopropyl alcohol
LC	liquid chromatography
LC-MS	liquid chromatography – mass spectrometry
M	Molar
MeOH	Methanol
MTBE	Methyl tert-butyl ether
<i>m/z</i>	mass-to-charge ratio
MsOH	methanesulfonic acid
N	Normal
NBS	N-Bromosuccinimide
NHC-1	5,7-di-tert-butyl-3-phenylbenzo[d]oxazol-3-ium tetrafluoroborate
PBS	phosphate-buffered saline
Pd ₂ (dba) ₃	tris(dibenzylideneacetone)dipalladium(0)
Pd(OAc) ₂	palladium (II) acetate
PE	Petroleum Ether
pM	Picomolar
q.s.	amount which is sufficient
rt	room temperature
SEM	trimethylsilylethoxymethyl
SFC	supercritical fluid chromatography
<i>t</i> -Bu	tert-butyl
TEA	Triethylamine
TFA	trifluoroacetic acid
TFP	tri(2-furyl)phosphine
THF	tetrahydrofuran
TMP	2,2,6,6-tetramethylpiperidine

T ₃ P	propanephosphonic acid anhydride
TRITC	tetramethylrhodamine
TsCl	4-toluenesulfonyl chloride
TsOH	4-toluenesulfonic acid
UV	Ultraviolet
v/v	volume/volume ratio
wt %	weight percent
NMR abbreviations	br = broad
	d = doublet
	dd = doublet of doublets
	m = multiplet
	q = quartet
	quin = quintet
	s = singlet
	t = triplet

Synthesis of intermediate 1

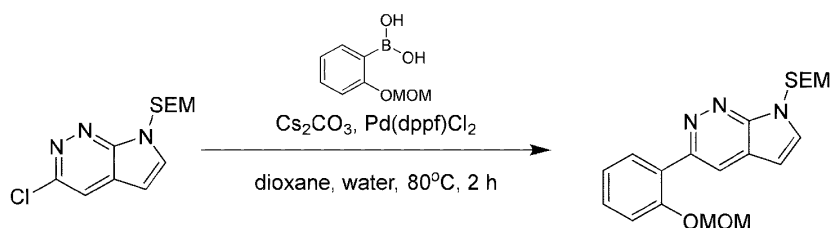


Step 1:



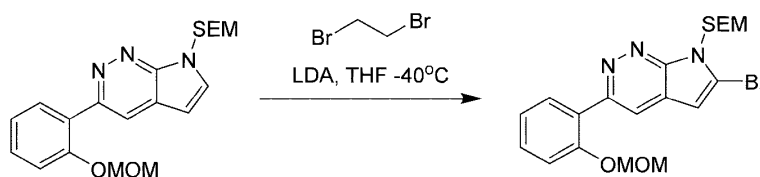
To a solution of 3-chloro-7H-pyrrolo[2,3-c]pyridazine (100 g, 651.17 mmol, 1 eq) in DMF (1100 mL) was added NaH (39.07 g, 976.76 mmol, 60% purity, 1.5 eq) in portions at 0 °C under N₂. After addition, the mixture was stirred at this temperature for 30 min, then 2-(trimethylsilyl)ethoxymethyl chloride (162.85 g, 976.76 mmol, 172.87 mL, 1.5 eq) was added dropwise over 40 min at 0 °C. The resulting mixture was stirred at 0 °C for 5 min. The reaction mixture was quenched by addition of H₂O (100 mL) at 0 °C, then diluted with brine (1 L) and extracted with EtOAc (1 L × 3). The combined organic layers were washed with brine (500 mL × 2), dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (SiO₂, petroleum ether/ethyl acetate = 10/1 to 1/1) to give 3-chloro-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazine (130 g, 448.86 mmol, 68.93% yield) as a yellow solid. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ 7.69 (s, 1H), 7.66 (d, *J*=3.50 Hz, 1H), 6.52 (d, *J*=3.63 Hz, 1H), 5.81 (s, 2H), 3.51-3.63 (m, 2H), 0.83-0.96 (m, 2H), -0.07 (s, 9H),

Step 2



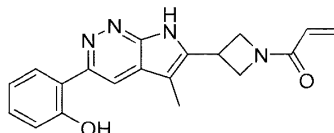
To a solution of 3-chloro-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazine (130 g, 458.02 mmol, 1 eq) and [2-(methoxymethoxy)phenyl]boronic acid (100.02 g, 549.63 mmol, 1.2 eq) in dioxane (1300 mL) and H₂O (650 mL) was added Pd(dppf)Cl₂ (33.51 g, 45.80 mmol, 0.1 eq) and Cs₂CO₃ (447.70 g, 1.37 mol, 3 eq) under N₂. The mixture was stirred at 80 °C for 2 h. The reaction mixture was diluted with water (1000 mL) and extracted with EtOAc (1500 mL × 2). The combined organic layers were washed with brine (2000 mL), dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (SiO₂, petroleum ether/ethyl acetate = 10/1 to 5/1) to give 3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazine (120 g, 298.81 mmol, 65.24% yield) as a yellow oil. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ 8.14 (s, 1H), 7.91 (dd, *J*=7.67, 1.36 Hz, 1H), 7.60 (d, *J*=3.46 Hz, 1H), 7.34-7.43 (m, 1H), 7.25 (s, 1H), 7.17 (t, *J*=7.48 Hz, 1H), 6.57 (d, *J*=3.46 Hz, 1H), 5.87 (s, 2H), 5.19 (s, 2H), 3.57-3.71 (m, 2H), 3.41 (s, 3H), 0.84-1.01 (m, 2H), -0.08 (s, 10H).

Step 3

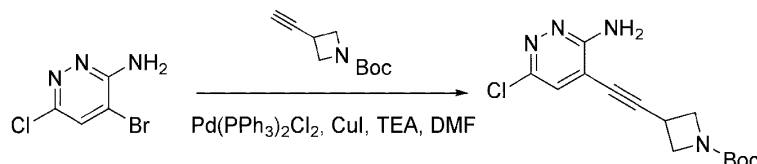


In a flow chemistry setup, LDA (2M in THF, 1.26 L, 2.5 eq) was added to a solution of 3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazine (390 g, 1.01 mol, 1 eq) in THF (7800 mL) at -40 °C to which was subsequently added a solution of 1,2-dibromoethane (665.14 g, 3.54 mol, 267.12 mL, 3.5 eq) in THF (3900 mL). The reaction was then quenched by addition of saturated NH₄Cl (1 L) at 10 °C, then diluted with H₂O (300 mL) and extracted with EtOAc (500 mL × 3). The combined organic layers were washed with brine (500 mL × 2), dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (SiO₂, petroleum ether/ethyl acetate=1/0 to 10/1) to give 6-bromo-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazine (570 g, 1.20 mol, 59.39% yield,) as a yellow solid. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.14 (s, 1H), 7.71 (dd, 1H, *J*=1.8, 7.6 Hz), 7.4-7.5 (m, 1H), 7.29 (d, 1H, *J*=8.3 Hz), 7.1-7.2 (m, 1H), 6.98 (s, 1H), 5.85 (s, 2H), 5.22 (s, 2H), 3.64 (t, 2H, *J*=7.9 Hz), 3.27 (s, 3H), 0.86 (t, 2H, *J*=7.9 Hz), -0.10 (s, 8H); LCMS (ESI⁺): *m/z* 466 (M+H)⁺.

Example 1: Synthesis of 1-{3-[5-(*o*-hydroxyphenyl)-1*H*-1,6,7-triazainden-2-yl]-1-azetidiny]-2-propen-1-one (Compound 216):

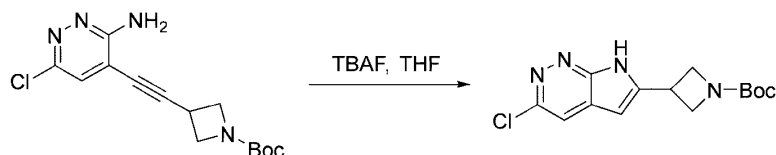


Step 1:



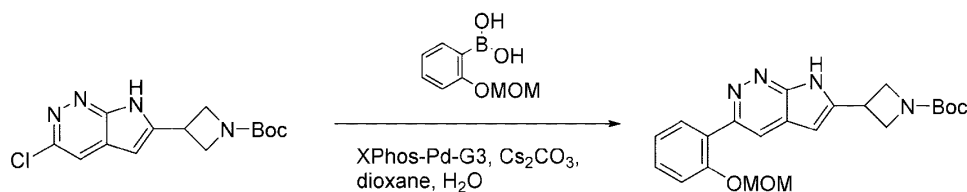
[0377] A mixture of 4-bromo-6-chloropyridazin-3-amine (10 g, 47.98 mmol, 1 eq), *tert*-butyl 3-ethynylazetidine-1-carboxylate (10 g, 55.18 mmol, 1.15 eq), Pd(PPh₃)₂Cl₂ (3.37 g, 4.80 mmol, 0.1 eq), CuI (913.80 mg, 4.80 mmol, 0.1 eq), and TEA (4.86 g, 47.98 mmol, 6.68 mL, 1 eq) in DMF (300 mL) was degassed and purged with N₂. The mixture was stirred at 120 °C for 2 h under a N₂ atmosphere. The reaction mixture was diluted with water (200 mL) and extracted with EtOAc (2 × 200 mL). The combined organic layers were washed with brine (200 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO₂, 50% petroleum ether in ethyl acetate) to give *tert*-butyl 3-((3-amino-6-chloropyridazin-4-yl)ethynyl)azetidine-1-carboxylate. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ = 8.06 (s, 1H), 5.84 (s, 2H), 4.30 (t, *J* = 8.4 Hz, 2H), 4.07 (dd, *J* = 6.4, 8.4 Hz, 2H), 3.70 - 3.60 (m, 1H), 1.50 (s, 9H).

Step 2:



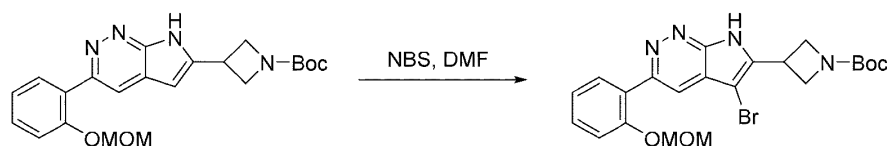
[0378] To a solution of *tert*-butyl 3-((3-amino-6-chloropyridazin-4-yl)ethynyl)azetidine-1-carboxylate (4.3 g, 13.93 mmol, 1 eq) in THF (43 mL) was added TBAF (1M, 55.71 mL, 4 eq) at 25 °C. The mixture was stirred at 80 °C for 1 h. The reaction mixture was diluted with water (50 mL) and extracted with EtOAc (2 × 50 mL). The combined organic layers were washed with brine (50 mL), dried over Na₂SO₄, filtered, and concentrated under reduced pressure to give *tert*-butyl 3-(3-chloro-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)azetidine-1-carboxylate, which was used in the next step without further purification. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ 11.32 - 10.84 (m, 1H), 7.78 - 7.65 (m, 1H), 6.48 (s, 1H), 4.47 (t, *J* = 8.0 Hz, 2H), 4.18 - 4.07 (m, 3H), 1.48 (s, 9H).

Step 3:



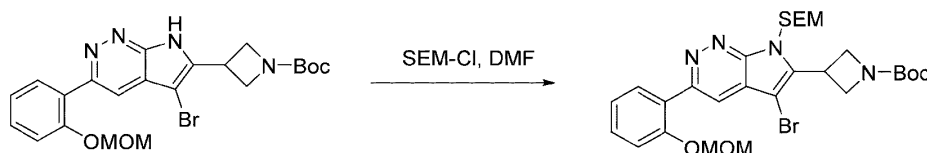
[0379] A mixture of *tert*-butyl 3-(3-chloro-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)azetidine-1-carboxylate, (4.2 g, 13.60 mmol, 1 eq), (2-(methoxymethoxy)phenyl)boronic acid (3.71 g, 20.40 mmol, 1.5 eq), Cs₂CO₃ (13.30 g, 40.81 mmol, 3 eq), and XPhos-Pd-G3 (1.73 g, 2.04 mmol, 0.15 eq) in dioxane (42 mL) and water (21 mL) was degassed and purged with N₂. The mixture was stirred at 80 °C for 1 h under a N₂ atmosphere. The reaction mixture was diluted with water (50 mL) and extracted with EtOAc (2 × 50 mL). The combined organic layers were washed with brine (50 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO₂, 35% petroleum ether in ethyl acetate) to give *tert*-butyl 3-(3-(2-(methoxymethoxy)phenyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)azetidine-1-carboxylate. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ 12.08 (br s, 1H), 8.12 (s, 1H), 7.88 (dd, *J* = 1.6, 7.6 Hz, 1H), 7.44 - 7.38 (m, 1H), 7.29 (d, *J* = 8.4 Hz, 1H), 7.24 - 7.18 (m, 1H), 6.49 (s, 1H), 5.21 (s, 2H), 4.54 - 4.42 (m, 2H), 4.21 - 4.10 (m, 3H), 3.43 (s, 3H), 1.47 (s, 9H).

Step 4:



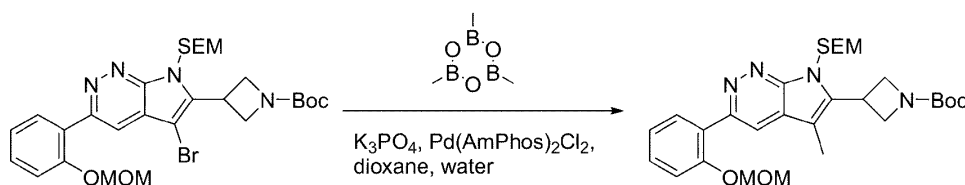
[0380] A solution of *tert*-butyl 3-(3-(2-(methoxymethoxy)phenyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)azetidine-1-carboxylate (3 g, 7.31 mmol, 1 eq) in DMF (50 mL) was cooled to 0 °C. NBS (1.30 g, 7.31 mmol, 1 eq) in DMF (10 mL) was added dropwise to the solution. The mixture was stirred at 0 °C for 0.5 h. The reaction mixture was poured into ice water (100 mL) and filtered. The filter cake was dried to give *tert*-butyl 3-(5-bromo-3-(2-(methoxymethoxy)phenyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)azetidine-1-carboxylate, which was used in the next step without further purification. ¹H NMR (400 MHz, DMSO-*d*₆) δ 13.25 (s, 1H), 7.95 (d, *J* = 5.2 Hz, 1H), 7.77 (d, *J* = 7.6 Hz, 1H), 7.49 - 7.39 (m, 1H), 7.28 (d, *J* = 8.0 Hz, 1H), 7.17 (t, *J* = 7.2 Hz, 1H), 5.25 (s, 2H), 4.25 (s, 5H), 3.33 (s, 3H), 1.49 - 1.39 (m, 9H).

Step 5:



[0381] To a solution of *tert*-butyl 3-(5-bromo-3-(2-(methoxymethoxy)phenyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)azetidine-1-carboxylate (3 g, 6.13 mmol, 1 eq) and TEA (2.48 g, 24.52 mmol, 3.41 mL, 4 eq) in DMF (30 mL) was added SEM-Cl (2.04 g, 12.26 mmol, 2.17 mL, 2 eq) dropwise at 0 °C under a N₂ atmosphere. The mixture was stirred at 0 °C for 1 h. The reaction mixture was quenched by addition of ice water (10 mL) at 0 °C and extracted with EtOAc (2 × 30 mL). The combined organic layers were washed with brine (30 mL), dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (SiO₂, 25% ethyl acetate in petroleum ether) to give *tert*-butyl 3-(5-bromo-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)azetidine-1-carboxylate. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.24 (s, 1H), 7.63 (dd, *J* = 1.6, 7.6 Hz, 1H), 7.48 (dt, *J* = 1.6, 8.0 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 1H), 7.17 (dt, *J* = 0.8, 7.6 Hz, 1H), 6.21 (s, 2H), 5.27 (s, 2H), 4.34 - 4.10 (m, 5H), 3.84 (t, *J* = 8.0 Hz, 2H), 3.34 - 3.34 (m, 3H), 1.42 (s, 9H), 0.96 - 0.86 (m, 2H), 0.11 (s, 9H).

Step 6:



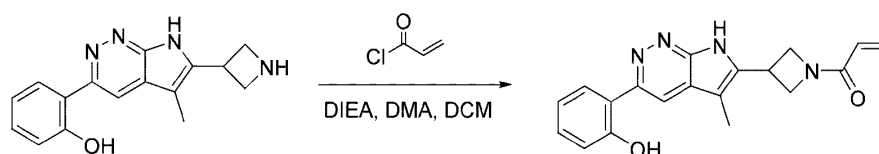
[0382] A mixture of *tert*-butyl 3-(5-bromo-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)azetidine-1-carboxylate (250.0 mg, 403.5 μmol, 1.0 eq), 2,4,6-trimethyl-1,3,5,2,4,6-trioxatriborinane (202.6 mg, 806.9 μmol, 225.6 μL, 2.0 eq), K₃PO₄ (171.3 mg, 806.9 μmol, 2.0 eq), and bis(4-(di-*tert*-butylphosphanyl)-*N,N*-dimethylaniline)-palladium chloride (42.8 mg, 60.5 μmol, 42.8 μL, 0.15 eq) in dioxane (5 mL) and H₂O (2.5 mL) was degassed and purged with N₂. The mixture was stirred at 60 °C for 4 h under N₂. The reaction mixture was partitioned between ethyl acetate (5 mL) and H₂O (5 mL). The organic phase was separated, washed with brine (5 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO₂, 10 to 15% ethyl acetate in petroleum ether) to give *tert*-butyl 3-(3-(2-(methoxymethoxy)phenyl)-5-methyl-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)azetidine-1-carboxylate. ¹H NMR (400 MHz, METHANOL-*d*₄) δ 8.23 (s, 1H), 7.64 (dd, *J* = 1.6, 7.6 Hz, 1H), 7.47 - 7.39 (m, 1H), 7.31 (d, *J* = 8.0 Hz, 1H), 7.15 (dt, *J* = 0.8, 7.6 Hz, 1H), 6.23 (s, 2H), 5.24 (s, 2H), 4.36 - 4.23 (m, 5H), 3.87 (t, *J* = 8.0 Hz, 2H), 3.39 (s, 3H), 2.31 (s, 3H), 1.49 (s, 9H), 0.96 - 0.91 (m, 2H), -0.10 (s, 9H).

Step 7:



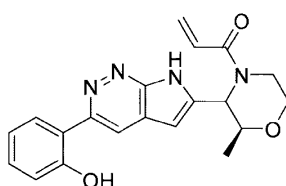
[0383] A solution of *tert*-butyl 3-(3-(2-(methoxymethoxy)phenyl)-5-methyl-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)azetidine-1-carboxylate (160.0 mg, 288.4 μ mol, 1.0 *eq*) in DCM (2 mL) and TFA (1 mL) was stirred at 25 °C for 1 h. The reaction mixture was concentrated under reduced pressure. The residue was triturated with *tert*-butyl methyl ether (5 mL) to give 2-(6-(azetidin-3-yl)-5-methyl-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)phenol (TFA salt), which was used in the subsequent step without purification. ¹H NMR (400 MHz, METHANOL-*d*₄) δ 8.58 (s, 1H), 7.76 - 7.70 (m, 1H), 7.44 (dt, *J* = 1.6, 7.6 Hz, 1H), 7.12 - 7.04 (m, 2H), 4.65 - 4.56 (m, 2H), 4.54 - 4.47 (m, 2H), 4.43 - 4.39 (m, 1H), 2.42 - 2.37 (m, 3H).

Step 8:

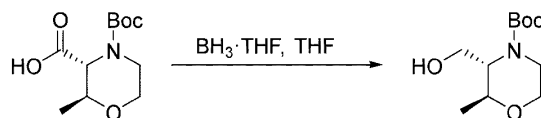


[0384] To a solution of 2-(6-(azetidin-3-yl)-5-methyl-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)phenol (TFA salt) (100.0 mg, 253.6 μ mol, 1.0 *eq*, TFA) and DIEA (98.3 mg, 760.7 μ mol, 132.5 μ L, 3.0 *eq*) in DMA (2 mL) was added prop-2-enoyl chloride (16.1 mg, 177.5 μ mol, 14.4 μ L, 0.7 *eq*) in DCM (0.2 mL) dropwise at 0 °C. The mixture was stirred at 25 °C for 1 h. The reaction mixture was concentrated under reduced pressure, and the residue was purified by prep-HPLC (Instrument: Gilson 281 semi-preparative HPLC system; Mobile phase: A: H₂O (10 mM NH₄HCO₃); B: ACN; Column: Waters Xbridge BEH C₁₈ 100 mm $\times$ 30 mm $\times$ 10 μ m; Flow rate: 25.00 ml/min) to give 1-{3-[5-(*o*-hydroxyphenyl)-1*H*-1,6,7-triazainden-2-yl]-1-azetidinyl}-2-propen-1-one. ¹H NMR (400 MHz, METHANOL-*d*₄) δ 8.56 (s, 1H), 7.64 (dd, *J* = 1.6, 7.6 Hz, 1H), 7.49 (dt, *J* = 1.6, 8.0 Hz, 1H), 7.15 - 7.07 (m, 2H), 6.49 - 6.39 (m, 1H), 6.36 - 6.28 (m, 1H), 5.82 (dd, *J* = 2.4, 10.4 Hz, 1H), 4.66 - 4.57 (m, 3H), 4.57 - 4.52 (m, 1H), 4.40 - 4.33 (m, 1H), 2.42 (s, 3H).

Example 2: Synthesis of 1-{(2*S*)-3-[5-(*o*-hydroxyphenyl)-1*H*-1,6,7-triazainden-2-yl]-2-methyl-4-morpholinyl}-2-propen-1-one (Compound 11):



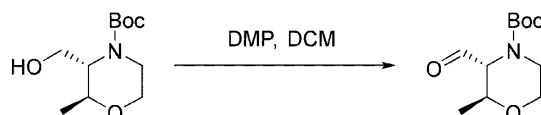
Step 1:



[0385] To a solution of (2*S*,3*R*)-4-(*tert*-butoxycarbonyl)-2-methylmorpholine-3-carboxylic acid (900.0 mg, 3.7 mmol, 1.0 *eq*) in THF (18 mL) was added BH₃·THF (1M, 11.0 mL, 3.0 *eq*) dropwise under nitrogen at 0 °C. After the addition was completed, the reaction mixture was warmed to 25 °C and

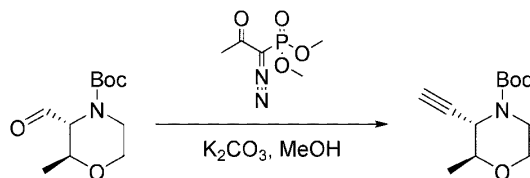
stirred at the same temperature for 2 h. The reaction mixture was quenched by addition of MeOH (10 mL) at 0 °C, then stirred at 25 °C for 2 h. The mixture was concentrated under reduced pressure to give *tert*-butyl (2*S*,3*S*)-3-(hydroxymethyl)-2-methylmorpholine-4-carboxylate, which was used in the next step without further purification. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ 3.97 - 3.91 (m, 1H), 3.91 - 3.84 (m, 2H), 3.84 - 3.79 (m, 1H), 3.79 - 3.74 (m, 1H), 3.73 - 3.66 (m, 1H), 3.60 - 3.51 (m, 1H), 3.32 - 3.21 (m, 1H), 1.48 (s, 9H), 1.34 (d, *J* = 6.4 Hz, 3H).

Step 2:



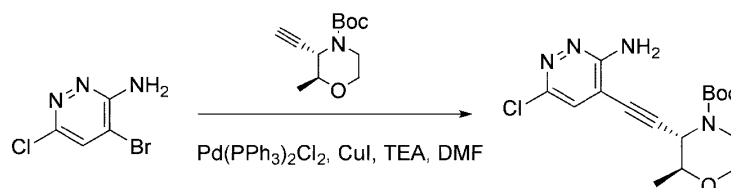
[0386] To a solution of *tert*-butyl (2*S*,3*S*)-3-(hydroxymethyl)-2-methylmorpholine-4-carboxylate (0.6 g, 2.6 mmol, 1.0 eq) in DCM (14 mL) was added DMP (1.7 g, 3.9 mmol, 1.2 mL, 1.5 eq) at 0 °C. The mixture was warmed up to 25 °C and stirred for 2 h. The reaction mixture was quenched by addition of NaHCO₃ (10 mL) at 0 °C, then diluted with H₂O (10 mL) and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine (10 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure to give *tert*-butyl (2*S*,3*R*)-3-formyl-2-methylmorpholine-4-carboxylate, which was used in the next step without further purification. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ 10.04 - 9.44 (m, 1H), 4.10 - 3.98 (m, 1H), 3.95 - 3.86 (m, 1H), 3.77 (dd, *J* = 2.0, 6.0 Hz, 1H), 3.57 (td, *J* = 5.2, 11.2 Hz, 1H), 3.45 (s, 2H), 1.48 (s, 9H), 1.34 (d, *J* = 6.4 Hz, 3H).

Step 3:



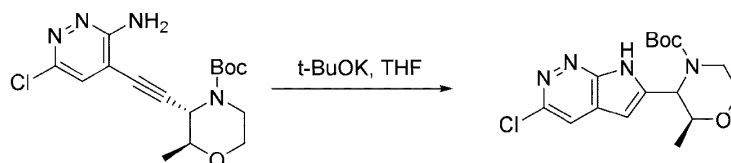
[0387] To a solution of *tert*-butyl (2*S*,3*R*)-3-formyl-2-methylmorpholine-4-carboxylate (440 mg, 1.9 mmol, 1.0 eq) in MeOH (5 mL) was added K₂CO₃ (795.7 mg, 5.8 mmol, 3.0 eq) and 1-diazo-1-dimethoxyphosphoryl-propan-2-one (442.4 mg, 2.3 mmol, 1.2 eq) at 0 °C. The mixture was warmed up to 25 °C and stirred for 2 h. The reaction mixture was quenched by addition of H₂O (5 mL) and extracted with EtOAc (2 × 5 mL). The combined organic layers were washed with brine (5 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO₂, 2 to 10% EtOAc in petroleum ether) to give *tert*-butyl (2*S*,3*S*)-3-ethynyl-2-methylmorpholine-4-carboxylate. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ 4.56 (s, 1H), 4.08 (dq, *J* = 1.6, 6.8 Hz, 1H), 3.84 (dt, *J* = 3.6, 12.0 Hz, 1H), 3.73 (dd, *J* = 3.6, 13.6 Hz, 1H), 3.63 (ddd, *J* = 1.2, 4.0, 11.6 Hz, 1H), 3.37 (ddd, *J* = 4.0, 12.0, 13.6 Hz, 1H), 2.36 - 2.31 (m, 1H), 1.49 (s, 9H), 1.33 (d, *J* = 6.8 Hz, 3H).

Step 4:



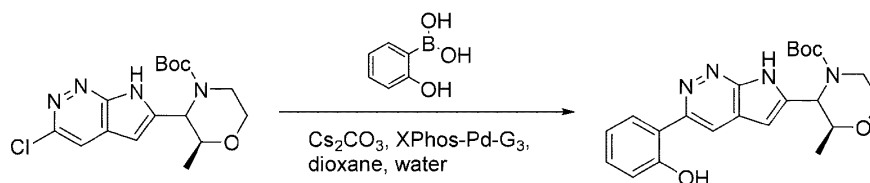
[0388] A mixture of 4-bromo-6-chloropyridazin-3-amine (291.5 mg, 1.4 mmol, 1.1 eq), *tert*-butyl (2*S*,3*S*)-3-ethynyl-2-methylmorpholine-4-carboxylate (300.0 mg, 1.3 mmol, 1.0 eq), CuI (38.0 mg, 199.8 μ mol, 0.15 eq), Pd(PPh₃)₂Cl₂ (93.5 mg, 133.2 μ mol, 0.1 eq), and TEA (673.8 mg, 6.7 mmol, 926.8 μ L, 5.0 eq) in DMF (3 mL) was degassed and purged with N₂. The mixture was then stirred at 40 °C for 2 h under a N₂ atmosphere. The reaction mixture was diluted with H₂O (5 mL) and extracted with EtOAc (2 $\times$ 5 mL). The combined organic layers were washed with brine (2 $\times$ 5 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO₂, 15 to 25% EtOAc in petroleum ether) to give *tert*-butyl (2*S*,3*S*)-3-((3-amino-6-chloropyridazin-4-yl)ethynyl)-2-methylmorpholine-4-carboxylate. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.60 (s, 1H), 6.92 - 6.62 (m, 2H), 4.20 - 4.10 (m, 1H), 3.81 - 3.68 (m, 1H), 3.63 (d, *J* = 13.6 Hz, 1H), 3.55 (dd, *J* = 2.4, 11.6 Hz, 1H), 3.50 - 3.37 (m, 1H), 3.30 - 3.24 (m, 1H), 1.43 (s, 9H), 1.28 - 1.20 (m, 3H).

Step 5:



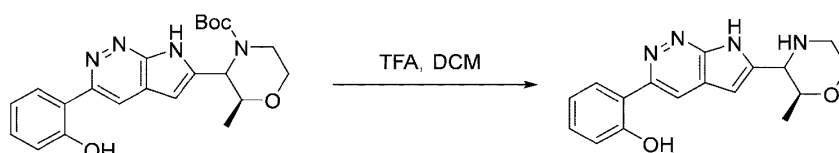
[0389] To a solution of *tert*-butyl (2*S*,3*S*)-3-((3-amino-6-chloropyridazin-4-yl)ethynyl)-2-methylmorpholine-4-carboxylate (300 mg, 850.3 μ mol, 1.0 eq) in THF (9 mL) was added potassium *tert*-butoxide (1M, 1.7 mL, 2.0 eq) at 25 °C. The mixture was stirred at the same temperature for 2 h. The reaction mixture was quenched with H₂O (5 mL) and extracted with EtOAc (2 $\times$ 5 mL). The combined organic layers were washed with brine (5 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO₂, 20 to 50% EtOAc in petroleum ether) to give *tert*-butyl (2*S*)-3-(3-chloro-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-2-methylmorpholine-4-carboxylate. ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.72 - 12.42 (m, 1H), 8.09 - 7.81 (m, 1H), 6.60 - 6.32 (m, 1H), 5.17 - 4.81 (m, 1H), 4.43 - 3.95 (m, 1H), 3.93 - 3.78 (m, 1H), 3.70 - 3.54 (m, 3H), 1.45 - 1.28 (m, 9H), 1.22 - 0.88 (m, 3H).

Step 6:



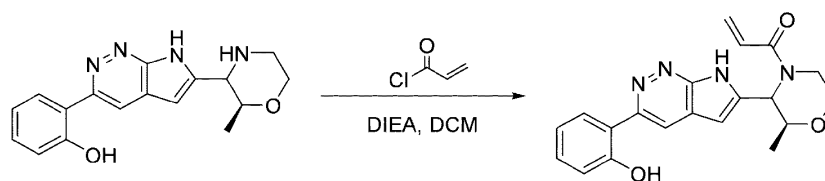
[0390] A mixture of *tert*-butyl (2*S*)-3-(3-chloro-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-2-methylmorpholine-4-carboxylate (130 mg, 368.5 μ mol, 1.0 eq), (2-hydroxyphenyl)boronic acid (152.5 mg, 1.1 mmol, 3.0 eq), Cs₂CO₃ (720.3 mg, 2.2 mmol, 6.0 eq), and Xphos-Pd-G₃ (46.8 mg, 55.3 μ mol, 0.15 eq) in dioxane (1.4 mL) and H₂O (0.7 mL) was degassed and purged with N₂. The resulting mixture was stirred at 100 °C for 2 h under a N₂ atmosphere. The reaction mixture was partitioned between EtOAc (5 mL) and H₂O (5 mL). The organic phase was separated, washed with brine (5 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO₂, 15 to 25% EtOAc in petroleum ether) to give *tert*-butyl (2*S*)-3-(3-(2-hydroxyphenyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-2-methylmorpholine-4-carboxylate. ¹H NMR (400 MHz, METHANOL-*d*₄) δ 8.87 - 8.46 (m, 1H), 8.15 - 7.90 (m, 1H), 7.51 - 7.24 (m, 1H), 7.17 - 7.03 (m, 1H), 6.88 - 6.73 (m, 1H), 6.72 - 6.50 (m, 1H), 5.28 - 5.05 (m, 1H), 5.01 - 4.92 (m, 1H), 4.02 - 3.92 (m, 1H), 3.84 - 3.66 (m, 2H), 3.47 - 3.35 (m, 1H), 1.42 - 1.38 (m, 9H), 1.17 - 1.00 (m, 3H).

Step 7:



[0391] To a solution of *tert*-butyl (2*S*)-3-(3-(2-hydroxyphenyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-2-methylmorpholine-4-carboxylate (100 mg, 243.6 μ mol, 1.0 eq) in DCM (2 mL) was added TFA (1.5 g, 13.5 mmol, 1.0 mL, 55.3 eq) at 25 °C. The mixture was stirred at the same temperature for 2 h. The mixture was concentrated under reduced pressure to remove DCM, and the residue was triturated with methyl *tert*-butyl ether (3 mL) at 25 °C for 30 min to give 2-(6-((2*S*)-2-methylmorpholin-3-yl)-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)phenol, which was used in the subsequent step without purification. *m/z* (ESI⁺): 311.1 (M+H)⁺.

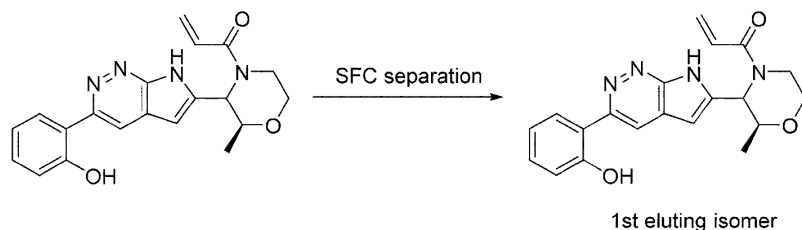
Step 8:



[0392] To a solution of 2-(6-((2*S*)-2-methylmorpholin-3-yl)-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)phenol (70 mg, 165.0 μ mol, 1.0 eq, TFA salt) and DIEA (213.2 mg, 1.7 mmol, 287.3 μ L, 10.0 eq) in DCM (0.4 mL) was added prop-2-enoyl chloride (11.9 mg, 132.0 μ mol, 10.7 μ L, 0.8 eq) in DCM (0.1 mL) dropwise at 0 °C. The resulting mixture was stirred at 25 °C for 2 h. The reaction mixture was quenched by addition of MeOH (0.5 mL) at 25 °C, and the mixture was concentrated under reduced pressure. The residue was purified by prep-TLC (SiO₂, 20% THF in DCM) to give 1-((2*S*)-3-(3-(2-hydroxyphenyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-2-methylmorpholino)prop-2-en-1-one. ¹H NMR (400 MHz, DMSO-*d*₆) δ 14.09 - 13.57 (m, 1H), 12.77 - 12.38 (m, 1H), 8.73 - 8.45 (m, 1H), 8.00 (d, *J* = 7.6 Hz, 1H), 7.40 - 7.20 (m, 1H), 7.12 -

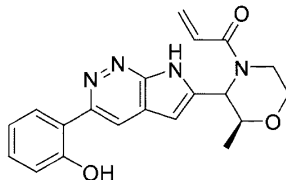
6.66 (m, 4H), 6.28 - 6.08 (m, 1H), 5.82 - 5.67 (m, 1H), 5.66 - 5.28 (m, 1H), 4.74 - 4.10 (m, 1H), 4.10 - 3.96 (m, 1H), 3.93 - 3.75 (m, 1H), 3.73 - 3.56 (m, 2H), 1.37 - 1.32 (m, 1H), 1.23 (s, 1H), 1.04 - 0.98 (m, 2H).

Step 9:

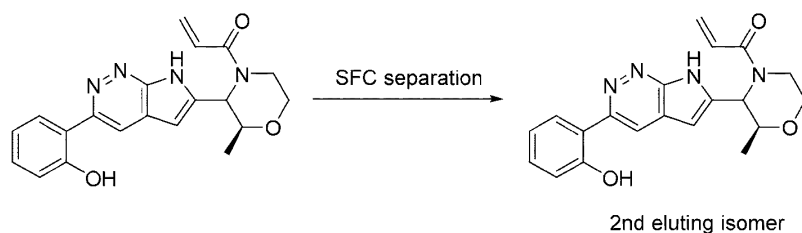


[0393] 1-((2*S*)-3-(3-(2-hydroxyphenyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-2-methylmorpholino)prop-2-en-1-one (24 mg, 65.9 μ mol) was separated by SFC (Column: DAICEL CHIRALCEL OJ 250mm $\times$ 30mm 10 μ m; mobile phase: [CO₂-MeOH]; B%: 46%, isocratic elution mode) to give 1-((2*S*)-3-[5-(*o*-hydroxyphenyl)-1*H*-1,6,7-triazainden-2-yl]-2-methyl-4-morpholinyl)-2-propen-1-one (1st eluting isomer). ¹H NMR (400 MHz, METHANOL-*d*₄) δ 8.49 (s, 1H), 7.94 (d, *J* = 8.4 Hz, 1H), 7.34 - 7.22 (m, 1H), 7.04 - 6.93 (m, 2H), 6.86 (dd, *J* = 10.4, 16.8 Hz, 1H), 6.72 (s, 1H), 6.35 (dd, *J* = 1.6, 16.8 Hz, 1H), 5.85 (dd, *J* = 2.0, 10.4 Hz, 1H), 5.54 (s, 1H), 4.67 (dq, *J* = 2.0, 6.4 Hz, 1H), 4.14 - 4.05 (m, 1H), 4.04 - 3.95 (m, 1H), 3.71 (dd, *J* = 2.8, 11.6 Hz, 1H), 3.52 - 3.39 (m, 1H), 1.45 (d, *J* = 6.4 Hz, 3H).

Example 3: Synthesis of 1-((2*S*)-3-[5-(*o*-hydroxyphenyl)-1*H*-1,6,7-triazainden-2-yl]-2-methyl-4-morpholinyl)-2-propen-1-one (Compound 10):



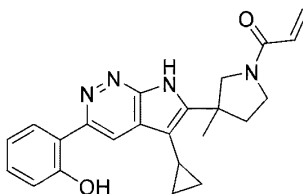
Step 1:



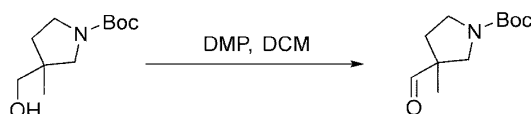
[0394] 1-((2*S*)-3-(3-(2-hydroxyphenyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-2-methylmorpholino)prop-2-en-1-one (24 mg, 65.9 μ mol) was separated by SFC (Column: DAICEL CHIRALCEL OJ 250mm $\times$ 30mm 10 μ m; mobile phase: [CO₂-MeOH]; B%: 46%, isocratic elution mode) to give 1-((2*S*)-3-[5-(*o*-hydroxyphenyl)-1*H*-1,6,7-triazainden-2-yl]-2-methyl-4-morpholinyl)-2-propen-1-one (2nd eluting isomer). ¹H NMR (400 MHz, METHANOL-*d*₄) δ 8.51 (s, 1H), 7.94 (d, *J* = 8.4 Hz, 1H), 7.34 - 7.23 (m, 1H), 7.01 - 6.93 (m, 2H), 6.87 - 6.79 (m, 1H), 6.72 (dd, *J* = 10.8, 16.8 Hz, 1H), 6.32 - 6.18 (m, 1H), 5.91

- 5.77 (m, 1H), 5.75 (s, 1H), 4.40 - 4.13 (m, 1H), 4.08 - 3.87 (m, 2H), 3.85 - 3.73 (m, 1H), 3.71 - 3.60 (m, 1H), 1.23 - 1.07 (m, 3H).

Example 4: Synthesis of 1-{3-[3-cyclopropyl-5-(o-hydroxyphenyl)-1H-1,6,7-triazainden-2-yl]-3-methyl-1-pyrrolidiny}-2-propen-1-one (Compound 31):

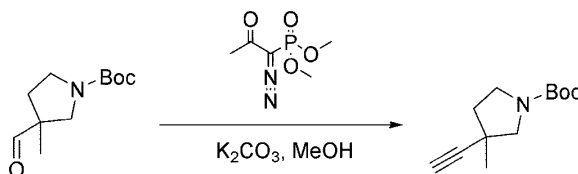


Step 1:



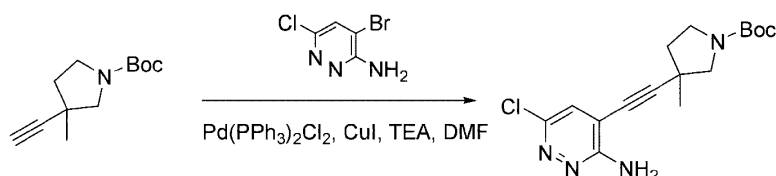
[0395] To a solution of *tert*-butyl 3-(hydroxymethyl)-3-methylpyrrolidine-1-carboxylate (3.9 g, 18.1 mmol, 1.0 *eq*) in DCM (50 mL) was added DMP (11.5 g, 27.2 mmol, 8.4 mL, 1.5 *eq*) at 0 °C and the mixture was warmed up to 25 °C and stirred for 1 h. The reaction mixture was filtered, and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (SiO₂, 5 to 15% EtOAc in petroleum ether) to give *tert*-butyl 3-formyl-3-methylpyrrolidine-1-carboxylate. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ 9.55 (s, 1H), 3.83 - 3.70 (m, 1H), 3.50 - 3.35 (m, 2H), 3.18 - 3.05 (m, 1H), 2.25 (s, 1H), 1.76 - 1.66 (m, 1H), 1.47 (s, 9H), 1.24 (s, 3H).

Step 2:



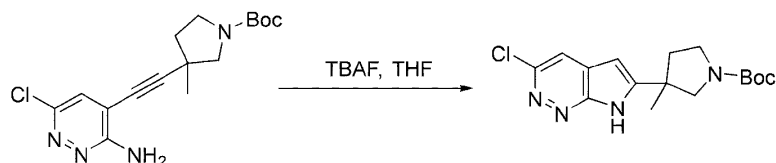
[0396] To a solution of *tert*-butyl 3-formyl-3-methylpyrrolidine-1-carboxylate (3.2 g, 15.0 mmol, 1.0 *eq*) and K₂CO₃ (6.2 g, 45.0 mmol, 3.0 *eq*) in MeOH (40 mL) was added 1-diazo-1-dimethoxyphosphorylpropan-2-one (3.5 g, 18.0 mmol, 1.2 *eq*) at 0 °C. The mixture was warmed up to 25 °C and stirred for 2 hours. The reaction mixture was partitioned between ethyl acetate (30 mL) and H₂O (20 mL). The organic phase was separated, washed with brine (20 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure to give *tert*-butyl 3-ethynyl-3-methylpyrrolidine-1-carboxylate, which was used in the subsequent step without purification. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ 3.61 - 3.38 (m, 3H), 3.26 - 3.15 (m, 1H), 2.16 - 2.10 (m, 2H), 1.86 - 1.76 (m, 1H), 1.47 (s, 9H), 1.36 (s, 3H).

Step 3:



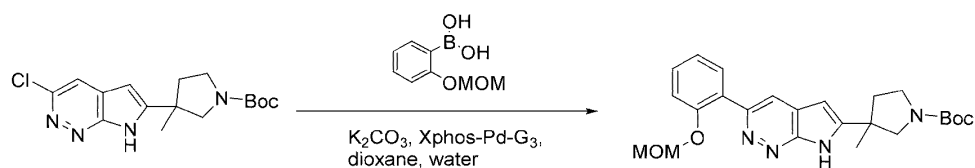
[0397] To a solution of 4-bromo-6-chloropyridazin-3-amine (2.2 g, 10.6 mmol, 1.0 *eq*) and *tert*-butyl 3-ethynyl-3-methylpyrrolidine-1-carboxylate (2.6 g, 12.7 mmol, 1.2 *eq*) in DMF (25 mL) was added Pd(PPh₃)₂Cl₂ (740.8 mg, 1.1 mmol, 0.1 *eq*), CuI (301.5 mg, 1.6 mmol, 0.15 *eq*), and TEA (5.3 g, 52.8 mmol, 7.3 mL, 5.0 *eq*) at 20 °C under N₂. The mixture was then heated to 40 °C and stirred for 2 h. Another 750 mg scale reaction was set up as described above; both reactions were combined for workup and purification. The combined reaction mixtures were diluted with water (15 mL) and extracted with ethyl acetate (2 × 15 mL). The combined organic layers were washed with brine (20 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO₂, 5 to 20% EtOAc in petroleum ether) to give *tert*-butyl 3-((3-amino-6-chloropyridazin-4-yl)ethynyl)-3-methylpyrrolidine-1-carboxylate. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.52 (s, 1H), 6.79 (s, 2H), 3.62 (d, *J* = 10.4 Hz, 1H), 3.46 - 3.38 (m, 2H), 3.23 (dd, *J* = 6.8, 10.4 Hz, 1H), 2.30 - 2.19 (m, 1H), 1.98 - 1.86 (m, 1H), 1.41 (s, 12H).

Step 4:



[0398] A mixture of *tert*-butyl 3-((3-amino-6-chloropyridazin-4-yl)ethynyl)-3-methylpyrrolidine-1-carboxylate (2.5 g, 7.4 mmol, 1.0 *eq*) and TBAF (1.0 M, 29.7 mL, 4.0 *eq*) in THF (25 mL) was degassed and purged with N₂. The mixture was then stirred at 80 °C for 2 h under a N₂ atmosphere. Another 1.1 g scale reaction was set up as described above; both reactions were combined for workup and purification. The combined reaction mixtures were partitioned between ethyl acetate (30 mL) and water (20 mL). The organic layer was washed with brine (20 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure to give *tert*-butyl 3-(3-chloro-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-methylpyrrolidine-1-carboxylate, which was used in the subsequent step without purification. ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.62 (s, 1H), 7.89 (s, 1H), 6.37 (s, 1H), 3.69 (dd, *J* = 2.8, 10.8 Hz, 1H), 3.41 (d, *J* = 10.8 Hz, 2H), 3.30 (s, 1H), 2.40 - 2.30 (m, 1H), 2.09 - 2.00 (m, 1H), 1.45 (s, 3H), 1.39 (d, *J* = 4.0 Hz, 9H).

Step 5:



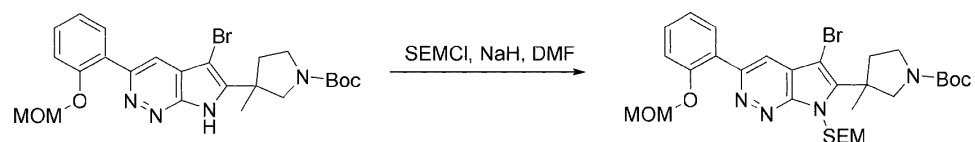
[0399] To a solution of *tert*-butyl 3-(3-chloro-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-methylpyrrolidine-1-carboxylate (2.7 g, 8.0 mmol, 1.0 *eq*) and [2-(methoxymethoxy)phenyl]boronic acid (1.9 g, 10.4 mmol, 1.3 *eq*) in dioxane (54 mL) and H₂O (27 mL) was added Cs₂CO₃ (15.7 g, 48.1 mmol, 6.0 *eq*) and XPhos-Pd-G₃ (1.0 g, 1.2 mmol, 0.15 *eq*) at 20 °C under N₂. The mixture was then heated to 100 °C and stirred for 2 h. The reaction mixture was partitioned between ethyl acetate (40 mL) and H₂O (20 mL). The organic phase was separated, washed with brine (20 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO₂, 25 to 75% EtOAc in petroleum ether) to give *tert*-butyl 3-(3-(2-(methoxymethoxy)phenyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-methylpyrrolidine-1-carboxylate. ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.37 (d, *J* = 4.4 Hz, 1H), 8.01 (s, 1H), 7.69 (dd, *J* = 1.6, 7.6 Hz, 1H), 7.42 - 7.37 (m, 1H), 7.26 (d, *J* = 8.0 Hz, 1H), 7.17 - 7.11 (m, 1H), 6.39 (d, *J* = 1.6 Hz, 1H), 5.20 (s, 2H), 3.73 (dd, *J* = 5.2, 10.8 Hz, 1H), 3.46 - 3.40 (m, 2H), 3.38 - 3.33 (m, 1H), 3.30 (s, 3H), 2.44 - 2.34 (m, 1H), 2.11 - 2.00 (m, 1H), 1.48 (s, 3H), 1.40 (d, *J* = 4.8 Hz, 9H).

Step 6:



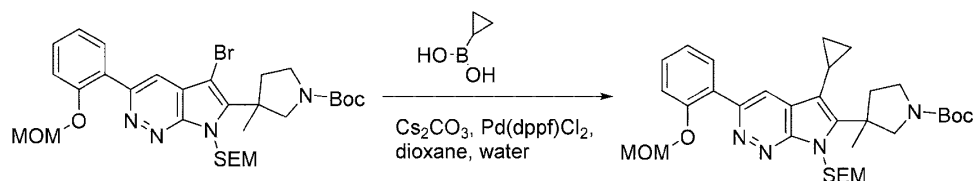
[0400] To a solution of *tert*-butyl 3-(3-(2-(methoxymethoxy)phenyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-methylpyrrolidine-1-carboxylate (1.0 g, 2.3 mmol, 1.0 *eq*) in DMF (20 mL) was added NBS (426.2 mg, 2.4 mmol, 1.05 *eq*) in portions at 0 °C under N₂. The mixture was then warmed up to 25 °C and stirred for 1 h. The reaction mixture was quenched by addition of H₂O (40 mL) at 0 °C, which resulted in a precipitate. The mixture was filtered, and the filter cake was triturated with H₂O (50 mL). The solid was dried under vacuum to give *tert*-butyl 3-(5-bromo-3-(2-(methoxymethoxy)phenyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-methylpyrrolidine-1-carboxylate, which was used in the subsequent step without purification. ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.80 (s, 1H), 8.00 - 7.94 (m, 1H), 7.75 (d, *J* = 7.2 Hz, 1H), 7.47 - 7.41 (m, 1H), 7.28 (d, *J* = 8.0 Hz, 1H), 7.18 (t, *J* = 7.6 Hz, 1H), 5.25 (s, 2H), 3.89 - 3.71 (m, 2H), 3.44 (s, 2H), 3.35 (s, 3H), 2.43 - 2.35 (m, 2H), 1.46 (d, *J* = 4.8 Hz, 3H), 1.43 (s, 9H).

Step 7:



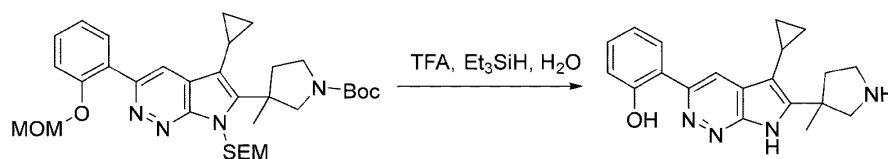
[0401] To a solution of *tert*-butyl 3-(5-bromo-3-(2-(methoxymethoxy)phenyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-methylpyrrolidine-1-carboxylate (1.4 g, 2.7 mmol, 1.0 *eq*) in DMF (25 mL) was added NaH (216.5 mg, 5.4 mmol, 60% purity, 2.0 *eq*) in portions at 0 °C under N₂. After addition, the mixture was stirred at the same temperature for 10 minutes. Subsequently, (2-chloromethoxyethyl)trimethylsilane (676.7 mg, 4.1 mmol, 718.32 µL, 1.5 *eq*) was added dropwise at 0 °C. The resulting mixture was warmed up to 25 °C and stirred for 30 minutes. The reaction mixture was quenched by addition of H₂O (50 mL) at 0 °C and extracted with ethyl acetate (50 mL). The organic layer was washed with brine (20 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO₂, 5 to 15% EtOAc in petroleum ether) to give *tert*-butyl 3-(5-bromo-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-methylpyrrolidine-1-carboxylate. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.35 (s, 1H), 7.73 (dd, *J* = 1.6, 7.6 Hz, 1H), 7.62 - 7.55 (m, 1H), 7.41 (d, *J* = 8.4 Hz, 1H), 7.29 (t, *J* = 7.6 Hz, 1H), 6.33 - 6.23 (m, 2H), 5.39 (s, 2H), 4.00 - 3.90 (m, 2H), 3.73 - 3.59 (m, 2H), 3.47 (s, 3H), 3.44 - 3.37 (m, 2H), 2.76 - 2.68 (m, 1H), 2.34 (td, *J* = 6.0, 12.4 Hz, 1H), 1.60 (s, 3H), 1.52 (d, *J* = 6.8 Hz, 9H), 1.01 (t, *J* = 8.0 Hz, 2H), 0.00 (d, *J* = 3.2 Hz, 9H).

Step 8:



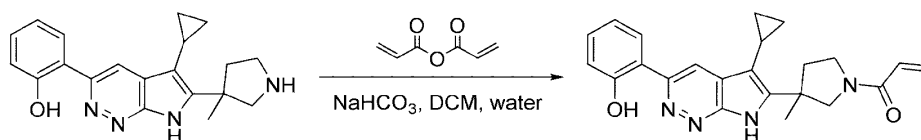
[0402] To a solution of *tert*-butyl 3-(5-bromo-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-methylpyrrolidine-1-carboxylate (420.0 mg, 648.5 µmol, 1.0 *eq*) and cyclopropylboronic acid (1.1 g, 12.9 mmol, 20.0 *eq*) in dioxane (22 mL) and H₂O (11 mL) was added Cs₂CO₃ (1.3 g, 3.9 mmol, 6.0 *eq*) and Pd(dppf)Cl₂ (71.2 mg, 97.3 µmol, 0.15 *eq*) under N₂. The mixture was heated to 100 °C and stirred for 3 h. The reaction mixture was partitioned between ethyl acetate (10 mL) and H₂O (5 mL). The organic phase was separated, washed with brine (5 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO₂, 5 to 25% EtOAc in petroleum ether) to give *tert*-butyl 3-(5-cyclopropyl-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-methylpyrrolidine-1-carboxylate. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.25 (s, 1H), 7.59 (d, *J* = 7.6 Hz, 1H), 7.50 - 7.41 (m, 1H), 7.28 (d, *J* = 8.4 Hz, 1H), 7.20 - 7.10 (m, 1H), 6.17 - 6.06 (m, 2H), 5.26 (s, 2H), 4.06 - 3.98 (m, 1H), 3.83 (t, *J* = 8.0 Hz, 2H), 3.68 - 3.56 (m, 1H), 3.45 - 3.38 (m, 2H), 3.37 (s, 3H), 2.56 (s, 1H), 2.30 - 2.23 (m, 1H), 1.96 - 1.88 (m, 1H), 1.45 (s, 3H), 1.42 (d, *J* = 3.2 Hz, 9H), 0.96 (d, *J* = 8.0 Hz, 2H), 0.90 (t, *J* = 8.0 Hz, 2H), 0.78 - 0.67 (m, 2H), -0.10 (s, 9H).

Step 9:



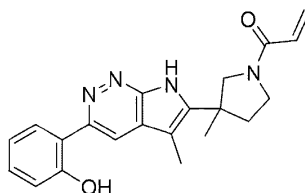
[0403] A solution of *tert*-butyl 3-(5-cyclopropyl-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-methylpyrrolidine-1-carboxylate (70.0 mg, 114.9 μmol , 1.0 *eq*) in TFA (1 mL), Et_3SiH (0.05 mL), and H_2O (0.05 mL) was stirred at 25 $^\circ\text{C}$ for 1 h. The reaction mixture was concentrated under reduced pressure to afford 2-(5-cyclopropyl-6-(3-methylpyrrolidin-3-yl)-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)phenol, which was used in the subsequent step without purification. m/z (ESI^+): 335.1 ($\text{M}+\text{H}^+$).

Step 10:

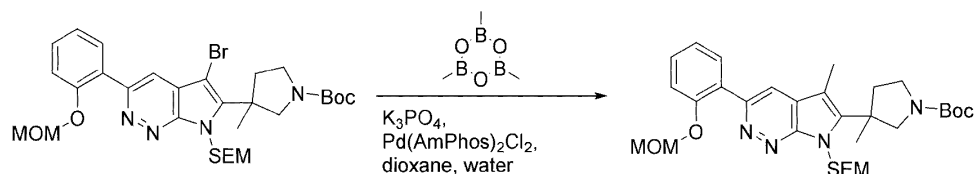


[0404] To a solution of 2-(5-cyclopropyl-6-(3-methylpyrrolidin-3-yl)-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)phenol (60.0 mg, 106.7 μmol , 1.0 *eq*, 2·TFA salt) in DCM (1 mL) and saturated NaHCO_3 aqueous solution (1 mL) was added prop-2-enoyl prop-2-enoate (13.5 mg, 106.7 μmol , 1.0 *eq*) dropwise at 25 $^\circ\text{C}$. The mixture was stirred at the same temperature for 30 minutes. The reaction mixture was partitioned between dichloromethane (5 mL) and H_2O (5 mL). The organic phase was separated, washed with brine (5 mL), dried over Na_2SO_4 , and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by prep-TLC (SiO_2 , 30% ethyl acetate in dichloromethane) to give 1-{3-[3-cyclopropyl-5-(*o*-hydroxyphenyl)-1*H*-1,6,7-triazainden-2-yl]-3-methyl-1-pyrrolidinyl}-2-propen-1-one. ^1H NMR (400 MHz, $\text{METHANOL-}d_4$) δ 8.43 (s, 1H), 7.93 (d, $J = 8.0$ Hz, 1H), 7.33 - 7.25 (m, 1H), 7.02 - 6.95 (m, 2H), 6.75 - 6.62 (m, 1H), 6.33 (dd, $J = 1.6, 16.8$ Hz, 1H), 5.80 (ddd, $J = 1.6, 8.0, 10.4$ Hz, 1H), 4.32 - 4.05 (m, 2H), 3.87 (dd, $J = 6.4, 10.0$ Hz, 1H), 3.78 - 3.68 (m, 1H), 2.69 - 2.59 (m, 1H), 2.58 - 2.51 (m, 1H), 1.99 - 1.90 (m, 1H), 1.56 (d, $J = 4.0$ Hz, 3H), 1.19 - 1.13 (m, 2H), 0.87 - 0.80 (m, 2H).

Example 5: Synthesis of 1-{3-[5-(*o*-hydroxyphenyl)-3-methyl-1*H*-1,6,7-triazainden-2-yl]-3-methyl-1-pyrrolidinyl}-2-propen-1-one (Compound 32):

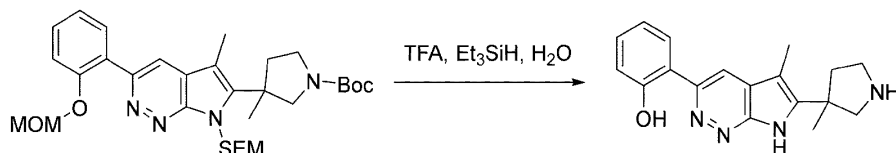


Step 1:



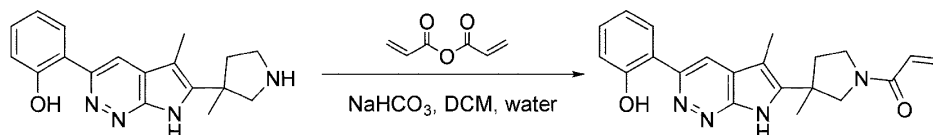
[0405] A mixture of *tert*-butyl 3-(5-bromo-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-methylpyrrolidine-1-carboxylate (200.0 mg, 308.8 μ mol, 1.0 *eq*), 2,4,6-trimethyl-1,3,5,2,4,6-trioxatriborinane (77.5 mg, 617.6 μ mol, 86.3 μ L, 2.0 *eq*), K_3PO_4 (131.1 mg, 617.6 μ mol, 2.0 *eq*), and bis(4-(di-*tert*-butylphosphanyl)-*N,N*-dimethylaniline)-palladium chloride (32.8 mg, 46.3 μ mol, 32.8 μ L, 0.15 *eq*) in dioxane (4 mL) and H_2O (2 mL) was degassed and purged with N_2 . The mixture was heated to 60 $^{\circ}C$ and stirred for 2 h under a N_2 atmosphere. The reaction mixture was partitioned between ethyl acetate (10 mL) and H_2O (10 mL). The organic phase was separated, washed with brine (10 mL), dried over Na_2SO_4 , and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by prep-HPLC to give *tert*-butyl 3-(3-(2-(methoxymethoxy)phenyl)-5-methyl-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-methylpyrrolidine-1-carboxylate. 1H NMR (400 MHz, $DMSO-d_6$) δ 8.21 (s, 1H), 7.55 (dd, J = 1.6, 7.6 Hz, 1H), 7.47 - 7.40 (m, 1H), 7.28 (d, J = 8.0 Hz, 1H), 7.15 (t, J = 7.2 Hz, 1H), 6.10 (s, 2H), 5.24 (s, 2H), 3.82 (t, J = 8.0 Hz, 2H), 3.54 (dd, J = 10.8, 16.4 Hz, 1H), 3.44 - 3.36 (m, 3H), 3.33 (s, 3H), 2.47 - 2.40 (m, 1H), 2.36 (s, 3H), 2.20 - 2.13 (m, 1H), 1.41 (d, J = 6.8 Hz, 12H), 0.92 - 0.88 (m, 2H), -0.11 (d, J = 2.4 Hz, 9H).

Step 2:



[0406] A solution of *tert*-butyl 3-(3-(2-(methoxymethoxy)phenyl)-5-methyl-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-methylpyrrolidine-1-carboxylate (57.0 mg, 97.8 μ mol, 1.0 *eq*) in TFA (1 mL), Et_3SiH (0.05 mL), and H_2O (0.05 mL) was stirred at 25 $^{\circ}C$ for 1 h. The reaction mixture was concentrated under reduced pressure to afford 2-(5-methyl-6-(3-methylpyrrolidin-3-yl)-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)phenol, which was used in the subsequent step without purification. m/z (ESI $^{+}$): 309.1 (M+H) $^{+}$.

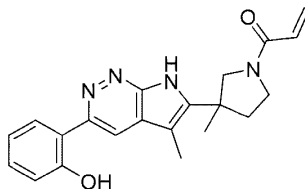
Step 3:



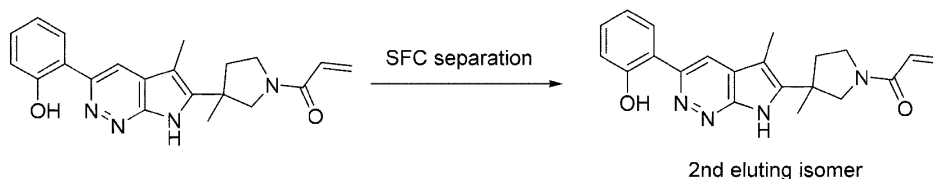
[0407] To a solution of 2-(5-methyl-6-(3-methylpyrrolidin-3-yl)-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)phenol (50.0 mg, 93.2 μ mol, 1.0 *eq*, 2 $\cdot$ TFA salt) in DCM (1 mL) and saturated aqueous $NaHCO_3$ solution (1

mL) was added prop-2-enoyl prop-2-enoate (11.7 mg, 93.2 μmol , 1.0 *eq*) dropwise at 25 °C. The mixture was stirred at 25 °C for 30 minutes. The reaction mixture was partitioned between dichloromethane (5 mL) and H₂O (5 mL). The organic phase was separated, washed with brine (5 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by prep-TLC (SiO₂, 30% ethyl acetate in dichloromethane) to give 1-{3-[5-(*o*-hydroxyphenyl)-3-methyl-1*H*-1,6,7-triazainden-2-yl]-3-methyl-1-pyrrolidinyl}-2-propen-1-one. ¹H NMR (400 MHz, METHANOL-*d*₄) δ 8.44 (s, 1H), 7.99 (dd, *J* = 1.6, 8.4 Hz, 1H), 7.28 (dt, *J* = 1.6, 7.2 Hz, 1H), 7.01 - 6.95 (m, 2H), 6.74 - 6.63 (m, 1H), 6.33 (dd, *J* = 1.6, 17.6 Hz, 1H), 5.80 (ddd, *J* = 2.0, 6.4, 10.4 Hz, 1H), 4.16 - 4.05 (m, 1H), 3.93 - 3.84 (m, 2H), 3.78 - 3.67 (m, 1H), 2.62 - 2.49 (m, 2H), 2.45 (d, *J* = 1.6 Hz, 3H), 1.54 (d, *J* = 3.6 Hz, 3H).

Example 6: Synthesis of 1-{3-[5-(*o*-hydroxyphenyl)-3-methyl-1*H*-1,6,7-triazainden-2-yl]-3-methyl-1-pyrrolidinyl}-2-propen-1-one (Compound 19):

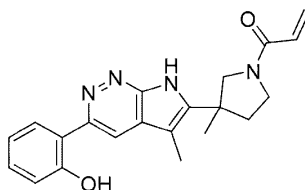


Step 1:

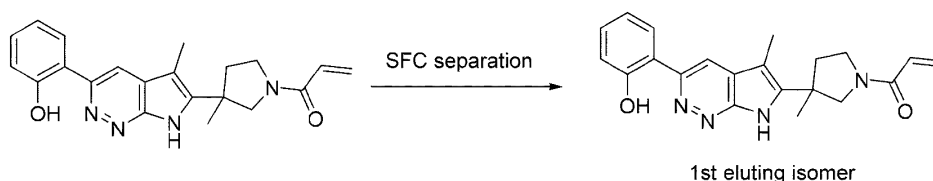


[0408] 1-{3-[5-(*o*-hydroxyphenyl)-3-methyl-1*H*-1,6,7-triazainden-2-yl]-3-methyl-1-pyrrolidinyl}-2-propen-1-one was separated by SFC (Column: DAICEL CHIRALCEL OJ (250mm $\times$ 30mm $\times$ 10 μm); mobile phase: [CO₂-MeOH(0.1%NH₃H₂O)]; B%: 45%, isocratic elution mode) to give 1-{3-[5-(*o*-hydroxyphenyl)-3-methyl-1*H*-1,6,7-triazainden-2-yl]-3-methyl-1-pyrrolidinyl}-2-propen-1-one (2nd eluting isomer). ¹H NMR (400 MHz, METHANOL-*d*₄) δ 8.43 (s, 1H), 8.01 (d, *J* = 8.4 Hz, 1H), 7.32 - 7.23 (m, 1H), 7.01 - 6.94 (m, 2H), 6.76 - 6.59 (m, 1H), 6.33 (td, *J* = 0.8, 16.8 Hz, 1H), 5.80 (ddd, *J* = 2.0, 6.4, 10.4 Hz, 1H), 4.18 - 4.05 (m, 1H), 3.92 - 3.84 (m, 2H), 3.80 - 3.66 (m, 1H), 2.65 - 2.47 (m, 2H), 2.45 (d, *J* = 2.0 Hz, 3H), 1.54 (d, *J* = 3.6 Hz, 3H).

Example 7: Synthesis of 1-{3-[5-(*o*-hydroxyphenyl)-3-methyl-1*H*-1,6,7-triazainden-2-yl]-3-methyl-1-pyrrolidinyl}-2-propen-1-one (Compound 20):

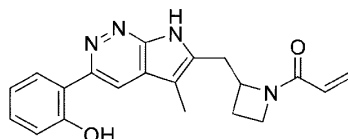


Step 1:

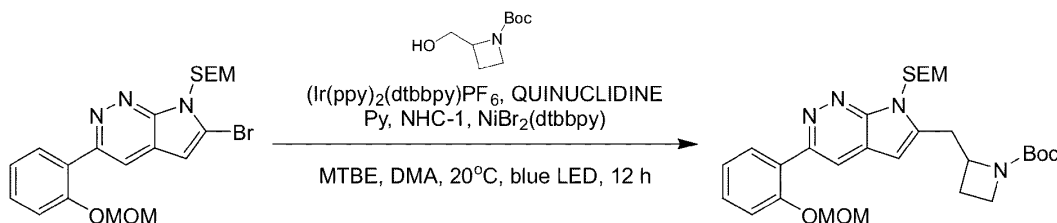


[0409] 1-{3-[5-(*o*-hydroxyphenyl)-3-methyl-1*H*-1,6,7-triazainden-2-yl]-3-methyl-1-pyrrolidinyl}-2-propen-1-one was separated by SFC (Column: DAICEL CHIRALCEL OJ (250mm × 30mm × 10μm); mobile phase: [CO₂-MeOH(0.1%NH₃H₂O)]; B%: 45%, isocratic elution mode) to give 1-{3-[5-(*o*-hydroxyphenyl)-3-methyl-1*H*-1,6,7-triazainden-2-yl]-3-methyl-1-pyrrolidinyl}-2-propen-1-one (1st eluting isomer). ¹H NMR (400 MHz, METHANOL-*d*₄) δ 8.44 (s, 1H), 8.01 (d, *J* = 8.0 Hz, 1H), 7.33 - 7.24 (m, 1H), 7.01 - 6.95 (m, 2H), 6.75 - 6.61 (m, 1H), 6.36 - 6.29 (m, 1H), 5.80 (ddd, *J* = 2.0, 6.4, 10.4 Hz, 1H), 4.18 - 4.04 (m, 1.5H), 3.92 - 3.85 (m, 1.5H), 3.79 - 3.66 (m, 1H), 2.67 - 2.47 (m, 2H), 2.45 (d, *J* = 2.4 Hz, 3H), 1.54 (d, *J* = 4.0 Hz, 3H).

Example 8: 1-(2-((3-(2-hydroxyphenyl)-5-methyl-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)methyl)azetidin-1-yl)prop-2-en-1-one (Compound 295)



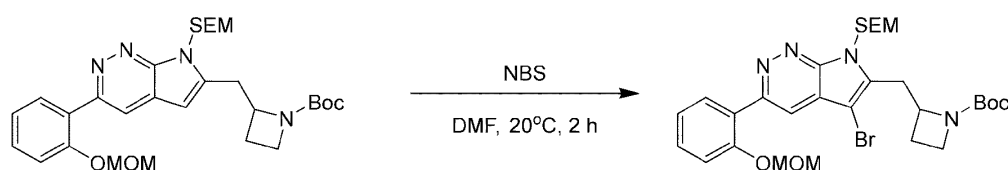
Step 1:



[0410] To a solution of tert-butyl 2-(hydroxymethyl)azetidine-1-carboxylate (241.89 mg, 1.29 mmol, 2 eq) in MTBE (6 mL) was added 5,7-di-*tert*-butyl-3-phenylbenzo[d]oxazol-3-ium tetrafluoroborate (459.56 mg, 1.16 mmol, 1.8 eq) in one portion. The resulting mixture was stirred at 20 °C for 5 min. Subsequently, a solution of pyridine (91.97 mg, 1.16 mmol, 93.85 μL, 1.8 eq) in MTBE (1.5 mL) was added dropwise to the reaction mixture, which was then stirred at 20 °C for 15 min. The mixture was filtered, and the filtrate was added to a solution of **intermediate 1** (300 mg, 645.96 μmol, 1 eq), quinuclidine (143.65 mg, 1.29 mmol, 2 eq), NiBr₂(dtbbpy) (31.45 mg, 64.60 μmol, 0.1 eq), and Ir(ppy)₂(dtbbpy)PF₆ (29.52 mg, 32.30 μmol, 0.05 eq) in DMA (6 mL). The resulting mixture was purged 3 times with N₂ and stirred at 20 °C for 12 h under 34W blue LED (455 nm). An additional five reactions were set up as described above; all six reactions were combined for workup and purification. The combined reaction mixtures were partitioned between ethyl acetate (20 mL) and H₂O (20 mL). The organic phase was separated, washed with brine (20 mL), dried over Na₂SO₄, and filtered. The filtrate

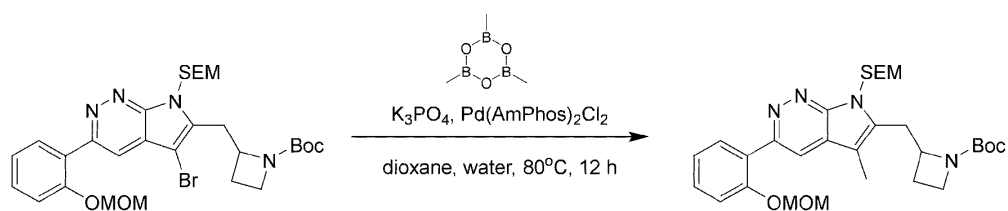
was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO₂, Petroleum ether: Ethyl acetate = 2: 1) to give *tert*-butyl 2-((3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)methyl)azetidine-1-carboxylate (2 g, 3.14 mmol, 80.93% yield) as a white solid. ¹H NMR (400 MHz, METHANOL-*d*₄) δ 8.06 (s, 1H), 7.63 - 7.59 (m, 1H), 7.45 - 7.39 (m, 1H), 7.31 (d, *J* = 7.6 Hz, 1H), 7.19 - 7.14 (m, 1H), 6.53 (s, 1H), 5.93 (s, 2H), 5.19 (s, 2H), 4.76 - 4.67 (m, 1H), 3.93 - 3.80 (m, 2H), 3.68 - 3.59 (m, 3H), 3.40 - 3.35 (m, 1H), 3.33 (s, 3H), 2.48 - 2.36 (m, 1H), 2.14 - 2.04 (m, 1H), 1.45 - 1.41 (m, 9H), 0.94 - 0.89 (m, 2H), -0.07 (s, 9H).

Step 2:



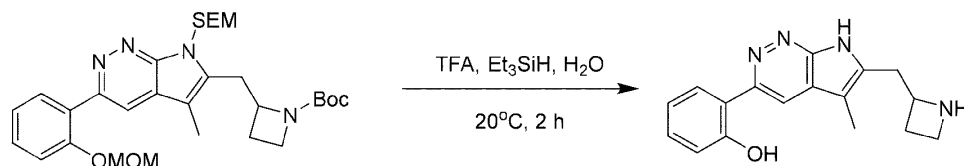
[0411] To a solution of *tert*-butyl 2-((3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)methyl)azetidine-1-carboxylate (700 mg, 1.26 mmol, 1 eq) in DMF (10 mL) was added NBS (235.81 mg, 1.32 mmol, 1.05 eq) at 20 °C. The resulting mixture was stirred at the same temperature for 2 h. An additional reaction was set up as described above; both reactions were combined for workup and purification. The combined reaction mixtures were diluted with water (20 mL) and extracted with ethyl acetate (10 mL × 2). The combined organic layers were washed with brine (10 mL × 2), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure to give *tert*-butyl 2-((5-bromo-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)methyl)azetidine-1-carboxylate (1.8 g, 93.80% yield) as a yellow oil, which was used in the subsequent step without purification. ¹H NMR (400 MHz, METHANOL-*d*₄) δ = 8.01 (s, 1H), 7.68 - 7.64 (m, 1H), 7.48 - 7.41 (m, 1H), 7.32 (d, *J* = 8.4 Hz, 1H), 7.18 (t, *J* = 7.6 Hz, 1H), 6.03 - 5.93 (m, 2H), 5.22 (s, 2H), 4.79 - 4.71 (m, 1H), 3.93 - 3.84 (m, 2H), 3.70 - 3.66 (m, 2H), 3.65 - 3.60 (m, 1H), 3.47 - 3.41 (m, 1H), 3.37 (s, 3H), 2.47 - 2.36 (m, 1H), 2.24 - 2.12 (m, 1H), 1.31 - 1.22 (m, 9H), 0.96 - 0.91 (m, 2H), -0.06 (s, 9H).

Step 3:

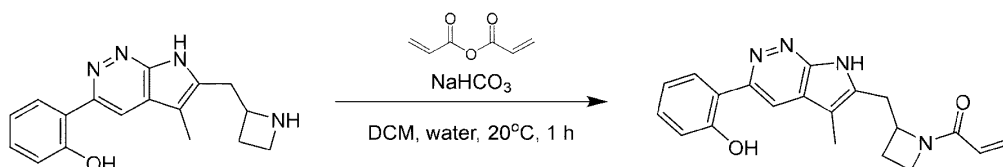


[0412] A mixture of *tert*-butyl 2-((5-bromo-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)methyl)azetidine-1-carboxylate (250 mg, 394.54 μmol, 1 eq), 2,4,6-trimethyl-1,3,5,2,4,6-trioxatrimborinane (148.59 mg, 1.18 mmol, 165.46 μL, 3 eq), tripotassium phosphate (251.24 mg, 1.18 mmol, 3 eq), and bis(4-(di-*tert*-butylphosphanyl)-*N,N*-dimethylaniline)-palladium chloride (41.90 mg, 59.18 μmol, 41.90 μL, 0.15 eq) in dioxane (5 mL) and

water (2.5 mL) was degassed and purged 3-times with N₂. The mixture was then heated to 80 °C and stirred for 12 h under N₂ atmosphere. An additional reaction was set up as described above; both reactions were combined for workup and purification. The combined reaction mixtures were diluted with water (10 mL) and extracted with ethyl acetate (10 mL × 2). The combined organic layers were washed with brine (10 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO₂, petroleum ether: ethyl acetate = 10: 1 to 1: 1) to give *tert*-butyl 2-((3-(2-(methoxymethoxy)phenyl)-5-methyl-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)azetidine-1-carboxylate (460 mg) as a yellow oil. ¹H NMR (400 MHz, METHANOL-*d*₄) δ 8.02 (s, 1H), 7.60 (d, *J* = 7.6 Hz, 1H), 7.46 - 7.38 (m, 1H), 7.30 (d, *J* = 8.0 Hz, 1H), 7.16 (t, *J* = 7.6 Hz, 1H), 5.96 - 5.80 (m, 2H), 5.22 - 5.16 (m, 2H), 4.72 - 4.61 (m, 1H), 4.32 - 4.23 (m, 0.5H), 4.15 - 4.05 (m, 0.5H), 3.85 (t, *J* = 7.6 Hz, 2H), 3.66 - 3.58 (m, 3H), 3.35 - 3.33 (m, 3H), 2.36 (s, 3H), 2.26 - 2.13 (m, 1H), 2.10 - 2.03 (m, 1H), 1.33 - 1.24 (m, 9H), 0.94 - 0.88 (m, 2H), -0.07 (s, 9H).

Step 4:

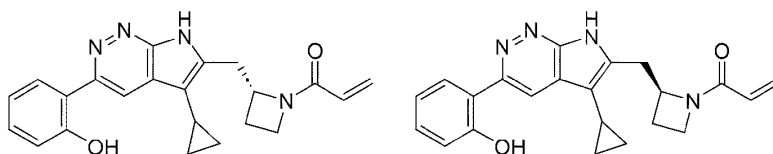
[0413] A mixture of *tert*-butyl 2-((3-(2-(methoxymethoxy)phenyl)-5-methyl-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)azetidine-1-carboxylate (130 mg, 228.56 μmol, 1 eq) in TFA (3.07 g, 26.92 mmol, 2 mL, 117.80 eq), Et₃SiH (0.1 mL), and water (0.1 mL) was stirred at 20 °C for 2 h under N₂ atmosphere. The reaction mixture was concentrated under reduced pressure to give 2-(6-(azetidin-2-ylmethyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-3-yl)phenol (65 mg, 220.83 μmol, 96.62% yield) as a yellow oil, which was used in the subsequent step without purification. LCMS (ESI⁺): *m/z* 295.1 (M+H)⁺.

Step 5:

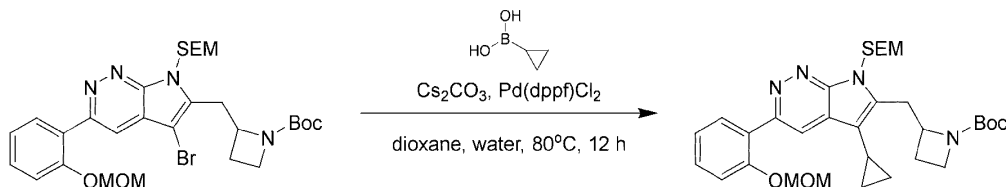
[0414] To a solution of 2-(6-(azetidin-2-ylmethyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-3-yl)phenol (65 mg, 220.83 μmol, 1 eq) in NaHCO₃ aq. (1N, 1 mL) and DCM (1 mL) was added acrylic anhydride (27.85 mg, 220.83 μmol, 1 eq) in DCM (0.3 mL) dropwise at 20 °C. The resulting mixture was stirred at the same temperature for 1 h. The reaction mixture was diluted with water (5 mL) and extracted with DCM (5 mL × 2). The combined organic layers were washed with brine (5 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by prep-TLC (SiO₂, DCM: THF = 2: 1) to give 1-(2-((3-(2-(2-acryloyloxyethyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)azetidin-2-yl)-6-hydroxyphenyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)azetidine-1-carboxylate.

yl)methyl)azetidin-1-yl)prop-2-en-1-one (45 mg, 23.40% yield) as a white solid. ^1H NMR (400 MHz, $\text{Me}_2\text{SO}-d_6$) δ 8.43 - 8.38 (m, 1H), 8.01 - 7.97 (m, 1H), 7.31 - 7.25 (m, 1H), 7.01 - 6.94 (m, 2H), 6.38 - 6.22 (m, 1.4H), 6.16 - 6.08 (m, 0.3H), 6.02 - 5.93 (m, 0.3H), 5.79 - 5.73 (m, 0.7H), 5.39 (d, $J = 9.6$ Hz, 0.3H), 4.95 - 4.90 (m, 0.3H), 4.83 - 4.77 (m, 0.7H), 4.18 (t, $J = 8.0$ Hz, 1.4H), 4.07 - 3.98 (m, 0.6H), 3.59 - 3.42 (m, 1H), 3.42 - 3.34 (m, 1H), 2.64 - 2.41 (m, 1H), 2.37 - 2.34 (m, 3H), 2.22 - 2.01 (m, 1H); LCMS (ESI^+): m/z 349.1 ($\text{M}+\text{H}$) $^+$.

Example 9: Synthesis of (S)-1-(2-((5-cyclopropyl-3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)azetidin-1-yl)prop-2-en-1-one and (R)-1-(2-((5-cyclopropyl-3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)azetidin-1-yl)prop-2-en-1-one (Compounds 296 and 297)

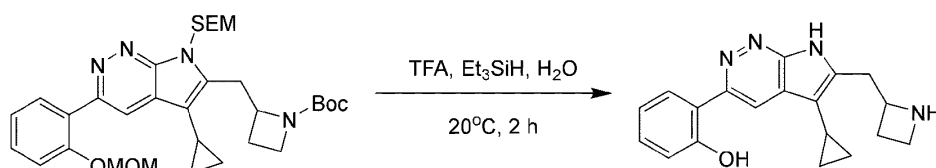


Step 1:



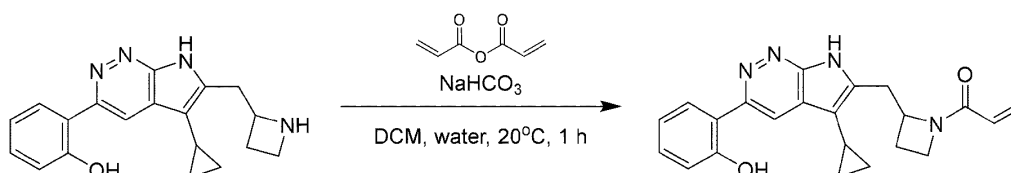
[0415] A mixture of *tert*-butyl 2-((5-bromo-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)azetidine-1-carboxylate (250 mg, 394.54 μmol , 1 eq), cyclopropylboronic acid (677.80 mg, 7.89 mmol, 20 eq), $\text{Pd}(\text{dppf})\text{Cl}_2$ (32.22 mg, 39.45 μmol , 0.1 eq) and Cs_2CO_3 (1.29 g, 3.95 mmol, 10 eq) in dioxane (5 mL) and water (2.5 mL) was degassed and purged 3 times with N_2 . The mixture was then heated to 80°C and stirred for 12 h under N_2 atmosphere. An additional reaction was set up as described above; both reactions were combined for workup and purification. The combined reaction mixtures were diluted with water (10 mL) and extracted with ethyl acetate (10 mL $\times$ 2). The combined organic layers were washed with brine (5 mL), dried over Na_2SO_4 , and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO_2 , petroleum ether/ethyl acetate = 10/1 to 2/1) to give *tert*-butyl 2-((5-cyclopropyl-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)azetidine-1-carboxylate (390 mg, 83.09% yield) as a yellow oil. ^1H NMR (400 MHz, $\text{Me}_2\text{SO}-d_6$) δ 8.08 (s, 1H), 7.65 - 7.62 (m, 1H), 7.45 - 7.40 (m, 1H), 7.32 - 7.28 (m, 1H), 7.19 - 7.14 (m, 1H), 5.94 - 5.89 (m, 2H), 5.21 - 5.19 (m, 2H), 4.77 - 4.72 (m, 1H), 3.87 (t, $J = 7.6$ Hz, 2H), 3.65 - 3.61 (m, 3H), 3.38 - 3.35 (m, 3H), 2.47 - 2.38 (m, 1H), 2.24 - 2.10 (m, 2H), 1.99 - 1.89 (m, 1H), 1.33 - 1.25 (m, 9H), 1.08 - 1.02 (m, 2H), 0.92 - 0.87 (m, 2H), 0.85 - 0.76 (m, 2H), -0.07 (s, 9H).

Step 2:



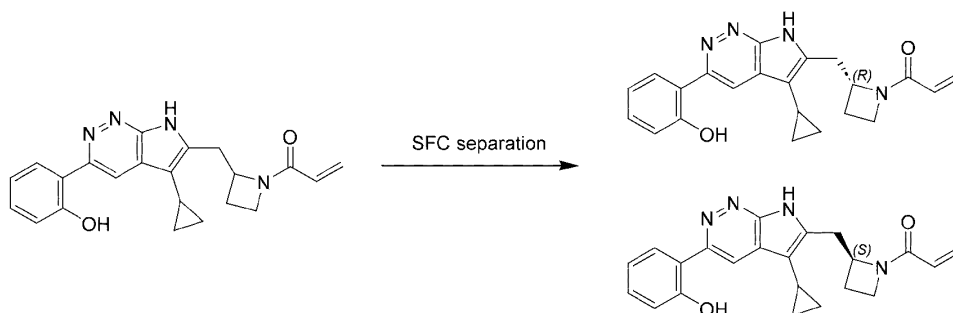
[0416] A mixture of *tert*-butyl 2-((5-cyclopropyl-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)methyl)azetidine-1-carboxylate (200 mg, 336.24 μ mol, 1 eq), TFA (6.14 g, 53.85 mmol, 4 mL, 160.15 eq), Et₃SiH (0.2 mL), and water (0.2 mL) was stirred at 20 °C for 2 h under N₂ atmosphere. The reaction mixture was concentrated under reduced pressure to give 2-(6-(azetidin-2-ylmethyl)-5-cyclopropyl-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)phenol (100 mg, 92.83% yield) as a yellow oil, which was used in the subsequent step without purification. LCMS (ESI⁺): *m/z* 321.1 (M+H).

Step 3:



[0417] To a solution of 2-(6-(azetidin-2-ylmethyl)-5-cyclopropyl-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)phenol (50 mg, 156.06 μ mol, 1 eq) in NaHCO₃ aq. (1N, 1 mL) and DCM (1 mL) was added acrylic anhydride (19.68 mg, 156.06 μ mol, 1 eq) in DCM (0.1 mL) dropwise at 20 °C. The resulting mixture was stirred at the same temperature for 1 h. An additional reaction was set up as described above; both reactions were combined for workup and purification. The combined reaction mixtures were diluted with water (5 mL) and extracted with DCM (5 mL $\times$ 2). The combined organic layers were washed with brine (5 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by prep-TLC (SiO₂, petroleum ether/ethyl acetate = 0/1) to give 1-(2-((5-cyclopropyl-3-(2-hydroxyphenyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)methyl)azetidin-1-yl)prop-2-en-1-one (21 mg, 17.97% yield) as a white solid. ¹H NMR (400 MHz, METHANOL-*d*₄) δ 8.39 - 8.33 (m, 1H), 7.94 (d, *J* = 8.4 Hz, 1H), 7.32 - 7.25 (m, 1H), 7.02 - 6.95 (m, 2H), 6.34 - 6.28 (m, 1H), 6.18 - 5.98 (m, 1H), 5.78 - 5.73 (m, 0.5H), 5.52 - 5.39 (m, 0.5H), 5.03 - 4.94 (m, 0.5H), 4.77 (s, 0.5H), 4.60 (s, 0.5H), 4.26 - 4.18 (m, 1H), 4.06 - 4.00 (m, 0.5H), 3.72 - 3.63 (m, 0.5H), 3.61 - 3.53 (m, 0.5H), 3.49 - 3.40 (m, 1H), 2.66 - 2.45 (m, 1H), 2.24 - 2.12 (m, 1H), 1.92 - 1.83 (m, 1H), 1.10 - 1.03 (m, 2H), 0.83 - 0.75 (m, 2H); LCMS (ESI⁺): *m/z* 375.1 (M+H)⁺.

Step 4:

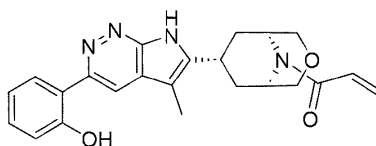


[0418] 1-(2-((5-cyclopropyl-3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)azetidin-1-yl)prop-2-en-1-one (38 mg) was separated by SFC (column: DAICEL CHIRALCEL OJ(250mm*30mm, 10um); mobile phase: [CO₂-EtOH]; B%:40%, isocratic elution mode) to give (S)-1-(2-((5-cyclopropyl-3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)azetidin-1-yl)prop-2-en-1-one and (R)-1-(2-((5-cyclopropyl-3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)azetidin-1-yl)prop-2-en-1-one.

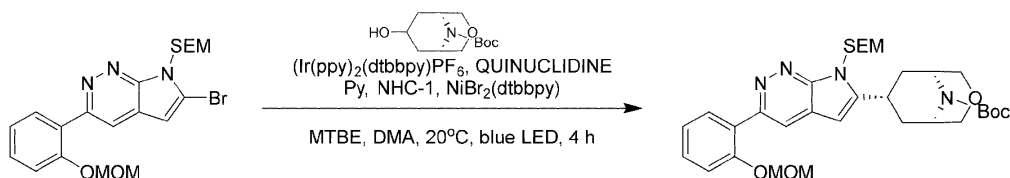
[0419] Compound 296 (1st eluting isomer, 9 mg, 23.68% yield) was obtained as a white solid. ¹H NMR (400 MHz, METHANOL-*d*₄) δ 8.40 - 8.34 (m, 1H), 7.98 - 7.91 (m, 1H), 7.28 (t, *J* = 7.2 Hz, 1H), 7.02 - 6.95 (m, 2H), 6.38 - 6.22 (m, 1.4H), 6.18 - 5.97 (m, 0.6H), 5.79 - 5.72 (m, 0.6H), 5.41 (d, *J* = 8.8 Hz, 0.4H), 4.29 - 4.16 (m, 1.3H), 4.09 - 3.98 (m, 0.7H), 3.72 - 3.64 (m, 0.6H), 3.61 - 3.54 (m, 0.4H), 3.50 - 3.40 (m, 1.4H), 3.35 (s, 0.6H), 2.67 - 2.45 (m, 1H), 2.26 - 2.09 (m, 1H), 1.96 - 1.81 (m, 1H), 1.11 - 1.02 (m, 2H), 0.84 - 0.75 (m, 2H); LCMS (ESI⁺): *m/z* 375.1 (M+H)⁺.

[0420] Compound 297 (2nd eluting isomer, 6 mg, 15.79% yield) was obtained as a white solid. ¹H NMR (400 MHz, METHANOL-*d*₄) δ 8.39 - 8.35 (m, 1H), 7.94 (d, *J* = 8.4 Hz, 1H), 7.29 (t, *J* = 7.6 Hz, 1H), 7.02 - 6.95 (m, 2H), 6.39 - 6.23 (m, 1.3H), 6.16 - 5.98 (m, 0.7H), 5.79 - 5.73 (m, 0.6H), 5.44 - 5.38 (m, 0.4H), 4.26 - 4.18 (m, 1.3H), 4.10 - 3.98 (m, 1H), 3.73 - 3.64 (m, 0.7H), 3.63 - 3.52 (m, 0.5H), 3.50 - 3.45 (m, 1H), 3.43 (d, *J* = 7.6 Hz, 0.5H), 2.67 - 2.45 (m, 1H), 2.25 - 2.10 (m, 1H), 1.95 - 1.83 (m, 1H), 1.10 - 1.04 (m, 2H), 0.84 - 0.72 (m, 2H); LCMS (ESI⁺): *m/z* 375.1 (M+H)⁺.

Example 10: 1-((1R,5S,7r)-7-(3-(2-hydroxyphenyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one (Compound 312)

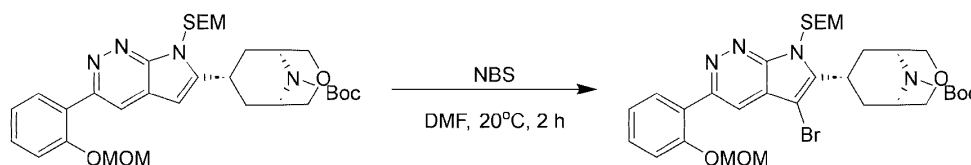


Step 1:



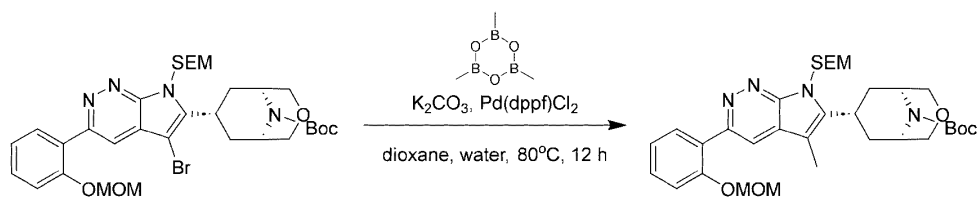
[0421] To a solution of *tert*-butyl (1*R*,5*S*)-7-hydroxy-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (1.89 g, 7.75 mmol, 2 eq) in MTBE (12 mL) was added NHC-1 (2.76 g, 6.98 mmol, 1.8 eq) in one portion at 20 °C. After addition, the mixture was stirred at the same temperature for 5 min. Subsequently, a solution of pyridine (551.83 mg, 6.98 mmol, 1.8 eq) in MTBE (2 mL) was added dropwise at 20 °C. The resulting mixture was stirred at the same temperature for 15 min, then filtered to remove the formed precipitate. A solution of **intermediate 1** (1.8 g, 3.88 mmol, 1 eq), quinuclidine (861.85 mg, 7.75 mmol, 2 eq), NiBr₂(dtbbpy) (188.71 mg, 387.57 μmol, 0.1 eq) and (Ir(ppy)₂(dtbbpy)PF₆) (177.11 mg, 193.79 μmol, 0.05 eq) in DMA (12 mL) was prepared, then mixed with the filtrate obtained. The resulting mixture was stirred at 20 °C for 4 h under 34W blue LED (455 nm). The reaction mixture was diluted with water (20 mL) and extracted with MTBE (20 mL × 2). The combined organic layers were washed with brine (20 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO₂, petroleum ether: ethyl acetate = 10: 1 to 2: 1) to give *tert*-butyl (1*R*,5*S*,7*r*)-7-(3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (1.9 g, 3.11 mmol, 80.26% yield) as a white solid. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.13 (s, 1H), 7.85 - 7.74 (m, 1H), 7.57 - 7.47 (m, 1H), 7.41 - 7.33 (m, 1H), 7.28 - 7.21 (m, 1H), 6.61 (s, 1H), 5.97 (s, 2H), 5.37 - 5.25 (m, 2H), 4.62 - 4.48 (m, 1H), 4.14 - 4.04 (m, 4H), 3.80 (br d, *J* = 11.6 Hz, 2H), 3.73 - 3.64 (m, 2H), 3.42 (s, 3H), 2.38 - 2.23 (m, 2H), 2.04 - 1.93 (m, 2H), 1.50 (s, 9H), 0.97 - 0.89 (m, 2H), 0.00 (s, 9H).

Step 2:



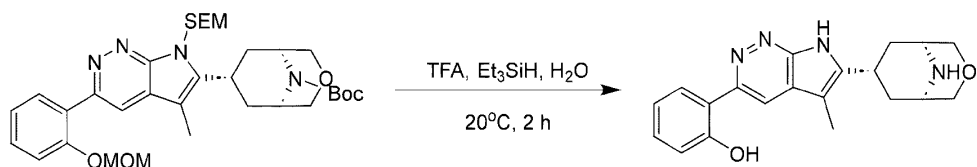
[0422] To a solution of *tert*-butyl (1*R*,5*S*,7*r*)-7-(3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (200 mg, 327.43 μmol, 1 eq) in DMF (2 mL) was added NBS (64.11 mg, 360.17 μmol, 1.1 eq) in one portion at 20 °C. The resulting mixture was stirred at 20 °C for 2 h. The reaction mixture was then quenched with ice water (10 mL), and the resulting precipitate was collected by vacuum filtration. The solid was washed with water and dried under high vacuum at 30 °C. *Tert*-butyl (1*R*,5*S*,7*r*)-7-(5-bromo-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (170 mg, 246.48 μmol, 75.28% yield) was obtained as a white solid, which was used in the next step without purification. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.05 (s, 1H), 7.85 - 7.74 (m, 1H), 7.57 - 7.47 (m, 1H), 7.40 - 7.31 (m, 1H), 7.28 - 7.18 (m, 1H), 6.02 (s, 2H), 5.31 (s, 2H), 4.81 - 4.67 (m, 1H), 4.14 - 4.04 (m, 4H), 3.79 (d, *J* = 11.6 Hz, 2H), 3.73 - 3.61 (m, 2H), 3.38 (s, 3H), 2.10 - 2.01 (m, 2H), 2.04 - 1.93 (m, 2H), 1.55 (s, 9H), 0.97 - 0.81 (m, 2H), 0.00 (s, 9H).

Step 3:



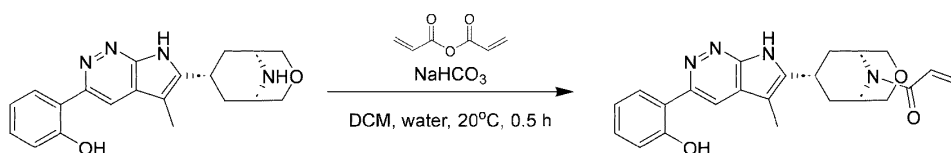
[0423] A mixture of *tert*-butyl (1*R*,5*S*,7*r*)-7-(5-bromo-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (150 mg, 217.48 μ mol, 1 eq), 2,4,6-trimethyl-1,3,5,2,4,6-trioxatriborinane (273.02 mg, 2.17 mmol, 304.03 μ L, 10 eq), Pd(dppf)Cl₂ (15.91 mg, 21.75 μ mol, 0.1 eq), and K₂CO₃ (90.17 mg, 652.45 μ mol, 3 eq) in dioxane (2 mL) and water (0.2 mL) was degassed and purged 3-times with N₂. The mixture was then heated to 80 °C and stirred for 12 h under N₂. The reaction mixture was diluted with water (5 mL) and extracted with EtOAc (5 mL $\times$ 2). The combined organic layers were washed with brine (5 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by prep-TLC (SiO₂, petroleum ether: ethyl acetate = 2: 1) to give *tert*-butyl (1*R*,5*S*,7*r*)-7-(3-(2-(methoxymethoxy)phenyl)-5-methyl-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (120 mg, 192.05 μ mol, 88.31% yield) as a white solid. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.09 (s, 1H), 7.81 - 7.71 (m, 1H), 7.55 - 7.43 (m, 1H), 7.39 - 7.31 (m, 1H), 7.23 (t, *J* = 7.6 Hz, 1H), 5.99 - 5.89 (m, 2H), 5.28 (s, 2H), 4.81 - 4.67 (m, 1H), 4.12 - 3.99 (m, 4H), 3.79 (d, *J* = 11.6 Hz, 2H), 3.73 - 3.61 (m, 2H), 3.38 (s, 3H), 2.38 (s, 3H), 2.33 - 2.24 (m, 2H), 2.13 - 1.92 (m, 2H), 1.55 (s, 9H), 1.01 - 0.89 (m, 2H), 0.00 (s, 9H).

Step 4:



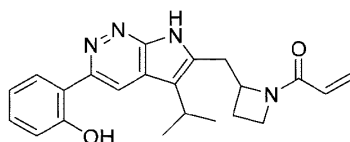
[0424] A solution of *tert*-butyl (1*R*,5*S*,7*r*)-7-(3-(2-(methoxymethoxy)phenyl)-5-methyl-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (50 mg, 80.02 μ mol, 1 eq) in TFA (1 mL), Et₃SiH (0.2 mL), and water (0.2 mL) was stirred at 20 °C for 2 h under N₂ atmosphere. The reaction mixture was concentrated under reduced pressure to give 2-(6-((1*R*,5*S*,7*r*)-3-oxa-9-azabicyclo[3.3.1]nonan-7-yl)-5-methyl-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)phenol (40 mg, 114.15 μ mol, 71.33% yield) as a yellow oil, which was used in the next step without purification. LCMS (ESI⁺): *m/z* 351.1 (M+H)⁺.

Step 5:

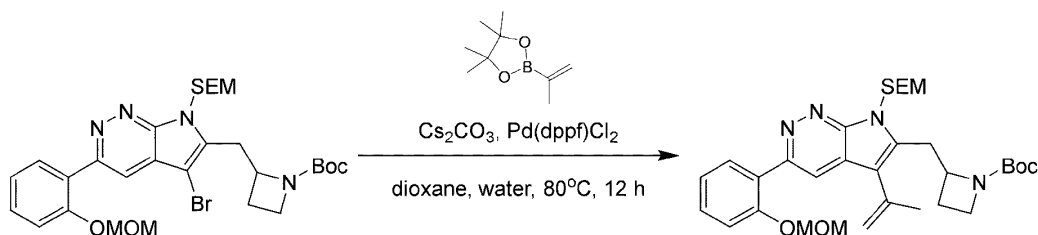


[0425] To a solution of 2-((1*R*,5*S*,7*r*)-3-oxa-9-azabicyclo[3.3.1]nonan-7-yl)-5-methyl-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)phenol (40 mg, 114.15 μ mol, 1 eq) in DCM (0.5 mL) and NaHCO₃ aq. (1*N*, 0.5 mL) was added acrylic anhydride (21.59 mg, 171.23 μ mol, 1.5 eq) at 20 °C. The resulting mixture was stirred at the same temperature for 0.5 h. The reaction mixture was diluted with water (1 mL) and extracted with DCM (1 mL $\times$ 2). The combined organic layers were washed with brine (1 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by prep-HPLC to give 1-((1*R*,5*S*,7*r*)-7-(3-(2-hydroxyphenyl)-5-methyl-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one (7.3 mg, 18.05 μ mol, 15.81% yield) as a white solid. ¹H NMR (400 MHz, DMSO-*d*₆) δ 14.38 (br s, 1H), 12.30 (s, 1H), 8.57 (s, 1H), 8.11 (dd, *J* = 1.2, 8.4 Hz, 1H), 7.30 - 7.25 (m, 1H), 6.97 - 6.92 (m, 2H), 6.89 - 6.81 (m, 1H), 6.25 (dd, *J* = 2.4, 16.8 Hz, 1H), 5.77 (dd, *J* = 2.4, 10.4 Hz, 1H), 4.57 (s, 1H), 4.53 - 4.41 (m, 1H), 4.301 (s, 1H), 4.05 (dd, *J* = 5.6, 11.2 Hz, 2H), 3.76 - 3.65 (m, 2H), 2.32 (s, 3H), 2.24 - 1.99 (m, 4H); LCMS (ESI⁺): *m/z* 405.1 (M+H)⁺.

Example 11: 1-(2-((3-(2-hydroxyphenyl)-5-isopropyl-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)methyl)azetidin-1-yl)prop-2-en-1-one (Compound 319)



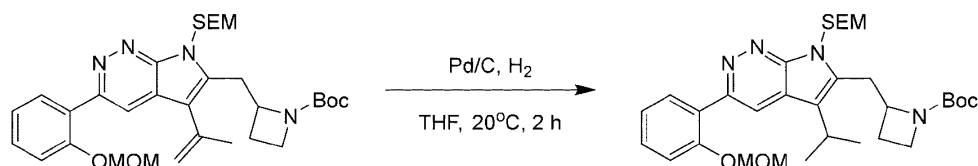
Step 1:



[0426] A mixture of *tert*-butyl 2-((5-bromo-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)methyl)azetidine-1-carboxylate (250 mg, 394.54 μ mol, 1 eq), 2-isopropenyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (99.45 mg, 591.81 μ mol, 1.5 eq), Pd(dppf)Cl₂ (28.87 mg, 39.45 μ mol, 0.1 eq), and Cs₂CO₃ (771.29 mg, 2.37 mmol, 6 eq) in dioxane (5 mL) and water (2.5 mL) was degassed and purged 3 times with N₂. The mixture was then heated to 80 °C and stirred for 12 h under N₂ atmosphere. An additional reaction was set up as described above; both reactions were combined for workup and purification. The combined reaction mixtures were diluted with water (10 mL) and extracted with ethyl acetate (10 mL $\times$ 2). The combined organic layers were washed with brine (10 mL $\times$ 2), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO₂, petroleum ether/ethyl acetate = 10/1 to 2/1) to give *tert*-butyl 2-((3-(2-(methoxymethoxy)phenyl)-5-(prop-1-en-2-yl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)methyl)azetidine-1-carboxylate (350 mg,

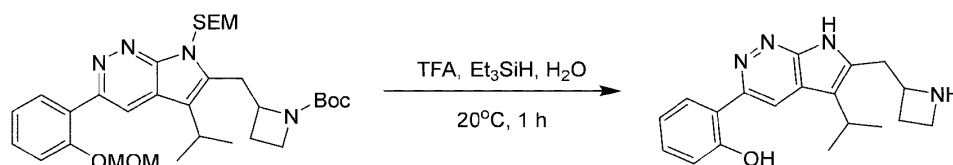
588.42 μmol , 74.57% yield) as a yellow oil. ^1H NMR (400 MHz, METHANOL- d_4) δ 8.06 (s, 1H), 7.66 - 7.63 (m, 1H), 7.45 - 7.39 (m, 1H), 7.29 (d, J = 7.6 Hz, 1H), 7.19 - 7.14 (m, 1H), 6.02 - 5.95 (m, 2H), 5.45 - 5.42 (m, 1H), 5.20 - 5.17 (m, 3H), 4.74 - 4.65 (m, 1H), 3.87 - 3.80 (m, 3H), 3.68 - 3.65 (m, 2H), 3.50 - 3.41 (m, 1H), 3.34 (s, 3H), 2.43 - 2.33 (m, 1H), 2.09 - 1.97 (m, 1H), 1.44 (s, 3H), 1.30 - 1.23 (m, 9H), 0.95 - 0.89 (m, 2H), -0.07 (s, 9H).

Step 2:



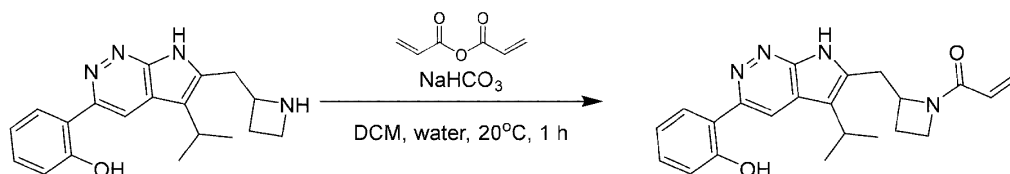
[0427] To a solution of *tert*-butyl 2-((3-(2-(methoxymethoxy)phenyl)-5-(prop-1-en-2-yl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)azetidine-1-carboxylate (350.00 mg, 588.42 μmol , 1 eq) in THF (4 mL) was added Pd/C (125.24 mg, 117.68 μmol , 10% purity, 0.2 eq) under N_2 atmosphere. The suspension was degassed and purged 3-times with H_2 . The mixture was stirred under H_2 (15 Psi) at 20 $^\circ\text{C}$ for 2 h. The mixture was filtered through a Celite pad, and the filtrate was concentrated under reduced pressure to give *tert*-butyl 2-((5-isopropyl-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)azetidine-1-carboxylate (320 mg, 91.12% yield) as a yellow oil. ^1H NMR (400 MHz, METHANOL- d_4) δ 8.21 (s, 1H), 7.68 - 7.63 (m, 1H), 7.46 - 7.40 (m, 1H), 7.30 (d, J = 8.0 Hz, 1H), 7.18 (t, J = 7.6 Hz, 1H), 5.98 - 5.86 (m, 2H), 5.20 (s, 2H), 4.66 - 4.59 (m, 1H), 3.88 - 3.78 (m, 3H), 3.67 - 3.61 (m, 2H), 3.57 - 3.50 (m, 1H), 3.41 (d, J = 6.4 Hz, 1H), 3.36 (s, 3H), 2.44 - 2.35 (m, 1H), 2.11 - 2.02 (m, 1H), 1.45 (d, J = 1.6 Hz, 3H), 1.44 (s, 3H), 1.29 (s, 9H), 0.90 - 0.86 (m, 2H), -0.09 (s, 9H).

Step 3:



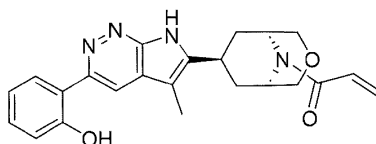
[0428] A solution of *tert*-butyl 2-((5-isopropyl-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)azetidine-1-carboxylate (205 mg, 343.48 μmol , 1 eq) in TFA (3.07 g, 26.92 mmol, 2 mL, 78.39 eq), Et_3SiH (1 mL), and water (1 mL) was stirred at 20 $^\circ\text{C}$ for 1 h under N_2 atmosphere. The reaction mixture was concentrated under reduced pressure to give 2-(6-(azetidin-2-ylmethyl)-5-isopropyl-7H-pyrrolo[2,3-c]pyridazin-3-yl)phenol (110 mg, 99.33% yield) as a yellow oil, which was used in the subsequent step without purification. LCMS (ESI $^+$): m/z 323.1 ($\text{M}+\text{H}$) $^+$.

Step 4:

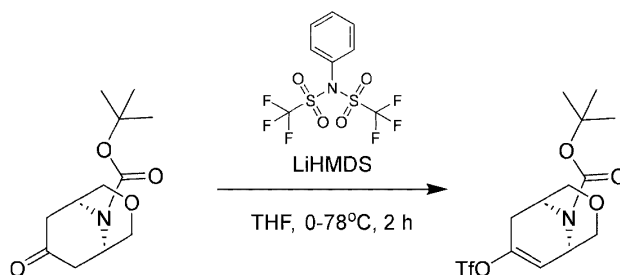


[0429] To a solution of 2-(6-(azetidin-2-ylmethyl)-5-isopropyl-7H-pyrrolo[2,3-c]pyridazin-3-yl)phenol (60 mg, 186.10 μmol , 1 eq) in NaHCO_3 aq. (1N, 1 mL) and DCM (1 mL) was added a solution of acrylic anhydride (23.47 mg, 186.10 μmol , 1 eq) in DCM (0.5 mL) dropwise at 20 °C. The resulting mixture was stirred at the same temperature for 1 h. The reaction mixture was diluted with water (5 mL) and extracted with DCM (5 mL $\times$ 2). The combined organic layers were washed with brine (5 mL), dried over Na_2SO_4 , and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by prep-TLC (SiO_2 , DCM: THF = 2: 1) to give 1-(2-((3-(2-hydroxyphenyl)-5-isopropyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)azetidin-1-yl)prop-2-en-1-one (47 mg, 67.09% yield) as a white solid. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 14.15 - 14.02 (m, 1H), 12.37 (s, 1H), 8.58 - 8.53 (m, 1H), 8.17 (d, J = 8.4 Hz, 1H), 7.28 (t, J = 7.6 Hz, 1H), 6.99 - 6.92 (m, 2H), 6.34 - 6.24 (m, 0.5H), 6.18 - 6.01 (m, 1.5H), 5.72 - 5.66 (m, 0.6H), 5.47 - 5.39 (m, 0.4H), 4.83 (s, 0.4H), 4.72 - 4.61 (m, 0.6H), 4.15 - 4.05 (m, 1.3H), 3.95 - 3.81 (m, 1H), 3.56 - 3.49 (m, 0.7H), 3.28 - 3.17 (m, 2H), 2.25 (s, 1.4H), 2.15 - 2.03 (m, 1H), 2.01 - 1.91 (m, 0.6H), 1.44 - 1.37 (m, 6H); LCMS (ESI^+): m/z 377.1 ($\text{M}+\text{H}^+$).

Example 12: 1-((1*R*,5*S*,7*S*)-7-(3-(2-hydroxyphenyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one (Compound 439)



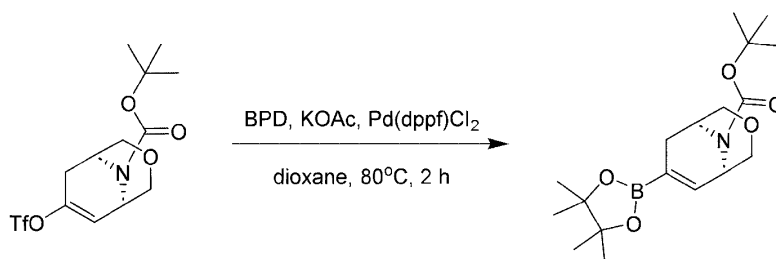
Step 1:



[0430] To a solution of *tert*-butyl (1*R*,5*S*)-7-oxo-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (5 g, 20.72 mmol, 1 eq) in THF (100 mL) was added dropwise LiHMDS (1M, 31.08 mL, 1.5 eq) at -78 °C. The reaction was then stirred at the same temperature for 30 min before a solution of 1,1,1-trifluoro-*N*-phenyl-*N*-[(trifluoromethyl)sulfonyl]methanesulfonamide (11.10 g, 31.08 mmol, 1.5 eq) in THF (100 mL) was added dropwise. The solution was allowed to warm to 0 °C and stirred at the same temperature

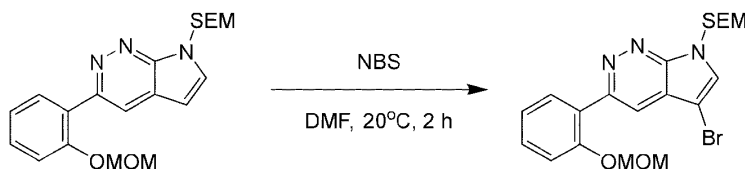
for 2 h. The reaction mixture was quenched by addition of aqueous NH_4Cl (100 mL), then diluted with H_2O (100 mL) and extracted with MTBE (100 mL $\times 2$). The combined organic layers were washed with brine (100 mL), dried over Na_2SO_4 , and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO_2 , petroleum ether/ethyl acetate=5/1 to 1/1) to give *tert*-butyl (1*S*,5*R*)-7-(((trifluoromethyl)sulfonyl)oxy)-3-oxa-9-azabicyclo[3.3.1]non-6-ene-9-carboxylate (3.1 g, 8.30 mmol, 40.07% yield) as an off-white oil. ^1H NMR (400 MHz, CHCl_3 -*d*) δ 5.90 (t, J = 6.4 Hz, 1H), 4.69 - 4.54 (m, 1H), 4.35 - 4.21 (m, 1H), 3.88 - 3.82 (m, 1H), 3.74 - 3.61 (m, 3H), 2.95 - 2.84 (m, 1H), 2.39-2.32 (m, 1H), 1.48 (s, 9H).

Step 2:



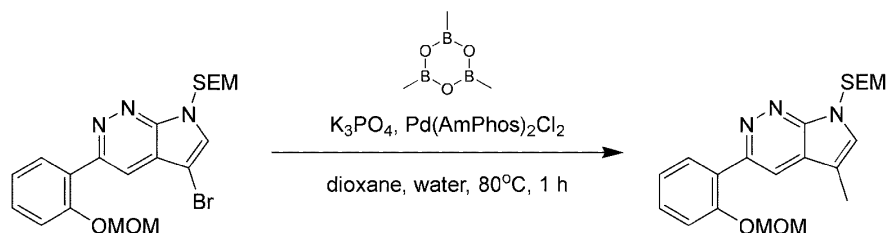
[0431] A mixture of *tert*-butyl (1*S*,5*R*)-7-(((trifluoromethyl)sulfonyl)oxy)-3-oxa-9-azabicyclo[3.3.1]non-6-ene-9-carboxylate (3 g, 8.04 mmol, 1 *eq*), 4,4,5,5-tetramethyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3,2-dioxaborolane (2.45 g, 9.64 mmol, 1.2 *eq*), KOAc (2.37 g, 24.11 mmol, 3 *eq*), and $\text{Pd}(\text{dppf})\text{Cl}_2$ (587.96 mg, 803.55 μmol , 0.1 *eq*) in dioxane (30 mL) was degassed and purged 3 times with N_2 . The resulting mixture was heated to 80°C and stirred for 2 h under N_2 atmosphere. The reaction mixture was diluted with H_2O (50 mL) and extracted with EtOAc (50 mL $\times 2$). The combined organic layers were washed with brine (50 mL), dried over Na_2SO_4 , and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO_2 , petroleum ether/ethyl acetate=5/1 to 1/1) to give *tert*-butyl (1*S*,5*R*)-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-oxa-9-azabicyclo[3.3.1]non-6-ene-9-carboxylate (2.3 g, 6.55 mmol, 81.49% yield) as a white solid. ^1H NMR (400 MHz, CHCl_3 -*d*) δ 6.61 - 6.53 (m, 1H), 4.52 - 4.39 (m, 1H), 4.21 - 4.06 (m, 1H), 3.82 - 3.73 (m, 2H), 3.63-3.59 (m, 2H), 2.68 - 2.62 (m, 1H), 2.27-2.21 (m, 1H), 1.46 (s, 9H), 1.27 (d, J = 2.0 Hz, 12H).

Step 3:

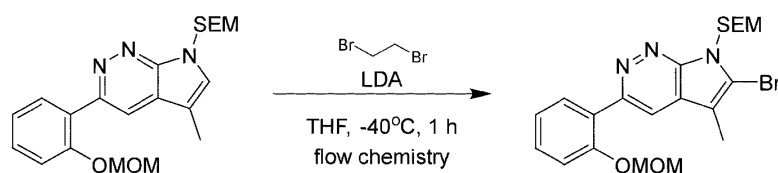


[0432] To a solution of 3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-*c*]pyridazine (80 g, 207.51 mmol, 1 *eq*) in DMF (800 mL) was added NBS (35.09 g, 197.13 mmol, 0.95 *eq*) in portions at 20°C . The mixture was stirred at 20°C for 2 h. The reaction mixture was diluted with water (800 mL) and extracted with ethyl acetate (500 mL $\times 2$). The combined organic layers

were washed with brine (1 L), dried over Na_2SO_4 , filtered and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2 , PE/EA = 10/1 to 3/1) to give 5-bromo-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazine (78 g, 167.95 mmol, 80.94% yield) as a brown oil. ^1H NMR (400 MHz, $\text{METHANOL-}d_4$) δ 8.08 (d, J = 4.8 Hz, 2H), 7.68 (dd, J = 1.6, 7.6 Hz, 1H), 7.52 - 7.42 (m, 1H), 7.36 - 7.28 (m, 1H), 7.18 (t, J = 7.2 Hz, 1H), 5.86 (s, 2H), 5.23 (s, 2H), 3.66 (t, J = 8.0 Hz, 2H), 3.37 (s, 3H), 0.98 - 0.85 (m, 2H), -0.07 (s, 9H)

Step 4:

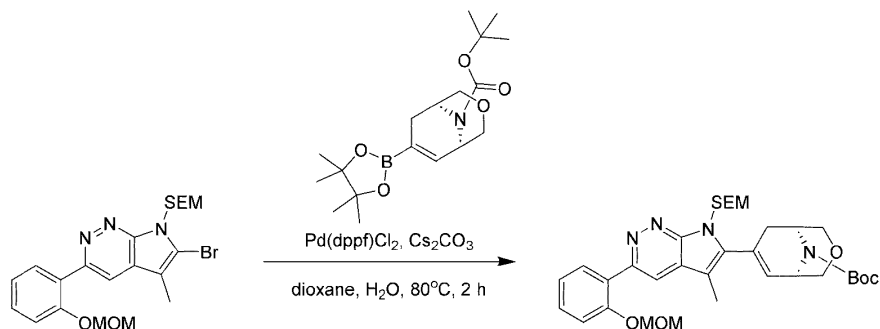
A solution of 5-bromo-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazine (60 g, 129.19 mmol, 1 eq), 2,4,6-trimethyl-1,3,5,2,4,6-trioxatriborinane (64.87 g, 258.38 mmol, 72.24 mL, 2 eq), $\text{Pd}(\text{AmPhos})_2\text{Cl}_2$ (13.72 g, 19.38 mmol, 13.72 mL, 0.15 eq) and K_3PO_4 (54.85 g, 258.38 mmol, 2 eq) in dioxane (300 mL) and water (150 mL) was degassed and then heated to 80°C for 1 h under N_2 . The reaction mixture was diluted with H_2O (500 mL) and extracted with EtOAc (500 mL $\times$ 2). The combined organic layers were washed with brine (500 mL), dried over Na_2SO_4 , filtered and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2 , PE/EA = 10/1 to 0/1) to give 3-(2-(methoxymethoxy)phenyl)-5-methyl-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazine (50 g, 110.12 mmol, 85.24% yield) as a yellow oil. ^1H NMR (400 MHz, $\text{METHANOL-}d_4$) δ = 8.11 (s, 1H), 7.69 - 7.58 (m, 2H), 7.49 - 7.35 (m, 1H), 7.31 (d, J = 8.0 Hz, 1H), 7.17 (t, J = 7.2 Hz, 1H), 5.80 (s, 2H), 5.20 (s, 2H), 3.62 (t, J = 8.0 Hz, 2H), 3.34 (s, 3H), 2.39 - 2.33 (m, 3H), 0.90 (t, J = 8.0 Hz, 2H), -0.08 (s, 9H).

Step 5:

[0433] LDA (2 M, 156.42 mL, 2.5 eq) was added into a solution of 3-(2-(methoxymethoxy)phenyl)-5-methyl-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazine (45 g, 1 eq) in THF (900 mL) at -40°C . Then 1, 2-dibromoethane (74.052 g 3.5 eq) in THF (450 mL) was added into the above solution at -40°C using a flow reactor for 1 h. The reaction mixture was diluted with H_2O (1000 mL) and extracted with ethyl acetate (500 mL $\times$ 2). The combined organic layers were washed with brine (500 mL), dried over Na_2SO_4 , filtered and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2 , PE/EA = 10/1 to 0/1) to give 6-bromo-3-(2-(methoxymethoxy)phenyl)-5-methyl-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazine

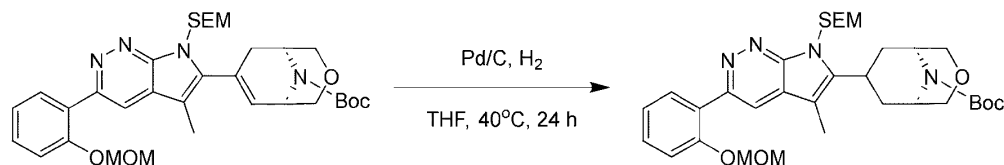
(40 g, 83.60 mmol, 66.81% yield) as a yellow solid. ^1H NMR (400 MHz, $\text{METHANOL-}d_4$) δ 8.08 (s, 1H), 7.62 (dd, $J = 1.6, 7.6$ Hz, 1H), 7.48 - 7.37 (m, 1H), 7.30 (dd, $J = 0.8, 8.4$ Hz, 1H), 7.16 (dt, $J = 1.2, 7.6$ Hz, 1H), 5.88 (s, 2H), 5.20 (s, 2H), 3.71 - 3.61 (m, 2H), 3.34 (s, 3H), 2.32 (s, 3H), 0.92 - 0.83 (m, 2H), -0.09 (s, 9H).

Step 6:



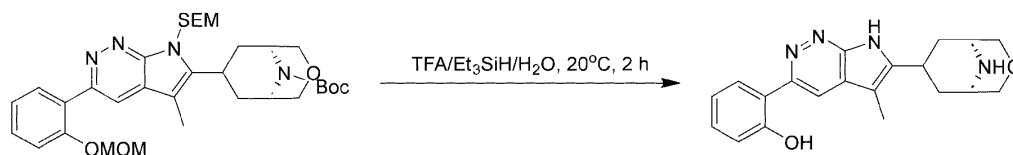
[0434] A mixture of 6-bromo-3-(2-(methoxymethoxy)phenyl)-5-methyl-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazine (100 mg, 209.01 μmol , 1 *eq*), *tert*-butyl (1*S*,5*R*)-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-oxa-9-azabicyclo[3.3.1]non-6-ene-9-carboxylate (88.09 mg, 250.81 μmol , 1.2 *eq*), Cs_2CO_3 (204.29 mg, 627.02 μmol , 3 *eq*), and $\text{Pd}(\text{dppf})\text{Cl}_2$ (15.29 mg, 20.90 μmol , 0.1 *eq*) in dioxane (1 mL) and H_2O (0.2 mL) was degassed and purged 3 times with N_2 . The resulting mixture was heated to 80 $^\circ\text{C}$ and stirred for 12 h under N_2 atmosphere. The reaction mixture was diluted with H_2O (2 mL) and extracted with EtOAc (2 mL $\times$ 2). The combined organic layers were washed with brine (2 mL), dried over Na_2SO_4 , and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO_2 , petroleum ether/ethyl acetate=2/1 to 1/1) to give *tert*-butyl (1*S*,5*R*)-7-(3-(2-(methoxymethoxy)phenyl)-5-methyl-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]non-6-ene-9-carboxylate (100 mg, 160.56 μmol , 76.82% yield) as a light green solid. ^1H NMR (400 MHz, $\text{CHLOROFORM-}d$) δ 8.02 (s, 1H), 7.89 (dd, $J = 1.2, 7.6$ Hz, 1H), 7.43 - 7.35 (m, 1H), 7.25 (s, 1H), 7.18 (t, $J = 7.6$ Hz, 1H), 6.08 (d, $J = 5.2$ Hz, 1H), 5.82 - 5.73 (m, 2H), 5.20 (s, 2H), 4.75 - 4.56 (m, 1H), 4.37 - 4.19 (m, 1H), 3.99 - 3.91 (m, 1H), 3.89 - 3.82 (m, 1H), 3.81 - 3.74 (m, 3H), 3.74 - 3.66 (m, 1H), 3.44 (s, 3H), 2.99 - 2.87 (m, 1H), 2.54 (dd, $J = 9.6, 18.0$ Hz, 1H), 2.26 (s, 3H), 1.53 (s, 9H), 0.93 (dd, $J = 7.2, 9.3$ Hz, 2H), 0.03 (s, 9H); LCMS (ESI $^+$): m/z 625.5 ($\text{M}+\text{H}$) $^+$.

Step 7:

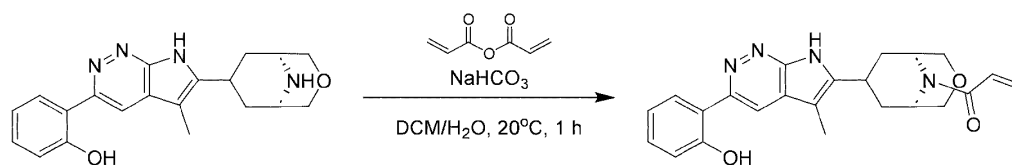


[0435] To a solution of *tert*-butyl (1*S*,5*R*)-7-(3-(2-(methoxymethoxy)phenyl)-5-methyl-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]non-6-ene-9-

carboxylate (100 mg, 160.56 μmol , 1 *eq*) in THF (3 mL) was added Pd/C (100 mg, 93.97 μmol , 10% purity) under N_2 atmosphere. The suspension was degassed and purged 3 times with H_2 . The mixture was stirred under H_2 (15 Psi), heated to 40 $^\circ\text{C}$, and stirred for 24 h. The reaction mixture was filtered, and the filtrate was concentrated under reduced pressure to afford *tert*-butyl (1*R*,5*S*)-7-(3-(2-(methoxymethoxy)phenyl)-5-methyl-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (92 mg, 147.24 μmol , 91.70% yield) as a white solid, which was used in the next step without purification. ^1H NMR (400 MHz, $\text{CHLOROFORM-}d$) δ 8.03 (d, J = 6.0 Hz, 1H), 7.90 - 7.79 (m, 1H), 7.46 - 7.38 (m, 1H), 7.22 - 7.17 (m, 1H), 7.06 - 6.93 (m, 1H), 5.23 (s, 2H), 4.43 - 4.31 (m, 1H), 4.29 - 4.19 (m, 1H), 3.81 - 3.72 (m, 2H), 3.72 - 3.66 (m, 2H), 3.63 (dd, J = 6.4, 9.6 Hz, 1H), 3.44 (s, 3H), 2.52 - 2.42 (m, 2H), 2.29 - 2.25 (m, 2H), 1.73 (s, 3H), 1.57 - 1.53 (m, 9H), 1.44 (s, 4H), 0.94 - 0.88 (m, 2H), 0.08 (s, 9H); LCMS (ESI^+): m/z 625.4 ($\text{M}+\text{H}$) $^+$.

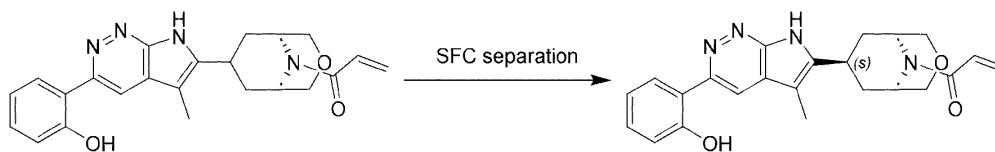
Step 8:

[0436] A solution of *tert*-butyl (1*R*,5*S*)-7-(3-(2-(methoxymethoxy)phenyl)-5-methyl-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (80 mg, 128.04 μmol , 1 *eq*) in TFA (1 mL), Et_3SiH (0.05 mL), and H_2O (0.05 mL) was stirred at 20 $^\circ\text{C}$ for 2 h. The reaction mixture was concentrated under reduced pressure to give 2-(6-((1*R*,5*S*)-3-oxa-9-azabicyclo[3.3.1]nonan-7-yl)-5-methyl-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)phenol (40 mg, 114.15 μmol , 89.16% yield) as a red solid, which was used in the next step without purification. LCMS (ESI^+): m/z 351.1 ($\text{M}+\text{H}$) $^+$.

Step 9:

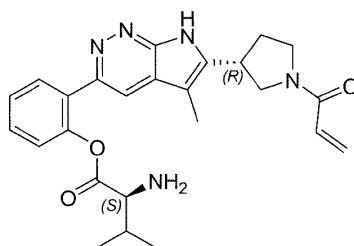
[0437] To a solution of 2-(6-((1*R*,5*S*)-3-oxa-9-azabicyclo[3.3.1]nonan-7-yl)-5-methyl-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)phenol (40 mg, 114.16 μmol , 1 *eq*) in DCM (1 mL) was added NaHCO_3 (47.94 mg, 570.76 μmol , 22.20 μL , 5 *eq*) in H_2O (1 mL) and prop-2-enyl prop-2-enoate (21.60 mg, 171.22 μmol , 1.5 *eq*) at 20 $^\circ\text{C}$. The mixture was stirred at the same temperature for 1 h. The reaction mixture was diluted with H_2O (3 mL) and extracted with DCM (3 mL $\times$ 2). The combined organic layers were concentrated under reduced pressure, and the residue was purified by column chromatography (SiO_2 , DCM/THF =2/1 to 1/1) to give 1-((1*R*,5*S*)-7-(3-(2-(2-allyloxyprop-2-en-1-yl)-2-hydroxyphenyl)-5-methyl-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one (15 mg, 37.09 μmol , 32.49% yield) as a white solid. LCMS (ESI^+): m/z 405.2 ($\text{M}+\text{H}$) $^+$.

Step 10:

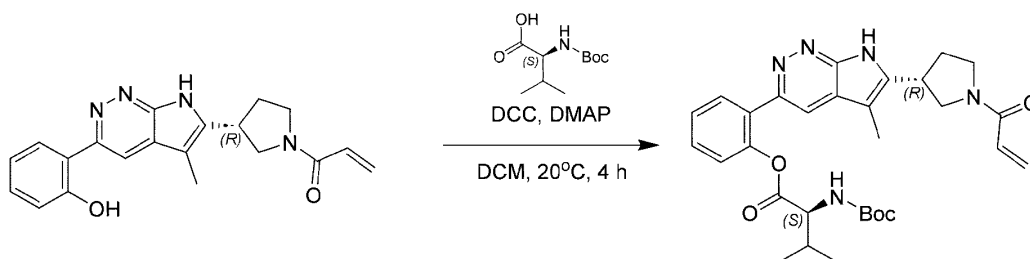


[0438] 1-((1*R*,5*S*)-7-(3-(2-hydroxyphenyl)-5-methyl-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one was purified by SFC (column: DAICEL CHIRALPAK IG (250 mm×30 mm, 10 μm); mobile phase: [CO₂-EtOH (0.1% NH₃H₂O)]; B%: 50%, isocratic elution mode) to give 1-((1*R*,5*S*,7*S*)-7-(3-(2-hydroxyphenyl)-5-methyl-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one (4 mg, 9.89 μmol, 26.67% yield) as a white solid. ¹H NMR (400 MHz, DMSO-*d*₆) δ 14.41 (s, 1H), 12.36 (s, 1H), 8.58 (s, 1H), 8.12 (d, *J* = 7.2 Hz, 1H), 7.28 (t, *J* = 7.6 Hz, 1H), 6.98 - 6.92 (m, 2H), 6.92 - 6.85 (m, 1H), 6.29 - 6.21 (m, 1H), 5.79 (dd, *J* = 2.4, 10.0 Hz, 1H), 4.72 (d, *J* = 8.0 Hz, 1H), 4.44 (d, *J* = 10.0 Hz, 1H), 3.69 (t, *J* = 11.2 Hz, 2H), 3.51 (t, *J* = 10.0 Hz, 2H), 3.39 (s, 1H), 2.72 (dt, *J* = 6.4, 12.4 Hz, 1H), 2.27 (s, 3H), 2.20 - 2.09 (m, 3H).

Example 13: Synthesis of 2-(6-((*R*)-1-acryloylpyrrolidin-3-yl)-5-methyl-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)phenyl *L*-valinate (Compound 460)



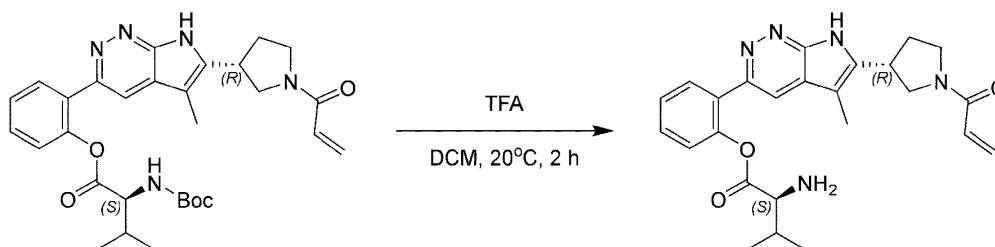
Step 1:



[0439] To a solution of (*R*)-1-(3-(3-(2-hydroxyphenyl)-5-methyl-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)pyrrolidin-1-yl)prop-2-en-1-one (50 mg, 143.51 μmol, 1 *eq*) in DCM (2 mL) was added (*2S*)-2-(*tert*-butoxycarbonylamino)-3-methylbutanoic acid (37.42 mg, 172.22 μmol, 1.2 *eq*), DCC (29.61 mg, 143.51 μmol, 29.03 μL, 1 *eq*), and DMAP (2.10 mg, 17.22 μmol, 0.12 *eq*) at 20° C. The mixture was stirred at the same temperature for 4 h. The reaction mixture was then partitioned between dichloromethane (4 mL) and H₂O (4 mL). The organic phase was separated, washed with brine (4 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by prep-TLC (SiO₂, dichloromethane/tetrahydrofuran = 2:1) to give 2-(6-((*R*)-1-acryloylpyrrolidin-3-yl)-5-methyl-7*H*-

pyrrolo[2,3-c]pyridazin-3-yl)phenyl (*tert*-butoxycarbonyl)-*L*-valinate (40 mg, 73.04 μ mol, 50.89% yield) as a yellow solid.

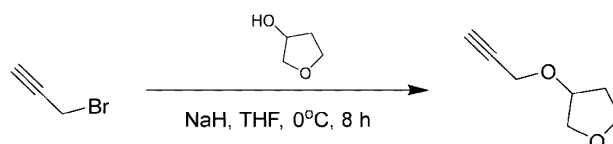
Step 2:



[0440] To a solution of 2-(6-((*R*)-1-acryloylpyrrolidin-3-yl)-5-methyl-7*H*-pyrrolo[2,3-c]pyridazin-3-yl)phenyl (*tert*-butoxycarbonyl)-*L*-valinate (40 mg, 73.04 μ mol, 1 *eq*) in DCM (1 mL) was added TFA (3.07 g, 26.93 mmol, 2.00 mL, 368.63 *eq*) at 20 °C. The mixture was stirred at the same temperature for 2 h. The reaction mixture was then concentrated under reduced pressure, and the residue was triturated with methyl *tert*-butyl ether (2 mL) at 25 °C for 10 min to give 2-(6-((*R*)-1-acryloylpyrrolidin-3-yl)-5-methyl-7*H*-pyrrolo[2,3-c]pyridazin-3-yl)phenyl *L*-valinate (34.4 mg, 61.26 μ mol, 83.87% yield, TFA salt) as a yellow solid. ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.37 - 12.28 (m, 1 H), 8.40 - 8.30 (m, 2 H), 7.98 (d, *J* = 1.6 Hz, 1 H), 7.78 (d, *J* = 7.6 Hz, 1 H), 7.65 - 7.57 (m, 1 H), 7.52 (t, *J* = 7.2 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 1 H), 6.64 (dt, *J* = 10.4, 16.4 Hz, 1 H), 6.18 (d, *J* = 16.4 Hz, 1 H), 5.76 - 5.65 (m, 1 H), 4.12 - 4.05 (m, 2 H), 4.00 - 3.90 (m, 4 H), 3.53 - 3.47 (m, 1 H), 2.35 (s, 1 H), 2.31 - 2.25 (m, 4 H), 2.21 - 2.12 (m, 2 H), 1.10 (s, 18 H), 0.81 (dd, *J* = 2.4, 6.8 Hz, 3 H), 0.68 (t, *J* = 8.0 Hz, 3 H); LCMS: (ESI⁺): *m/z* 448.2 (M+H)⁺.

Example 14: Synthesis of 1-((1*R*,5*S*,7*r*)-7-(3-(2-hydroxyphenyl)-5-(3-((tetrahydrofuran-3-yl)oxy)propyl)-7*H*-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one (Compound 465)

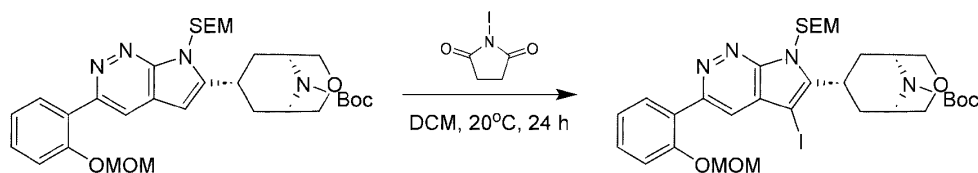
Step 1:



[0441] To a solution of tetrahydrofuran-3-ol (1 g, 8.25 mmol, 1 *eq*) in THF (30 mL) was added NaH (907.92 mg, 22.70 mmol, 60% purity, 2 *eq*) in portions at 0 °C. The reaction mixture was degassed and purged with N₂ 3 times, then stirred at 0 °C for 30 min under N₂. To the mixture was added propargyl bromide (1.62 g, 13.62 mmol, 1.17 mL, 1.2 *eq*) at the same temperature, and the reaction mixture was allowed to stir for 8 h. The crude mixture was poured carefully into sat. aqueous NH₄Cl (10.0 mL) under a blanket of N₂ at 10 °C. The mixture was then diluted with ethyl acetate (30.0 mL), and the layers were separated. The organic layer was washed with brine (10.0 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (SiO₂, petroleum ether/ethyl acetate=1/0 to 10/1). 3-(Prop-2-yn-1-yloxy)tetrahydrofuran (400 mg, 3.17 mmol,

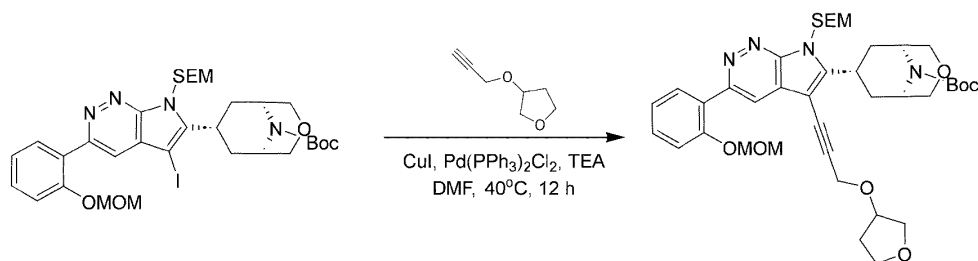
27.94% yield) was obtained as a white oil. ^1H NMR (400 MHz, $\text{CHLOROFORM-}d$) δ 4.37 - 4.36 (m, 1 H), 4.16 (d, $J = 2.4$ Hz, 2 H), 3.94 - 3.78 (m, 4 H), 2.44 (t, $J = 2.4$ Hz, 1 H), 2.05 - 1.99 (m, 2 H).

Step 2:



[0442] To a solution of *tert*-butyl (1*R*,5*S*,7*r*)-7-(3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (240 mg, 392.92 μmol , 1 *eq*) in DMF (2 mL) was added *N*-iodosuccinimide (176.80 mg, 785.84 μmol , 2 *eq*) at 20 $^{\circ}\text{C}$. The mixture was stirred at the same temperature for 24 h. The reaction mixture was diluted with H_2O (4 mL) and extracted with ethyl acetate (6 mL). The combined organic layers were washed with brine (4 mL), dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The residue was purified by prep-TLC (SiO_2 , petroleum ether: ethyl acetate = 1:1) to give *tert*-butyl (1*R*,5*S*,7*r*)-7-(5-iodo-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (240 mg, 325.77 μmol , 82.91% yield) as a white solid. ^1H NMR (400 MHz, $\text{METHANOL-}d_4$) δ 7.88 (s, 1 H), 7.66 (dd, $J = 1.6$, 7.6 Hz, 1 H), 7.47 - 7.40 (m, 1 H), 7.31 (d, $J = 8.0$ Hz, 1 H), 7.17 (dt, $J = 0.8$, 7.6 Hz, 1 H), 6.00 (s, 2 H), 5.22 (s, 2 H), 4.20 - 4.12 (m, 2 H), 3.83 (d, $J = 11.6$ Hz, 2 H), 3.67 - 3.58 (m, 2 H), 3.38 (s, 3 H), 2.99 (s, 1 H), 2.90 - 2.73 (m, 4 H), 2.68 (s, 1 H), 1.56 (s, 9 H), 0.99 - 0.90 (m, 2 H), -0.05 (s, 9 H).

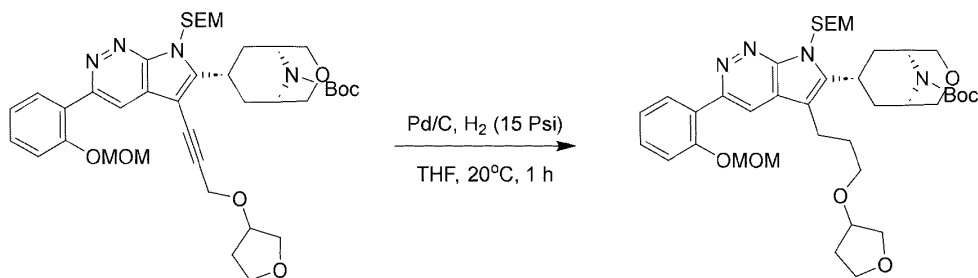
Step 3:



[0443] To a solution of *tert*-butyl (1*R*,5*S*,7*r*)-7-(5-iodo-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (80 mg, 108.60 μmol , 1 *eq*) in DMF (1.6 mL) was added 3-(prop-2-yn-1-yloxy)tetrahydrofuran (68.48 mg, 542.96 μmol , 5 *eq*), CuI (3.10 mg, 16.28 μmol , 0.15 *eq*), $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (15.24 mg, 21.72 μmol , 0.2 *eq*), and TEA (109.88 mg, 1.09 mmol, 151.16 μL , 10 *eq*). The solution was degassed and purged with N_2 3 times, and the reaction mixture was heated to 40 $^{\circ}\text{C}$ and stirred for 12 h under N_2 atmosphere. The reaction mixture was diluted with H_2O (2 mL) and extracted with EtOAc (4 mL). The combined organic layers were washed with brine (2 mL), dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The residue was purified by prep-TLC (SiO_2 , petroleum ether: ethyl acetate = 1:2) to give *tert*-butyl (1*R*,5*S*,7*r*)-7-(3-(2-(methoxymethoxy)phenyl)-5-(3-((tetrahydrofuran-3-

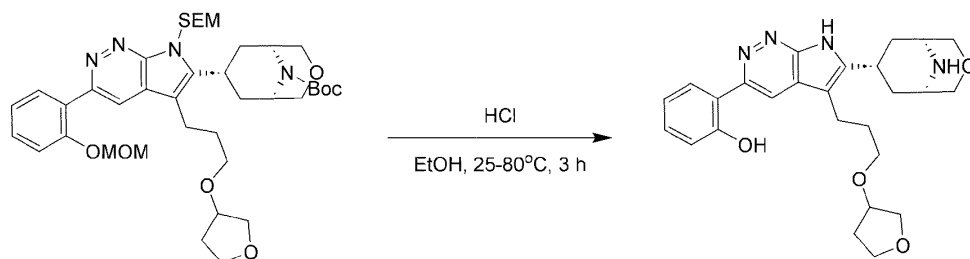
yl)oxy)prop-1-yn-1-yl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (70 mg, 95.24 μ mol, 87.71% yield) as a white solid. ^1H NMR (400 MHz, METHANOL- d_4) δ 8.12 (s, 1 H), 7.66 (dd, J = 1.6, 7.6 Hz, 1 H), 7.49 - 7.40 (m, 1 H), 7.31 (d, J = 8.0 Hz, 1 H), 7.18 (t, J = 8.0 Hz, 1 H), 6.00 (s, 2 H), 5.22 (s, 3 H), 4.47 (s, 3 H), 4.27 (s, 1 H), 4.17 (s, 2 H), 4.04 (t, J = 11.2 Hz, 3 H), 3.88 - 3.78 (m, 7 H), 3.73 (t, J = 6.8 Hz, 6 H), 2.95 - 2.76 (m, 2 H), 2.63 - 2.52 (m, 1 H), 1.54 (s, 9 H), 1.40 (s, 1 H), -0.05 (s, 9 H).

Step 4:



[0444] To a solution of *tert*-butyl (1*R*,5*S*,7*r*)-7-(3-(2-(methoxymethoxy)phenyl)-5-(3-((tetrahydrofuran-3-yl)oxy)prop-1-yn-1-yl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (70 mg, 95.24 μ mol, 1 *eq*) in THF (0.7 mL) was added Pd/C (175.35 mg, 164.77 μ mol, 10% purity, 1.73 *eq*) at 20 °C under N_2 . The suspension was degassed and purged with H_2 three times, then stirred under H_2 atmosphere (15 Psi) at 20 °C for 1 h. The reaction mixture was then filtered and concentrated under reduced pressure to give *tert*-butyl (1*R*,5*S*,7*r*)-7-(3-(2-(methoxymethoxy)phenyl)-5-(3-((tetrahydrofuran-3-yl)oxy)propyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (70 mg, 94.72 μ mol, crude) as a white solid, which was used in the next step without purification. ^1H NMR (400 MHz, METHANOL- d_4) δ 8.08 (s, 1 H), 7.62 (dd, J = 1.6, 7.6 Hz, 1 H), 7.46 - 7.40 (m, 1 H), 7.30 (d, J = 8.0 Hz, 1 H), 7.17 (dt, J = 0.8, 7.6 Hz, 1 H), 5.95 (s, 2 H), 5.19 (s, 2 H), 3.89 - 3.81 (m, 3 H), 3.77 - 3.69 (m, 6 H), 3.65 - 3.59 (m, 2 H), 3.52 - 3.40 (m, 3 H), 2.93 (t, J = 6.8 Hz, 2 H), 2.48 - 2.34 (m, 2 H), 2.22 (s, 1 H), 2.18 - 2.08 (m, 2 H), 2.02 - 1.91 (m, 5 H), 1.56 (s, 9 H), 1.48 (d, J = 9.2 Hz, 1 H), 1.40 (s, 3 H), 1.29 (s, 2 H), -0.06 (s, 8 H).

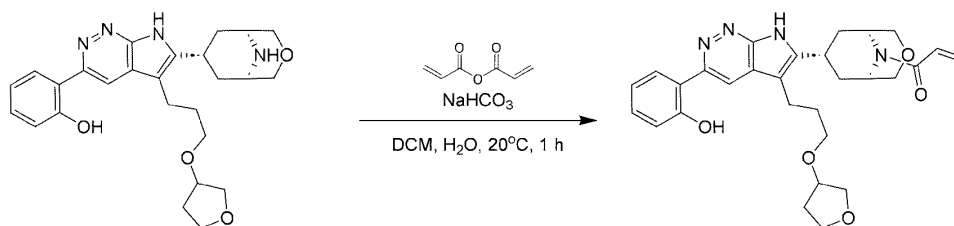
Step 5:



[0445] To a solution of *tert*-butyl (1*R*,5*S*,7*r*)-7-(3-(2-(methoxymethoxy)phenyl)-5-(3-((tetrahydrofuran-3-yl)oxy)propyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-

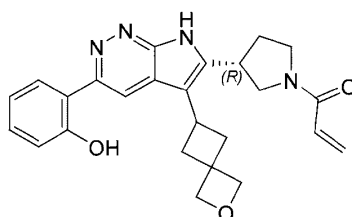
azabicyclo[3.3.1]nonane-9-carboxylate (65 mg, 87.96 μmol , 1 eq) in EtOH (0.8 mL) was added HCl (12M, 0.2 mL, 27.29 eq) and the reaction was heated to 80 °C and stirred for 3 h. The reaction mixture was then cooled to 25 °C and concentrated under reduced pressure to give 2-(6-((1*R*,5*S*,7*r*)-3-oxa-9-azabicyclo[3.3.1]nonan-7-yl)-5-(3-((tetrahydrofuran-3-yl)oxy)propyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)phenol (40 mg, crude) as a yellow oil, which was used in the next step without purification.

Step 6:

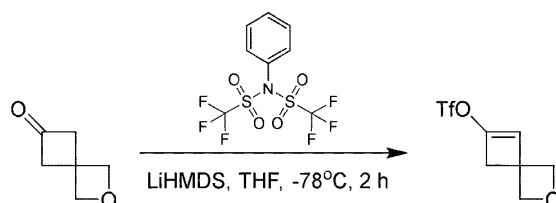


[0446] To a solution of 2-(6-((1*R*,5*S*,7*r*)-3-oxa-9-azabicyclo[3.3.1]nonan-7-yl)-5-(3-((tetrahydrofuran-3-yl)oxy)propyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)phenol (40 mg, 86.10 μmol , 1 eq) in DCM (3 mL) and H₂O (0.3 mL) was added Na₂CO₃ (3.62 mg, 43.05 μmol , 1 eq) and acrylic anhydride (16.28 mg, 129.16 μmol , 1.5 eq) at 20 °C. The mixture was then stirred at the same temperature for 1 h. The reaction was quenched with H₂O (2 mL) and extracted with DCM (6 mL). The combined organic layers were washed with brine (2 mL), dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was purified by prep-TLC (SiO₂, ethyl acetate: methanol =15:1) to give 1-((1*R*,5*S*,7*r*)-7-(3-(2-hydroxyphenyl)-5-(3-((tetrahydrofuran-3-yl)oxy)propyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one (9 mg, 17.35 μmol , 20.16% yield) as a white solid. ¹H NMR (400 MHz, DMSO-*d*₆) δ 14.30 (d, *J* = 1.6 Hz, 1 H), 12.35 (s, 1 H), 8.53 (s, 1 H), 8.10 (d, *J* = 8.0 Hz, 1 H), 7.28 (t, *J* = 7.2 Hz, 1 H), 7.00 - 6.90 (m, 2 H), 6.85 (dd, *J* = 10.4, 16.8 Hz, 1 H), 6.25 (dd, *J* = 2.4, 16.8 Hz, 1 H), 5.77 (dd, *J* = 2.4, 10.4 Hz, 1 H), 4.61 - 4.41 (m, 2 H), 4.31 (s, 1 H), 4.02 (dd, *J* = 5.6, 12.0 Hz, 3 H), 3.76 - 3.61 (m, 6 H), 3.37 (d, *J* = 5.2 Hz, 2 H), 2.82 (t, *J* = 7.2 Hz, 2 H), 2.30 - 2.11 (m, 2 H), 2.06 - 1.95 (m, 2 H), 1.94 - 1.80 (m, 4 H); LCMS: (ESI⁺): *m/z* 519.2 (M+H)⁺.

Example 15: (*R*)-1-(3-(3-(2-hydroxyphenyl)-5-(2-oxaspiro[3.3]heptan-6-yl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)pyrrolidin-1-yl)prop-2-en-1-one (Compound 467)

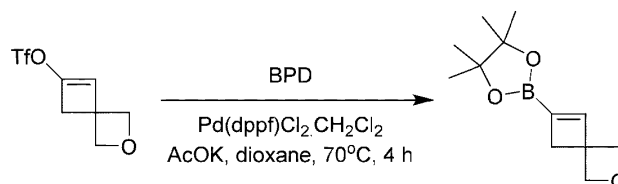


Step 1:



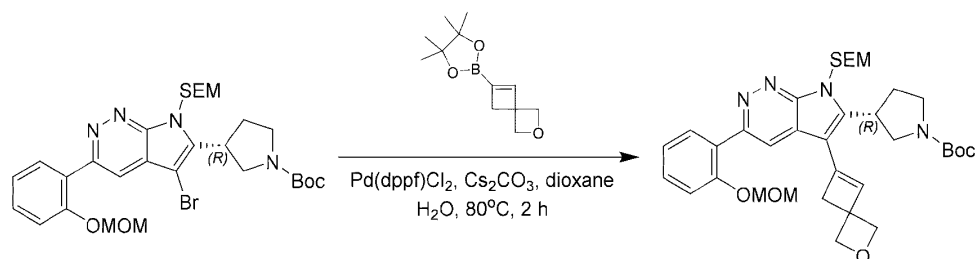
[0447] To a solution of 2-oxaspiro[3.3]heptan-6-one (850 mg, 7.58 mmol, 1 *eq*) in THF (9 mL) was added dropwise LiHMDS (1M, 9.10 mL, 1.2 *eq*) at -78 °C under N₂ atmosphere. After addition, the mixture was stirred at the same temperature for 30 min, then 1,1,1-trifluoro-N-phenyl-N-[(trifluoromethyl)sulfonyl]methanesulfonamide (3.25 g, 9.10 mmol, 1.2 *eq*) in THF (9 mL) was added dropwise. The resulting mixture was stirred at -78 °C for 2 h under N₂. The reaction mixture was quenched by addition of sat. NH₄Cl solution (10 mL) at 0 °C, then diluted with H₂O (20 mL) and extracted with ethyl acetate (20 mL × 2). The combined organic layers were washed with brine (20 mL), dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The residue was purified by prep-TLC (SiO₂, petroleum ether: ethyl acetate = 3:1) to give 2-oxaspiro[3.3]hept-5-en-6-yl trifluoromethanesulfonate (1.5 g, 6.14 mmol, 81.03% yield) as a yellow oil. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ = 5.51 (s, 1 H), 4.75 (s, 4 H), 3.00 (s, 2 H).

Step 2:



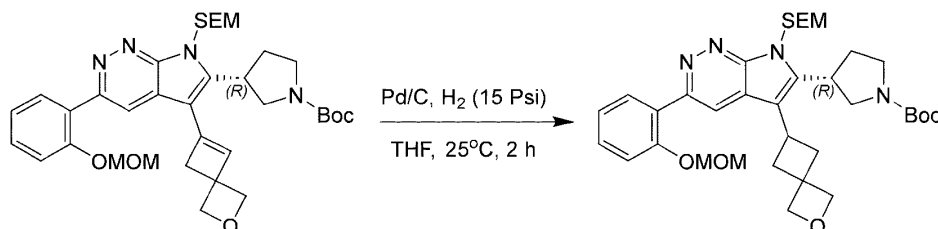
[0448] To a solution of 2-oxaspiro[3.3]hept-5-en-6-yl trifluoromethanesulfonate (540 mg, 2.21 mmol, 1 *eq*), and bis(pinacolato)diboron (561.56 mg, 2.21 mmol, 1 *eq*) in dioxane (5.4 mL) was added KOAc (434.07 mg, 4.42 mmol, 2 *eq*) and Pd(dppf)Cl₂·CH₂Cl₂ (180.59 mg, 221.14 μmol, 0.1 *eq*). The mixture was heated to 70 °C and stirred under N₂ atmosphere for 4 h. The reaction mixture was washed with methyl *tert*-butyl ether (10 mL), filtered, and concentrated under reduced pressure. The residue was purified by prep-TLC (SiO₂, petroleum ether: ethyl acetate = 10:1) to give 4,4,5,5-tetramethyl-2-(2-oxaspiro[3.3]hept-5-en-6-yl)-1,3,2-dioxaborolane (168 mg, 0.76 mmol, 34.21% yield) as a yellow solid. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ = 6.95 (s, 1 H), 4.84 (s, 4 H), 2.80 (s, 2 H), 1.28 (s, 12 H).

Step 3:



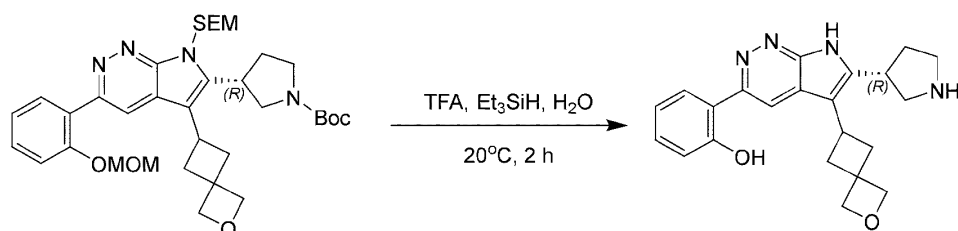
[0449] To a solution of *tert*-butyl (*R*)-3-(5-bromo-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)pyrrolidine-1-carboxylate (150 mg, 236.72 μmol , 1 *eq*) and 4,4,5,5-tetramethyl-2-(2-oxaspiro[3.3]hept-5-en-6-yl)-1,3,2-dioxaborolane (78.86 mg, 355.09 μmol , 1.5 *eq*) in dioxane (0.5 mL) and H_2O (0.375 mL) was added Cs_2CO_3 (154.26 mg, 473.45 μmol , 2 *eq*) and $\text{Pd}(\text{dppf})\text{Cl}_2$ (17.32 mg, 23.67 μmol , 0.1 *eq*) at 25 °C under N_2 . The mixture was degassed and purged with N_2 3 times, then the mixture was stirred at 80 °C for 2 h under N_2 atmosphere. The reaction mixture was cooled to 25 °C and partitioned between ethyl acetate (2 mL) and H_2O (2 mL). The organic phase was separated, washed with brine (2 mL), dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The residue was purified by prep-TLC (SiO_2 , petroleum ether: ethyl acetate = 2:1) to give *tert*-butyl (*R*)-3-(3-(2-(methoxymethoxy)phenyl)-5-(2-oxaspiro[3.3]hept-5-en-6-yl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)pyrrolidine-1-carboxylate (100 mg, 154.12 μmol , 65.10% yield) as a red solid.

Step 4:



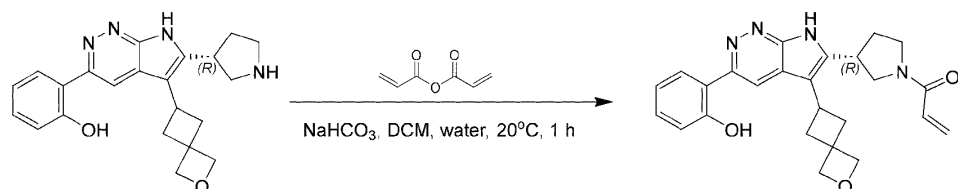
[0450] To a solution of *tert*-butyl (*R*)-3-(3-(2-(methoxymethoxy)phenyl)-5-(2-oxaspiro[3.3]hept-5-en-6-yl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)pyrrolidine-1-carboxylate (50 mg, 77.06 μmol , 1 *eq*) in THF (1 mL) was added Pd/C (50.00 mg, 46.98 μmol , 10% purity, 0.61 *eq*) at 25 °C under Ar. The suspension was degassed and purged with H_2 three times. The mixture was stirred under a blanket of H_2 (15 Psi) at 25 °C for 2 h. The reaction mixture was filtered and concentrated under reduced pressure to give *tert*-butyl (*R*)-3-(3-(2-(methoxymethoxy)phenyl)-5-(2-oxaspiro[3.3]heptan-6-yl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)pyrrolidine-1-carboxylate (90 mg, 138.27 μmol , crude) as yellow oil. The crude product was used in the next step without purification.

Step 5:



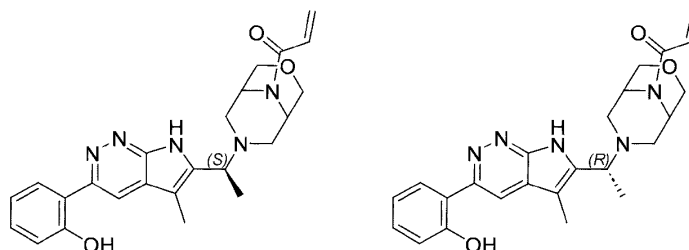
[0451] To a solution of *tert*-butyl (*R*)-3-(3-(2-(methoxymethoxy)phenyl)-5-(2-oxaspiro[3.3]heptan-6-yl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)pyrrolidine-1-carboxylate (50 mg, 76.82 μ mol, 1 *eq*) in H₂O (0.1 mL) was added Et₃SiH (0.1 mL) and TFA (2 mL) at 20 °C. The mixture was stirred at at the same temperature for 2 h. The reaction mixture was concentrated under reduced pressure to give (*R*)-2-(6-(pyrrolidin-3-yl)-5-(2-oxaspiro[3.3]heptan-6-yl)-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)phenol (25 mg, 66.41 μ mol, 43.22% yield) as green oil, which was used in the next step without purification.

Step 6:

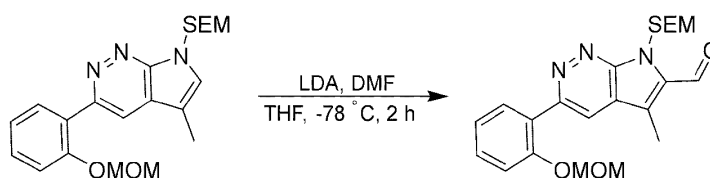


[0452] To a solution of (*R*)-2-(6-(pyrrolidin-3-yl)-5-(2-oxaspiro[3.3]heptan-6-yl)-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)phenol (25 mg, 66.41 μ mol, 1 *eq*) in DCM (1 mL) and H₂O (1 mL) was added NaHCO₃ (5.58 mg, 66.41 μ mol, 2.58 μ L, 1 *eq*) and acrylic anhydride (12.56 mg, 99.61 μ mol, 1.5 *eq*) at 20 °C. The mixture was stirred at the same temperature for 1 h. The reaction mixture was partitioned between ethyl acetate (1 mL) and H₂O (1 mL). The organic phase was separated, washed with brine (2 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by prep-HPLC (0.1% FA condition) to give (*R*)-1-(3-(3-(2-hydroxyphenyl)-5-(2-oxaspiro[3.3]heptan-6-yl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)pyrrolidin-1-yl)prop-2-en-1-one (3.4 mg, 7.9 μ mol, 5.9% yield) as a white solid. ¹H NMR (400 MHz, DMSO-*d*₆) δ = 13.88 - 13.87 (m, 1 H), 12.42 - 12.34 (m, 1 H), 8.43 (d, *J* = 4.8 Hz, 1 H), 8.07 (d, *J* = 8.4 Hz, 1 H), 7.32 - 7.28 (m, 1 H), 6.99 - 6.96 (m, 2 H), 6.67 - 6.61 (m, 1 H), 6.18 (d, *J* = 2.8 Hz, 1 H), 5.74 - 5.67 (m, 1 H), 4.78 (s, 2 H), 4.60 (d, *J* = 2.0 Hz, 2 H), 4.06 - 4.02 (m, 1 H), 3.94 - 3.89 (m, 1 H), 3.80 - 3.75 (m, 1 H), 3.74 - 3.57 (m, 3 H), 3.51 - 3.42 (m, 1 H), 2.77 - 2.72 (m, 2 H), 2.73 - 2.71 (m, 2 H), 2.33 - 2.30 (m, 1 H), 2.32 - 2.19 (m, 1 H); LCMS (ESI⁺): *m/z* 431.2 (M+H)⁺.

Example 16: Synthesis of 1-(7-((*S*)-1-(3-(2-hydroxyphenyl)-5-methyl-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)ethyl)-3-oxa-7,9-diazabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one and 1-(7-((*R*)-1-(3-(2-hydroxyphenyl)-5-methyl-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)ethyl)-3-oxa-7,9-diazabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one (Compounds 491 and 492):

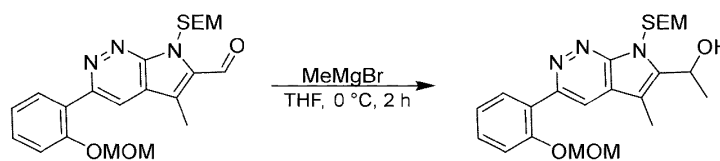


Step 1:



[0453] To a solution of 3-(2-(methoxymethoxy)phenyl)-5-methyl-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazine (3 g, 7.51 mmol, 1 eq) in THF (30 mL) was added dropwise LDA (2 M, 11.26 mL, 3 eq) at -78 °C under N₂, and the mixture was stirred at the same temperature for 30 min. Then, DMF (1.65 g, 22.52 mmol, 1.73 mL, 3 eq) was added dropwise to the mixture at -78 °C under N₂. The mixture was stirred at -78 °C for 2 h. The mixture was quenched with saturated aq. NH₄Cl (20 mL) at 0 °C and partitioned between ethyl acetate (50 mL) and H₂O (50 mL). The organic phase was separated, washed with brine (50 mL × 2), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO₂, PE/EA = 10/1 to 3/1) to give 3-(2-(methoxymethoxy)phenyl)-5-methyl-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazine-6-carbaldehyde (2.4 g, 5.61 mmol, 74.76% yield) as a yellow solid. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ 10.46 (s, 1H), 8.26 (s, 1H), 7.93 (dd, *J* = 1.6, 7.6 Hz, 1H), 7.44 - 7.39 (m, 1H), 7.29 (d, *J* = 0.8 Hz, 1H), 7.27 (d, *J* = 0.8 Hz, 1H), 7.20 (dt, *J* = 1.2, 7.6 Hz, 1H), 6.25 (s, 2H), 5.22 (s, 2H), 3.71 - 3.59 (m, 2H), 3.43 (s, 3H), 2.69 (s, 3H), 1.00 - 0.87 (m, 2H), -0.07 (s, 9H).

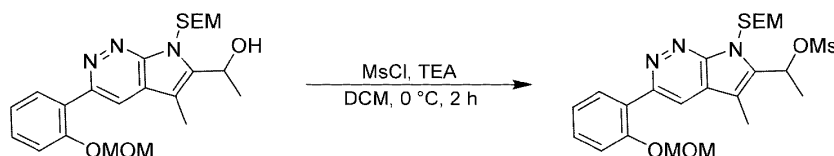
Step 2:



[0454] To a solution of 3-(2-(methoxymethoxy)phenyl)-5-methyl-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazine-6-carbaldehyde (2.30 g, 5.38 mmol, 1 eq) in THF (25 mL) was added MeMgBr (3M, 5.38 mL, 3 eq) dropwise at 0 °C. The mixture was stirred at the same temperature for 2 h. The mixture was quenched with saturated NH₄Cl (10 mL) at 0 °C and partitioned between ethyl acetate

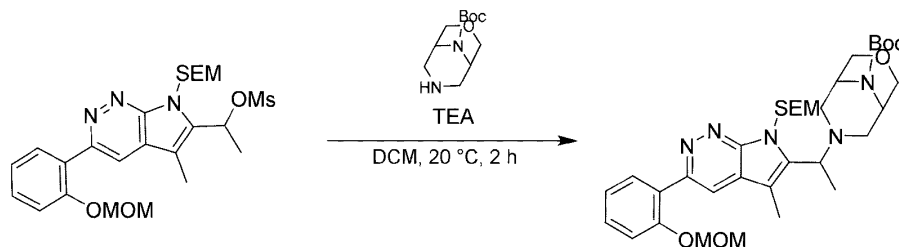
(30 mL) and H₂O (30 mL). The organic phase was separated, washed with brine (30 mL × 2), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure and the residue was purified by column chromatography (SiO₂, PE/EA = 10/1 to 3/1) to give 1-(3-(2-(methoxymethoxy)phenyl)-5-methyl-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)ethan-1-ol (1.2 g, 2.71 mmol, 50.29% yield) as a brown solid. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ 8.03 (s, 1H), 7.83 (dd, *J* = 1.2, 7.6 Hz, 1H), 7.47 - 7.37 (m, 1H), 7.29 (s, 0.6H), 7.27 (s, 0.4H), 7.19 (t, *J* = 7.6 Hz, 1H), 6.16 (d, *J* = 11.2 Hz, 1H), 5.99 (d, *J* = 11.2 Hz, 1H), 5.41 (q, *J* = 6.8 Hz, 1H), 5.22 (s, 2H), 3.71 - 3.60 (m, 2H), 3.43 (s, 3H), 2.38 (s, 3H), 1.72 (d, *J* = 6.8 Hz, 3H), 0.95 (ddd, *J* = 6.8, 8.8, 10.0 Hz, 2H), -0.04 (s, 9H).

Step 3:



[0455] To a solution of 1-(3-(2-(methoxymethoxy)phenyl)-5-methyl-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)ethan-1-ol (450 mg, 1.01 mmol, 1 *eq*) and TEA (1.03 g, 10.14 mmol, 1.41 mL, 10 *eq*) in DCM (5 mL) was added MsCl (232.40 mg, 2.03 mmol, 157.03 μL, 2 *eq*) under N₂ at 0 °C. The mixture was stirred at the same temperature for 2 h under N₂. At this point, the reaction mixture containing the product, 1-(3-(2-(methoxymethoxy)phenyl)-5-methyl-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)ethyl methanesulfonate, was taken to the next step without work up or purification.

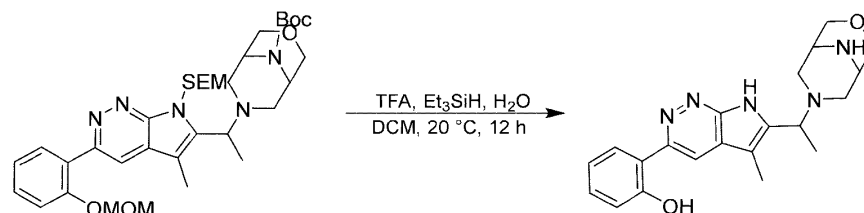
Step 4:



[0456] A solution of 1-(3-(2-(methoxymethoxy)phenyl)-5-methyl-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)ethyl methanesulfonate (520 mg, 996.74 μmol, 1 *eq*), *tert*-butyl 3-oxa-7,9-diazabicyclo[3.3.1]nonane-9-carboxylate (341.31 mg, 1.50 mmol, 1.5 *eq*), and TEA (302.58 mg, 2.99 mmol, 416.20 μL, 3 *eq*) in DCM (5 mL) was stirred at 20 °C for 2 h. The reaction mixture was partitioned between ethyl acetate (5 mL) and H₂O (5 mL). The organic phase was separated, washed with brine (5 mL × 2), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure and the residue was purified by column chromatography (SiO₂, PE/EA = 10/1 to 3/1) to give *tert*-butyl 7-(1-(3-(2-(methoxymethoxy)phenyl)-5-methyl-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)ethyl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane-9-carboxylate (250 mg, 382.33 μmol, 38.36% yield) as a brown solid. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ 7.99 (s, 1H), 7.88 (d, *J* = 7.6 Hz, 1H), 7.42 - 7.35 (m, 1H), 7.31 - 7.28 (m, 0.6H), 7.26 (s, 0.4H), 7.20 - 7.15 (m, 1H), 6.45 - 6.35 (m,

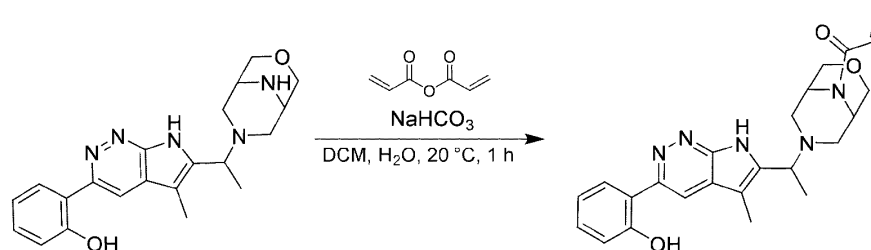
1H), 6.07 (dd, $J = 3.6, 10.8$ Hz, 1H), 5.21 (s, 2H), 4.00 - 3.89 (m, 2H), 3.84 (t, $J = 11.2$ Hz, 1H), 3.78 - 3.62 (m, 6H), 3.45 (s, 3H), 3.35 (d, $J = 10.4$ Hz, 1H), 2.78 - 2.69 (m, 1H), 2.51 - 2.42 (m, 1H), 2.39 (d, $J = 3.6$ Hz, 3H), 2.37 - 2.33 (m, 1H), 1.58 (d, $J = 6.8$ Hz, 3H), 1.48 (d, $J = 13.6$ Hz, 9H), 0.92 - 0.82 (m, 2H), -0.05 (s, 9H).

Step 5:



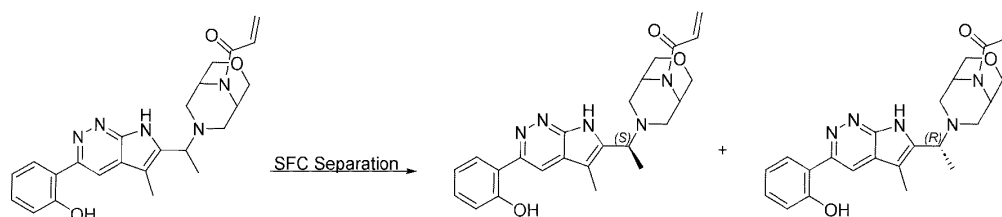
[0457] A solution of *tert*-butyl 7-(1-(3-(2-(methoxymethoxy)phenyl)-5-methyl-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)ethyl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane-9-carboxylate (250 mg, 382.33 μmol , 1 *eq*) in TFA (4 mL), Et_3SiH (0.02 mL), and H_2O (0.02 mL) was stirred at 20 $^\circ\text{C}$ for 12 h. The mixture was concentrated under reduced pressure to give crude 2-(6-(1-(3-oxa-7,9-diazabicyclo[3.3.1]nonan-7-yl)ethyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-3-yl)phenol (188 mg, 380.97 μmol , 99.64% yield, TFA) as a yellow oil, which was used in the next step without purification. LCMS (ESI⁺): m/z 380.2 (M+H)⁺.

Step 6:



[0458] To a solution of 2-(6-(1-(3-oxa-7,9-diazabicyclo[3.3.1]nonan-7-yl)ethyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-3-yl)phenol (180 mg, 364.76 μmol , 1 *eq*, TFA) in DCM (4 mL) and NaHCO_3 aq. (1N, 4 mL) was added prop-2-enyl prop-2-enoate (46.00 mg, 364.76 μmol , 1 *eq*) at 20 $^\circ\text{C}$, and the mixture was stirred at the same temperature for 1 h. The reaction mixture was diluted with H_2O (5 mL) and extracted with DCM (5 mL $\times$ 2). The combined organic layers were washed with brine (5 mL), dried over Na_2SO_4 , and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by prep-TLC (SiO_2 , PE/EA = 1/1) to give 1-(7-(1-(3-(2-hydroxyphenyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)ethyl)-3-oxa-7,9-diazabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one (50 mg, 115.34 μmol , 31.62% yield) as a white solid. ^1H NMR (400 MHz, $\text{CHLOROFORM-}d$) δ 8.08 (d, $J = 4.8$ Hz, 1H), 7.82 (d, $J = 8.8$ Hz, 1H), 7.37 - 7.29 (m, 1H), 7.13 (d, $J = 8.0$ Hz, 1H), 7.02 - 6.92 (m, 1H), 6.61 - 6.49 (m, 1H), 6.48 - 6.38 (m, 1H), 5.88 - 5.71 (m, 1H), 4.85 - 4.53 (m, 1H), 4.28 - 4.14 (m, 1H), 4.13 - 4.02 (m, 2H), 4.00 - 3.82 (m, 4H), 3.50 - 3.34 (m, 0.5H), 3.05 - 2.90 (m, 0.5H), 2.88 - 2.75 (m, 2H), 2.32 (s, 3H), 1.57 - 1.47 (m, 3H).

Step 7:

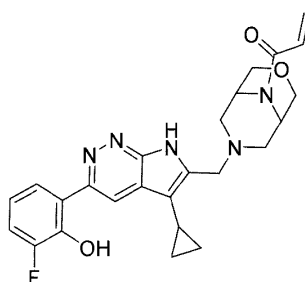


[0459] 1-(7-(1-(3-(2-hydroxyphenyl)-5-methyl-7H-pyrrolo[2,3-c]pyridazin-6-yl)ethyl)-3-oxa-7,9-diazabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one (50 mg, 115.34 μmol) was separated by SFC (Column: DAICEL CHIRALCEL OD (250mm*30mm,10 μm);mobile phase: $[\text{CO}_2\text{-MeOH}$ (0.1% $\text{NH}_3\text{H}_2\text{O}$)]); gradient:30%-50% B over 14.0 min) to give 492 (1st eluting isomer, 18.7 mg, 42.27 μmol) and 491 (2nd eluting isomer, 19 mg, 42.95 μmol).

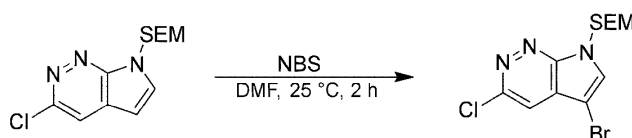
[0460] **492:** (ESI⁺): m/z 434.1 (M+H)⁺. ¹H NMR (400 MHz, METHANOL-*d*₄) δ 8.40 (s, 1H), 7.98 (d, J = 8.0 Hz, 1H), 7.28 (t, J = 7.6 Hz, 1H), 7.04 - 6.92 (m, 2H), 6.84 - 6.60 (m, 1H), 6.30 (d, J = 16.4 Hz, 1H), 5.87 - 5.74 (m, 1H), 4.63 (s, 0.5H), 4.46 - 4.26 (m, 1H), 4.15 (dd, J = 4.8, 11.6 Hz, 1H), 4.09 (s, 0.5H), 3.94 (dd, J = 7.2, 11.6 Hz, 1H), 3.87 (d, J = 11.2 Hz, 1H), 3.82 - 3.75 (m, 1H), 3.61 (dd, J = 3.2, 6.8 Hz, 1H), 3.55 (d, J = 11.2 Hz, 1H), 2.87 - 2.80 (m, 1H), 2.49 (t, J = 11.6 Hz, 1H), 2.38 (d, J = 2.8 Hz, 1H), 2.35 (s, 3H), 1.51 (d, J = 6.4 Hz, 3H).

[0461] **491:** LCMS (ESI⁺): m/z 434.1 (M+H)⁺. ¹H NMR (400 MHz, METHANOL-*d*₄) δ 8.43 (s, 1H), 8.00 (d, J = 7.6 Hz, 1H), 7.34 - 7.25 (m, 1H), 7.03 - 6.95 (m, 2H), 6.84 - 6.61 (m, 1H), 6.35 - 6.23 (m, 1H), 5.80 (ddd, J = 2.0, 10.4, 16.8 Hz, 1H), 4.63 (d, J = 1.2 Hz, 0.5H), 4.42 (s, 0.5H), 4.30 (s, 0.5H), 4.15 (dd, J = 4.8, 11.2 Hz, 1H), 4.09 (s, 0.5H), 3.94 (dd, J = 6.4, 11.6 Hz, 1H), 3.90 - 3.84 (m, 1H), 3.78 (dd, J = 2.0, 11.6 Hz, 1H), 3.62 (dd, J = 2.8, 6.8 Hz, 1H), 3.56 (d, J = 10.8 Hz, 1H), 2.83 (dd, J = 5.2, 11.6 Hz, 1H), 2.49 (t, J = 11.6 Hz, 1H), 2.36 (s, 4H), 1.58 - 1.46 (m, 3H).

Example 17: Synthesis of 1-(7-((5-Cyclopropyl-3-(3-fluoro-2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)-3-oxa-7,9-diazabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one (Compound 494):

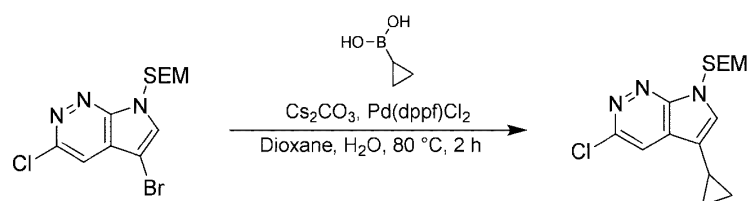


Step 1:



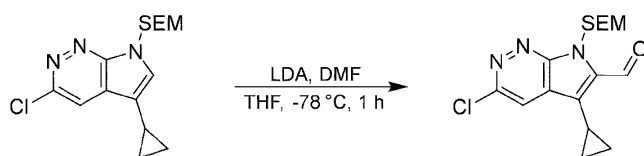
[0462] To a solution of 3-chloro-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazine (3 g, 10.57 mmol, 1 eq) in DMF (10 mL) was added NBS (2.07 g, 11.63 mmol, 1.1 eq). The mixture was stirred at 25 °C for 2 h. The reaction mixture was quenched by addition of H₂O (5 mL), then diluted with H₂O (5 mL) and extracted with MTBE (10 mL × 2). The combined organic layers were washed with brine (100 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure to give 5-bromo-3-chloro-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazine (3.5 g, 9.65 mmol, 91.29% yield) as a yellow solid, which was used in the next step without purification. ¹H NMR (400 MHz, METHANOL-*d*₄) δ 8.15 (s, 1H), 7.88 (s, 1H), 5.81 (s, 2H), 3.70 - 3.55 (m, 2H), 0.96 - 0.82 (m, 2H), 0.01 - -0.15 (m, 9H).

Step 2:



[0463] A mixture of 5-bromo-3-chloro-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazine (3.5 g, 9.65 mmol, 1 eq), cyclopropylboronic acid (1.66 g, 19.30 mmol, 2 eq), Cs₂CO₃ (9.43 g, 28.95 mmol, 3 eq), and Pd(dppf)Cl₂ (706.04 mg, 964.92 μmol, 0.1 eq) in dioxane (32 mL) and H₂O (8 mL) was degassed and purged with N₂ 3 times, then the mixture was stirred at 80 °C for 2 h under N₂ atmosphere. The reaction mixture was quenched by addition of H₂O (20 mL), then diluted with additional H₂O (20 mL) and extracted with EtOAc (40 mL × 2). The combined organic layers were washed with brine (40 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO₂, Petroleum ether/Ethyl acetate=4:1) to give 3-chloro-5-cyclopropyl-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazine (2.1 g, 6.48 mmol, 67.19% yield) as a yellow solid. ¹H NMR (400 MHz, METHANOL-*d*₄) δ 8.00 (s, 1H), 7.68 (d, *J* = 0.8 Hz, 1H), 5.72 (s, 2H), 3.65 - 3.49 (m, 2H), 2.00 - 1.90 (m, 1H), 1.01 - 0.94 (m, 2H), 0.90 - 0.83 (m, 2H), 0.73 - 0.67 (m, 2H), -0.08 - -0.11 (m, 9H).

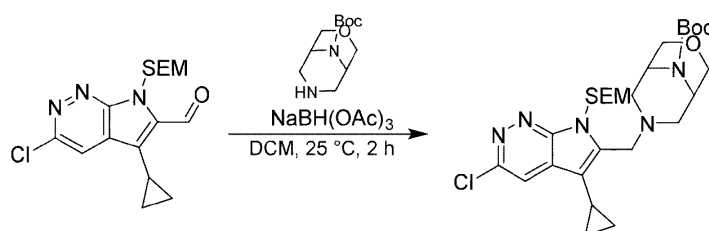
Step 3:



[0464] To a solution of 3-chloro-5-cyclopropyl-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazine (1 g, 3.09 mmol, 1 eq) in THF (10 mL) was added dropwise LDA (2 M, 4.63 mL, 3 eq) at -78 °C over 5 min. The resulting mixture was stirred at the same temperature for 30 min, after which DMF (1.35 g, 18.52 mmol, 1.43 mL, 6 eq) in THF (0.5 mL) was added dropwise to the mixture. The resulting mixture was stirred at -78 °C for 1 h. The reaction mixture was quenched by addition of aqueous NH₄Cl (5 mL) at 0 °C under N₂ atmosphere, then diluted with H₂O (5 mL) and extracted with EtOAc (10

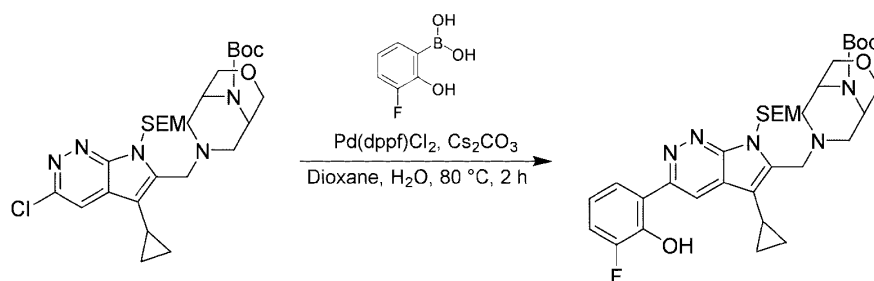
ml $\times$ 2). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4 , and filtered. The filtrate was concentrated under reduced pressure and the residue was purified by column chromatography (SiO_2 , Petroleum ether/Ethyl acetate=3:1) to give 3-chloro-5-cyclopropyl-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazine-6-carbaldehyde (600 mg, 1.71 mmol, 55.22% yield) as a yellow solid. ^1H NMR (400 MHz, $\text{METHANOL-}d_4$) δ 10.58 (s, 1H), 8.16 (s, 1H), 6.14 (s, 2H), 3.71 - 3.64 (m, 2H), 3.61 (d, J = 4.8 Hz, 1H), 1.26 - 1.21 (m, 4H), 0.75 - 0.71 (m, 2H), -0.07 (s, 9H).

Step 4:



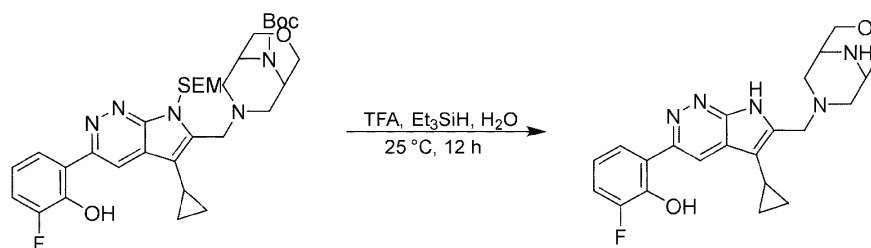
[0465] To a solution of 3-chloro-5-cyclopropyl-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazine-6-carbaldehyde (600 mg, 1.71 mmol, 1 eq) in DCM (6 mL) was added *tert*-butyl 3-oxa-7,9-diazabicyclo [3.3.1] nonane-9-carboxylate (778.47 mg, 3.41 mmol, 2 eq). The mixture was stirred at 25 °C for 1 h. Then, $\text{NaBH}(\text{OAc})_3$ (722.72 mg, 3.41 mmol, 2 eq) was added to the mixture. The resulting mixture was stirred at 25 °C for 1 h. The reaction mixture was quenched by addition of H_2O (6 mL) at 25°C, then diluted with additional H_2O (6 mL) and extracted with DCM (12 mL $\times$ 2). The combined organic layers were washed with brine (12 mL), dried over Na_2SO_4 , and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO_2 , petroleum ether/ethyl acetate=3:1) to give *tert*-butyl 7-((3-chloro-5-cyclopropyl-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)methyl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane-9-carboxylate (400 mg, 708.98 μmol , 41.58% yield) as a yellow solid. ^1H NMR (400 MHz, $\text{METHANOL-}d_4$) δ 7.87 (s, 1H), 6.23 (s, 2H), 3.98 - 3.91 (m, 4H), 3.85 (dd, J = 8.4, 11.2 Hz, 2H), 3.77 - 3.67 (m, 2H), 3.57 - 3.50 (m, 2H), 2.99 (d, J = 10.8 Hz, 2H), 2.56 (d, J = 11.2 Hz, 2H), 1.86 (tt, J = 5.2, 8.4 Hz, 1H), 1.49 (s, 9H), 1.09 - 1.00 (m, 2H), 0.91 - 0.86 (m, 2H), 0.77 - 0.71 (m, 2H), -0.08 - -0.10 (m, 9H).

Step 5:



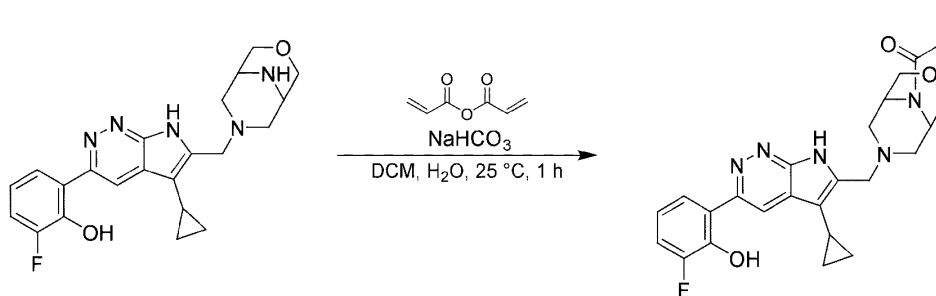
[0466] A mixture of *tert*-butyl 7-((3-chloro-5-cyclopropyl-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)methyl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane-9-carboxylate (200 mg, 354.49 μ mol, 1 eq), (3-fluoro-2-hydroxy-phenyl) boronic acid (165.82 mg, 1.06 mmol, 3 eq), Pd(dppf)Cl₂ (25.94 mg, 35.45 μ mol, 0.1 eq), and Cs₂CO₃ (693.00 mg, 2.13 mmol, 6 eq) in dioxane (2 mL) and H₂O (0.4 mL) was degassed and purged with N₂ 3 times. Then, the mixture was heated to 80 °C and stirred for 2 h under N₂ atmosphere. The reaction mixture was quenched by addition of H₂O (1 mL) at 25 °C, then diluted with additional H₂O (1 mL) and extracted with EtOAc (2 mL $\times$ 2). The combined organic layers were washed with brine (2 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO₂, petroleum ether/ethyl acetate=3:1) to give *tert*-butyl 7-((5-cyclopropyl-3-(3-fluoro-2-hydroxyphenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)methyl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane-9-carboxylate (100 mg, 156.29 μ mol, 44.09% yield) as a yellow solid. ¹H NMR (400 MHz, METHANOL-*d*₄) δ 8.43 (s, 1H), 7.91 - 7.71 (m, 1H), 7.32 - 7.03 (m, 1H), 6.95 (dt, *J* = 5.2, 8.0 Hz, 1H), 6.33 - 6.18 (m, 2H), 4.01 - 3.92 (m, 4H), 3.90 - 3.81 (m, 2H), 3.73 (dt, *J* = 2.4, 5.6 Hz, 2H), 3.62 - 3.50 (m, 2H), 3.05 - 2.93 (m, 2H), 2.62 - 2.52 (m, 2H), 1.95 - 1.81 (m, 1H), 1.51 - 1.48 (m, 9H), 1.14 - 1.01 (m, 2H), 0.94 - 0.85 (m, 2H), 0.81 - 0.70 (m, 2H), -0.01 - -0.13 (m, 9H).

Step 6:



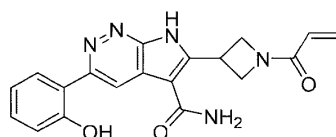
[0467] A solution of *tert*-butyl 7-((5-cyclopropyl-3-(3-fluoro-2-hydroxyphenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)methyl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane-9-carboxylate (90 mg, 140.66 μ mol, 1 eq) in TFA (1 mL), Et₃SiH (0.05 mL), and H₂O (0.05 mL) was stirred at 25 °C for 12 h. The reaction mixture was concentrated under reduced pressure to give 2-(6-((3-oxa-7,9-diazabicyclo[3.3.1]nonan-7-yl)methyl)-5-cyclopropyl-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)-6-fluorophenol (50 mg, 122.11 μ mol, 86.81% yield) as yellow oil, which was used in the next step without workup or purification. LCMS (ESI⁺): *m/z* 410.3 (M+H)⁺.

Step 7:

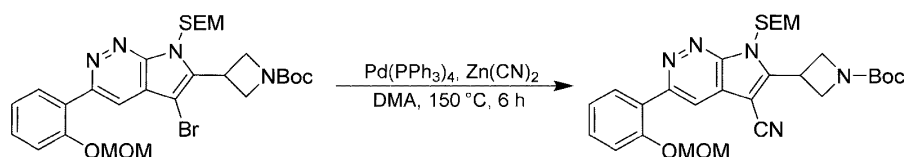


[0468] To a solution of 2-(6-((3-oxa-7,9-diazabicyclo[3.3.1]nonan-7-yl)methyl)-5-cyclopropyl-7H-pyrrolo[2,3-c]pyridazin-3-yl)-6-fluorophenol (50 mg, 122.11 μmol , 1 eq) and NaHCO_3 (51.29 mg, 610.57 μmol , 23.76 μL , 5 eq) in DCM (1 mL) and H_2O (1 mL) was added prop-2-enoyl prop-2-enoate (23.10 mg, 183.17 μmol , 1.5 eq). The resulting mixture was stirred at 25 $^\circ\text{C}$ for 1 h. The reaction mixture was quenched by addition of MeOH (1 mL) at 25 $^\circ\text{C}$, then diluted with H_2O (1 mL) and extracted with DCM (2 mL $\times$ 2). The combined organic layers were washed with brine (2 mL), dried over Na_2SO_4 , and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by prep-HPLC (FA condition) to give **494** (9.5 mg, 20.49 μmol , 16.78% yield). LCMS (ESI^+): m/z 464.1 ($\text{M}+\text{H}^+$). ^1H NMR (400 MHz, $\text{METHANOL}-d_4$) δ 8.42 (s, 1H), 7.77 (d, $J = 8.0$ Hz, 1H), 7.15 (ddd, $J = 1.2, 8.0, 10.8$ Hz, 1H), 6.94 (dt, $J = 5.2, 8.0$ Hz, 1H), 6.76 (dd, $J = 10.8, 16.8$ Hz, 1H), 6.32 (dd, $J = 2.0, 16.8$ Hz, 1H), 5.82 (dd, $J = 2.0, 10.8$ Hz, 1H), 4.23 (s, 1H), 4.08 (dd, $J = 7.2, 11.6$ Hz, 2H), 3.90 - 3.81 (m, 4H), 3.15 (d, $J = 11.6$ Hz, 2H), 2.87 - 2.72 (m, 1H), 2.61 - 2.51 (m, 2H), 1.93 - 1.81 (m, 1H), 1.09 - 1.01 (m, 2H), 0.77 - 0.71 (m, 2H).

Example 18: Synthesis of 6-(1-Acryloylazetidin-3-yl)-3-(2-hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazine-5-carboxamide (Compound 505):



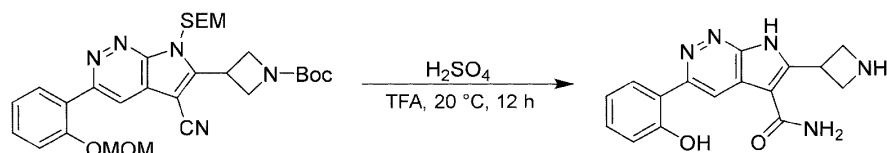
Step 1:



[0469] To a solution of *tert*-butyl 3-(5-bromo-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)azetidine-1-carboxylate (250 mg, 403.47 μmol , 1 eq) in DMA (8 mL) was added $\text{Pd}(\text{PPh}_3)_4$ (93.25 mg, 80.69 μmol , 0.2 eq) and $\text{Zn}(\text{CN})_2$ (142.13 mg, 1.21 mmol, 76.83 μL , 3 eq) at 20 $^\circ\text{C}$ under N_2 atmosphere. The mixture was heated to 150 $^\circ\text{C}$ and stirred for 6 h. The reaction mixture was quenched by addition of aqueous NaHCO_3 (5 mL) and extracted with EtOAc (5 mL $\times$ 2). The combined organic layers were washed with brine (5 mL), dried over Na_2SO_4 , and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified

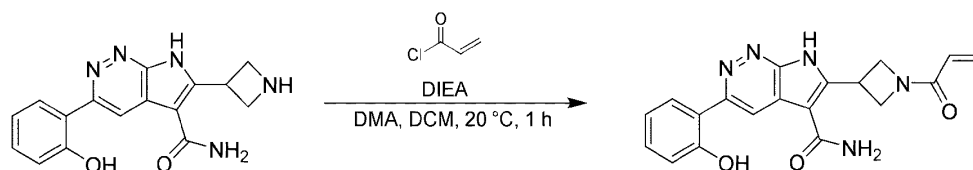
by column chromatography (SiO₂, PE/EA = 10/1 to 2/1) to give *tert*-butyl 3-(5-cyano-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)azetidine-1-carboxylate (80 mg, 141.41 μmol, 35.05% yield) as a yellow solid. ¹H NMR (400 MHz, METHANOL-*d*₄) δ 8.56 (s, 1H), 7.71 (dd, *J* = 1.6, 7.6 Hz, 1H), 7.52 - 7.45 (m, 1H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.21 - 7.12 (m, 1H), 6.32 (s, 2H), 5.29 (s, 2H), 4.45 - 4.31 (m, 5H), 3.92 (t, *J* = 8.0 Hz, 2H), 3.42 (s, 3H), 1.49 (s, 9H), 0.99 - 0.92 (m, 2H), -0.08 (s, 9H).

Step 2:



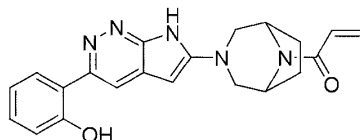
[0470] To a solution of *tert*-butyl 3-(5-cyano-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)azetidine-1-carboxylate (60 mg, 106.06 μmol, 1 *eq*) in TFA (1 mL) was added H₂SO₄ (104.02 mg, 1.06 mmol, 56.53 μL, 10 *eq*) at 20 °C. The mixture was stirred at the same temperature for 12 h. The reaction mixture was then concentrated under reduced pressure and the residue was purified by prep-HPLC (TFA condition) to give 6-(azetidin-3-yl)-3-(2-hydroxyphenyl)-7*H*-pyrrolo[2,3-*c*]pyridazine-5-carboxamide (6 mg, 19.40 μmol, 18.29% yield) as a yellow solid. LCMS (ESI⁺): *m/z* 310.2 (M+H)⁺.

Step 3:

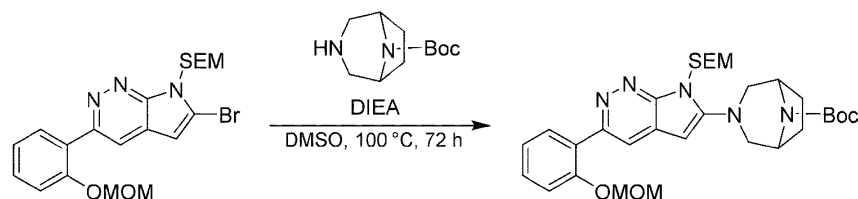


[0471] To a solution of 6-(azetidin-3-yl)-3-(2-hydroxyphenyl)-7*H*-pyrrolo[2,3-*c*]pyridazine-5-carboxamide (6 mg, 19.40 μmol, 1 *eq*) and DIEA (12.53 mg, 96.99 μmol, 16.89 μL, 5 *eq*) in DMA (0.5 mL) was added prop-2-enoyl chloride (1.23 mg, 13.58 μmol, 1.10 μL, 0.7 *eq*) at 20 °C. The mixture was stirred at 20 °C for 1 h. The reaction mixture was diluted with H₂O (5 mL) and extracted with EtOAc (5 mL × 2). The combined organic layers were washed with brine (5 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by prep-HPLC (FA condition) to give 6-(1-acryloylazetidin-3-yl)-3-(2-hydroxyphenyl)-7*H*-pyrrolo[2,3-*c*]pyridazine-5-carboxamide (3 mg, 8.26 μmol, 42.56% yield). LCMS (ESI⁺): *m/z* 364.2 (M+H)⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 13.84 (br s, 1H), 8.63 (s, 1H), 8.13 (d, *J* = 7.2 Hz, 1H), 7.45 (br s, 1H), 7.36 - 7.27 (m, 1H), 7.07 - 6.92 (m, 2H), 6.37 (dd, *J* = 10.4, 17.2 Hz, 1H), 6.15 (dd, *J* = 2.4, 17.2 Hz, 1H), 5.71 (dd, *J* = 2.4, 10.4 Hz, 1H), 4.98 - 4.81 (m, 1H), 4.67 (t, *J* = 8.8 Hz, 1H), 4.57 - 4.46 (m, 1H), 4.39 - 4.31 (m, 1H), 4.29 - 4.20 (m, 1H).

Example 19: Synthesis of 1-(3-(3-(2-Hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3,8-diazabicyclo[3.2.1]octan-8-yl)prop-2-en-1-one (Compound 533):

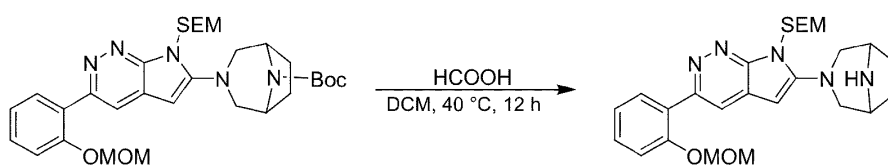


Step 1:



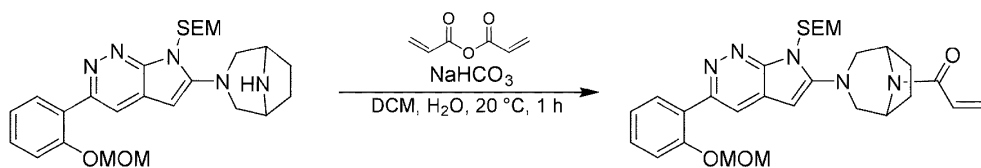
[0472] A mixture of **intermediate 1** (200 mg, 430.64 μmol , 1 *eq*), *tert*-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate (182.84 mg, 861.28 μmol , 2 *eq*) and DIEA (556.57 mg, 4.31 mmol, 750.09 μL , 10 *eq*) in DMSO (4 mL) was degassed and purged with N_2 3 times. The mixture was then heated to 100 $^\circ\text{C}$ and stirred for 72 h under N_2 atmosphere. The reaction mixture was diluted with H_2O (10 mL) and extracted with EtOAc (10 mL $\times$ 2). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4 , and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by prep-TLC (SiO_2 , PE/EA = 1/1) to give *tert*-butyl 3-(3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate (120 mg, 201.41 μmol , 46.77% yield) as a yellow oil. ^1H NMR (400 MHz, $\text{METHANOL-}d_4$) δ 7.81 (s, 1H), 7.59 - 7.54 (m, 1H), 7.44 - 7.37 (m, 1H), 7.29 (d, J = 8.4 Hz, 1H), 7.18 - 7.10 (m, 1H), 5.96 (s, 1H), 5.73 (s, 2H), 5.17 (s, 2H), 4.36 (s, 2H), 3.90 (t, J = 8.0 Hz, 2H), 3.65 (d, J = 10.4 Hz, 2H), 3.33 (s, 3H), 3.17 - 3.08 (m, 2H), 2.14 - 2.03 (m, 4H), 1.51 (s, 9H), 0.98 (t, J = 8.0 Hz, 2H), -0.02 (s, 9H).

Step 2:



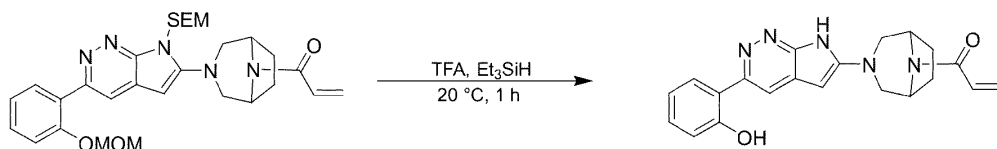
[0473] To a solution of *tert*-butyl 3-(3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate (60 mg, 100.70 μmol , 1 *eq*) in DCM (0.4 mL) was added formic acid (0.2 mL). The mixture was stirred at 40 $^\circ\text{C}$ for 12 h. The reaction mixture was concentrated under reduced pressure, and the residue was triturated with MTBE (5 mL) at 20 $^\circ\text{C}$ for 10 min to give 6-(3,8-diazabicyclo[3.2.1]octan-3-yl)-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazine (60 mg, crude, FA salt) as a yellow oil, which was used in the subsequent step without purification. LCMS (ESI^+): m/z 496.3 ($\text{M}+\text{H}^+$).

Step 3:



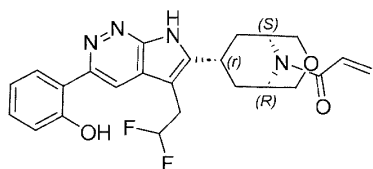
[0474] To a solution of 6-(3,8-diazabicyclo[3.2.1]octan-3-yl)-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazine (60 mg, 110.76 μ mol, 1 *eq*, FA salt) in DCM (3 mL) and NaHCO₃ aq. (1M, 3 mL, 27.09 *eq*) was added prop-2-enoyl prop-2-enoate (13.97 mg, 110.76 μ mol, 1 *eq*) in DCM (0.2 mL) dropwise at 20 °C. The resulting mixture was stirred at the same temperature for 1 h. The reaction mixture was diluted with H₂O (10 mL) and extracted with DCM (5 mL $\times$ 2). The combined organic layers were washed with brine (10 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by prep-TLC (SiO₂, PE/EA = 0/1) to give 1-(3-(3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3,8-diazabicyclo[3.2.1]octan-8-yl)prop-2-en-1-one (15 mg, 27.29 μ mol, 24.64% yield) as a yellow oil. ¹H NMR (400 MHz, METHANOL-*d*₄) δ 7.82 (s, 1H), 7.60 - 7.54 (m, 1H), 7.45 - 7.38 (m, 1H), 7.29 (d, *J* = 8.4 Hz, 1H), 7.18 - 7.11 (m, 1H), 6.83 - 6.72 (m, 1H), 6.40 - 6.32 (m, 1H), 5.98 (s, 1H), 5.86 - 5.80 (m, 1H), 5.76 (s, 2H), 5.17 (s, 2H), 4.83 (s, 1H), 4.69 (d, *J* = 5.2 Hz, 1H), 3.93 - 3.87 (m, 2H), 3.81 - 3.70 (m, 2H), 3.33 (s, 3H), 3.23 - 3.10 (m, 2H), 2.27 - 2.12 (m, 3H), 2.09 - 1.99 (m, 1H), 1.02 - 0.96 (m, 2H), 0.01 (s, 9H).

Step 4:

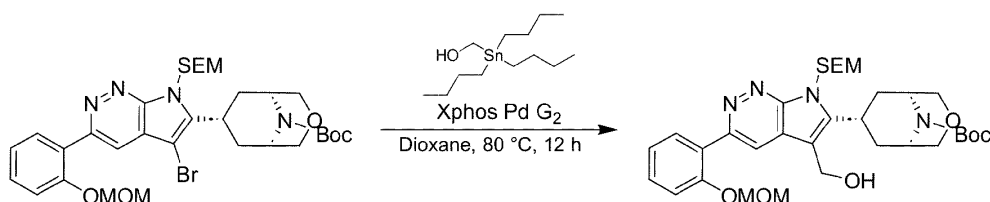


[0475] A solution of 1-(3-(3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3,8-diazabicyclo[3.2.1]octan-8-yl)prop-2-en-1-one (30 mg, 54.57 μ mol, 1 *eq*) in TFA (0.2 mL) and Et₃SiH (0.02 mL) was stirred at 20 °C for 1 h. The reaction mixture was diluted with H₂O (10 mL) and extracted with petroleum ether (5 mL $\times$ 2). The aqueous phase was lyophilized to give **533** (8 mg, 15.95 μ mol, 29.23% yield, TFA salt). LCMS (ESI⁺): *m/z* 376.1 (M+H)⁺. ¹H NMR (400 MHz, METHANOL-*d*₄) δ 7.67 (s, 1H), 7.56 - 7.47 (m, 1H), 7.46 - 7.38 (m, 1H), 7.08 - 7.01 (m, 2H), 6.84 - 6.72 (m, 1H), 6.46 - 6.32 (m, 1H), 6.06 (s, 1H), 5.89 - 5.81 (m, 1H), 4.92 - 4.88 (m, 1H), 4.79 - 4.75 (m, 1H), 3.95 - 3.83 (m, 2H), 3.60 - 3.47 (m, 2H), 2.19 (dd, *J* = 5.2 Hz, 1H), 2.10 - 1.89 (m, 3H).

Example 20: Synthesis of 1-((1*R*,5*S*,7*r*)-7-(5-(2,2-difluoroethyl)-3-(2-hydroxyphenyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one (Compound 537):

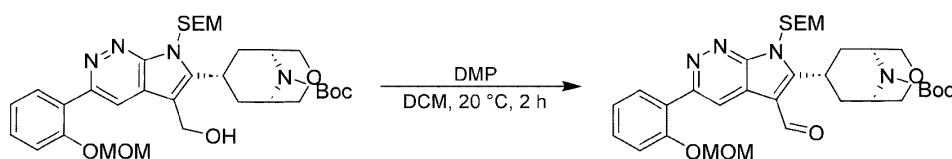


Step 1:



[0476] A mixture of *tert*-butyl (1*R*,5*S*,7*r*)-7-(5-bromo-3-(2-(methoxymethoxy)phenyl)-7-(2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (3.5 g, 5.07 mmol, 1 eq), tributylstannylmethanol (4.89 g, 15.22 mmol, 3 eq), and Xphos Pd G₂ (399.27 mg, 507.46 μmol, 0.1 eq) in dioxane (70 mL) was degassed and purged with N₂ 3 times. The resulting mixture was stirred at 80 °C for 12 h under N₂ atmosphere. The reaction mixture was filtered, and the resulting filtrate was concentrated under reduced pressure. The crude residue was purified by column chromatography (SiO₂, PE/EA = 10/1 to 1/1) to give *tert*-butyl (1*R*,5*S*,7*r*)-7-(5-(hydroxymethyl)-3-(2-(methoxymethoxy)phenyl)-7-(2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (2.1 g, 3.20 mmol, 63.15% yield) as a yellow solid. ¹H NMR (400 MHz, METHANOL-*d*₄) δ 8.19 (s, 1H), 7.62 - 7.59 (m, 1H), 7.46 - 7.39 (m, 1H), 7.30 (d, *J* = 8.4 Hz, 1H), 7.17 - 7.14 (m, 1H), 5.98 (s, 2H), 5.19 (s, 2H), 4.92 - 4.87 (m, 2H), 4.83 - 4.77 (m, 1H), 4.13 (s, 2H), 4.10 - 4.01 (m, 2H), 3.83 (d, *J* = 11.2 Hz, 2H), 3.68 - 3.59 (m, 2H), 3.36 - 3.33 (m, 3H), 2.52 - 2.34 (m, 2H), 2.20 - 2.13 (m, 2H), 1.55 (s, 9H), 0.99 - 0.89 (m, 2H), -0.05 (s, 9H).

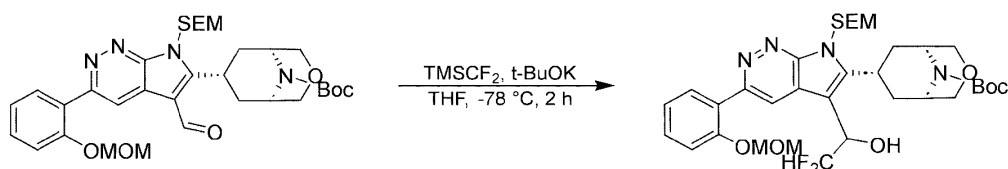
Step 2:



[0477] To a solution of *tert*-butyl (1*R*,5*S*,7*r*)-7-(5-(hydroxymethyl)-3-(2-(methoxymethoxy)phenyl)-7-(2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (0.9 g, 1.40 mmol, 1 eq) in DCM (20 mL) was added Dess-Martin periodinane (DMP) (714.80 mg, 1.69 mmol, 522.13 μL, 1.2 eq) in portions at 0 °C under N₂. The resulting mixture was warmed up to 20 °C and stirred for 2 h under N₂. An additional two reactions were set up as described above, and all three reactions were combined for workup and purification. The combined reaction

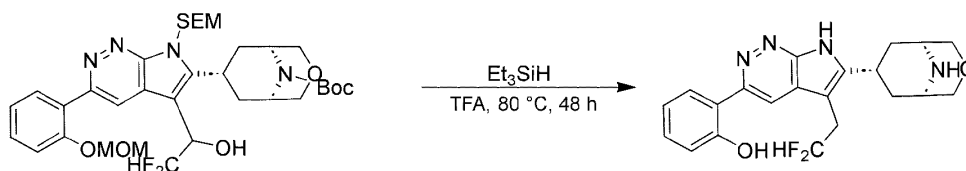
mixtures were filtered, and the filtrate was concentrated under reduced pressure. The crude material was diluted with aqueous NaHCO₃ (100 mL) at 20 °C and extracted with MTBE (100 mL × 2). The combined organic layers were washed with brine (100 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO₂, PE/EA = 10/1 to 1/1) to give *tert*-butyl (1*R*,5*S*,7*r*)-7-(5-formyl-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (1.6 g, 1.78 mmol, 54.58% yield) as a yellow solid. ¹H NMR (400 MHz, METHANOL-*d*₄) δ 10.44 (s, 1H), 8.66 (s, 1H), 7.67 - 7.64 (m, 1H), 7.48 - 7.42 (m, 1H), 7.35 - 7.29 (m, 1H), 7.19 - 7.15 (m, 1H), 6.08 (s, 2H), 5.22 (s, 2H), 5.09 - 4.97 (m, 1H), 4.17 (s, 2H), 4.08 - 4.02 (m, 2H), 3.85 (d, *J* = 11.6 Hz, 2H), 3.75 - 3.68 (m, 2H), 3.39 (s, 3H), 2.60 - 2.47 (m, 2H), 2.30 - 2.21 (m, 2H), 1.56 (s, 9H), 1.03 - 0.95 (m, 2H), -0.04 (s, 9H).

Step 3:



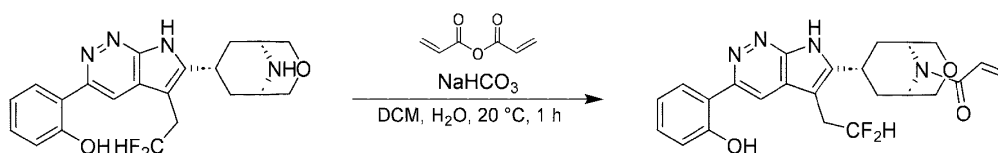
[0478] To a solution of *tert*-butyl (1*R*,5*S*,7*r*)-7-(5-formyl-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (200 mg, 313.07 μmol, 1 eq) and TMSCF₂ (233.31 mg, 1.88 mmol, 6 eq) in THF (4 mL) was added a solution of potassium *tert*-butoxide (1M, 469.61 μL, 1.5 eq) dropwise at -78 °C under N₂. The mixture was stirred at the same temperature for 2 h. Five additional reactions were set up as described above, and all six reactions were combined for workup and purification. The combined reaction mixtures were diluted with H₂O (50 mL) at 20 °C and extracted with EtOAc (50 mL × 3). The combined organic layers were washed with brine (50 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO₂, PE/EA = 10/1 to 1/1) to give *tert*-butyl (1*R*,5*S*,7*r*)-7-(5-(2,2-difluoro-1-hydroxyethyl)-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (680 mg, 915.40 μmol, 48.73% yield) as a yellow solid. ¹H NMR (400 MHz, METHANOL-*d*₄) δ 8.30 (s, 1H), 7.67 - 7.60 (m, 1H), 7.48 - 7.37 (m, 1H), 7.29 (d, *J* = 8.4 Hz, 1H), 7.20 - 7.11 (m, 1H), 6.29 - 6.26 (m, 0.3H), 6.15 - 6.12 (m, 0.5H), 5.99 (s, 2H), 5.33 - 5.21 (m, 1H), 5.19 (s, 2H), 4.83 (s, 1H), 4.12 (d, *J* = 7.2 Hz, 2H), 4.08 - 3.99 (m, 2H), 3.83 (d, *J* = 11.2 Hz, 2H), 3.67 - 3.63 (m, 2H), 3.36 (s, 3H), 2.52 - 2.32 (m, 2H), 2.24 - 2.07 (m, 2H), 1.55 (s, 9H), 0.94 - 0.90 (m, 2H), -0.06 (s, 9H).

Step 4:



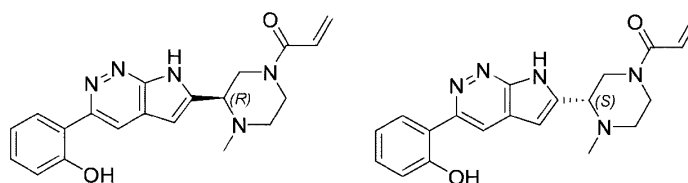
[0479] A mixture of (1*R*,5*S*,7*r*)-7-(5-(2,2-difluoro-1-hydroxyethyl)-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (100.0 mg, 144.7 μ mol, 1.0 eq) in TFA (5 mL) and Et₃SiH (5 mL) was stirred at 80 °C for 48 h. An additional two reactions were set up as described above, and all three reaction mixtures were combined for work-up. The combined reaction mixtures were concentrated under reduced pressure, and the crude material was purified by prep-HPLC (NH₄HCO₃ condition) to give 2-(6-((1*R*,5*S*,7*r*)-3-oxa-9-azabicyclo[3.3.1]nonan-7-yl)-5-(2,2-difluoroethyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)phenol (25.0 mg, 62.4 μ mol, 21.5% yield) as a white solid and byproduct 2-(6-((1*R*,5*S*,7*r*)-3-oxa-9-azabicyclo[3.3.1]nonan-7-yl)-5-(2,2-difluoro-1-hydroxyethyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)phenol (25.0 mg, 60.0 μ mol, 20.7% yield) as a white solid. ¹H NMR (400 MHz, METHANOL-*d*₄) δ 8.45 (s, 1H), 7.98 (d, *J* = 8.4 Hz, 1H), 7.35 - 7.24 (m, 1H), 7.06 - 6.91 (m, 2H), 6.36 - 5.91 (m, 1H), 4.79 (d, *J* = 1.2 Hz, 1H), 3.99 (s, 4H), 3.49 - 3.38 (m, 2H), 3.06 (s, 2H), 2.34 - 2.19 (m, 2H), 2.16 - 2.05 (m, 2H).

Step 5:

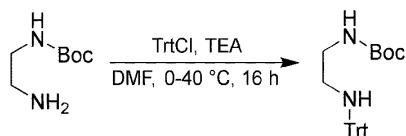


[0480] To a solution of 2-(6-((1*R*,5*S*,7*r*)-3-oxa-9-azabicyclo[3.3.1]nonan-7-yl)-5-(2,2-difluoroethyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)phenol (20.0 mg, 49.9 μ mol, 1.0 eq) in DCM (2 mL) and aq. NaHCO₃ (1M, 2 mL) was added a solution of prop-2-enoyl prop-2-enoate (9.4 mg, 74.9 μ mol, 1.5 eq) in DCM (0.1 mL) dropwise at 20 °C. The resulting mixture was stirred at the same temperature for 1 h. The reaction mixture was then partitioned between DCM (5 mL) and H₂O (5 mL). The organic phase was separated, washed with brine (5 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified via prep-HPLC (TFA condition) to give **537** (10.0 mg, 17.0 μ mol, 34.1% yield). LCMS (ESI⁺): *m/z* 455.1 (M+H)⁺. ¹H NMR (400 MHz, METHANOL-*d*₄) δ 8.58 (s, 1H), 7.64 (dd, *J* = 1.6, 7.6 Hz, 1H), 7.53 - 7.44 (m, 1H), 7.15 - 7.05 (m, 2H), 6.84 (dd, *J* = 10.4, 16.8 Hz, 1H), 6.40 - 6.05 (m, 2H), 5.86 (dd, *J* = 2.0, 10.4 Hz, 1H), 4.80 (s, 1H), 4.73 (s, 1H), 4.37 (s, 1H), 4.13 (dd, *J* = 3.6, 11.6 Hz, 2H), 3.91 - 3.82 (m, 2H), 3.54 (dt, *J* = 3.2, 18.4 Hz, 2H), 2.31 - 2.20 (m, 4H).

Example 21: (R)-1-(3-(3-(2-hydroxyphenyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-4-methylpiperazin-1-yl)prop-2-en-1-one and (S)-1-(3-(3-(2-hydroxyphenyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-4-methylpiperazin-1-yl)prop-2-en-1-one (Compounds **569 and **570**):**

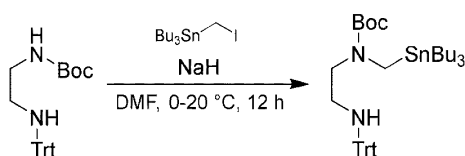


Step 1:



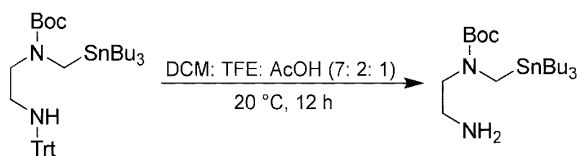
[0481] Trityl chloride (18.27 g, 65.54 mmol, 1.05 eq) in DMF (50 mL) was added dropwise to a solution of *tert*-butyl (2-aminoethyl)carbamate (10 g, 62.42 mmol, 9.84 mL, 1 eq) and TEA (6.95 g, 68.66 mmol, 9.56 mL, 1.1 eq) in DMF (350 mL) at 0 °C. The resulting yellow suspension was warmed to 40 °C and stirred for 16 h. The reaction mixture was poured into water (100 mL) and extracted with EtOAc (100 mL $\times$ 2). The combined organic layers were washed with brine (100 mL $\times$ 3), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was triturated with MTBE (100 mL) at 25 °C for 10 min and filtered. The filter cake was dried to give *tert*-butyl (2-(tritylamino)ethyl)carbamate (20 g, 49.69 mmol, 79.60% yield) as a white solid, which was used in the subsequent step without purification. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ 7.50 (d, *J* = 7.2 Hz, 6H), 7.34 - 7.27 (m, 6H), 7.26 - 7.18 (m, 3H), 5.04 - 4.48 (m, 1H), 3.26 (d, *J* = 5.4 Hz, 2H), 2.29 (t, *J* = 5.6 Hz, 2H), 1.68 (s, 1H), 1.50 (s, 9H).

Step 2:



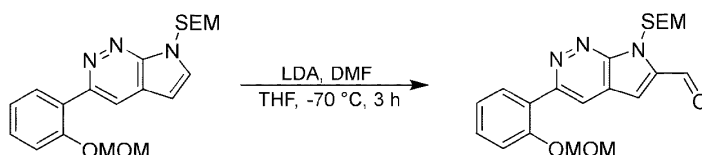
[0482] *Tert*-butyl (2-(tritylamino)ethyl)carbamate (4.2 g, 10.43 mmol, 1 eq) in DMF (20 mL) was added dropwise into a solution of NaH (542.57 mg, 13.56 mmol, 60% purity, 1.3 eq) in DMF (60 mL) at 0 °C under N₂ atmosphere. The resulting suspension was allowed to gradually warm to 20 °C. After 1 h, the reaction mixture was re-cooled to 0 °C and tributyl(iodomethyl)stannane (4.95 g, 11.48 mmol, 1.1 eq) was added dropwise over 10 min under N₂. The resulting suspension was allowed to warm to 20 °C and stir at the same temperature for 12 h under N₂ atmosphere. An additional 3 reactions were set up as described above. All 4 reaction mixtures were combined for work-up. The combined reaction mixtures were quenched by addition of aqueous NH₄Cl (50 mL) at 0 °C under N₂ atmosphere, then diluted with water (50 mL) and extracted with EtOAc (50 mL $\times$ 2). The combined organic layers were washed with brine (50 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure to give *tert*-butyl ((tributylstannyl)methyl)(2-(tritylamino)ethyl)carbamate (20 g, 28.34 mmol, 67.91% yield) as a colorless oil, which was used in the next step without purification. LCMS (ESI⁺): *m/z* 707.5 (M+H)⁺. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ 7.49 (d, *J* = 8.0 Hz, 6H), 7.33 - 7.24 (m, 6H), 7.24 - 7.14 (m, 3H), 3.32 (d, *J* = 5.6 Hz, 2H), 3.04 (s, 1H), 2.85 - 2.70 (m, 1H), 2.32 (d, *J* = 6.8 Hz, 2H), 1.54 - 1.44 (m, 8H), 1.40 (s, 7H), 1.32 - 1.25 (m, 6H), 0.93 - 0.80 (m, 15H).

Step 3:



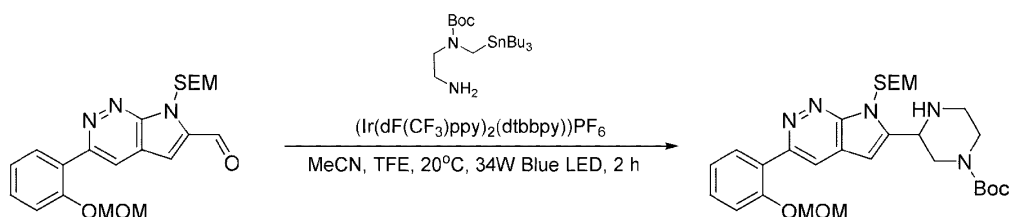
[0483] To a solution of *tert*-butyl ((tributylstannyl)methyl)(2-(tritylamino)ethyl)carbamate (6 g, 8.50 mmol, 1 eq) in DCM (84 mL) was added 2,2,2-Trifluoroethanol (24 mL) and AcOH (12 mL). The mixture was stirred at 20 °C for 12 h. An additional 2 reactions were set up as described above. All 3 reaction mixtures were combined for work-up. The combined reaction mixtures were diluted with DCM (200 mL) and carefully adjusted to pH ~ 8 by addition of saturated aqueous NaHCO₃ (1000 mL) at 0 °C. The layers were separated, and the aqueous layer was extracted with DCM (3 × 200 mL). The combined organic layers were washed with brine (200 mL), dried over Na₂SO₄, and filtered. The residue was purified by prep-HPLC (FA condition) to give *tert*-butyl (2-aminoethyl)((tributylstannyl)methyl)carbamate (8 g, 17.27 mmol, 67.69% yield) as a yellow oil. LCMS (ESI⁺): *m/z* 465.2 (M+H)⁺. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ 3.27 - 3.17 (m, 2H), 3.06 (s, 1H), 2.90 - 2.78 (m, 3H), 1.57 - 1.39 (m, 15H), 1.30 (m, 6H), 1.09 (s, 2H), 0.96 - 0.78 (m, 15H).

Step 4:



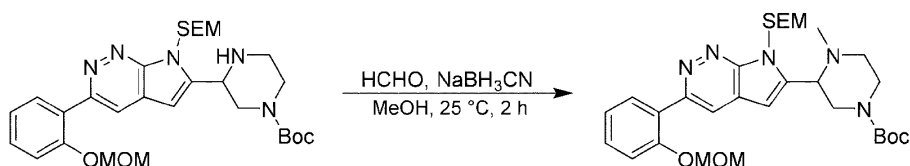
[0484] To a solution of 3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazine (500 mg, 1.30 mmol, 1 eq) in THF (2 mL) was added LDA (2 M, 1.30 mL, 2 eq) at -70 °C over 1 h under N₂. Then, DMF (104.28 mg, 1.43 mmol, 109.76 μL, 1.1 eq) was added dropwise to the resulting mixture at -70 °C under N₂. The mixture was then stirred at -70 °C for 2 h under N₂ atmosphere. An additional 3 reactions were set up as described above. All 4 reaction mixtures were combined for work up. The combined reaction mixtures were quenched by addition of aqueous NH₄Cl (12 mL) at 0 °C under N₂, then diluted with EtOAc (20 mL), and extracted with H₂O (20 mL × 2). The combined organic layers were washed with brine (10 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by prep-HPLC (FA condition) to give 3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazine-6-carbaldehyde (750 mg, 1.81 mmol, 34.96% yield) as a yellow solid. LCMS (ESI⁺): *m/z* 414.2 (M+H)⁺. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ 10.22 - 10.18 (m, 1H), 8.34 (s, 1H), 7.97 (d, *J* = 7.6 Hz, 1H), 7.46 - 7.38 (m, 1H), 7.33 (s, 1H), 7.30 (d, *J* = 8.4 Hz, 1H), 7.21 (t, *J* = 7.6 Hz, 1H), 6.29 (s, 2H), 5.23 (s, 2H), 3.69 (t, *J* = 8.0 Hz, 2H), 3.43 (s, 3H), 0.94 (t, *J* = 8.0 Hz, 2H), -0.07 (s, 9H).

Step 5:



[0485] A solution of 3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazine-6-carbaldehyde (100 mg, 241.81 μmol , 1 eq), *tert*-butyl 2-aminoethyl((tributylstannyl)methyl)carbamate (168.04 mg, 362.72 μmol , 1.5 eq), and 4Å MS (100 mg, 241.81 μmol , 1 eq) in CH_2Cl_2 (0.1 mL) was stirred at 25 °C for 16 h. The resulting mixture was filtered under N_2 atmosphere. To the filtrate was added $(\text{Ir}(\text{dF}(\text{CF}_3)\text{ppy})_2(\text{dtbbpy}))\text{PF}_6$ (6.78 mg, 6.05 μmol , 0.025 eq) in MeCN (0.1 mL) and TFE (0.1 mL). The mixture was then degassed and purged with argon 3 times, and the mixture was stirred at 25 °C for 2 h under argon with blue LEDs. An additional 9 vials were set up in parallel as described above. All 10 reaction mixtures were combined for work-up. The combined reaction mixtures were diluted with water (5 mL) and extracted with EtOAc (5 mL $\times$ 2). The combined organic layers were washed with brine (5 mL), dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2 , dichloromethane/methanol = 1/60) to give *tert*-butyl 3-(3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)piperazine-1-carboxylate (310 mg, 544.08 μmol , 22.50% yield) as an orange oil. LCMS (ESI⁺): m/z 570.4 ($\text{M}+\text{H}$)⁺. ¹H NMR (400 MHz, $\text{CHLOROFORM-}d$) δ 8.10 (s, 1H), 7.91 (dd, J = 1.6, 7.6 Hz, 1H), 7.43 - 7.34 (m, 1H), 7.29 - 7.28 (m, 1H), 7.26 (s, 1H), 7.18 (t, J = 7.2 Hz, 1H), 6.59 (s, 1H), 6.25 - 6.11 (m, 1H), 5.96 - 5.78 (m, 1H), 5.20 (s, 2H), 4.34 - 4.22 (m, 1H), 3.76 - 3.56 (m, 3H), 3.48 - 3.39 (m, 3H), 3.37 - 3.21 (m, 2H), 3.17 - 3.02 (m, 2H), 2.98 - 2.88 (m, 1H), 1.54 - 1.48 (m, 9H), 0.97 - 0.92 (m, 2H), -0.03 - -0.10 (m, 9H).

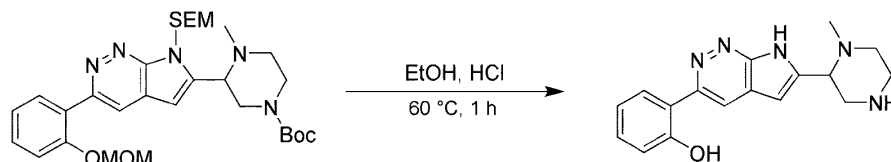
Step 6:



[0486] To a solution of *tert*-butyl 3-(3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)piperazine-1-carboxylate (280 mg, 491.43 μmol , 1 eq) in MeOH (1 mL) was added formaldehyde (159.52 mg, 1.97 mmol, 146.35 μL , 37% purity, 4 eq) and NaBH_3CN (154.41 mg, 2.46 mmol, 5 eq). The mixture was stirred at 25 °C for 2 h. The reaction mixture was diluted with water (2 mL) and extracted with EtOAc (2 mL $\times$ 2). The combined organic layers were washed with brine (2 mL), dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2 , dichloromethane/methanol = 0/1) to give *tert*-butyl 3-(3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-4-methylpiperazine-1-carboxylate (120 mg, 205.55 μmol , 41.83% yield) as

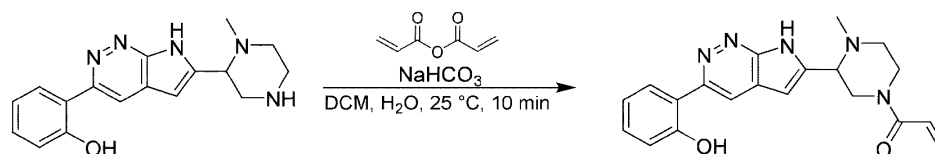
a yellow oil. LCMS (ESI⁺): m/z 584.4 (M+H)⁺. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ 8.11 (s, 1H), 7.96 - 7.90 (m, 1H), 7.46 - 7.38 (m, 2H), 7.21 (t, J = 7.6 Hz, 1H), 6.61 (s, 1H), 6.11 (s, 2H), 5.24 (s, 2H), 4.24 - 4.05 (m, 2H), 3.78 - 3.62 (m, 3H), 3.57 (m, 1H), 3.47 (s, 3H), 3.26 - 3.10 (m, 2H), 3.04 - 2.95 (m, 1H), 2.23 (s, 3H), 1.32 (s, 10H), 0.93 (s, 2H), -0.03 (s, 10H).

Step 7:



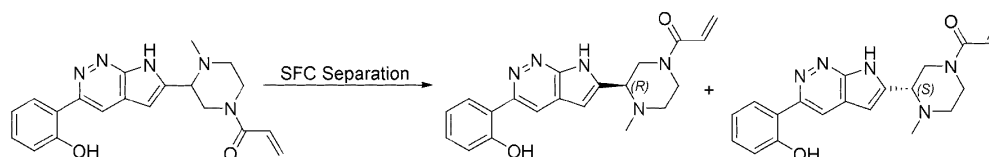
[0487] To a solution of *tert*-butyl 3-(3-(2-(methoxymethoxy)phenyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-4-methylpiperazine-1-carboxylate (75 mg, 128.47 μ mol, 1 eq) in EtOH (0.4 mL) was added HCl (0.2 mL). The mixture was stirred at 60 °C for 1 h. The reaction mixture was concentrated under reduced pressure to give 2-(6-(1-methylpiperazin-2-yl)-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)phenol (60 mg, crude, HCl salt) as a yellow oil, which was used in the next step without purification. LCMS (ESI⁺): m/z 310.1 (M+H)⁺.

Step 8:



[0488] To a solution of 2-(6-(1-methylpiperazin-2-yl)-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)phenol (40 mg, 115.67 μ mol, 1 eq, HCl) in DCM (0.2 mL) was added NaHCO₃ (48.58 mg, 578.33 μ mol, 22.50 μ L, 5 eq) in H₂O (0.2 mL), then prop-2-en-1-yl prop-2-enoate (20.42 mg, 161.93 μ mol, 1.4 eq) in DCM (0.2 mL) was added dropwise to the mixture. The resulting mixture was stirred at 25 °C for 10 min. The reaction mixture was diluted with DCM (1 mL) and extracted with water (1 mL $\times$ 2). The organic layer was washed with brine (1 mL), dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (SiO₂, dichloromethane/tetrahydrofuran = 1/1) to give 1-(3-(3-(2-(6-(1-methylpiperazin-2-yl)-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)phenyl)prop-2-en-1-yl)-4-methylpiperazin-1-yl)prop-2-en-1-one (40 mg, 110.07 μ mol, 63.44% yield) as a yellow solid. LCMS (ESI⁺): m/z 364.2 (M+H)⁺.

Step 9:



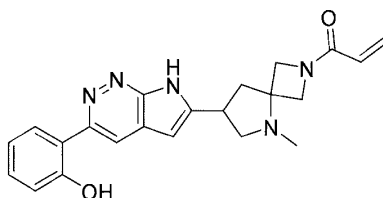
[0489] 1-(3-(3-(2-(6-(1-methylpiperazin-2-yl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-4-methylpiperazin-1-yl)prop-2-en-1-yl)prop-2-en-1-one (40 mg, 110.07 μ mol) was separated by SFC (Column: Waters Xbridge BEH C18

100*30mm*10um; mobile phase: [H₂O (10mM NH₄HCO₃)-ACN]; gradient: 30%-70% B over 8.0 min) to give **570** (1st eluting isomer, 8 mg, 22.01 μmol) and **569** (2nd eluting isomer, 11 mg, 30.27 μmol).

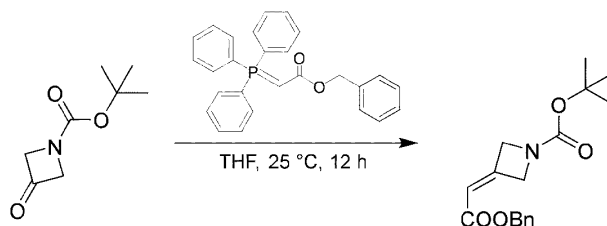
[0490] 570: LCMS (ESI⁺): *m/z* 364.1 (M+H)⁺. ¹H NMR (400 MHz, METHANOL-*d*₄) δ 8.50 (s, 1H), 7.94 (d, *J* = 7.6 Hz, 1H), 7.32 - 7.25 (m, 1H), 7.02 - 6.94 (m, 2H), 6.80 (m, 1H), 6.68 (s, 1H), 6.26 (dd, *J* = 5.4, 16.8 Hz, 1H), 5.78 (dd, *J* = 10.4, 17.6 Hz, 1H), 4.63 - 4.51 (m, 1H), 4.17 (d, *J* = 11.2 Hz, 1H), 3.57 - 3.47 (m, 1H), 3.47 - 3.37 (m, 1H), 3.19 - 3.05 (m, 2H), 2.40 - 2.27 (m, 1H), 2.21 (s, 3H).

[0491] 569: LCMS (ESI⁺): *m/z* 364.1 (M+H)⁺. ¹H NMR (400 MHz, METHANOL-*d*₄) δ 8.50 (s, 1H), 7.94 (d, *J* = 8.0 Hz, 1H), 7.33 - 7.25 (m, 1H), 7.02 - 6.93 (m, 2H), 6.81 (dt, *J* = 10.6, 17.4 Hz, 1H), 6.68 (s, 1H), 6.26 (dd, *J* = 6.4, 16.4 Hz, 1H), 5.78 (dd, *J* = 10.6, 18.0 Hz, 1H), 4.65 - 4.51 (m, 1H), 4.24 - 4.12 (m, 1H), 3.57 - 3.47 (m, 1H), 3.47 - 3.37 (m, 1H), 3.19 - 3.04 (m, 2H), 2.39 - 2.26 (m, 1H), 2.21 (s, 3H).

Example 22: Synthesis of 1-(7-(3-(2-Hydroxyphenyl)-7H-pyrrolo[2,3-*c*]pyridazin-6-yl)-5-methyl-2,5-diazaspiro[3.4]octan-2-yl)prop-2-en-1-one (Compound 591):

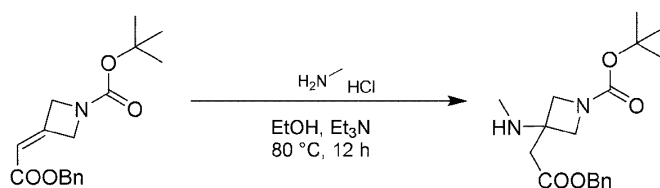


Step 1:



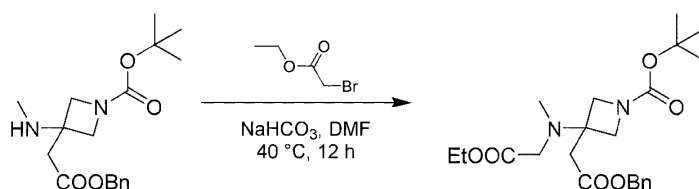
[0492] To a solution of *tert*-butyl 3-oxoazetidine-1-carboxylate (2 g, 11.68 mmol, 1 eq) in THF (20 mL) was added benzyl 2-(triphenyl-phosphanylidene)acetate (5.75 g, 14.02 mmol, 1.2 eq) at 25 °C. The mixture was stirred at the same temperature for 12 h. The mixture was diluted with water (20 mL) and extracted with ethyl acetate (20 mL x 3). The combined organic layers were washed with brine (20 mL x 3), dried over anhydrous Na₂SO₄, filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 5/1) to afford *tert*-butyl 3-(2-(benzyloxy)-2-oxoethylidene)azetidine-1-carboxylate (3.2 g, 10.54 mmol, 90.29% yield) as a yellow oil. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.44 - 7.29 (m, 5H), 6.00 - 5.89 (m, 1H), 5.14 (s, 2H), 4.68 (brs, 2H), 4.57 (brs, 2H), 1.39 (s, 9H).

Step 2:



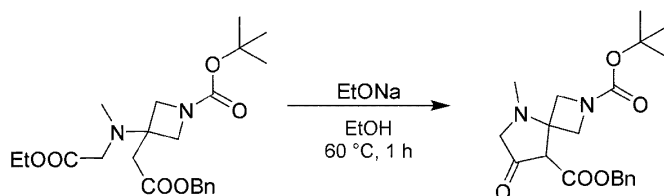
[0493] To a solution of methanamine hydrochloride (2.14 g, 31.65 mmol, 1.2 eq) in EtOH (80 mL) was added Et₃N (2.67g, 26.37 mmol, 3.67 mL, 1 eq) at 25 °C. The resulting mixture was stirred at the same temperature for 1 h. To this mixture was added *tert*-butyl 3-(2-(benzyloxy)-2-oxoethylidene)azetidine-1-carboxylate (8 g, 26.37 mmol, 1 eq) at 25 °C. The mixture was heated to 80 °C and stirred for 11 h. The mixture was filtered, and the filtrate was concentrated in vacuo. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1) to afford *tert*-butyl 3-(2-(benzyloxy)-2-oxoethyl)-3-(methyamino)azetidine-1-carboxylate (6.5 g, 19.43 mmol, 73.70% yield) as a yellow oil. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.38 - 7.31 (m, 5H), 5.08 (s, 2H), 3.74 (brs, 2H), 3.65 (brs, 2H), 2.77 (s, 2H), 2.31 (brs, 1H), 2.17 (s, 3H), 1.37 (s, 9H).

Step 3:



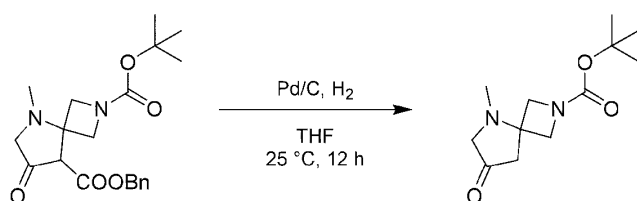
[0494] To a solution of *tert*-butyl 3-(2-(benzyloxy)-2-oxoethyl)-3-(methyamino)azetidine-1-carboxylate (26 g, 77.75 mmol, 1 eq) in DMF (200 mL) were added aqueous NaHCO₃ (13.06 g, 155.50 mmol, 6.05 mL, 2 eq) and ethyl 2-bromoacetate (15.58 g, 93.30 mmol, 10.33 mL, 1.2 eq) at 25 °C. The mixture was heated to 40 °C and stirred for 12 h. The mixture was diluted with water (200 mL) and extracted with ethyl acetate (200 mL x 3). The combined organic layers were washed with brine (200 mL x 3), dried over anhydrous Na₂SO₄, filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 5/1) to afford *tert*-butyl 3-(2-(benzyloxy)-2-oxoethyl)-3-((2-ethoxy-2-oxoethyl)(methyl)amino)azetidine-1-carboxylate (27 g, 64.21 mmol, 82.59% yield) as a yellow oil. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.40 - 7.30 (m, 5H), 5.09 (s, 2H), 4.06 (q, *J* = 7.2 Hz, 2H), 3.80 (brs, 2H), 3.68 (brs, 2H), 3.18 (s, 2H), 2.74 (s, 2H), 2.18 (s, 3H), 1.37 (s, 9H), 1.20 (t, *J* = 7.2 Hz, 3H).

Step 4:



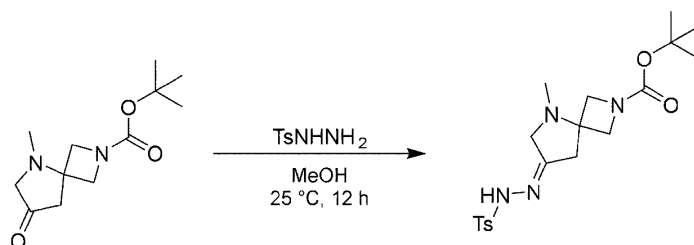
[0495] A mixture of *tert*-butyl 3-(2-(benzyloxy)-2-oxoethyl)-3-((2-ethoxy-2-oxoethyl)(methyl)amino)azetidine-1-carboxylate (26 g, 61.83 mmol, 1 eq) and sodium ethoxide (105.19 g, 309.16 mmol, 20% purity in EtOH, 5 eq) in EtOH (300 mL) was heated to 60 °C and stirred for 1 h under N₂. The mixture was concentrated in vacuo, and the residue was purified by preparative HPLC (column: Daisogel C18 250*70mm*10um; mobile phase: [water (NH₄HCO₃) - ACN]; gradient: 15% - 45% B over 5 min) to afford 8-benzyl 2-(*tert*-butyl) 5-methyl-7-oxo-2,5-diazaspiro[3.4]octane-2,8-dicarboxylate (4.5 g, 12.02 mmol, 19.44% yield) as a yellow oil. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.45 - 7.25 (m, 5H), 5.25 - 5.14 (m, 2H), 4.18 - 3.78 (m, 5H), 3.47 (s, 1H), 3.25 - 3.09 (m, 1H), 2.47 (s, 3H), 1.37 (s, 9H).

Step 5:



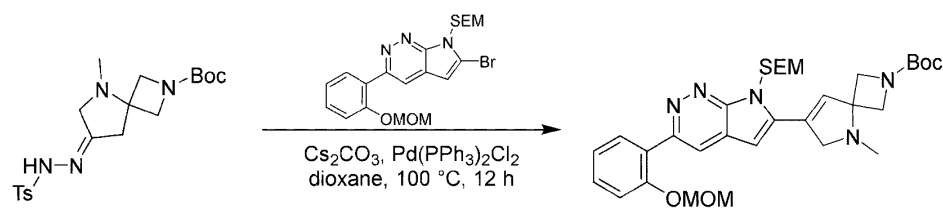
[0496] To a solution of 8-benzyl 2-(*tert*-butyl) 5-methyl-7-oxo-2,5-diazaspiro[3.4]octane-2,8-dicarboxylate (4.5 g, 12.02 mmol, 1 eq) in THF (50 mL) was added Pd/C (2 g) under N₂. The mixture was stirred at 25 °C for 12 h under H₂ (45 Psi). The mixture was filtered, and the filtrate was concentrated in vacuo to afford *tert*-butyl 5-methyl-7-oxo-2,5-diazaspiro[3.4]octane-2-carboxylate (2.5 g, 10.40 mmol, 86.57% yield) as a yellow oil, which was used directly in the subsequent step without purification. ¹H NMR (400 MHz, DMSO-*d*₆) δ 4.20 (d, *J* = 9.6 Hz, 2H), 3.78 (d, *J* = 9.6 Hz, 2H), 3.12 (s, 2H), 2.67 (s, 2H), 2.56 (s, 3H), 1.46 (s, 9H).

Step 6:



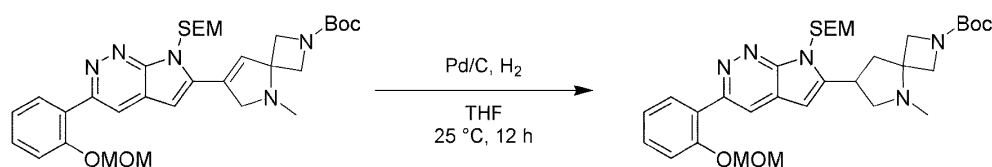
[0497] To a solution of *tert*-butyl 5-methyl-7-oxo-2,5-diazaspiro[3.4]octane-2-carboxylate (1 g, 4.16 mmol, 1 eq) in MeOH (10 mL) was added 4-methylbenzenesulfonohydrazide (775.00 mg, 4.16 mmol, 1 eq) at 25 °C. The mixture was stirred at 25 °C for 12 h under N₂. The resultant precipitate was collected by filtration and dried in vacuo to afford *tert*-butyl (Z)-5-methyl-7-(2-tosylhydrazineylidene)-2,5-diazaspiro[3.4]octane-2-carboxylate (670 mg, 1.64 mmol, 39.41% yield) as a white solid, which was used in the subsequent step without purification. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.16 (s, 1H), 7.71 (d, *J* = 8.4 Hz, 2H), 7.39 (d, *J* = 8.0 Hz, 2H), 4.04 - 3.92 (m, 2H), 3.67 - 3.59 (m, 2H), 3.13 (s, 2H), 2.74 (s, 2H), 2.38 (s, 3H), 2.33 (s, 3H), 1.41 - 1.33 (s, 9H).

Step 7:



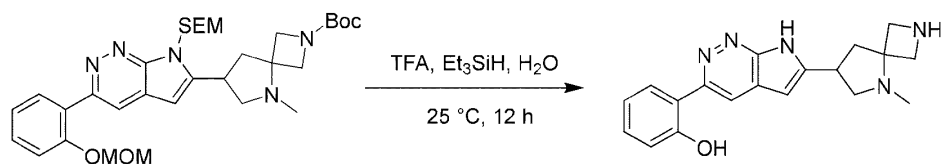
[0498] A mixture of 6-bromo-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazine (420.64 mg, 905.72 μmol , 1 eq), *tert*-butyl (Z)-5-methyl-7-(2-tosylhydrazineylidene)-2,5-diazaspiro[3.4]octane-2-carboxylate (370 mg, 905.72 μmol , 1 eq), Cs_2CO_3 (590.20 mg, 1.81 mmol, 2 eq), and $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (63.57 mg, 90.57 μmol , 0.1 eq) in dioxane (6 mL) was heated to 100 $^\circ\text{C}$ and stirred for 12 h under N_2 . The mixture was diluted with water (10 mL) and extracted with ethyl acetate (10 mL x 3). The combined organic layers were washed with brine (10 mL x 3), dried over anhydrous Na_2SO_4 , filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1) to afford *tert*-butyl 7-(3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-5-methyl-2,5-diazaspiro[3.4]oct-7-ene-2-carboxylate (250 mg) as a yellow oil. QC (ESI+): m/z 608.7 ($\text{M}+\text{H}$) $^+$.

Step 8:



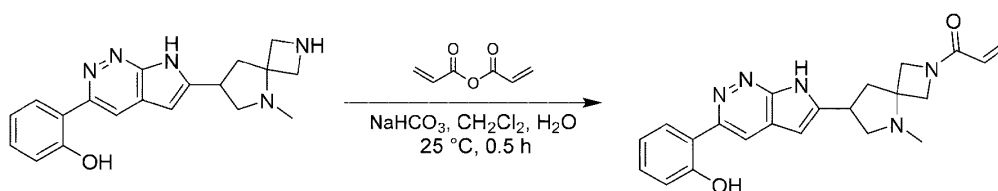
[0499] To a solution of *tert*-butyl 7-(3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-5-methyl-2,5-diazaspiro[3.4]oct-7-ene-2-carboxylate (400 mg, 658.10 μmol , 1 eq) in THF (6 mL) was added Pd/C (200 mg) under N_2 . The mixture was stirred at 25 $^\circ\text{C}$ for 12 h under H_2 (15 Psi). The mixture was filtered, and the filtrate was concentrated in vacuo. The residue was purified by prep-TLC on silica gel (petroleum ether/ethyl acetate = 2/1) to afford *tert*-butyl 7-(3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-5-methyl-2,5-diazaspiro[3.4]octane-2-carboxylate (100 mg, 163.98 μmol , 24.92% yield) as a yellow oil. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 8.06 (s, 1H), 7.68 (d, J = 7.6 Hz, 1H), 7.46 - 7.37 (m, 1H), 7.27 (d, J = 8.4 Hz, 1H), 7.17 - 7.14 (m, 1H), 6.55 (s, 1H), 5.93 - 5.80 (m, 2H), 5.21 (s, 2H), 4.21 - 3.88 (m, 4H), 3.61 - 3.53 (m, 3H), 3.29 (s, 3H), 2.37 (s, 3H), 2.34 - 2.30 (m, 1H), 2.22 - 2.15 (m, 1H), 2.04 - 2.01 (m, 1H), 1.86 - 1.76 (m, 1H), 1.40 (s, 9H), 0.88 - 0.82 (m, 2H), -0.10 (s, 9H).

Step 9:



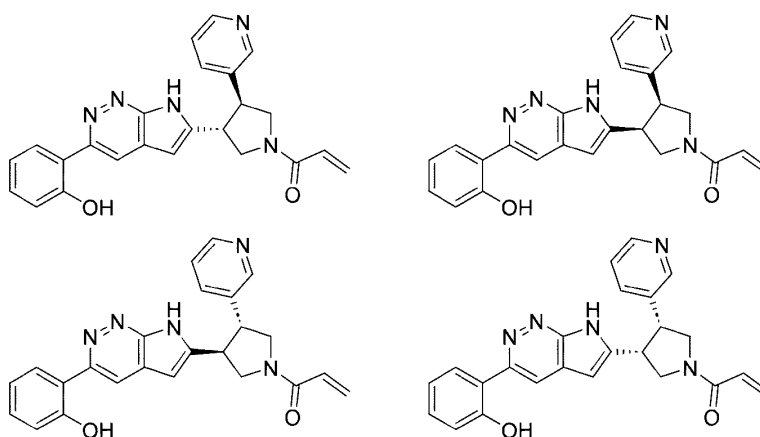
[0500] To a solution of *tert*-butyl 7-(3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-5-methyl-2,5-diazaspiro[3.4]octane-2-carboxylate (90 mg, 147.58 μ mol, 1 eq) and TFA (1 mL) in H₂O (0.1 mL) was added Et₃SiH (1 mL) at 25 °C. The mixture was stirred at 25 °C for 12 h. The mixture was concentrated in vacuo to afford 2-(6-(5-methyl-2,5-diazaspiro[3.4]octan-7-yl)-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)phenol (80 mg, 141.98 μ mol, 96.21% yield, TFA salt) as a yellow oil, which was used in the subsequent step without purification. QC (ESI⁺): *m/z* 336.1 (M+H)⁺.

Step 10:

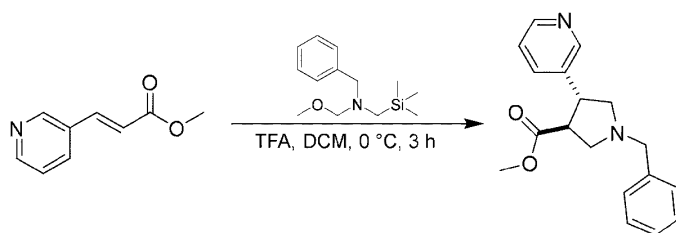


[0501] To a solution of 2-(6-(5-methyl-2,5-diazaspiro[3.4]octan-7-yl)-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)phenol (75 mg, 133.11 μ mol, 1 eq, TFA salt) in CH₂Cl₂ (1 mL) and aqueous NaHCO₃ (1M, 1 mL, 1.0 mmol) was added prop-2-enoyl prop-2-enoate (13.43 mg, 106.49 μ mol, 0.8 eq) at 0 °C. The mixture was stirred at 0 °C for 0.5 h. The mixture was diluted with water (3 mL) and extracted with CH₂Cl₂ (5 mL x 3). The combined organic layers were washed with brine (5 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated in vacuo. The residue was purified by preparative HPLC (column: CD01-Phenomenex luna C18 150*25*10um; mobile phase: [water (FA) - ACN]; gradient: 13% - 43% B over 10 min) to afford **591** (5.1 mg, 13.02 μ mol, 9.78% yield). QC (ESI⁺): *m/z* 390.2 (M+H)⁺, RT: 2.053 min. ¹H NMR (400 MHz, DMSO-*d*₆) δ 14.13 (s, 1H), 12.55 (brs, 1H), 8.56 (s, 1H), 8.02 (d, *J* = 8.0 Hz, 1H), 7.29 (t, *J* = 7.6 Hz, 1H), 7.03 - 6.89 (m, 2H), 6.53 (s, 1H), 6.44 - 6.32 (m, 1H), 6.17 - 6.08 (m, 1H), 5.69 (d, *J* = 10.4 Hz, 1H), 4.57 - 4.35 (m, 1H), 4.32 - 4.22 (m, 1H), 4.11 - 3.99 (m, 1H), 3.95 - 3.57 (m, 2H), 2.36 (s, 3H), 2.28 - 2.17 (m, 3H), 1.90 - 1.80 (m, 1H).

Example 23: Synthesis of 1-(3-(3-(2-hydroxyphenyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-4-(pyridin-3-yl)pyrrolidin-1-yl)prop-2-en-1-one (Compounds 595, 596, and 597):

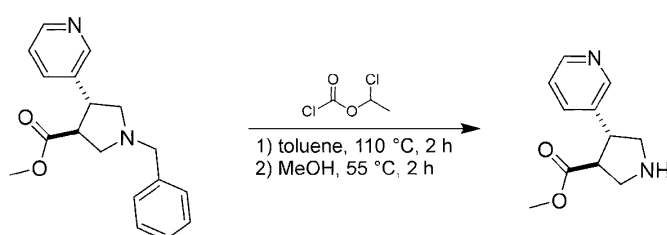


Step 1:



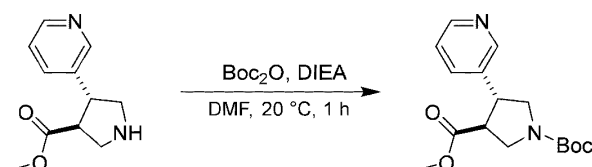
[0502] To a solution of methyl (E)-3-(pyridin-3-yl)acrylate (22 g, 134.82 mmol, 1 eq) and N-benzyl-1-methoxy-N-((trimethylsilyl)methyl)methanamine (24.01 g, 101.12 mmol, 1.5 eq) in DCM (200 mL) was added dropwise TFA (4.62 g, 140.44, 3 mL, 0.3 eq) at 0 °C under N₂. The mixture was stirred at 0 °C for 3 h under N₂. The mixture was quenched with water (200 mL) and extracted with methyl *tert*-butyl ether (200 mL × 3). The combined organic phases were washed with brine (200 mL), dried over anhydrous sodium sulfate, filtered, and concentrated to give the crude product, which was purified by column chromatography (SiO₂, petroleum ether: ethyl acetate = 20: 1 to 2: 1) to give *rel*-methyl (3S,4R)-1-benzyl-4-(pyridin-3-yl)pyrrolidine-3-carboxylate (36 g, 121.464 mmol, 75.08% yield) as a yellow oil. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ 8.50 (d, *J* = 2.0 Hz, 1 H), 8.39 - 8.38 (dd, *J* = 1.2, 3.6 Hz, 1 H), 7.6 (d, *J* = 8 Hz, 1H), 7.28 - 7.24 (m, 4 H), 7.22 - 7.16 (m, 2 H), 3.76 - 3.70 (m, 1H), 3.60 (s, 6 H), 3.07 - 3.04 (m, 1 H), 2.90 - 2.88 (m, 1 H), 2.87 - 2.86 (m, 1 H), 2.74 - 2.71 (m, 2 H).

Step 2:



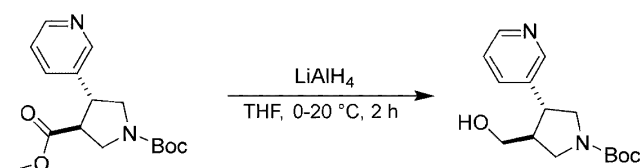
[0503] To a solution of *rel*-methyl (3S,4R)-1-benzyl-4-(pyridin-3-yl)pyrrolidine-3-carboxylate (36 g, 121.464 mmol, 1 eq) in toluene (310 mL) was added 1-chloroethyl carbonochloridate (45.16 g, 157.91 mmol, 3 eq) at 25 °C. After addition, the mixture was heated to 110 °C and stirred for 2 h. The mixture was concentrated under reduced pressure to give a residue. MeOH (310 mL) was added to the residue and the mixture was stirred at 55 °C for 2 h. The mixture was concentrated under reduced pressure to give *rel*-methyl (3S,4R)-4-(pyridin-3-yl)pyrrolidine-3-carboxylate (16 g, 77.58 mmol, 73.69% yield) as a colorless oil, which was used in the next step without further purification. LCMS (ESI⁺): *m/z* 206.1 (M+H)⁺.

Step 3:



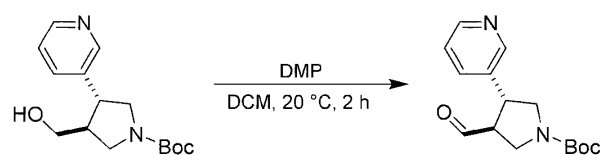
[0504] To a solution of *rel*-methyl (3*S*,4*R*)-4-(pyridin-3-yl)pyrrolidine-3-carboxylate (16 g, 77.58 mmol, 1 *eq*) in DMF (160 mL) was added DIEA (30.08 g, 232.74 mmol, 40.54 mL, 3 *eq*) and Boc₂O (33.86 g, 155.16 mmol, 35.64 mL, 2 *eq*) at 20 °C. The mixture was stirred at the same temperature for 1 h. The reaction mixture was partitioned between methyl *tert*-butyl ether (200 mL) and H₂O (200 mL). The organic phase was separated, washed with brine (150 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The crude material was purified by column chromatography (SiO₂, petroleum ether: ethyl acetate = 30: 1 to 1: 1) to give *rel*-1-(*tert*-butyl) 3-methyl (3*S*,4*R*)-4-(pyridin-3-yl)pyrrolidine-1,3-dicarboxylate (11.9 g, 39.18 mmol, 50.49% yield) as a yellow oil. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ 8.54 - 8.53 (m, 2H), 7.61 - 7.58 (m, 1H), 7.30 - 7.27 (m, 1H), 3.96 - 3.88 (m, 2H), 3.67 - 3.61 (m, 5H), 3.44 - 3.40 (m, 1H), 3.22 - 3.20 (m, 1H), 1.48 (s, 9H).

Step 4:



[0505] To a solution of *rel*-1-(*tert*-butyl) 3-methyl (3*S*,4*R*)-4-(pyridin-3-yl)pyrrolidine-1,3-dicarboxylate (11.9 g, 39.18 mmol, 1 *eq*) in THF (150 mL) was added dropwise a solution of LiAlH₄ (2.5 M, 15.67 mL, 2 *eq*) at 0 °C under N₂. The resulting mixture was warmed up to 20 °C and stirred for 2 h under N₂ atmosphere. The reaction mixture was quenched by addition of saturated NH₄Cl solution (20 mL) at 0 °C under N₂ atmosphere, then diluted with H₂O (300 mL) and extracted with ethyl acetate (200 mL × 2). The combined organic layers were washed with brine (150 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to give the crude product, which was purified by column chromatography (SiO₂, petroleum ether: ethyl acetate = 1: 1 to 1: 2) to give *rel*-*tert*-butyl (3*S*,4*R*)-3-(hydroxymethyl)-4-(pyridin-3-yl)pyrrolidine-1-carboxylate (8.2 g, 29.46 mmol, 97.22% yield) as a white solid. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ = 8.50 - 8.49 (m, 2H), 7.60 (d, *J* = 7.6 Hz, 1H), 7.30 - 7.28 (m, 1H), 3.90 - 3.66 (m, 2H), 3.57 - 3.55 (m, 1H), 3.38 - 3.37 (m, 1H), 3.35 - 3.34 (m, 2H), 3.22 - 3.21 (m, 1H), 2.52 - 2.47 (m, 1H), 1.48 (s, 9H).

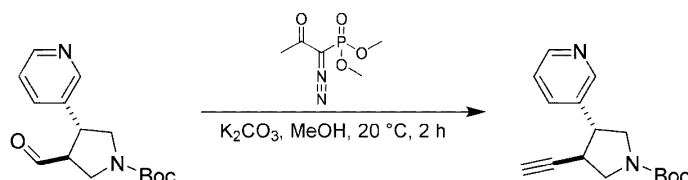
Step 5:



[0506] To a solution of *rel*-*tert*-butyl (3*S*,4*R*)-3-(hydroxymethyl)-4-(pyridin-3-yl)pyrrolidine-1-carboxylate (8.2 g, 29.46 mmol, 1 *eq*) in DCM (100 mL) was added Dess-Martin periodinane (18.74 g, 394.13 mmol, 8.35 mL, 1.5 *eq*) at 0 °C under N₂. The mixture was stirred at the same temperature for 2 h. The reaction mixture was partitioned between sat. Na₂S₂O₃ solution/sat. NaHCO₃ solution (25 mL/25 mL) and methyl *tert*-butyl ether (280 mL). The organic phase was separated, washed with brine (100 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue

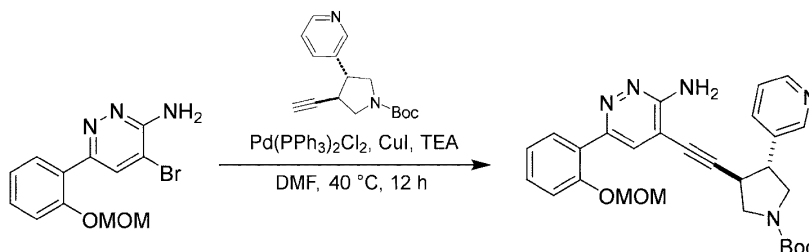
was purified by column chromatography (SiO₂, petroleum ether/ethyl acetate=100/1 to 1/1) to give *rel-tert*-butyl (3*S*,4*R*)-3-formyl-4-(pyridin-3-yl)pyrrolidine-1-carboxylate (3.5 g, 12.15 mmol, 50.36% yield) as a brown solid. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ 9.71 (d, *J* = 1.6 Hz, 1H), 8.56 - 8.53 (m, 2H), 7.59 (d, *J* = 8 Hz, 1H), 7.33 - 7.27 (m, 1H), 3.88 - 3.69 (m, 4H), 3.67 - 3.50 (m, 1H), 3.47 - 3.20 (m, 1H), 1.49 (s, 9H).

Step 6:



[0507] To a solution of *rel-tert*-butyl (3*S*,4*R*)-3-formyl-4-(pyridin-3-yl)pyrrolidine-1-carboxylate (3.5 g, 12.15 mmol, 1 *eq*) and K₂CO₃ (2.50 g, 18.09 mmol, 2 *eq*) in MeOH (35 mL) was added dimethyl (1-diazo-2-oxopropyl)phosphonate (2.09 g, 10.86 mmol, 1.2 *eq*) at 0 °C under N₂. The resulting mixture was warmed up to 20 °C and stirred for 2 h. The mixture was poured into water (30 mL) and extracted with ethyl acetate (20 mL × 3). The combined organic phases were washed with brine (20 mL), dried over Na₂SO₄, filtered, and concentrated to give the crude product, which was triturated with methyl *tert*-butyl ether (5 mL) at 25 °C to give *rel-tert*-butyl (3*R*,4*R*)-3-ethynyl-4-(pyridin-3-yl)pyrrolidine-1-carboxylate (945 mg, 3.47 mmol, 38.35% yield) as a white solid, which was used in the subsequent step without purification. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ 8.59 (d, *J* = 16.4 Hz, 2H), 7.65 (d, *J* = 8 Hz, 1H), 7.34 - 7.31 (m, 1H), 3.99 - 3.89 (m, 2H), 3.46 - 3.37 (m, 3H), 3.05 - 3.02 (q, *J* = 8.8 Hz, 1H), 2.15 (s, 1H), 1.49 (s, 9H).

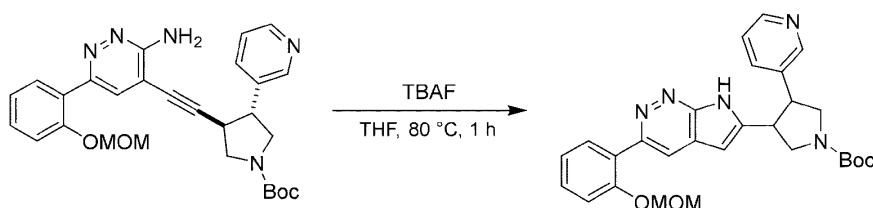
Step 7:



[0508] To a solution of 4-bromo-6-(2-(methoxymethoxy)phenyl)pyridazin-3-amine (680 mg, 1.93 mmol, 1 *eq*), *rel-tert*-butyl (3*R*,4*R*)-3-ethynyl-4-(pyridin-3-yl)pyrrolidine-1-carboxylate (790.30 mg, 2.90 mmol, 1.5 *eq*), and copper (I) iodide (110.53 mg, 580.37 μmol, 0.3 *eq*) in DMF (15 mL) was added Pd(PPh₃)₂Cl₂ (271.57 mg, 386.91 μmol, 0.2 *eq*) and TEA (587.27 mg, 5.80 mmol, 807.80 μL, 3 *eq*) at 20 °C under N₂. The resulting mixture was heated to 40 °C and stirred for 12 h under N₂. The reaction mixture was cooled to 25 °C and partitioned between ethyl acetate (30 mL) and H₂O (15 mL). The organic phase was separated, washed with brine (20 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The crude material was purified by column chromatography (SiO₂, petroleum ether: ethyl acetate = 80:1 to 50:1) to give *rel-tert*-butyl (3*R*,4*R*)-3-((3-amino-6-(2-

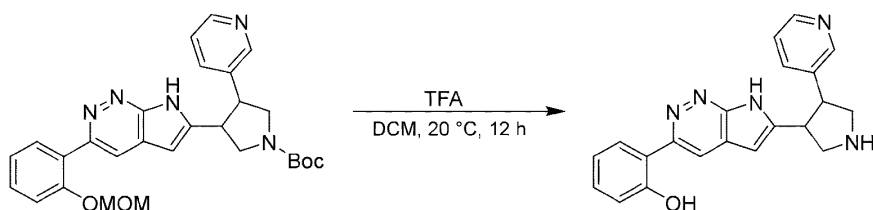
(methoxymethoxy)phenyl)pyridazin-4-yl)ethynyl)-4-(pyridin-3-yl)pyrrolidine-1-carboxylate (600 mg, 1.10 mmol, 56.68% yield) as a brown solid. ^1H NMR (400 MHz, $\text{METHANOL-}d_4$) δ 8.87 - 8.58 (m, 1H), 7.92 - 7.90 (m, 1H), 7.62 - 7.61 (m, 1H), 7.53 - 7.52 (m, 3H), 7.36 - 7.34 (m, 1H), 7.20 - 7.18 (d, J = 8.0 Hz, 1H), 7.11 - 7.09 (t, J = 8.0 Hz, 1H), 6.65 (s, 2H), 5.18 (s, 2H), 3.91 - 3.87 (m, 2H), 3.82 - 3.81 (d, J = 4.0 Hz, 3H), 3.52 - 3.27 (m, 3H), 1.42 (s, 9H).

Step 8:



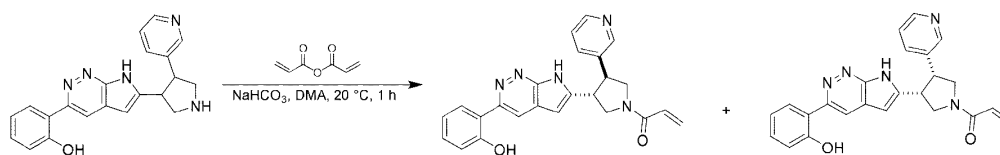
[0509] To a solution of *rel-tert*-butyl (3*R*,4*R*)-3-((3-amino-6-(2-(methoxymethoxy)phenyl)pyridazin-4-yl)ethynyl)-4-(pyridin-3-yl)pyrrolidine-1-carboxylate (600 mg, 1.10 mmol, 1 *eq*) in THF (12 mL) was added a solution of TBAF (1M, 4.39 mL, 4 *eq*) at 25 °C. The mixture was heated to 80 °C and stirred for 1 h. The reaction mixture was then cooled to 25 °C and partitioned between ethyl acetate (10 mL) and H_2O (10 mL). The organic phase was separated, washed with brine (15 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to give *tert*-butyl 3-(3-(2-(methoxymethoxy)phenyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-4-(pyridin-3-yl)pyrrolidine-1-carboxylate (550 mg, 179.79 μmol , 28.13% yield) as a yellow solid, which was used in the next step without purification. ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 12.43 (d, J = 10.8 Hz, 1 H), 8.61 - 8.45 (m, 2 H), 7.95 - 7.81 (m, 2 H), 7.66 - 7.64 (m, 2 H), 7.37 - 7.32 (m, 3 H), 7.25 - 7.10 (m, 3 H), 6.37 (d, J = 2.4 Hz, 1 H), 5.18 (s, 2 H), 4.03 - 3.93 (m, 4 H), 3.73 - 3.70 (m, 1 H), 3.56 - 3.45 (m, 1 H), 1.46 (d, J = 17.2 Hz, 9 H).

Step 9:



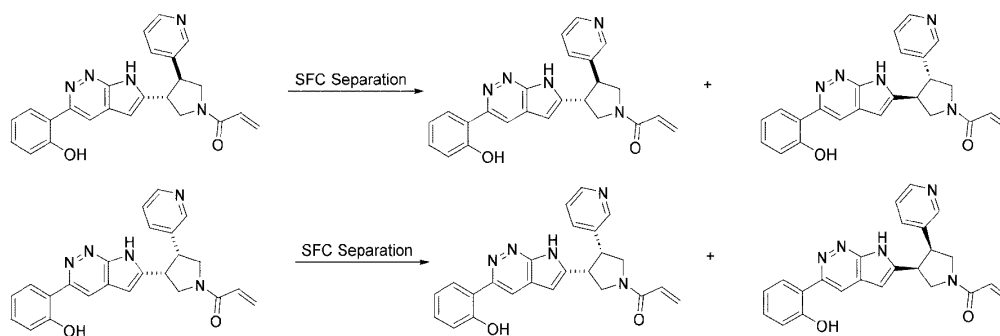
[0510] To a solution of *tert*-butyl 3-(3-(2-(methoxymethoxy)phenyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-4-(pyridin-3-yl)pyrrolidine-1-carboxylate (550 mg, 179.79 μmol , 1 *eq*) in DCM (2 mL) was added TFA (3.07 g, 26.92 mmol, 2 mL, 33.76 *eq*) at 20 °C. The mixture was stirred at the same temperature for 12 h. The mixture was concentrated under reduced pressure to give 2-(6-(4-(pyridin-3-yl)pyrrolidin-3-yl)-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)phenol (255 mg, 713.47 μmol , 89.46% yield) as a brown oil, which was used in the next step without purification. LCMS (ESI⁺): m/z 357.1 ($\text{M}+\text{H}$)⁺.

Step 10:



[0511] To a solution of 2-(6-(4-(pyridin-3-yl)pyrrolidin-3-yl)-7H-pyrrolo[2,3-c]pyridazin-3-yl)phenol (255 mg, 713.47 μmol , 1 *eq*) in DMA (5 mL) was added aqueous NaHCO_3 (12.95 g, 154.20 mmol, 6.00 mL, 216.13 *eq*) and acrylic anhydride (134.96 mg, 1.07 mmol, 1.5 *eq*) at 20 °C. The mixture was stirred at 20 °C for 1 hr. The reaction mixture was partitioned between ethyl acetate (5 mL) and H_2O (5 mL), dried over anhydrous sodium sulfate, filtered, and concentrated to give the crude product, which was purified by prep-HPLC (neutral condition) to give diastereomer 1 (1st eluting diastereomer, 14 mg, 37.56 μmol) as a white solid and diastereomer 2 (2nd eluting diastereomer, 24 mg, 63.43 μmol) as a white solid. Diastereomer 1: LCMS (ESI^+): m/z 411.1. ($\text{M}+\text{H}$)⁺. Diastereomer 2: LCMS (ESI^+): m/z 411.1 ($\text{M}+\text{H}$)⁺.

Step 11:



Diastereomer 1 (14 mg) was separated by SFC (Column: DAICEL CHIRALCEL OJ (250mm*30mm,10 μm); mobile phase: [CO_2 -IPA(0.1% $\text{NH}_3\text{H}_2\text{O}$)]; B%:40%, isocratic elution mode) to give **597** (1st eluting isomer, 4 mg, 9.72 μmol). LCMS (ESI^+): m/z 411.1 ($\text{M}+\text{H}$)⁺. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 14.61 (s, 1H), 8.34 (s, 1H), 8.26 - 8.21 (m, 2H), 7.92 (d, J = 4.0 Hz, 1H), 7.32 - 7.29 (m, 1H), 7.24 - 7.21 (m, 1H), 7.11 - 7.12 (m, 1H), 6.90 - 6.81 (m, 2H), 6.79 - 6.74 (m, 1H), 6.29 - 6.25 (dd, J = 1.6, 15.2 Hz, 1H), 6.08 (d, J = 16, 1H), 5.79 - 5.75 (m, 1H), 4.21 - 4.13 (m, 4H), 4.02 - 3.34 (m, 2H).

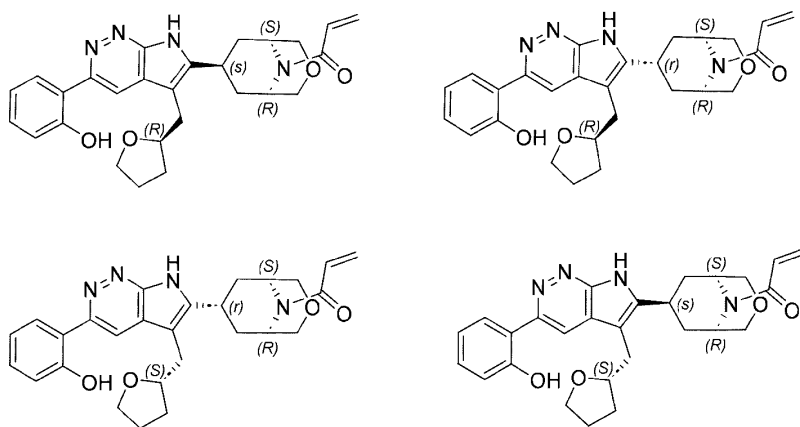
[0512] Diastereomer 2 (24 mg) was separated by SFC (Column: DAICEL CHIRALCEL OJ (250mm*30mm,10 μm); mobile phase: [CO_2 -IPA(0.1% $\text{NH}_3\text{H}_2\text{O}$)]; B%:40%, isocratic elution mode) to give **596** (1st eluting isomer, 10 mg, 24.30 μmol) and **595** (2nd eluting isomer, 8 mg, 19.44 μmol).

[0513] **596**: LCMS (ESI^+): m/z 411.1 ($\text{M}+\text{H}$)⁺. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 13.93 (s, 1H), 12.67 (s, 1H), 8.59 - 8.55 (m, 2H), 8.51 - 8.43 (m, 1H), 7.99 (d, J = 7.2 Hz, 1H), 7.98 - 7.87 (d, J = 7.2 Hz, 1H), 7.35 - 7.33 (m, 1H), 7.27 - 6.94 (m, 1H), 7.03 - 6.85 (m, 2H), 6.67 (d, J = 10.4, 16.0 Hz, 1H), 6.50 (d, J = 12.8 Hz, 1H), 6.22 (d, J = 16.4 Hz, 1H), 5.76 - 5.75 (m, 1H), 4.45 - 4.15 (m, 2H), 4.15 - 4.04 (m, 1H), 4.02 - 3.77 (m, 2H), 3.67 - 3.33 (m, 1H).

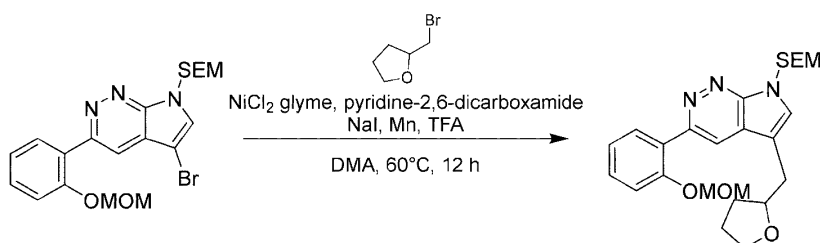
[0514] **595**: LCMS (ESI^+): m/z 411.1 ($\text{M}+\text{H}$)⁺. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 13.92 (s, 1H), 12.69 (s, 1H), 8.62 - 8.51 (m, 2H), 8.43 (t, J = 3.6 Hz, 1H), 7.97 (d, J = 7.6 Hz, 1H), 7.97 (d, J = 8.4 Hz, 1H), 7.35 (d, J = 4.0, 8.0 Hz, 1H), 7.34 - 7.27 (t, J = 7.6 Hz, 1H), 6.96 - 6.95 (m, 2H), 6.73 - 6.63 (m, 1H).

H), 6.50 (d, $J = 12.8$ Hz, 1 H), 6.22 (d, $J = 16.8$ Hz, 1 H), 5.75 - 5.74 (m, 1 H), 5.78 - 5.70 (m, 1 H), 4.38 - 4.23 (m, 1 H), 4.20 - 4.04 (m, 1 H), 4.03 - 3.67 (m, 3 H), 3.57 - 3.33 (m, 1 H).

Example 24: Synthesis of 1-((1*R*,5*S*,7*r*)-7-(3-(2-hydroxyphenyl)-5-(((*R*)-tetrahydrofuran-2-yl)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one, 1-((1*R*,5*S*,7*s*)-7-(3-(2-hydroxyphenyl)-5-(((*R*)-tetrahydrofuran-2-yl)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one, 1-((1*R*,5*S*,7*s*)-7-(3-(2-hydroxyphenyl)-5-(((*S*)-tetrahydrofuran-2-yl)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one, and 1-((1*R*,5*S*,7*r*)-7-(3-(2-hydroxyphenyl)-5-(((*S*)-tetrahydrofuran-2-yl)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one (Compounds 623, 624, 625, and 626):



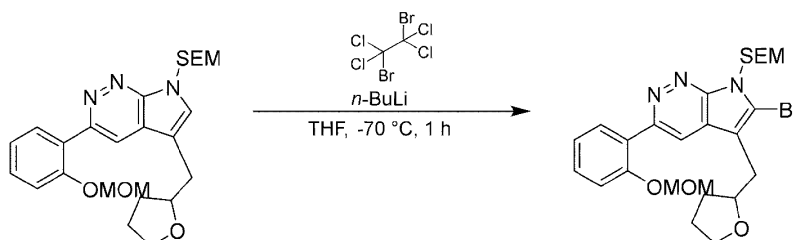
Step 1:



[0515] To a solution of 5-bromo-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazine (0.2 g, 430.64 μ mol, 1 *eq*), 2-(bromomethyl)tetrahydrofuran (213.20 mg, 1.29 mmol, 3 *eq*), pyridine-2,6-dicarboxamide (41.01 mg, 172.26 μ mol, 0.4 *eq*, 2·HCl salt), NiCl₂ glyme (37.85 mg, 172.26 μ mol, 0.4 *eq*), manganese (189.27 mg, 3.45 mmol, 187.58 μ L, 8 *eq*) and sodium iodide (64.55 mg, 430.64 μ mol, 1 *eq*) in *N,N*-dimethylacetamide (2 mL) was added trifluoroacetic acid (19.64 mg, 172.26 μ mol, 12.80 μ L, 0.4 *eq*). The mixture was heated to 60 °C and stirred for 12 h. Four additional reactions were set up as described above, and the five reaction mixtures were combined and diluted with water (30 mL) and extracted with ethyl acetate (20 mL $\times$ 3). The combined organic layers were washed with brine (20 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO₂, petroleum ether/ethyl

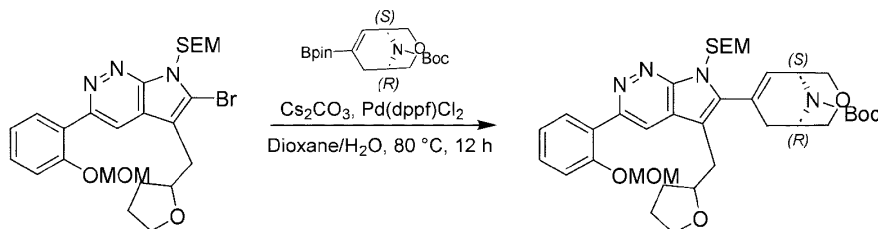
acetate=1/0 to 0/1) to give 3-(2-(methoxymethoxy)phenyl)-5-((tetrahydrofuran-2-yl)methyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazine (0.36 g, 766.53 μmol , 59.33% yield) as a colorless oil. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ -0.10 (s, 9H) 0.80 - 0.88 (m, 2H) 1.51 (dd, $J=11.82$, 7.73 Hz, 1H) 1.75 (quin, $J=7.05$ Hz, 2H) 1.89 (dd, $J=11.88$, 6.56 Hz, 1H) 2.90 (d, $J=5.94$ Hz, 2H) 3.29 (s, 3H) 3.53 - 3.63 (m, 3H) 3.70 - 3.77 (m, 1H) 4.02 - 4.10 (m, 1H) 5.21 (s, 2H) 5.77 (s, 2H) 7.13 - 7.20 (m, 1H) 7.27 (d, $J=7.92$ Hz, 1H) 7.38 - 7.45 (m, 1H) 7.71 (dd, $J=7.67$, 1.61 Hz, 1H) 7.84 (s, 1H) 8.19 (s, 1H).

Step 2:



[0516] To a solution of 3-(2-(methoxymethoxy)phenyl)-5-((tetrahydrofuran-2-yl)methyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazine (0.2 g, 425.85 μmol , 1 *eq*) in tetrahydrofuran (5 mL) was added a solution of *n*-BuLi (1.6 M, 399.24 μL , 1.5 *eq*) at -70 °C under N_2 . The mixture was stirred at the same temperature for 10 min, then a solution of 1,2-dibromo-1,1,2,2-tetrachloroethane (416.02 mg, 1.28 mmol, 153.34 μL , 3 *eq*) in tetrahydrofuran (5 mL) was added to the mixture. After addition, the resulting mixture was stirred at -70 °C for 1 h. The reaction mixture was quenched with saturated NH_4Cl solution (10 mL) and extracted with ethyl acetate (10 mL $\times$ 3). The organic layers were combined and washed with brine (10 mL), dried over Na_2SO_4 , and filtered. The filtrate was concentrated under reduced pressure. The residue was combined with that of another reaction (conducted as described above), and the combined residues were purified by prep-TLC (SiO_2 , PE: EA = 1:1) to give 6-bromo-3-(2-(methoxymethoxy)phenyl)-5-((tetrahydrofuran-2-yl)methyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazine (0.3 g, 546.90 μmol , 64.21% yield) as a colorless oil. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ -0.11 (s, 9H) 0.80 - 0.88 (m, 2H) 1.48 - 1.59 (m, 1H) 1.76 (quin, $J=7.00$ Hz, 2H) 1.83 - 1.94 (m, 1H) 2.86 - 3.01 (m, 2H) 3.29 (s, 3H) 3.55 - 3.66 (m, 3H) 3.67 - 3.76 (m, 1H) 4.05 - 4.12 (m, 1H) 5.19 - 5.25 (m, 2H) 5.84 (s, 2H) 7.17 (t, $J=7.44$ Hz, 1H) 7.28 (d, $J=8.13$ Hz, 1H) 7.40 - 7.47 (m, 1H) 7.72 (dd, $J=7.57$, 1.69 Hz, 1H) 8.22 (s, 1H).

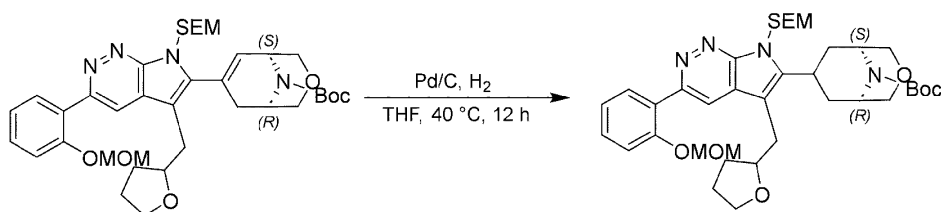
Step 3:



[0517] To a solution of 6-bromo-3-(2-(methoxymethoxy)phenyl)-5-((tetrahydrofuran-2-yl)methyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazine (0.3 g, 546.90 μmol , 1 *eq*) and *tert*-butyl

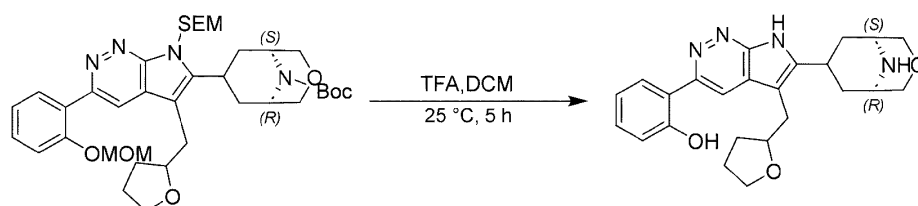
(1*R*,5*S*)-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-oxa-9-azabicyclo[3.3.1]non-6-ene-9-carboxylate (230.52 mg, 656.28 μmol , 1.2 *eq*) in dioxane (3 mL) and H₂O (0.6 mL) was added Cs₂CO₃ (534.57 mg, 1.64 mmol, 3 *eq*). The resulting mixture was degassed and purged with N₂, then Pd(dppf)Cl₂ (40.02 mg, 54.69 μmol , 0.1 *eq*) was added to the mixture. This mixture was heated to 80 °C and stirred for 2 h. The reaction mixture was diluted with water (5 mL) and extracted with ethyl acetate 15 mL (5 mL $\times$ 3). The combined organic layers were combined and washed with brine (5 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by prep-TLC (SiO₂, PE: EA = 1:1) to give *tert*-butyl (1*R*,5*S*)-7-(3-(2-(methoxymethoxy)phenyl)-5-((tetrahydrofuran-2-yl)methyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]non-6-ene-9-carboxylate (0.15 g, 216.48 μmol , 39.58% yield) as a colorless oil. ¹H NMR (400 MHz, DMSO-*d*₆) δ -0.08 (d, *J*=1.00 Hz, 9H) 0.82 - 0.87 (m, 2H) 1.46 (s, 9H) 1.70 - 1.90 (m, 4H) 2.42 (br d, *J*=17.64 Hz, 2H) 2.80 (br d, *J*=5.75 Hz, 3H) 3.53 - 3.77 (m, 9H) 3.84 - 3.95 (m, 2H) 4.09 - 4.18 (m, 1H) 4.54 (br s, 1H) 5.20 - 5.24 (m, 2H) 5.66 (br s, 2H) 6.10 (br d, *J*=4.63 Hz, 1H) 7.14 - 7.19 (m, 1H) 7.27 (d, *J*=8.13 Hz, 1H) 7.39 - 7.45 (m, 1H) 7.70 (d, *J*=7.25 Hz, 1H) 8.17 (s, 1H).

Step 4:



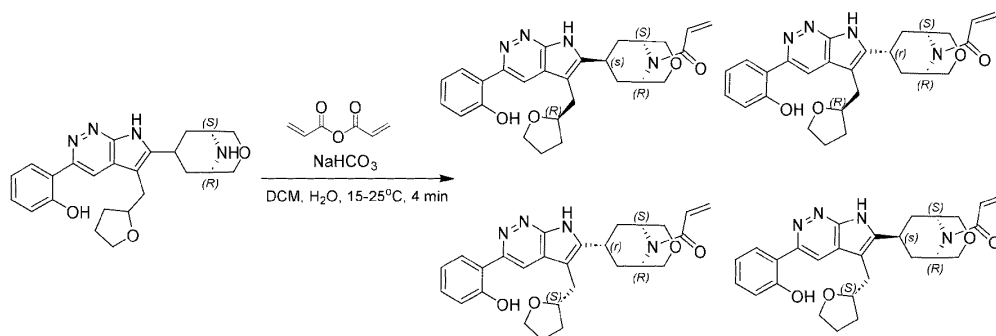
[0518] To a solution of *tert*-butyl (1*R*,5*S*)-7-(3-(2-(methoxymethoxy)phenyl)-5-((tetrahydrofuran-2-yl)methyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]non-6-ene-9-carboxylate (0.15 g, 216.48 μmol , 1 *eq*) in tetrahydrofuran (10 mL) was added Pd/C (150.00 mg, 140.95 μmol). The resulting mixture was stirred at 40 °C for 12 h under H₂ (15 Psi). The reaction mixture was filtered, and the filtrate was concentrated under reduced pressure to give a residue, which was used for the next step without purification. *Tert*-butyl (1*R*,5*S*)-7-(3-(2-(methoxymethoxy)phenyl)-5-((tetrahydrofuran-2-yl)methyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (0.12 g, 172.68 μmol , 79.77% yield) was obtained as a colorless oil. ¹H NMR (400 MHz, DMSO-*d*₆) δ -0.12 - -0.06 (m, 9H) 0.82 - 0.89 (m, 2H) 1.49 (s, 9H) 1.78 - 2.02 (m, 4H) 2.14 - 2.31 (m, 4H) 2.90 - 2.99 (m, 2H) 3.30 (s, 3H) 3.48 - 3.80 (m, 9H) 3.96 - 4.03 (m, 2H) 4.11 - 4.22 (m, 1H) 5.18 - 5.22 (m, 2H) 5.81 - 5.94 (m, 2H) 7.16 (t, *J*=7.50 Hz, 1H) 7.26 (d, *J*=8.38 Hz, 1H) 7.38 - 7.44 (m, 1H) 7.70 (dd, *J*=7.63, 1.38 Hz, 1H) 8.09 - 8.13 (m, 1H).

Step 5:



[0519] To a solution of *tert*-butyl (1*R*,5*S*)-7-(3-(2-(methoxymethoxy)phenyl)-5-((tetrahydrofuran-2-yl)methyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (0.12 g, 172.68 μ mol, 1 *eq*) in dichloromethane (1.2 mL) was added trifluoroacetic acid (1.84 g, 16.15 mmol, 1.20 mL, 93.55 *eq*). The resulting mixture was stirred at 25 °C for 5 h. The reaction mixture was concentrated under reduced pressure, and the residue was used for the next step without purification. 2-(6-((1*R*,5*S*)-3-oxa-9-azabicyclo[3.3.1]nonan-7-yl)-5-((tetrahydrofuran-2-yl)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)phenol (0.12 g, 195.27 μ mol) was obtained as a colorless oil. LCMS (ESI⁺): *m/z* 420.51, 421.3(M+H)⁺.

Step 6:



[0520] To a solution of 2-(6-((1*R*,5*S*)-3-oxa-9-azabicyclo[3.3.1]nonan-7-yl)-5-((tetrahydrofuran-2-yl)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)phenol (0.12 g, 185.03 μ mol, 1 *eq*, 2·TFA salt) in dichloromethane (0.8 mL) was added saturated NaHCO₃ (0.5 mL) to adjust the mixture to pH 8-9. Then, a solution of acrylic anhydride (18.67 mg, 148.02 μ mol, 0.8 *eq*) in dichloromethane (0.5 mL) was added dropwise to the mixture at 15 °C. The resulting mixture was stirred at the same temperature for 2 min, then warmed up to 25 °C and stirred for an additional 2 min. The reaction mixture was partitioned between organic and aqueous layers. The organic layer was washed with brine (0.5 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure to give a residue, which was purified by prep-HPLC (neutral condition:column: Waters Xbridge BEH C18 100*30mm*10um;mobile phase: [H₂O(10mM NH₄HCO₃)-ACN];gradient:45%-55% B over 8.0 min), then with SFC (column: DAICEL CHIRALPAK IG (250mm*30mm,10um);mobile phase: [CO₂-MeOH(0.1%NH₃H₂O)];B%:50%, isocratic elution mode) to give 15 mg of P1 (first eluting isomer), and 7.5 mg of P2 (second eluting isomer).

[0521] P1 was separated by SFC (Column: DAICEL CHIRALPAK IG (250mm*30mm,10um), mobile phase: A for CO₂ and B for MeOH(0.1%NH₃H₂O), gradient: B%=50.00% isocratic elution mode)

affording **626** (first eluting isomer, 3.1 mg, 6.53 μ mol, 3.53% yield) and **624** (fourth eluting isomer, 3.1 mg, 6.53 μ mol, 3.53% yield).

[0522] 626: LCMS (ESI⁺): m/z 474.23 (M+H)⁺, Rt: 2.760 min. ¹H NMR (400 MHz, DMSO-*d*₆) δ ppm 1.43 - 1.54 (m, 1H) 1.72 - 1.95 (m, 3H) 2.09 - 2.30 (m, 4H) 2.69 - 2.95 (m, 3H) 3.48 - 3.60 (m, 3H) 3.65 - 3.78 (m, 3H) 3.95 - 4.05 (m, 1H) 4.43 (br d, $J=6.80$ Hz, 1H) 4.70 (br d, $J=5.96$ Hz, 1H) 5.78 (dd, $J=10.43$, 2.32 Hz, 1H) 6.23 (dt, $J=16.69$, 2.74 Hz, 1H) 6.83 - 6.98 (m, 3H) 7.23 - 7.32 (m, 1H) 8.10 (dd, $J=8.40$, 1.49 Hz, 1H) 8.58 (d, $J=2.27$ Hz, 1H) 12.44 (br s, 1H) 14.36 (br s, 1H).

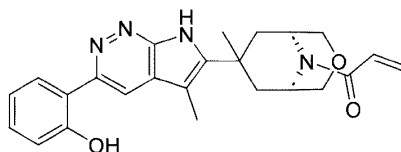
[0523] 624: LCMS (ESI⁺): m/z 474.23 (M+H)⁺, Rt: 2.772 min. ¹H NMR (400 MHz, DMSO-*d*₆) δ ppm 1.42 - 1.55 (m, 1H) 1.71 - 1.94 (m, 3H) 2.08 - 2.31 (m, 4H) 2.69 - 2.97 (m, 3H) 3.46 - 3.62 (m, 3H) 3.63 - 3.81 (m, 3H) 3.94 - 4.07 (m, 1H) 4.43 (br d, $J=7.15$ Hz, 1H) 4.70 (br d, $J=6.91$ Hz, 1H) 5.74 - 5.81 (m, 1H) 6.23 (dt, $J=16.63$, 2.71 Hz, 1H) 6.83 - 6.99 (m, 3H) 7.24 - 7.31 (m, 1H) 8.09 (br d, $J=8.23$ Hz, 1H) 8.51 - 8.61 (m, 1H) 12.18 - 12.71 (m, 1H) 14.08 - 14.68 (m, 1H).

[0524] P2 was separated by SFC (Column: DAICEL CHIRALPAK IG (250mm*30mm,10 μ m), mobile phase: A for CO₂ and B for MeOH(0.1%NH₃H₂O), gradient: B%=50.00% isocratic elution mode), affording **623** (second eluting isomer, 2.3 mg, 4.85 μ mol, 2.62% yield) and **625** (third eluting isomer, 4.1 mg, 8.64 μ mol, 4.67% yield).

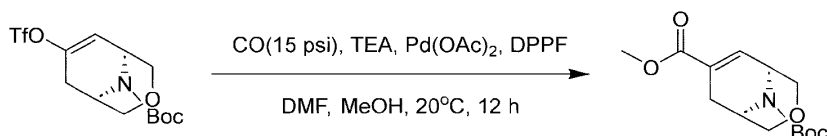
[0525] 623: LCMS (ESI⁺): m/z 474.23 (M+H)⁺, Rt: 2.847 min. ¹H NMR (400 MHz, DMSO-*d*₆) δ ppm 1.55 (br dd, $J=10.67$, 7.45 Hz, 1H) 1.76 - 1.95 (m, 3H) 1.98 - 2.10 (m, 2H) 2.14 - 2.26 (m, 2H) 2.91 - 2.98 (m, 2H) 3.62 - 3.80 (m, 4H) 4.02 (td, $J=11.44$, 6.20 Hz, 3H) 4.30 (br s, 1H) 4.45 - 4.60 (m, 2H) 5.77 (br d, $J=10.49$ Hz, 1H) 6.25 (br d, $J=16.57$ Hz, 1H) 6.85 (br dd, $J=16.63$, 10.43 Hz, 1H) 6.91 - 7.00 (m, 2H) 7.28 (br t, $J=7.51$ Hz, 1H) 8.10 (br d, $J=7.99$ Hz, 1H) 8.59 (s, 1H) 12.38 (br s, 1H) 14.08 - 14.46 (m, 1H).

[0526] 625: LCMS (ESI⁺): m/z 474.23 (M+H)⁺, Rt: 2.850 min. ¹H NMR (400 MHz, DMSO-*d*₆) δ ppm 1.49 - 1.60 (m, 1H) 1.76 - 2.07 (m, 5H) 2.10 - 2.27 (m, 2H) 2.88 - 3.00 (m, 2H) 3.59 - 3.83 (m, 4H) 3.93 - 4.08 (m, 3H) 4.30 (br s, 1H) 4.44 - 4.59 (m, 2H) 5.77 (dd, $J=10.43$, 2.44 Hz, 1H) 6.25 (dd, $J=16.69$, 2.38 Hz, 1H) 6.78 - 6.99 (m, 3H) 7.28 (t, $J=7.63$ Hz, 1H) 8.10 (br d, $J=7.99$ Hz, 1H) 8.59 (s, 1H) 12.20 - 12.52 (m, 1H) 14.33 (br s, 1H).

Example 25: Synthesis of 1-((1*R*,5*S*)-7-(3-(2-hydroxyphenyl)-5-methyl-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-7-methyl-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one (Compound 627):

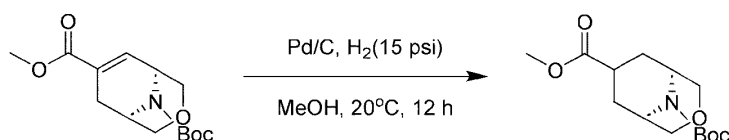


Step 1:



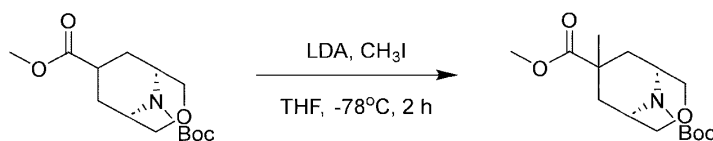
[0527] A solution of *tert*-butyl (1*R*,5*S*)-7-(((trifluoromethyl)sulfonyl)oxy)-3-oxa-9-azabicyclo[3.3.1]non-6-ene-9-carboxylate (14.44 g, 38.68 mmol, 1 *eq*), TEA (11.74 g, 116.03 mmol, 16.15 mL, 3 *eq*), Pd(OAc)₂ (868.34 mg, 3.87 mmol, 0.1 *eq*), and DPPF (2.14 g, 3.87 mmol, 0.1 *eq*) in DMF (150 mL) and MeOH (150 mL) under N₂ atmosphere was degassed and purged with carbon monoxide 3 times. The mixture was stirred under carbon monoxide (15 psi) at 20 °C for 12 h. The reaction mixture was partitioned between H₂O (200 mL) and ethyl acetate (200 mL). The organic phase was separated, washed with brine (200 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO₂, PE/EA = 10/1 to 2/1) to give 9-(*tert*-butyl) 7-methyl (1*R*,5*S*)-3-oxa-9-azabicyclo[3.3.1]non-6-ene-7,9-dicarboxylate (7.78 g, 27.46 mmol, 71.00% yield) as a colorless oil. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ 7.04 - 6.94 (m, 1H), 4.69 - 4.50 (m, 1H), 4.34 - 4.15 (m, 1H), 3.77 (s, 5H), 3.70 - 3.63 (m, 2H), 2.85 - 2.70 (m, 1H), 2.43 (d, *J* = 18.4 Hz, 1H), 1.46 (s, 9H).

Step 2:



[0528] To a solution of 9-(*tert*-butyl) 7-methyl (1*R*,5*S*)-3-oxa-9-azabicyclo[3.3.1]non-6-ene-7,9-dicarboxylate (6.8 g, 24.00 mmol, 1 *eq*) in MeOH (70 mL) was added Pd/C (680.00 mg, 1.92 mmol) under N₂ atmosphere. The suspension was degassed and purged with H₂ 3 times. The mixture was stirred under H₂ (15 Psi) at 20 °C for 12 h. The mixture was filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO₂, PE/EA = 5/1 to 1/1) to give 9-(*tert*-butyl) 7-methyl (1*R*,5*S*)-3-oxa-9-azabicyclo[3.3.1]nonane-7,9-dicarboxylate (4 g, 14.02 mmol, 58.41% yield) as a colorless oil. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ 4.05 - 3.86 (m, 2H), 3.79 (dd, *J* = 11.6, 13.4 Hz, 2H), 3.70 (s, 3H), 3.67 - 3.57 (m, 2H), 2.67 (t, *J* = 7.6 Hz, 1H), 2.50 (dd, *J* = 2.8, 14.4 Hz, 2H), 2.09 - 1.92 (m, 2H), 1.48 (s, 9H).

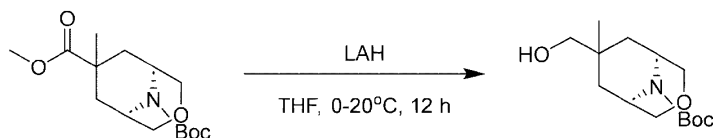
Step 3:



[0529] To a solution of 9-(*tert*-butyl) 7-methyl (1*R*,5*S*)-3-oxa-9-azabicyclo[3.3.1]nonane-7,9-dicarboxylate (3 g, 10.51 mmol, 1 *eq*) in THF (30 mL) was added dropwise LDA (2M, 7.89 mL, 1.5 *eq*) under N₂ at -78 °C. The mixture was then stirred at the same temperature for 0.5 h, and methyl iodide (4.48 g, 31.54 mmol, 1.96 mL, 3 *eq*) was added dropwise at -78 °C. The resulting mixture was stirred at -78 °C for 2 h. The reaction mixture was partitioned between ethyl acetate (30 mL) and H₂O (30 mL). The organic phase was separated, washed with brine (50 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO₂, PE/EA = 10/1 to 3/1) to give 9-(*tert*-butyl) 7-methyl (1*R*,5*S*)-7-methyl-3-oxa-9-azabicyclo[3.3.1]nonane-7,9-dicarboxylate (3 g, 10.51 mmol, 100% yield) as a colorless oil. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ 4.05 - 3.86 (m, 2H), 3.79 (dd, *J* = 11.6, 13.4 Hz, 2H), 3.70 (s, 3H), 3.67 - 3.57 (m, 2H), 2.67 (t, *J* = 7.6 Hz, 1H), 2.50 (dd, *J* = 2.8, 14.4 Hz, 2H), 2.09 - 1.92 (m, 2H), 1.48 (s, 9H).

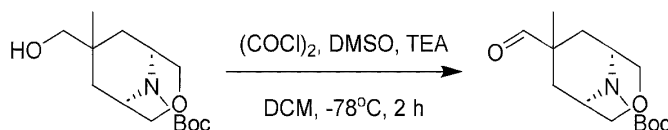
7,9-dicarboxylate (3.2 g, 10.69 mmol, 78.21% yield) as a colorless oil. ^1H NMR (400 MHz, CHLOROFORM-*d*) δ 4.01 (s, 1H), 3.89 (s, 1H), 3.78 (dd, J = 11.2, 14.4 Hz, 2H), 3.67 (s, 3H), 3.65 - 3.56 (m, 2H), 2.66 - 2.57 (m, 2H), 1.65 - 1.57 (m, 1H), 1.56 - 1.50 (m, 1H), 1.48 (s, 9H), 1.16 (s, 3H).

Step 4:



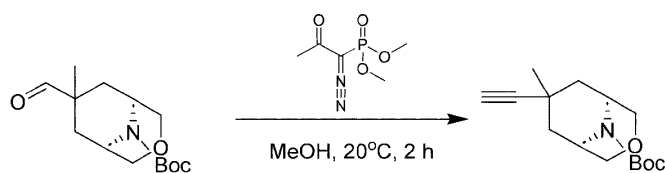
[0530] To a solution of 9-(*tert*-butyl) 7-methyl (1*R*,5*S*)-7-methyl-3-oxa-9-azabicyclo[3.3.1]nonane-7,9-dicarboxylate (3.1 g, 10.36 mmol, 1 *eq*) in THF (60 mL) was added LiAlH_4 (2.5M, 6.21 mL, 1.5 *eq*) dropwise at 0 °C under N_2 . The mixture was warmed up to 20 °C and stirred for 12 h. The reaction mixture was quenched with a 1N sodium potassium tartrate aqueous solution (10 mL), then diluted with H_2O (50 mL) and extracted with ethyl acetate (50 mL $\times$ 2). The combined organic layers were washed with brine (50 mL), dried over Na_2SO_4 , and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO_2 , PE/EA = 10/1 to 1/1) to give *tert*-butyl (1*R*,5*S*)-7-(hydroxymethyl)-7-methyl-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (2.8 g, 9.85 mmol, 95.11% yield) as a colorless oil. ^1H NMR (400 MHz, CHLOROFORM-*d*) δ 4.17 - 4.12 (m, 1H), 4.02 (br d, J = 7.6 Hz, 1H), 3.67 - 3.56 (m, 6H), 1.83 - 1.68 (m, 5H), 1.48 (s, 9H), 0.97 (s, 3H).

Step 5:



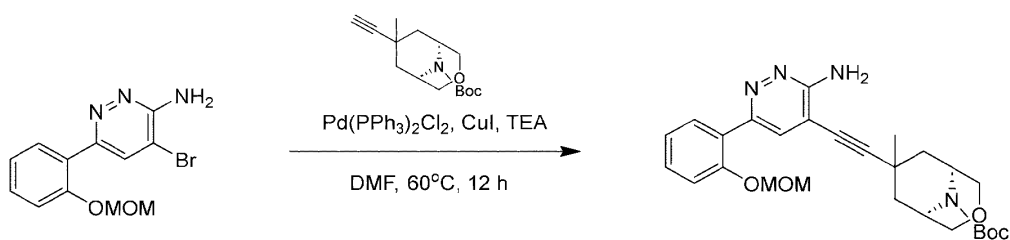
[0531] To a mixture of DMSO (1.04 g, 13.27 mmol, 1.04 mL, 2.4 *eq*) in DCM (20 mL) was added oxalyl chloride (841.96 mg, 6.63 mmol, 580.66 μL , 1.2 *eq*) in DCM (20 mL) dropwise at -78 °C under N_2 . After 30 min, *tert*-butyl (1*R*,5*S*)-7-(hydroxymethyl)-7-methyl-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (1.5 g, 5.53 mmol, 1 *eq*) in DCM (20 mL) was added dropwise to the reaction mixture. After 5 min, TEA (2.80 g, 27.64 mmol, 3.85 mL, 5 *eq*) was added dropwise and the reaction mixture was stirred at -78 °C for 2 h. The reaction mixture was then diluted with NaHCO_3 (50 mL). The organic layer was separated and washed with brine (50 mL), dried over Na_2SO_4 , and filtered. The filtrate was concentrated under reduced pressure to give *tert*-butyl (1*R*,5*S*)-7-formyl-7-methyl-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (1.1 g, 4.08 mmol, 73.88% yield) as a white solid, which was used in the subsequent step without purification. ^1H NMR (400 MHz, CHLOROFORM-*d*) δ 9.47 (s, 1H), 4.04 (s, 1H), 3.96 - 3.85 (m, 1H), 3.74 - 3.56 (m, 4H), 1.78 - 1.50 (m, 3H), 1.47 (s, 9H), 1.36 (t, J = 7.2 Hz, 1H), 0.90 (s, 3H).

Step 6:



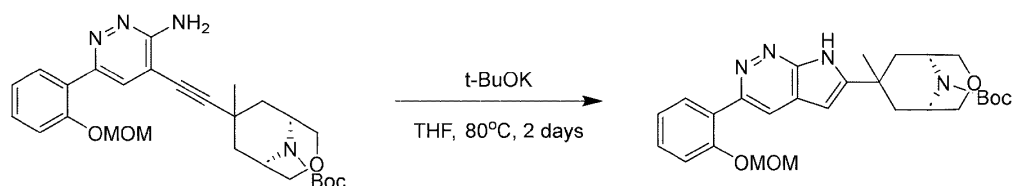
[0532] To a mixture of *tert*-butyl (1*R*,5*S*)-7-formyl-7-methyl-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (1.1 g, 4.08 mmol, 1 *eq*) and K_2CO_3 (2.26 g, 16.34 mmol, 4 *eq*) in MeOH (20 mL) was added 1-diazo-1-dimethoxyphosphoryl-propan-2-one (941.52 mg, 4.90 mmol, 1.2 *eq*) dropwise at 20 °C under N_2 . The mixture was stirred at the same temperature for 2 h. The reaction mixture was diluted with water (50 mL) and extracted with EtOAc (20 mL $\times$ 2). The combined organic layers were washed with brine (50 mL), dried over Na_2SO_4 , and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO_2 , PE/EA = 50/1 to 10/1) to give *tert*-butyl (1*R*,5*S*)-7-ethynyl-7-methyl-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (700 mg, 2.64 mmol, 64.59% yield) as a white solid. 1H NMR (400 MHz, $CHCl_3-d_3$) δ 4.07 (s, 1H), 3.96 - 3.84 (m, 3H), 3.76 - 3.67 (m, 2H), 2.11 (s, 1H), 2.07 (d, J = 14.4 Hz, 2H), 1.91 - 1.73 (m, 2H), 1.47 (s, 9H), 1.33 (s, 3H).

Step 7:



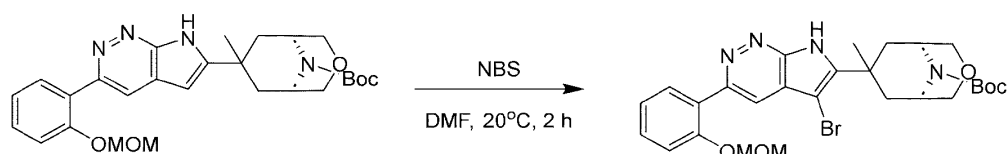
[0533] To a solution of 4-bromo-6-(2-(methoxymethoxy)phenyl)pyridazin-3-amine (700 mg, 2.26 mmol, 1 *eq*) and *tert*-butyl (1*R*,5*S*)-7-ethynyl-7-methyl-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (688.72 mg, 2.60 mmol, 1.15 *eq*) in DMF (10 mL) was added $Pd(PPh_3)_2Cl_2$ (158.42 mg, 225.70 μ mol, 0.1 *eq*), CuI (85.97 mg, 451.40 μ mol, 0.2 *eq*) and TEA (1.14 g, 11.29 mmol, 5 *eq*) under N_2 . The mixture was heated to 60 °C and stirred for 12 h. The reaction mixture was diluted with H_2O (20 mL) and extracted with EtOAc (20 mL $\times$ 2). The combined organic layers were washed with brine (20 mL $\times$ 2), dried over Na_2SO_4 , and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO_2 , PE/EA = 10/1 to 0/1) to give *tert*-butyl (1*R*,5*S*)-7-((3-amino-6-(2-(methoxymethoxy)phenyl)pyridazin-4-yl)ethynyl)-7-methyl-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (900 mg, 1.82 mmol, 80.63% yield) as a yellow solid. 1H NMR (400 MHz, $CHCl_3-d_3$) δ 7.75 (d, J = 7.2 Hz, 1H), 7.60 (s, 1H), 7.32 (d, J = 7.2 Hz, 1H), 7.18 (d, J = 8.0 Hz, 1H), 7.15 - 7.06 (m, 1H), 6.04 (s, 2H), 5.19 (s, 2H), 4.14 (s, 1H), 4.08 - 3.96 (m, 3H), 3.80 (t, J = 10.4 Hz, 2H), 3.44 (s, 3H), 2.16 (d, J = 14.4 Hz, 2H), 1.96 - 1.82 (m, 2H), 1.49 (s, 9H), 1.46 - 1.40 (m, 3H).

Step 8:



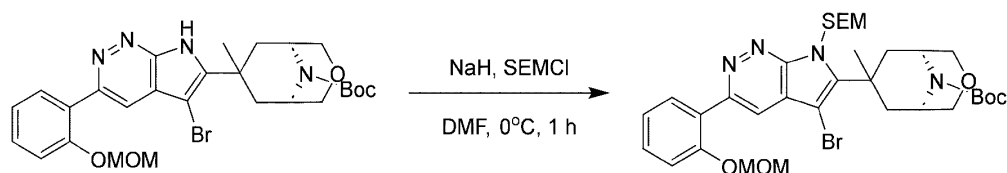
[0534] To a mixture of *tert*-butyl (1*R*,5*S*)-7-((3-amino-6-(2-(methoxymethoxy)phenyl)pyridazin-4-yl)ethynyl)-7-methyl-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (900 mg, 1.18 mmol, 1 *eq*) in THF (18 mL) was added a solution of potassium *tert*-butoxide (1*M*, 7.29 mL, 4 *eq*) in one portion. The mixture was then heated to 80 °C and stirred for 2 days. The reaction mixture was quenched with H₂O (20 mL) and extracted with EtOAc (20 mL × 2). The combined organic layers were washed with brine (20 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO₂, PE/EA = 10/1 to 0/1) to give *tert*-butyl (1*R*,5*S*)-7-(3-(2-(methoxymethoxy)phenyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-7-methyl-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (820 mg, 1.66 mmol, 91.1% yield) as a yellow solid. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ 13.56 (s, 1H), 8.08 (s, 1H), 7.83 (d, *J* = 7.6 Hz, 1H), 7.38 (t, *J* = 7.6 Hz, 1H), 7.33 - 7.29 (m, 1H), 7.18 (t, *J* = 7.2 Hz, 1H), 6.36 (s, 1H), 5.23 (s, 2H), 4.21 (s, 1H), 4.15 (d, *J* = 7.2 Hz, 1H), 3.93 (d, *J* = 11.2 Hz, 1H), 3.79 (d, *J* = 11.2 Hz, 1H), 3.54 (d, *J* = 16.4 Hz, 2H), 3.48 (s, 3H), 3.31 (d, *J* = 14.4 Hz, 1H), 2.87 (d, *J* = 14.8 Hz, 1H), 2.24 - 2.09 (m, 2H), 1.51 (s, 9H), 1.47 - 1.41 (m, 3H).

Step 9:



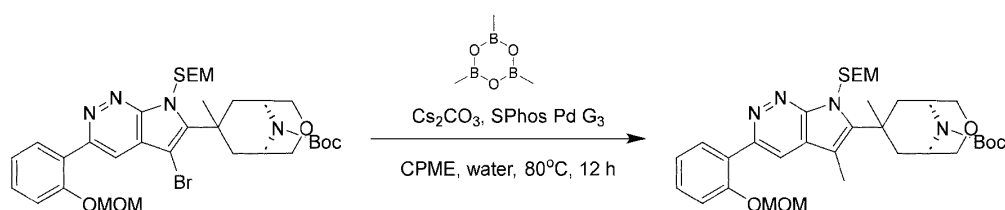
[0535] To a solution of *tert*-butyl (1*R*,5*S*)-7-(3-(2-(methoxymethoxy)phenyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-7-methyl-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (800 mg, 1.62 mmol, 1 *eq*) in DMF (10 mL) was added NBS (273.50 mg, 1.54 mmol, 0.95 *eq*) in one portion. The mixture was stirred at 20 °C for 2 h. The reaction mixture was diluted with water (10 mL) and extracted with ethyl acetate (10 mL × 2). The combined organic layers were washed with brine (10 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO₂, PE/EA = 10/1 to 1/1) to give *tert*-butyl (1*R*,5*S*)-7-(5-bromo-3-(2-(methoxymethoxy)phenyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-7-methyl-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (700 mg, 1.22 mmol, 75.46% yield) as a yellow solid. LCMS (ESI⁺): *m/z* 573.3 (M+H)⁺.

Step 10:



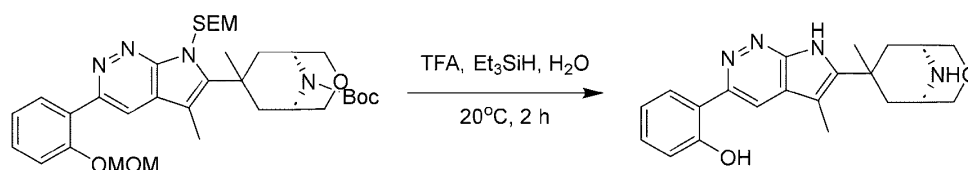
[0536] To a solution of *tert*-butyl (1*R*,5*S*)-7-(5-bromo-3-(2-(methoxymethoxy)phenyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-7-methyl-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (700 mg, 1.22 mmol, 1 *eq*) in DMF (10 mL) was added NaH (58.58 mg, 1.46 mmol, 60% purity, 1.2 *eq*) in portions at 0 °C under N₂. The mixture was stirred at the same temperature for 30 min before (2-chloromethoxyethyl)trimethylsilane (213.68 mg, 1.28 mmol, 226.84 μ L, 1.05 *eq*) was added dropwise at 0 °C. The resulting mixture was stirred at the same temperature for 1 h. The reaction mixture was quenched by addition of H₂O (20 mL) at 0 °C, then extracted with EtOAc (20 mL $\times$ 2). The combined organic layers were washed with brine (20 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO₂, PE/EA = 10/1 to 1/1) to give *tert*-butyl (1*R*,5*S*)-7-(5-bromo-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-7-methyl-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (700 mg, 1.22 mmol, 75.46% yield) as a yellow solid. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ 8.07 (s, 1H), 7.60 (dd, *J* = 1.6, 7.6 Hz, 1H), 7.43 - 7.36 (m, 1H), 7.29 (s, 1H), 7.13 (t, *J* = 7.6 Hz, 1H), 6.19 (s, 2H), 5.25 (s, 2H), 4.02 (s, 1H), 3.90 - 3.85 (m, 2H), 3.84 - 3.75 (m, 2H), 3.68 (t, *J* = 13.6 Hz, 2H), 3.50 (s, 3H), 3.47 (s, 1H), 1.92 - 1.76 (m, 2H), 1.52 (s, 9H), 1.35 (s, 3H), 1.30 - 1.24 (m, 2H), 1.04 - 0.97 (m, 2H), -0.03 (s, 9H).

Step 11:



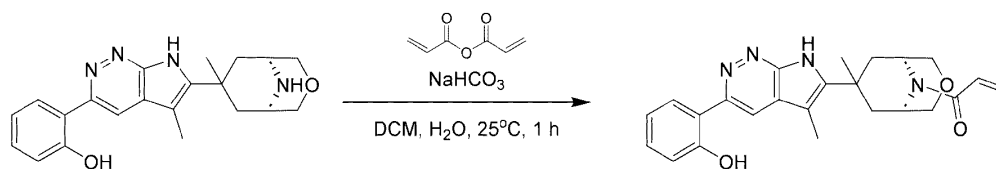
[0537] A solution of *tert*-butyl (1*R*,5*S*)-7-(5-bromo-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-7-methyl-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (200 mg, 284.20 μ mol, 1 *eq*), 2,4,6-trimethyl-1,3,5,2,4,6-trioxatriborinane (713.53 mg, 2.84 mmol, 794.58 μ L, 10 *eq*), SPhos Pd G₃ (22.17 mg, 28.42 μ mol, 0.1 *eq*) and Cs₂CO₃ (185.19 mg, 568.39 μ mol, 2 *eq*) in water (1 mL) and CPME (4 mL) was degassed and heated to 80 °C and stirred for 12 h under N₂. The reaction mixture was diluted with H₂O (20 mL) and extracted with EtOAc (10 mL $\times$ 2). The combined organic layers were washed with brine (20 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO₂, PE/EA = 10/1 to 0/1) to give *tert*-butyl (1*R*,5*S*)-7-(3-(2-(methoxymethoxy)phenyl)-5-methyl-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-7-methyl-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (160 mg, 250.44 μ mol, 88.12% yield) as a yellow solid. LCMS (ESI⁺): *m/z* 639.4 (M+H)⁺.

Step 12:



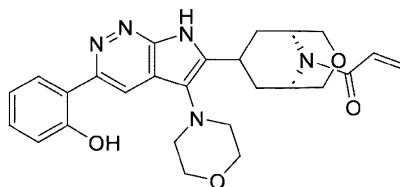
[0538] A solution of *tert*-butyl (1*R*,5*S*)-7-(3-(2-(methoxymethoxy)phenyl)-5-methyl-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-7-methyl-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (160 mg, 250.44 μ mol, 1 *eq*) in TFA (2 mL), Et₃SiH (72.80 mg, 626.09 μ mol, 0.1 mL, 2.50 *eq*), and water (100.00 mg, 5.55 mmol, 0.1 mL, 22.16 *eq*) was stirred at 20 °C for 2 h. The mixture was concentrated under reduced pressure to yield 2-(5-methyl-6-((1*R*,5*S*)-7-methyl-3-oxa-9-azabicyclo[3.3.1]nonan-7-yl)-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)phenol (120 mg, 208.17 μ mol, 83.12% yield) as a yellow solid, which was used in the next step directly without purification. LCMS (ESI⁺): *m/z* 365.2 (M+H)⁺.

Step 13:

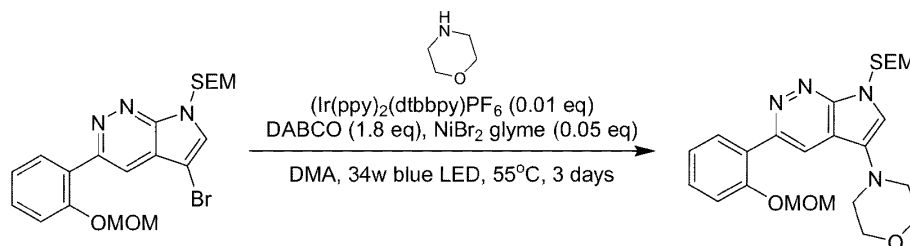


[0539] To a solution of crude 2-(5-methyl-6-((1*R*,5*S*)-7-methyl-3-oxa-9-azabicyclo[3.3.1]nonan-7-yl)-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)phenol (120 mg, 329.27 μ mol, 1 *eq*) in NaHCO₃ (1.09 M, 12.00 mL, 39.72 *eq*) and DCM (12 mL) was added prop-2-enyl prop-2-enoate (83.05 mg, 658.54 μ mol, 2 *eq*) at 25 °C. The mixture was stirred at the same temperature for 1 h. The layers were separated, and the organic layer was washed with brine (40 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by prep-HPLC (column: WePure Biotech XP tC18 150*40*7 μ m; mobile phase: [H₂O (0.05% NH₃H₂O+10mM NH₄HCO₃)-ACN]; gradient: 35%-65% B over 8.0 min) to give **627** (30 mg, 71.69 μ mol, 21.77% yield). ¹H NMR (400 MHz, METHANOL-*d*₄) δ 8.34 (s, 1H), 8.00 (d, *J* = 7.2 Hz, 1H), 7.27 (t, *J* = 7.2 Hz, 1H), 7.02 - 6.92 (m, 2H), 6.80 (dd, *J* = 10.8, 16.8 Hz, 1H), 6.32 (dd, *J* = 2.0, 16.8 Hz, 1H), 5.83 (dd, *J* = 2.0, 10.8 Hz, 1H), 4.72 - 4.58 (m, 1H), 4.30 (s, 1H), 3.81 (t, *J* = 12.1 Hz, 2H), 3.60 - 3.47 (m, 2H), 3.37 - 3.33 (m, 1H), 3.13 - 3.00 (m, 2H), 2.54 (s, 3H), 2.16 - 1.98 (m, 2H), 1.41 (s, 3H). LCMS (ESI⁺): *m/z* 419.1 (M+H)⁺.

Example 26: 1-((1*R*,5*S*)-7-(3-(2-hydroxyphenyl)-5-morpholino-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one (Compound 603):

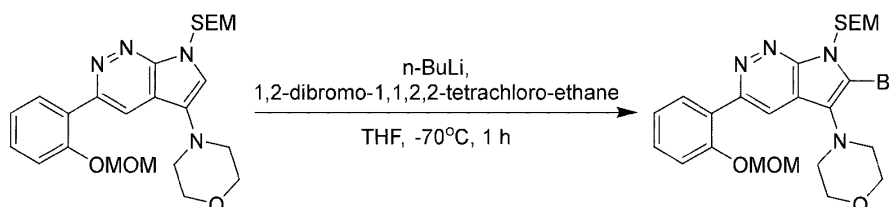


Step 1:



[0540] A mixture of 5-bromo-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazine (1 g, 2.16 mmol, 1 *eq*), morpholine (1.95 g, 21.54 mmol, 1.89 mL, 10 *eq*), DABCO (1.21 g, 10.76 mmol, 1.184 mL, 5 *eq*), (4,4'-di-*tert*-butyl-2,2'-bipyridine)bis[(2-pyridinyl)phenyl]iridium(III) hexafluorophosphate (98.4 mg, 107.66 μ mol, 0.05 *eq*), and dibromo(1,2-dimethoxyethane)nickel(II) (66.46 mg, 215.32 μ mol, 0.1 *eq*) in DMA (20 mL) was degassed and purged with N₂ 3 times. The reaction mixture was then heated to 55°C and stirred for 3 days under argon and blue LEDs. The reaction mixture was diluted with H₂O (30 mL) and extracted with MTBE (30 mL $\times$ 2). The combined organic layers were washed with brine (30 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO₂, petroleum ether/ethyl acetate=1/2) to give 4-(3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazin-5-yl)morpholine (570 mg, crude) as a yellow oil. ¹H NMR (400 MHz, METHANOL-*d*₄) δ 8.28 (s, 1H), 7.73 (d, *J* = 1.6, 7.6 Hz, 1H), 7.56 - 7.47 (m, 2H), 7.37 (d, *J* = 8.4 Hz, 1H), 7.29 - 7.20 (m, 1H), 5.88 (s, 2H), 5.31 - 5.26 (m, 2H), 3.99 - 3.95 (m, 4H), 3.73 - 3.66 (m, 2H), 3.42 (s, 3H), 3.23 - 3.17 (m, 4H), 0.99 - 0.92 (m, 2H), 0.02 - -0.02 (m, 9H). LCMS (ESI⁺): *m/z* 471.3 (M+H)⁺.

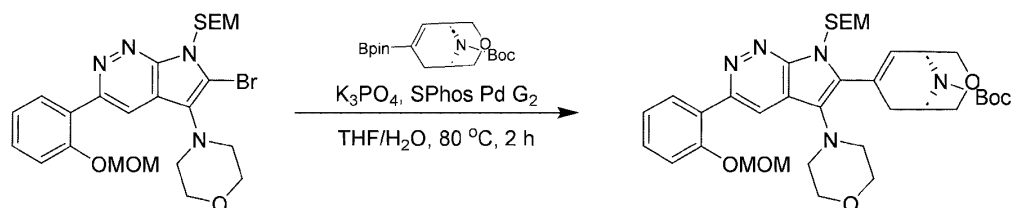
Step 2:



[0541] To a solution of 4-(3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazin-5-yl)morpholine (500 mg, 1.06 mmol, 1 *eq*) in THF (5 mL) was added *n*-BuLi (2.5 M, 637.44 μ L, 1.5 *eq*) dropwise at -70 °C under N₂. The mixture was then stirred at the same temperature for 10 min before a solution of 1,2-dibromo-1,1,2,2-tetrachloro-ethane (860.26 mg, 2.64 mmol, 317.08 μ L, 3 *eq*) in THF (0.5 mL) was added. The reaction mixture was stirred at -70°C for 1.5 h. The reaction mixture was then quenched via addition of saturated aqueous NH₄Cl (2 mL) at 0 °C, diluted with H₂O (2 mL), and extracted with ethyl acetate (3 mL $\times$ 2). The organic phase was separated, washed with brine (1 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO₂, petroleum ether/ethyl acetate=1/2) to give 4-(6-bromo-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-

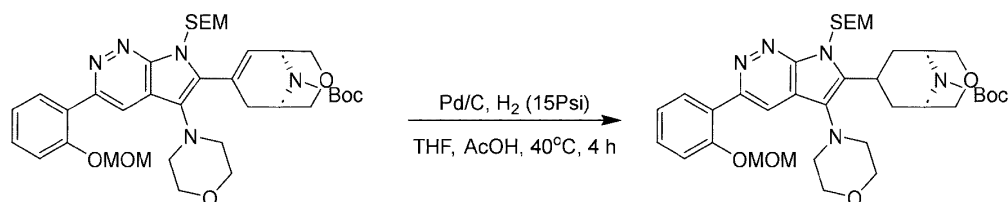
c]pyridazin-5-yl)morpholine (400 mg, 727.89 μmol , 68.51% yield) as a yellow oil. ^1H NMR (400 MHz, $\text{METHANOL-}d_4$) δ 8.37 (d, J = 12.0 Hz, 1H), 7.74 (d, J = 7.6 Hz, 1H), 7.57 - 7.47 (m, 1H), 7.39 (d, J = 8.4 Hz, 1H), 7.26 (t, J = 7.6 Hz, 1H), 5.99 (d, J = 8.8 Hz, 2H), 5.31 (s, 2H), 3.95 - 3.90 (m, 4H), 3.77 (t, J = 7.6 Hz, 2H), 3.46 (s, 3H), 3.37 - 3.34 (m, 4H), 0.98 (t, J = 8.0 Hz, 2H), 0.00 (s, 9H). LCMS (ESI^+): m/z 549.2 ($\text{M}+\text{H}$) $^+$.

Step 3:



[0542] A mixture of 4-(6-bromo-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazin-5-yl)morpholine (300 mg, 545.92 μmol , 1 *eq*), *tert*-butyl (1*R*,5*S*)-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-oxa-9-azabicyclo[3.3.1]non-6-ene-9-carboxylate (230.1 mg, 655.1 μmol , 1.2 *eq*), K_3PO_4 (231.76 mg, 1.09 mmol, 2 *eq*), and chloro(2-dicyclohexylphosphino-2',6'-dimethoxy-1,1'-biphenyl)[2-(2'-amino-1,1'-biphenyl)]palladium(II) (39.34 mg, 54.6 μmol , 0.1 *eq*) in THF (3 mL) and H_2O (0.6 mL) was degassed and purged with N_2 3 times. The reaction mixture was then heated to 80 $^\circ\text{C}$ and stirred for 2 h under N_2 atmosphere. The reaction mixture was diluted with H_2O (10 mL) and extracted with MTBE (5 mL $\times$ 2). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4 , and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO_2 , petroleum ether/ethyl acetate=1/1) to give *tert*-butyl (1*R*,5*S*)-7-(3-(2-(methoxymethoxy)phenyl)-5-morpholino-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]non-6-ene-9-carboxylate (180 mg, 259.40 μmol , 47.52% yield) as a yellow oil. ^1H NMR (400 MHz, $\text{METHANOL-}d_4$) δ 8.31 (d, J = 3.2 Hz, 1H), 7.72 (d, J = 1.6, 7.6 Hz, 1H), 7.50 (s, 1H), 7.36 (d, J = 8.0 Hz, 1H), 7.24 (s, 1H), 6.34 (s, 1H), 5.87 - 5.79 (m, 2H), 5.28 (s, 2H), 3.92 - 3.84 (m, 6H), 3.81 - 3.75 (m, 4H), 3.44 (s, 3H), 3.33 (d, J = 3.6 Hz, 2H), 3.29 - 3.22 (m, 2H), 1.59 (s, 9H), 1.51 (s, 2H), 1.35 - 1.24 (m, 4H), 0.01 - -0.02 (m, 9H). LCMS (ESI^+): m/z 694.5 ($\text{M}+\text{H}$) $^+$.

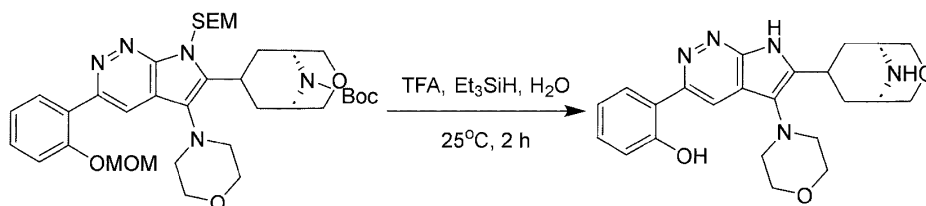
Step 4:



[0543] To a solution of *tert*-butyl (1*R*,5*S*)-7-(3-(2-(methoxymethoxy)phenyl)-5-morpholino-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]non-6-ene-9-carboxylate (80 mg, 129.70 μmol , 1 *eq*) in THF (1 mL) was added Pd/C (80 mg, 75.17 μmol) and AcOH

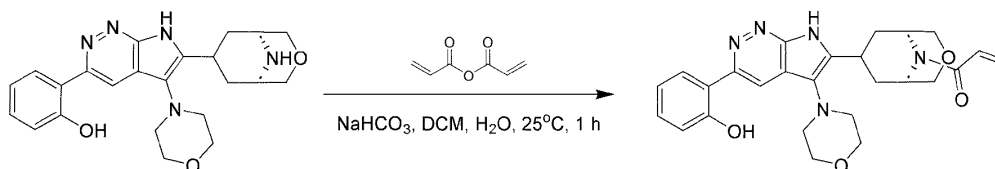
(0.1 mL) under N₂ atmosphere. The suspension was degassed and purged with H₂ 3 times. The mixture was heated to 40 °C and stirred under H₂ (15 Psi) for 4 h. The reaction mixture was filtered, and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (SiO₂, petroleum ether /ethyl acetate=1/2) to give *tert*-butyl (1*R*,5*S*)-7-(3-(2-(methoxymethoxy)phenyl)-5-morpholino-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (20 mg) as a white solid. LCMS (ESI⁺): *m/z* 696.5 (M+H)⁺.

Step 5:



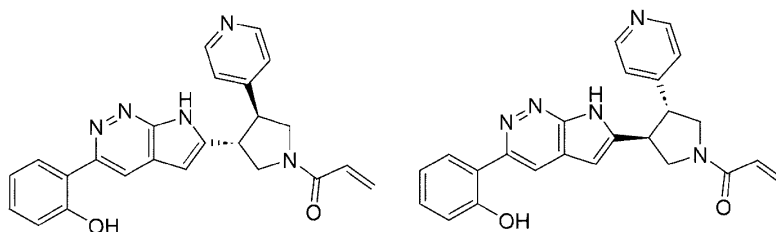
[0544] A solution of *tert*-butyl (1*R*,5*S*)-7-(3-(2-(methoxymethoxy)phenyl)-5-morpholino-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (20 mg, 28.74 μmol, 1 eq) in TFA (1 mL), Et₃SiH (0.05 mL), and H₂O (0.05 mL) was stirred at 25 °C for 2 h. The reaction mixture was concentrated under reduced pressure to give 2-(6-((1*R*,5*S*)-3-oxa-9-azabicyclo[3.3.1]nonan-7-yl)-5-morpholino-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)phenol (12 mg, 28.47 μmol, 99.07% yield) as a yellow oil, which was used in the next step without purification. LCMS (ESI⁺): *m/z* 422.2 (M+H)⁺.

Step 6:

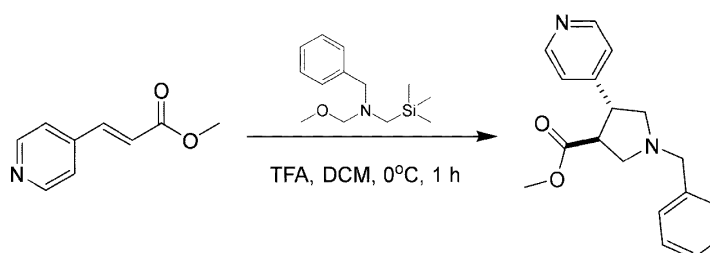


[0545] To a solution of 2-(6-((1*R*,5*S*)-3-oxa-9-azabicyclo[3.3.1]nonan-7-yl)-5-morpholino-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)phenol, and NaHCO₃ (11.96 mg, 142.35 μmol, 5.54 μL, 5 eq) in DCM (0.5 mL) and H₂O (0.5 mL) was added prop-2-enoyl prop-2-enoate (5.39 mg, 42.71 μmol, 1.5 eq). The mixture was stirred at 25 °C for 1 h. The reaction mixture was quenched by addition of MeOH (1 mL) at the same temperature, then diluted with H₂O (1 mL) and extracted with DCM (2 mL × 2). The combined organic layers were washed with brine (2 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by prep-HPLC (FA condition) to give **603** (3 mg, 6.31 μmol, 22.16% yield). ¹H NMR (400 MHz, DMSO-*d*₆) δ 14.11 (s, 1H), 12.41 (s, 1H), 8.63 (s, 1H), 8.21 (d, *J* = 7.2 Hz, 1H), 7.35 - 7.23 (m, 1H), 7.01 - 6.86 (m, 3H), 6.27 (dd, *J* = 2.4, 16.8 Hz, 1H), 5.89 - 5.65 (m, 1H), 4.69 (d, *J* = 10.4 Hz, 1H), 4.42 (s, 1H), 3.78 - 3.64 (m, 6H), 3.53 (t, *J* = 10.4 Hz, 2H), 3.12 (s, 4H), 3.00 - 2.76 (m, 1H), 2.34 - 2.10 (m, 4H). LCMS (ESI⁺): *m/z* 476.2 (M+H)⁺.

Example 27: 1-((3*R*,4*S*)-3-(3-(2-hydroxyphenyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-4-(pyridin-4-yl)pyrrolidin-1-yl)prop-2-en-1-one and 1-((3*S*,4*R*)-3-(3-(2-hydroxyphenyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-4-(pyridin-4-yl)pyrrolidin-1-yl)prop-2-en-1-one (Compound 608 and 609):

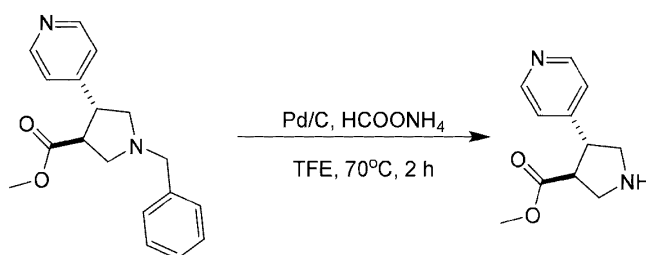


Step 1:



[0546] To a solution of methyl (*E*)-3-(pyridin-4-yl)acrylate (10.26 g, 43.21 mmol, 1.5 *eq*) and methyl (*E*)-3-(4-pyridyl) prop-2-enoate (4.7 g, 28.80 mmol, 1 *eq*) in DCM (70 mL) was added TFA (985.26 mg, 8.64 mmol, 641.87 μ L, 0.3 *eq*). The mixture was stirred at 0 °C for 1 hr. The mixture was poured into water (80 mL) and extracted with methyl *tert*-butyl ether (80 mL $\times$ 2). The combined organic phases were washed with brine (80 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO₂, petroleum ether: ethyl acetate = 1:0 to 0:1) to give *rel*-methyl (3*S*,4*R*)-1-benzyl-4-(pyridin-4-yl)pyrrolidine-3-carboxylate (7 g, 23.62 mmol, 82.00% yield) as a colorless oil. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.49 - 8.47 (m, 2 H), 7.35 - 7.31 (m, 5 H), 7.28 (s, 1 H), 7.27 - 7.25 (m, 1 H), 3.68 (s, 1 H), 3.59 (s, 3 H), 3.56 - 3.53 (m, 1 H), 3.33 (s, 1 H), 3.19 - 3.15 (m, 1 H), 3.00 (s, 2 H), 2.90 (s, 1 H), 2.58 (d, *J* = 14.0 Hz, 1 H).

Step 2:



[0547] To a solution of methyl *rel*-(3*S*,4*R*)-1-benzyl-4-(pyridin-4-yl)pyrrolidine-3-carboxylate (15 g, 50.61 mmol, 1 *eq*) in TFE (150 mL) was added ammonium formate (4.79 g, 75.92 mmol, 1.5 *eq*). After addition, Pd/C (1.50 g, 1.41 mmol) was added at 20 °C under argon atmosphere. The mixture was then heated to 70 °C and stirred for 2 h. The mixture was filtered and concentrated under reduced pressure to

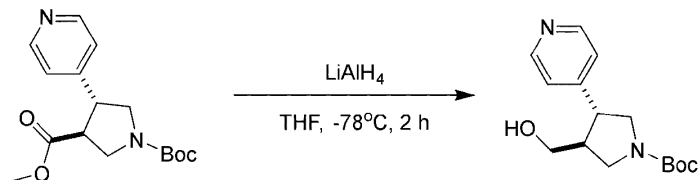
give methyl *rel*-(3*S*,4*R*)-4-(pyridin-4-yl)pyrrolidine-3-carboxylate (13 g, crude) as a yellow oil, which was used in the next step without purification. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.48 - 8.46 (m, 2 H), 7.31 (d, *J* = 6.0 Hz, 2 H), 3.88 (q, *J* = 9.6 Hz, 1 H), 3.60 - 3.55 (m, 3 H), 3.18 (s, 3 H), 3.05 - 3.03 (m, 2H), 2.74 - 2.71 (m, 1H).

Step 3:



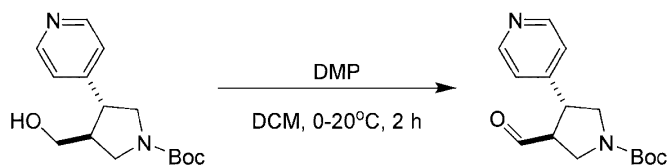
[0548] To a solution of *rel*-(3*S*,4*R*)-4-(pyridin-4-yl)pyrrolidine-3-carboxylate (6 g, 29.09 mmol, 1 *eq*) in DMF (60 mL) was added Boc₂O (12.70 g, 58.18 mmol, 13.37 mL, 2 *eq*) and DIEA (11.28 g, 87.28 mmol, 15.20 mL, 3 *eq*). The mixture was stirred at 0 °C for 1 h. The mixture was poured into water (100 mL) and extracted with ethyl acetate (100 mL × 2). The combined organic phases were washed with brine (200 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO₂, petroleum ether: ethyl acetate = 1:0 to 0:1) to give *rel*-*tert*-butyl 3-methyl (3*S*,4*R*)-4-(pyridin-4-yl)pyrrolidine-1,3-dicarboxylate (10 g, 32.64 mmol, 56.10% yield) as a yellow oil. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.49 - 8.45 (m, 2 H), 7.35 - 7.34 (s, 1 H), 7.11 (s, 1 H), 3.77 - 3.73 (m, 2 H), 3.72 - 3.70 (m, 1 H), 3.58 - 3.55 (m, 2H), 3.52 - 3.43 (m, 1H), 3.24 (s, 1 H), 1.41 - 1.36 (m, 9H).

Step 4:



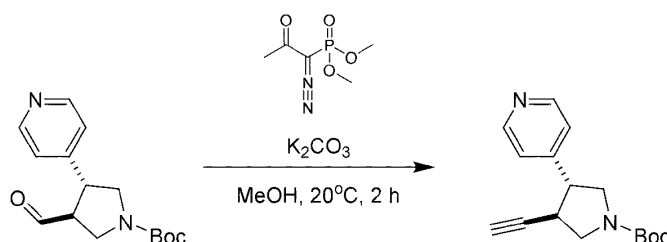
[0549] To a solution of *rel*-*tert*-butyl 3-methyl (3*S*,4*R*)-4-(pyridin-4-yl)pyrrolidine-1,3-dicarboxylate (4.5 g, 14.69 mmol, 1 *eq*) in THF (45 mL) was added LiAlH₄ (2.5 M, 11.75 mL, 2 *eq*) at -78 °C under N₂. The mixture was stirred at the same temperature for 2 h. The reaction mixture was then quenched with the addition of aqueous NH₄Cl (50 mL). This was diluted with H₂O (100 mL) and extracted with ethyl acetate (50 mL × 2). The combined organic layers were washed with brine (50 mL × 2), dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure to give *rel*-*tert*-butyl (3*S*,4*R*)-3-(hydroxymethyl)-4-(pyridin-4-yl)pyrrolidine-1-carboxylate (7.5 g, 26.94 mmol, 91.72% yield) as a yellow oil, which was used in the next step without purification. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.56 - 8.54 (m, 2H), 7.39 (d, *J* = 6.0 Hz, 1H), 7.22 (d, *J* = 4.4 Hz, 1H), 3.78 (dd, *J* = 8.0, 10.4 Hz, 1H), 3.62 - 3.58 (m, 2H), 3.36 - 3.31 (m, 1H), 3.26 - 3.23 (m, 2H), 3.05 - 3.04 (m, 1H), 2.69 - 2.65 (m, 1H), 1.50 - 1.46 (m, 9H).

Step 5:



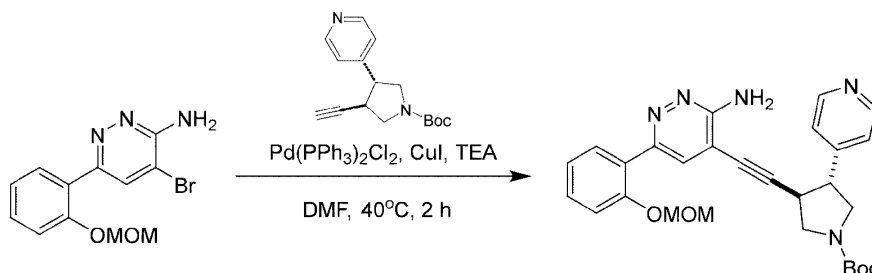
[0550] To a solution of *rel*-tert-butyl (3*S*,4*R*)-3-(hydroxymethyl)-4-(pyridin-4-yl)pyrrolidine-1-carboxylate (3.5 g, 12.57 mmol, 1 *eq*) in DCM (35 mL) was added DMP (8.00 g, 18.86 mmol, 5.84 mL, 1.2 *eq*) at 0 °C under N₂. The mixture was then warmed up to 20 °C and stirred for 2 h. The mixture was concentrated under reduced pressure, and the residue was triturated in MTBE (50 mL). The solid was discarded and the organic phase was washed with brine (50 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO₂, petroleum ether/ethyl acetate=1/0 to 0/1) to give *rel*-tert-butyl (3*S*,4*R*)-3-formyl-4-(pyridin-4-yl)pyrrolidine-1-carboxylate (4.5 g, 16.28 mmol, 64.75% yield) as a yellow oil. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ 9.63 (d, *J* = 1.6 Hz, 1 H), 8.52 - 8.49 (m, 2 H), 7.11 (d, *J* = 6.0 Hz, 2 H), 3.78 - 3.67 (m, 4 H), 3.45 - 3.34 (m, 1 H), 3.11 (d, *J* = 6.0 Hz, 1 H), 1.43 - 1.41 (m, 9H).

Step 6:



[0551] To a mixture of *rel*-tert-butyl (3*S*,4*R*)-3-formyl-4-(pyridin-4-yl)pyrrolidine-1-carboxylate (3.5 g, 12.67 mmol, 1 *eq*) and K₂CO₃ (3.50 g, 25.33 mmol, 2 *eq*) in MeOH (35 mL) was added 1-diazo-1-dimethoxyphosphoryl-propan-2-one (2.92 g, 15.20 mmol, 1.2 *eq*) at 0 °C. The mixture was stirred at 20 °C for 2 h. The mixture was poured into water (30 mL) and extracted with ethyl acetate (20 mL × 3). The combined organic phases were washed with brine (50 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was triturated with MTBE (30 mL) at 20 °C for 20 min to give *rel*-tert-butyl (3*R*,4*R*)-3-ethynyl-4-(pyridin-4-yl)pyrrolidine-1-carboxylate (2.3 g, 8.45 mmol, 66.68% yield) as a white solid. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ 8.52 - 8.51 (m, 2 H), 7.20 - 7.16 (m, 2 H), 3.88 - 3.80 (m, 2 H), 3.37 - 3.24 (m, 3 H), 3.00 - 2.95 (m, 1 H), 1.43 - 1.41 (m, 9 H).

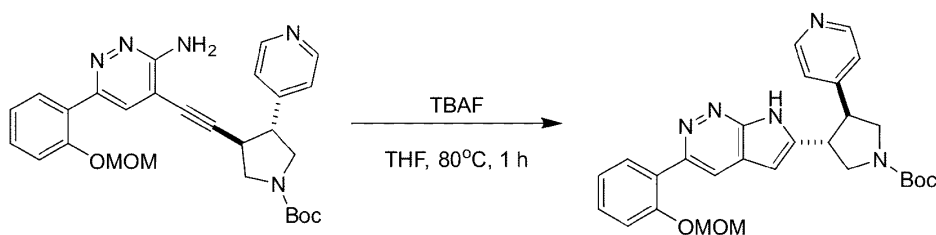
Step 7:



[0552] A mixture of 4-bromo-6-(2-(methoxymethoxy)phenyl)pyridazin-3-amine (800 mg, 2.58 mmol, 1 *eq*), *tert*-butyl *rel*-(3*R*,4*R*)-3-ethynyl-4-(pyridin-4-yl)pyrrolidine-1-carboxylate (1.05 g, 3.87 mmol, 1.5 *eq*), Pd(PPh₃)₂Cl₂ (362.10 mg, 515.89 μmol, 0.2 *eq*), CuI (147.38 mg, 773.83 μmol, 0.3 *eq*), and TEA (783.03 mg, 7.74 mmol, 1.08 mL, 3 *eq*) in DMF (20 mL) was degassed and purged with N₂ 3 times.

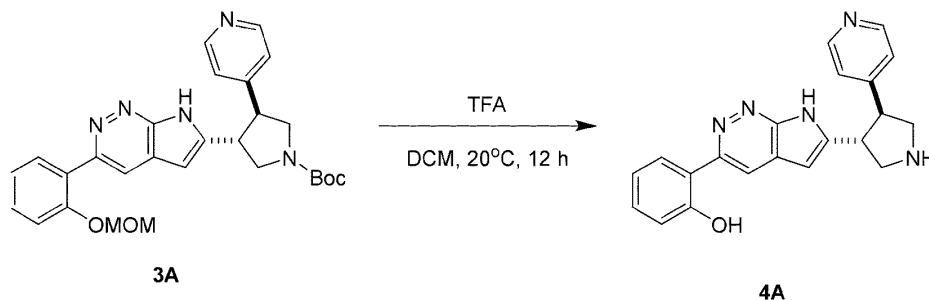
[0553] The mixture was then heated to 40 °C and stirred for 2 h under N₂ atmosphere. The mixture was poured into water (15 mL) and extracted with ethyl acetate (20 mL × 3). The combined organic phases were washed with brine (20 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by prep-HPLC (Column: Welch Xtimate C18 250*70mm*10um; Mobile phase: [H₂O (0.2%FA)-ACN]; gradient: 20%-50% B over 20.0 min.) to give *tert*-butyl *rel*-(3*R*,4*R*)-3-((3-amino-6-(2-(methoxymethoxy)phenyl)pyridazin-4-yl)ethynyl)-4-(pyridin-4-yl)pyrrolidine-1-carboxylate (500 mg, 996.86 μmol, 38.65% yield) as a yellow solid. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ 7.77 (d, *J* = 7.2 Hz, 1H), 7.70 - 7.62 (m, 1 H), 7.59 - 7.52 (m, 1 H), 7.51 - 7.43 (m, 1 H), 7.37 (t, *J* = 8.0 Hz, 1 H), 7.31 - 7.27 (m, 2 H), 7.21 (d, *J* = 8.4 Hz, 1 H), 7.13 (t, *J* = 7.2 Hz, 1 H), 5.43 - 5.28 (m, 1 H), 5.19 (s, 2 H), 4.07 - 3.82 (m, 2 H), 3.64 - 3.52 (m, 1 H), 3.42 (s, 5 H), 3.11 - 3.09 (m, 1 H), 1.51 - 1.49 (m, 9 H).

Step 8:

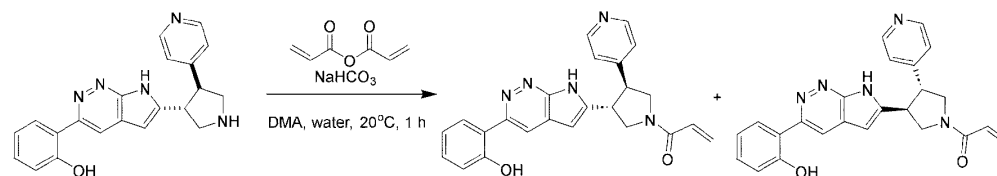


[0554] To a mixture of *rel*-*tert*-butyl (3*R*,4*R*)-3-((3-amino-6-(2-(methoxymethoxy)phenyl)pyridazin-4-yl)ethynyl)-4-(pyridin-4-yl)pyrrolidine-1-carboxylate (600 mg, 1.20 mmol, 1 *eq*) in THF (6 mL) was added TBAF (1M, 4.78 mL, 4 *eq*) under N₂ at 20 °C. The mixture was heated to 80 °C and stirred for 1 h. The mixture was poured into water (10 mL) and extracted with ethyl acetate (10 mL × 3). The combined organic phases were washed with brine (20 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by prep-HPLC (neutral condition) to give *rel*-*tert*-butyl (3*R*,4*S*)-3-(3-(2-(methoxymethoxy)phenyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-4-(pyridin-4-yl)pyrrolidine-1-carboxylate (80 mg, 159.50 μmol, 13.33% yield) as a yellow solid. ¹H NMR

(400 MHz, METHANOL- d_4) δ = 8.45 (d, J = 4.8 Hz, 2 H), 7.99 (s, 1 H), 7.60 (d, J = 7.6 Hz, 1 H), 7.44 - 7.36 (m, 3 H), 7.29 (d, J = 8.4 Hz, 1 H), 7.14 (t, J = 7.2 Hz, 1 H), 6.42 (s, 1 H), 5.17 (s, 2 H), 4.21 - 4.12 (m, 1 H), 4.09 - 4.02 (m, 1 H), 4.02 - 3.94 (m, 1 H), 3.87 (q, J = 9.6 Hz, 1 H), 3.75 - 3.70 (m, 1 H), 3.60 - 3.58 (m, 1 H), 3.34 - 3.32 (m, 3 H), 1.52 (s, 9 H).

Step 9:

[0555] To a mixture of *rel-tert*-butyl (3*R*,4*S*)-3-(3-(2-(methoxymethoxy)phenyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-4-(pyridin-4-yl)pyrrolidine-1-carboxylate (80 mg, 159.50 μ mol, 1 *eq*) in DCM (2 mL) was added TFA (1.54 g, 13.46 mmol, 1 mL, 84.40 *eq*) at 20 °C. The mixture was stirred at the same temperature for 12 h. The mixture was concentrated under reduced pressure to give *rel*-2-(6-((3*R*,4*S*)-4-(pyridin-4-yl)pyrrolidin-3-yl)-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)phenol (80 mg, 136.65 μ mol, 85.67% yield, 2·TFA salt) as a brown oil, which was used in the next step without purification. LCMS (ESI⁺): m/z 358.2 (M+H)⁺.

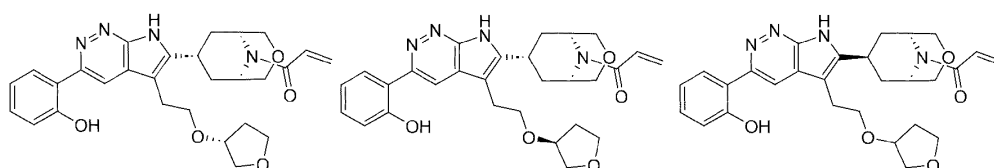
Step 10:

[0556] To a solution of crude *rel*-2-(6-((3*R*,4*S*)-4-(pyridin-4-yl)pyrrolidin-3-yl)-7*H*-pyrrolo[2,3-*c*]pyridazin-3-yl)phenol (20 mg, 42.42 μ mol, 1 *eq*, 2·TFA salt) in DMA (2 mL) was added NaHCO₃ (2.16 g, 25.70 mmol, 1 mL, 605.77 *eq*) and prop-2-enoyl prop-2-enoate (8.03 mg, 63.64 μ mol, 1.5 *eq*). The mixture was stirred at 20 °C for 1 hr. The mixture was poured into water (2 mL) and extracted with DCM (1 mL $\times$ 3). The combined organic phases were washed with brine (5 mL), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure to give a yellow solid, which was then purified by SFC to yield:

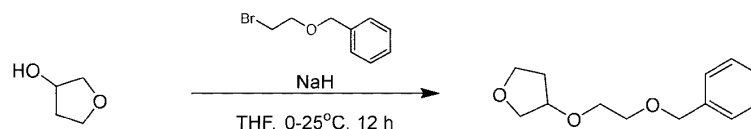
[0557] **609** (11.2 mg, 25.61 μ mol) as the first eluting isomer. ¹H NMR (400 MHz, DMSO- d_6) δ 13.92 (d, J = 5.2 Hz, 1H), 12.70 (s, 1H), 8.53 (d, J = 5.6 Hz, 1H), 8.49 (t, J = 6.0 Hz, 2H), 7.98 (d, J = 8.0 Hz, 1H), 7.47 - 7.37 (m, 2H), 7.28 (t, J = 7.6 Hz, 1H), 6.99 - 6.92 (m, 2H), 6.68 (dd, J = 10.4, 16.8 Hz, 1H), 6.50 (d, J = 14.8 Hz, 1H), 6.23 (td, J = 2.4, 16.8 Hz, 1H), 5.75 - 5.73 (m, 1H), 4.34 - 4.32 (m, 2H), 4.31 - 4.29 (m, 1H), 4.23 - 4.21 (m, 1H), 4.13 - 3.70 (m, 1H), 3.73 - 3.63 (m, 1H). LCMS (ESI⁺): m/z 412.1 (M+H)⁺.

[0558] **608** (10.9 mg, 25.62 μ mol) as the second eluting isomer. ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 13.96 (s, 1H), 12.67 (s, 1H), 8.55 - 8.46 (m, 3H), 7.96 (d, J = 8.0 Hz, 1H), 7.42 (dd, J = 6.0, 13.2 Hz, 2H), 7.28 (t, J = 7.6 Hz, 1H), 6.99 - 6.88 (m, 2H), 6.68 (dd, J = 10.4, 16.8 Hz, 1H), 6.49 (d, J = 13.6 Hz, 1H), 6.28 - 6.18 (m, 1H), 5.77 - 5.75 (m, 1H), 4.34 - 4.32 (m, 2H), 4.31 - 4.30 (m, 1H), 4.13 - 4.12 (m, 1H), 3.99 - 3.96 (m, 1H), 3.93 - 3.79 (m, 1H), 3.56 (t, J = 11.2 Hz, 1H). LCMS (ESI $^+$): m/z 412.1 ($\text{M}+\text{H}$) $^+$.

Example 28: 1-((1*R*,5*S*,7*r*)-7-(3-(2-hydroxyphenyl)-5-(2-(((*R*)-tetrahydrofuran-3-yl)oxy)ethyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one, 1-((1*R*,5*S*,7*r*)-7-(3-(2-hydroxyphenyl)-5-(2-(((*S*)-tetrahydrofuran-3-yl)oxy)ethyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one and 1-((1*R*,5*S*,7*s*)-7-(3-(2-hydroxyphenyl)-5-(2-(((tetrahydrofuran-3-yl)oxy)ethyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one (Compounds 620, 621, and 622)

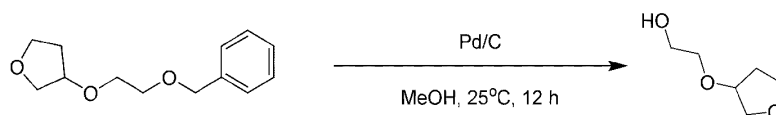


Step 1:



[0559] To a stirred solution of NaH (907.92 mg, 22.70 mmol, 60% purity, 2 *eq*) in tetrahydrofuran (100 mL) was added tetrahydrofuran-3-ol (2 g, 22.70 mmol, 1.83 mL, 2 *eq*) portionwise at 0 $^{\circ}\text{C}$ under N_2 . The resulting mixture was stirred at the same temperature for 20 min, then 2-bromoethoxymethylbenzene (2.93 g, 13.62 mmol, 2.15 mL, 1.2 *eq*) was added dropwise after warming the mixture to 15 $^{\circ}\text{C}$. The reaction mixture was then warmed up to 25 $^{\circ}\text{C}$ and stirred for 12 h. The mixture was quenched with 100 mL saturated ammonium chloride under N_2 at 0 $^{\circ}\text{C}$. The mixture was then extracted with ethyl acetate (100 mL $\times$ 3), and the combined organic layers were washed with brine. The dried organic layer was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO_2 , petroleum ether/ethyl acetate=1/0 to 0/1) to afford 3-(2-(benzyloxy)ethoxy)tetrahydrofuran (1 g, 4.50 mmol, 39.64% yield) as a colorless oil. ^1H NMR (400 MHz, $\text{CHLOROFORM-}d$) δ 1.89 - 2.01 (m, 2H), 3.49 - 3.59 (m, 4H), 3.70 - 3.79 (m, 3H), 3.84 (q, J =8.00 Hz, 1H), 4.05 - 4.15 (m, 1H), 4.50 (s, 2H), 7.19 - 7.24 (m, 1H), 7.25 - 7.33 (m, 4H).

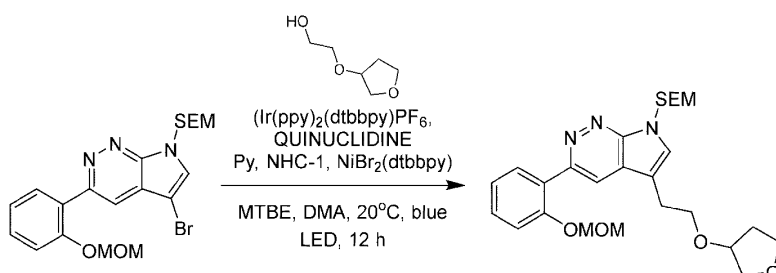
Step 2:



[0560] To a solution of 3-(2-(benzyloxy)ethoxy)tetrahydrofuran (1.4 g, 6.30 mmol, 1 *eq*) in methanol (140 mL) was added Pd/C (1.34 g, 1.26 mmol) under N_2 atmosphere. The suspension was degassed and

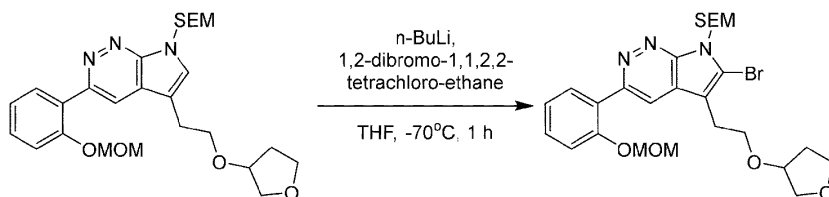
purged with H₂ 3 times. The mixture was stirred under H₂ (50 Psi) at 25 °C for 12 h. The mixture was then filtered, and the filtrate was concentrated under reduced pressure. The residue was purified by prep-TLC to yield 2-((tetrahydrofuran-3-yl)oxy)ethan-1-ol (700 mg, 5.30 mmol, 84.10% yield) as a colorless oil. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ 1.99 (ddd, *J*=7.54, 6.72, 4.25 Hz, 2H), 3.44 - 3.56 (m, 2H), 3.65 - 3.94 (m, 6H), 4.10 - 4.18 (m, 1H).

Step 3:



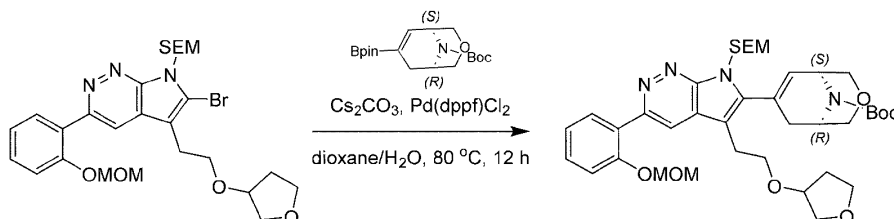
[0561] To a solution of 2-((tetrahydrofuran-3-yl)oxy)ethan-1-ol (113.82 mg, 861.28 μmol, 2 *eq*) in methyl *tert*-butyl ether (4 mL) was added 5,7-di-*tert*-butyl-3-phenylbenzo[d]oxazol-3-ium tetrafluoroborate (306.37 mg, 775.15 μmol, 1.8 *eq*). The solution was stirred at 20 °C for 5 min before pyridine (61.31 mg, 775.15 μmol, 62.57 μL, 1.8 *eq*) was added. The resulting mixture was then stirred at the same temperature for an additional 30 min and filtered to remove the white precipitate. To a solution of 5-bromo-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazine (200 mg, 430.64 μmol, 1 *eq*), quinuclidine (95.76 mg, 861.28 μmol, 2 *eq*), [4,4'-bis(*tert*-butyl)-2,2'-bipyridine]nickel dibromide (20.97 mg, 43.06 μmol, 0.1 *eq*), and (4,4'-di-*tert*-butyl-2,2'-bipyridine)bis[(2-pyridinyl)phenyl]iridium(III) hexafluorophosphate (19.68 mg, 21.53 μmol, 0.05 *eq*) in DMA (4 mL) was added the filtrate obtained. The mixture was stirred at 25 °C for 12 h under argon and blue LEDs. Five additional reactions were set up as described above. All six reaction mixtures were combined, diluted with H₂O (50 mL), and extracted with ethyl acetate 120 mL (40 mL × 3). The combined organic layers were washed with brine 50 mL (25 mL × 2), dried over Na₂SO₄, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO₂, petroleum ether/ethyl acetate=2/1 to 1/1) to yield 3-(2-(methoxymethoxy)phenyl)-5-(2-((tetrahydrofuran-3-yl)oxy)ethyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazine (220 mg, 440.29 μmol, 17.04% yield) as a yellow oil. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ -0.05 (s, 8H), 0.89 - 1.00 (m, 2H), 1.94 - 2.00 (m, 2H), 2.97 - 3.07 (m, 2H), 3.42 (s, 3H), 3.59 - 3.92 (m, 9H), 4.06 - 4.14 (m, 1H), 5.21 (s, 2H), 5.85 (s, 2H), 7.19 (t, *J*=7.50 Hz, 1H), 7.35 - 7.44 (m, 1H), 7.48 (br s, 1H), 7.89 (dd, *J*=7.63, 1.50 Hz, 1H), 8.13 (s, 1H).

Step 4:



[0562] To a solution of 3-(2-(methoxymethoxy)phenyl)-5-(2-((tetrahydrofuran-3-yl)oxy)ethyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazine (220 mg, 440.29 μmol , 1 *eq*) in tetrahydrofuran (2.2 mL) was added *n*-BuLi (1.6M, 412.77 μL , 1.5 *eq*) dropwise at -78°C under N_2 . The mixture was stirred at the same temperature for 10 min, after which a solution of 1,2-dibromo-1,1,2,2-tetrachloro-ethane (430.13 mg, 1.32 mmol, 158.54 μL , 3 *eq*) in tetrahydrofuran (0.5 mL) was added to the mixture at -78°C . The mixture was stirred at this same temperature for 1.5 h under N_2 . The reaction mixture was quenched by addition of saturated ammonium chloride (1 mL) at 0°C , then diluted with H_2O (1 mL) and extracted with ethyl acetate (1 mL $\times$ 3). The organic phase was separated, washed with brine (1 mL), dried over Na_2SO_4 , and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by prep-TLC. 6-bromo-3-(2-(methoxymethoxy)phenyl)-5-(2-((tetrahydrofuran-3-yl)oxy)ethyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazine (150 mg, 259.26 μmol , 58.88% yield) was obtained as a yellow oil. ^1H NMR (400 MHz, $\text{CHLOROFORM-}d$) δ -0.05 (s, 9H), 0.95 (t, $J=8.07$ Hz, 2 H), 1.85 - 2.01 (m, 2H), 3.05 (t, $J=6.82$ Hz, 2H), 3.41 (s, 3H), 3.63 (td, $J=6.69$, 4.63 Hz, 2 H), 3.68 - 3.84 (m, 6H), 4.04 - 4.12 (m, 1H), 5.21 (s, 2H), 5.94 (s, 2H), 7.19 (t, $J=7.50$ Hz, 1H), 7.28 (s, 1H), 7.36 - 7.45 (m, 1H), 7.87 (d, $J=7.63$ Hz, 1H), 8.10 (s, 1H).

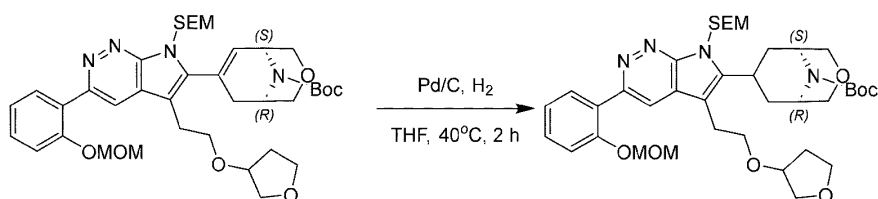
Step 5:



[0563] A mixture of 6-bromo-3-(2-(methoxymethoxy)phenyl)-5-(2-((tetrahydrofuran-3-yl)oxy)ethyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7H-pyrrolo[2,3-c]pyridazine (150 mg, 259.26 μmol , 1 *eq*), *tert*-butyl 7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-oxa-9-azabicyclo[3.3.1]non-6-ene-9-carboxylate (109.28 mg, 311.11 μmol , 1.2 *eq*), and Cs_2CO_3 (253.42 mg, 777.78 μmol , 3 *eq*) in dioxane (2 mL) and H_2O (0.4 mL) was degassed and purged 3 times with N_2 . Pd(dppf)Cl_2 (18.97 mg, 25.93 μmol , 0.1 *eq*) was then added and the mixture heated to 80°C and stirred for 16 h under N_2 atmosphere. The reaction mixture was diluted with H_2O (2 mL) and extracted with ethyl acetate (2 mL $\times$ 2). The combined organic layers were washed with brine (2 mL), dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The residue was purified by prep-TLC (SiO_2 , petroleum ether: ethyl acetate = 1:1). *Tert*-butyl (1*R*,5*S*)-7-(3-(2-(methoxymethoxy)phenyl)-5-(2-((tetrahydrofuran-3-yl)oxy)ethyl)-7-((2-

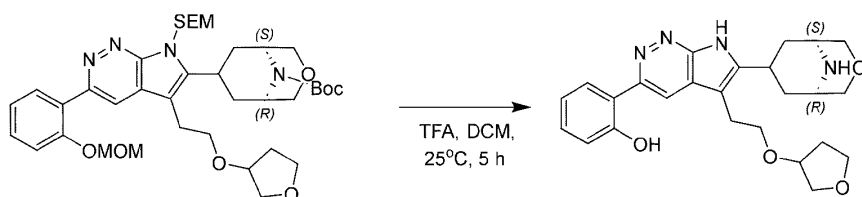
(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]non-6-ene-9-carboxylate (180 mg, 248.98 μ mol, 96.04% yield) was obtained as a yellow oil. ^1H NMR (400 MHz, CHLOROFORM-*d*) δ -0.03 (s, 9H), 0.93 (dd, $J=9.47$, 7.09 Hz, 2H), 1.53 (s, 9H), 1.82 - 1.95 (m, 2H), 2.52 - 2.63 (m, 1H), 2.87 - 3.02 (m, 3H), 3.42 (s, 3H), 3.55 - 3.64 (m, 2H), 3.68 - 3.88 (m, 9H), 3.89 - 3.99 (m, 1H), 4.01 - 4.08 (m, 1H), 4.18 - 4.37 (m, 1H), 4.55 - 4.76 (m, 1H), 5.20 (br s, 2H), 5.71 - 5.84 (m, 2H), 6.07 (br s, 1H), 7.19 (t, $J=7.28$ Hz, 1H), 7.28 (br d, $J=1.13$ Hz, 1H), 7.36 - 7.44 (m, 1H), 7.87 (br d, $J=6.65$ Hz, 1H), 8.09 (br d, $J=1.13$ Hz, 1H).

Step 6:



[0564] To a solution of *tert*-butyl (1*R*,5*S*)-7-(3-(2-(methoxymethoxy)phenyl)-5-(2-((tetrahydrofuran-3-yl)oxy)ethyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]non-6-ene-9-carboxylate (210 mg, 290.48 μ mol, 1 *eq*) in tetrahydrofuran (84 mL) was added Pd/C (309.13 mg, 290.48 μ mol) under N_2 atmosphere. The suspension was degassed and purged 3 times with H_2 . The mixture was heated to 40°C and stirred under H_2 (15 Psi) for 2 h. The reaction mixture was then filtered and concentrated under reduced pressure. The obtained residue was purified by prep-TLC (SiO_2 , petroleum ether/ethyl acetate = 2:1). *Tert*-butyl (1*R*,5*S*)-7-(3-(2-(methoxymethoxy)phenyl)-5-(2-((tetrahydrofuran-3-yl)oxy)ethyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (130 mg, 179.32 μ mol, 61.73% yield) was obtained as a yellow solid. ^1H NMR (400 MHz, CHLOROFORM-*d*) δ -0.14 - 0.07 (m, 9H), 0.84 - 1.00 (m, 2H), 1.56 (s, 8H), 1.81 - 2.01 (m, 3H), 2.12 - 2.47 (m, 4H), 3.03 - 3.22 (m, 2H), 3.38 - 3.48 (m, 3H), 3.59 - 3.81 (m, 11H), 3.85 - 3.91 (m, 1H), 3.96 - 4.10 (m, 2H), 4.18 - 4.29 (m, 1H), 4.37 (br d, $J=7.50$ Hz, 1H), 5.22 (br s, 2H), 5.81 - 6.13 (m, 2H), 7.14 - 7.23 (m, 1H), 7.29 - 7.36 (m, 1H), 7.38 - 7.50 (m, 1H), 7.85 (br d, $J=1.63$ Hz, 1H), 7.95 - 8.20 (m, 1H).

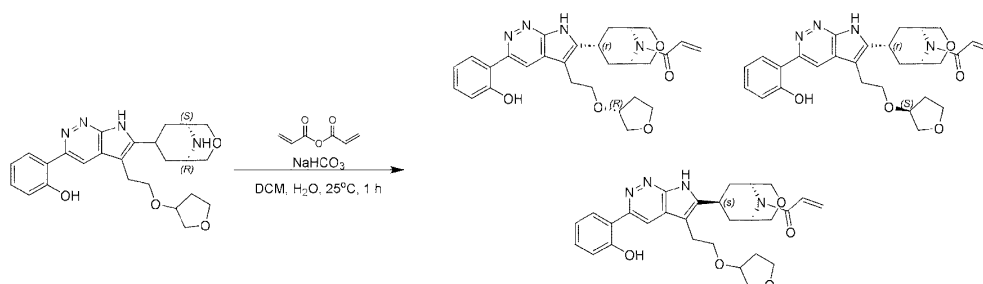
Step 7:



[0565] A solution of *tert*-butyl (1*R*,5*S*)-7-(3-(2-(methoxymethoxy)phenyl)-5-(2-((tetrahydrofuran-3-yl)oxy)ethyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (130 mg, 179.32 μ mol, 1 *eq*) in trifluoroacetic acid (0.65 mL) and dichloromethane (0.65 mL) was stirred at 25 °C for 5 h. The reaction mixture was concentrated under reduced pressure to give 2-(6-((1*R*,5*S*)-3-oxa-9-azabicyclo[3.3.1]nonan-7-yl)-5-(2-((tetrahydrofuran-3-

yl)oxy)ethyl]-7H-pyrrolo[2,3-c]pyridazin-3-yl)phenol, which was used in the next step without purification. LCMS: (ESI⁺): m/z 451.4 (M+H)⁺.

Step 8:



[0566] To a solution of crude 2-(6-((1R,5S)-3-oxa-9-azabicyclo[3.3.1]nonan-7-yl)-5-(2-((tetrahydrofuran-3-yl)oxy)ethyl)-7H-pyrrolo[2,3-c]pyridazin-3-yl)phenol (130 mg, 191.58 μmol , 1 *eq*, 2·TFA salt) in dichloromethane (1.3 mL) was added saturated sodium bicarbonate (1.3 mL) and a solution of prop-2-enyl prop-2-enoate (19.33 mg, 153.26 μmol , 0.8 *eq*) in dichloromethane (0.1 mL). The mixture was stirred at 25 °C for 1 h. The reaction mixture was partitioned between H₂O (2 mL) and ethyl acetate (2 mL). The organic phase was separated, washed with brine (1 mL), dried over Na₂SO₄, filtered and concentrated under reduced pressure. The obtained residue was first purified by prep-HPLC (neutral condition, column: Waters Xbridge Prep OBD C18 150*40mm*10 μm ; mobile phase: [H₂O(10mM NH₄HCO₃)-ACN]; gradient: 25%-55% B over 8.0 min) to give a yellow solid, which was further purified by SFC (column: REGIS(S,S)WHELK-O1(250mm*25mm,10 μm); mobile phase: [CO₂-EtOH(0.1% NH₃H₂O)]; B%: 50%, isocratic elution mode) to yield:

[0567] - a mixture of **621** and **622** (peak 1)

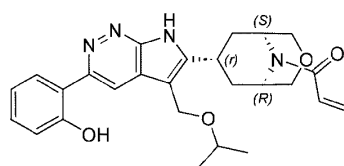
[0568] **620** (peak 2) (2 mg, 3.63 μmol , 1.90% yield). ¹H NMR (400 MHz, CHLOROFORM-*d*) δ 1.87 - 2.00 (m, 2H), 2.08 - 2.21 (m, 2H), 2.42 (br dd, *J*=13.26, 3.88 Hz, 1H), 2.59 - 2.74 (m, 1H), 3.11 (br t, *J*=6.00 Hz, 2H), 3.65 - 3.94 (m, 8H), 4.04 - 4.22 (m, 3H), 4.46 (br s, 1H), 4.71 - 4.83 (m, 2H), 5.23 (br d, *J*=9.38 Hz, 1H), 6.16 (br d, *J*=16.63 Hz, 1H), 6.58 (dd, *J*=16.70, 10.44 Hz, 1H), 6.97 - 7.05 (m, 1H), 7.12 (d, *J*=8.13 Hz, 1H), 7.31 - 7.40 (m, 1H), 7.88 (d, *J*=7.00 Hz, 1H), 8.29 (s, 1H), 12.00 (br d, *J*=5.63 Hz, 1H). (ESI⁺): m/z 505 (M+H)⁺

[0569] The mixture of **621** and **622** was further separated by SFC (column: Agilent Poroshell SB-C18 150*21.2*2.7; mobile phase: [Heptane-EtOH:ACN=4:1 (0.1% NH₃H₂O)]; B%: 20%, isocratic elution mode) to give:

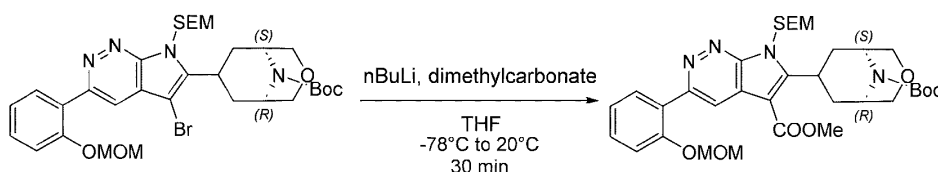
[0570] **622** (4 mg, 7.84 μmol , 4.09% yield) as a first eluting isomer. ¹H NMR (400 MHz, CHLOROFORM-*d*) δ 1.21 - 1.35 (m, 1H), 1.79 - 1.98 (m, 2H), 2.03 - 2.14 (m, 1H), 2.15 - 2.29 (m, 1H), 2.43 - 2.59 (m, 2H), 2.99 (br s, 2H), 3.09 - 3.24 (m, 1H), 3.53 - 3.66 (m, 2H), 3.68 - 3.92 (m, 8H), 4.00 - 4.11 (m, 1H), 4.30 (br d, *J*=9.76 Hz, 1H), 4.94 (br d, *J*=9.63 Hz, 1H), 5.85 (dd, *J*=10.44, 1.81 Hz, 1H), 6.41 - 6.51 (m, 1H), 6.65 (dd, *J*=16.76, 10.51 Hz, 1H), 6.96 - 7.02 (m, 1H), 7.17 (br d, *J*=7.50 Hz, 1H), 7.31 - 7.38 (m, 1H), 7.84 (d, *J*=7.00 Hz, 1H), 8.24 (s, 1H), 10.09 - 10.75 (m, 1H). (ESI⁺): m/z 505 (M+H)⁺,

[0571] **621** (4.5 mg, 8.89 μ mol, 4.64% yield) as a second eluting isomer. ^1H NMR (400 MHz, CHCl_3) δ 1.28 (br d, $J=10.76$ Hz, 1H), 1.80 - 1.98 (m, 2H), 2.03 - 2.13 (m, 1H), 2.14 - 2.28 (m, 1H), 2.51 (br dd, $J=11.38, 7.13$ Hz, 2H), 2.92 - 3.05 (m, 2H), 3.16 (td, $J=10.88, 5.00$ Hz, 1H), 3.53 - 3.65 (m, 2H), 3.69 - 3.90 (m, 8H), 4.02 - 4.10 (m, 1H), 4.31 (br d, $J=9.51$ Hz, 1H), 4.95 (br d, $J=10.26$ Hz, 1H), 5.85 (dd, $J=10.44, 1.81$ Hz, 1H), 6.42 - 6.51 (m, 1H), 6.66 (dd, $J=16.76, 10.51$ Hz, 1H), 6.94 - 7.05 (m, 1H), 7.14 (d, $J=8.13$ Hz, 1H), 7.30 - 7.39 (m, 1H), 7.85 (d, $J=7.13$ Hz, 1H), 8.24 (s, 1H), 10.36 - 10.62 (m, 1H). (ESI $^-$): m/z 505 ($\text{M}+\text{H}$) $^+$.

Example 29: Synthesis of 1-((1*R*,5*S*,7*r*)-7-(3-(2-hydroxyphenyl)-5-(isopropoxymethyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one (Compound 645)

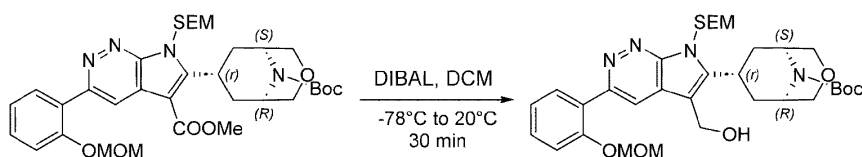


Step 1:



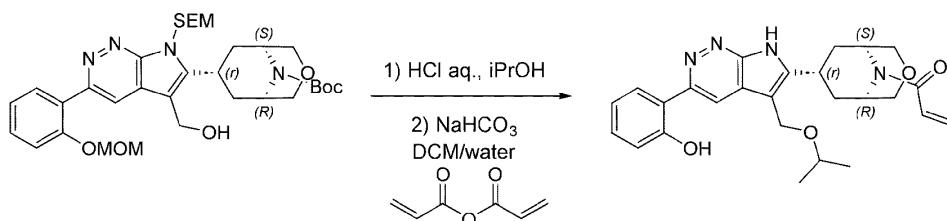
[0572] To a solution of *tert*-butyl (1*R*,5*S*,7*r*)-7-(5-bromo-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (250 mg, 362 μ mol) in THF (5 mL) was added a solution of *n*-BuLi in hexane (1.6M, 725 μ mol) at -78 $^{\circ}\text{C}$. After 5 min, dimethyl carbonate (327 mg, 3.62 mmol) in THF (1 mL) was added. After stirring at the same temperature for an additional 20 min, the reaction mixture was allowed up to room temperature, then stir for 30 min. The reaction mixture was quenched with 10% aqueous citric acid, then extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with heptane/etOAc = 100:0 - 70:30 to afford *tert*-butyl (1*R*,5*S*,7*r*)-7-(5-(methoxycarbonyl)-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (260 mg). LC/MS m/z [$\text{M}+\text{H}$] $^+$: 669. ^1H NMR (499 MHz, $\text{DMSO}-d_6$) δ 8.44 (s, 1H), 7.72 (dd, $J = 7.7, 1.8$ Hz, 1H), 7.47 - 7.42 (m, 1H), 7.27 (m, 1H), 7.16 (m, 1H), 6.01 (s, 2H), 5.25 (s, 2H), 4.05 - 3.90 (m, 5H), 3.82 (s, 3H), 3.70 (d, $J = 11.2$ Hz, 2H), 3.66 - 3.57 (m, 2H), 3.36 (s, 3H), 2.71 (d, $J = 12.9$ Hz, 2H), 1.92 - 1.80 (m, 2H), 1.50 (s, 9H), -0.07 (s, 9H).

Step 2:



[0573] To a solution of *tert*-butyl (1*R*,5*S*,7*r*)-7-(5-(methoxycarbonyl)-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (100 mg, 150 μ mol) in DCM (5 mL) was added a solution of DIBAL in hexane (755 μ mol) at -78 °C. The reaction mixture was stirred at the same temperature for 30 min, then warmed up to room temperature and allowed to stir for 30 min. The reaction mixture was quenched with 10% aqueous citric acid, then extracted with EtOAc. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with heptane/EtOAc = 100:0 - 50:50 to afford *tert*-butyl (1*R*,5*S*,7*r*)-7-(5-(hydroxymethyl)-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate as an off-white foam (32 mg, yield 36%). LC/MS *m/z* [M+H]⁺: 598.

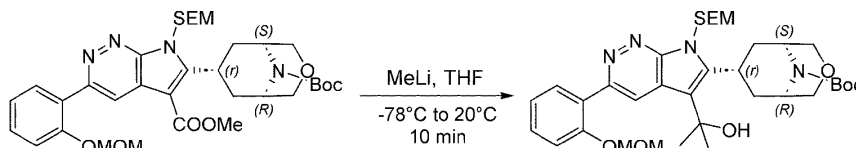
Step 3:



[0574] To a solution of *tert*-butyl (1*R*,5*S*,7*r*)-7-(5-(hydroxymethyl)-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (31 mg, 48 μ mol) in iPrOH (1 mL) was added a solution of 12N HCl (0.5 mL), then the reaction mixture was heated to 80 °C and stirred for 3 h. The reaction mixture was then concentrated under reduced pressure. To a solution of this residue in DCM (3 mL) and sat. aqueous NaHCO₃ (3 mL) was added acryloyl acrylate (30 mg, 240 μ mol). After 40 min, the organic layer was separated, and 7N NH₃ in MeOH solution (0.5 mL) was added. The mixture was then stirred at room temperature for 10 min. The reaction mixture was washed with brine, and the organic layer was dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was purified by preparative HPLC (column: 00F-4252-P0-AX Luna 5 mm C18 100Å 150*21.2 mm; water/CH₃CN with 0.1% FA = 90:10 - 50:50 to afford **645** (2 mg, 9% yield). LC/MS *m/z* [M+H]⁺: 463. ¹H NMR (499 MHz, DMSO-*d*₆) δ 14.15 (s, 1H), 12.58 (s, 1H), 8.59 (s, 1H), 8.07 (s, 1H), 7.28 (s, 1H), 6.96 (s, 1H), 6.98 – 6.93 (m, 2H), 6.25 (dd, *J* = 16.8, 2.5 Hz, 1H), 5.77 (dd, *J* = 10.4, 2.5 Hz, 1H), 4.69 (s, 2H), 4.56 (m, 2H), 4.31 (s, 1H), 4.04 – 3.96 (m, 2H), 3.76 – 3.66 (m, 3H), 2.31 – 2.15 (m, 2H), 2.08 – 2.00 (m, 2H), 1.17 (d, *J* = 6.0 Hz, 6H).

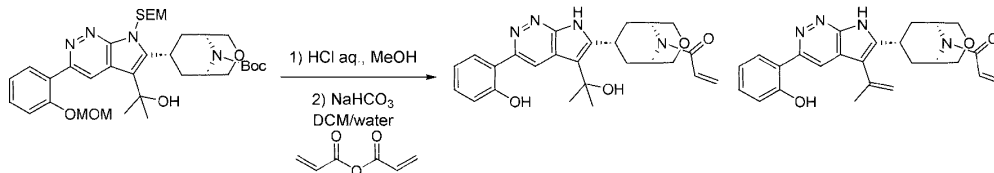
Example 30: Synthesis of 1-((1*R*,5*S*,7*r*)-7-(3-(2-hydroxyphenyl)-5-(2-hydroxypropan-2-yl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one (Compound 633) and 1-((1*R*,5*S*,7*r*)-7-(3-(2-hydroxyphenyl)-5-(prop-1-en-2-yl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonan-9-yl)prop-2-en-1-one (Compound 632)

Step 1:



[0575] To a solution of *tert*-butyl 1*R*,5*S*,7*r*)-7-(5-(methoxycarbonyl)-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (20 mg, 30 mmol) in THF (1.5 mL) was added a solution of MeLi in hexane (150 mmol) at -78 °C. The reaction mixture was stirred at the same temperature for 30 min, then warmed up to rt and stirred for 10 min. The reaction mixture was then quenched with water and extracted with EtOAc. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was purified by prep-TLC with heptane/etOAc = 1:1 to afford *tert*-butyl 1*R*,5*S*,7*r*)-7-(5-(2-hydroxypropan-2-yl)-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate as a colorless oil (11 mg, yield 55%). LC/MS *m/z* [M+H]⁺: 669.

Step 2:



[0576] To a solution of *tert*-butyl 1*R*,5*S*,7*r*)-7-(5-(2-hydroxypropan-2-yl)-3-(2-(methoxymethoxy)phenyl)-7-((2-(trimethylsilyl)ethoxy)methyl)-7*H*-pyrrolo[2,3-*c*]pyridazin-6-yl)-3-oxa-9-azabicyclo[3.3.1]nonane-9-carboxylate (11 mg, 16 mmol) in MeOH (1 mL) was added an aqueous 12*N* HCl solution (0.5 mL), then the reaction mixture was stirred at reflux. After 2.5 h, the reaction mixture was concentrated under reduced pressure. To this residue in a solution of DCM (3 mL) and sat. NaHCO₃ aqueous solution (3 mL) was added acryloyl acrylate (30 mg, 240 mmol). After 40 min, the organic layer was separated, and 7*N* NH₃ in MeOH solution (0.5 mL) was added. The resulting mixture was stirred at room temperature for 10 min. The reaction mixture was then washed with brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was purified by preparative HPLC (column: 00F-4252-P0-AX Luna 5 mm C18 100Å 150*21.2 mm; water/CH₃CN with 0.1% FA = 90:10 – 50:50 to afford:

[0577] **633** (1 mg, yield 14%). LC/MS *m/z* [M+H]⁺: 449.

[0578] **632** (2 mg, yield 28%). LC/MS m/z $[M+H]^+$: 431. 1H NMR (499 MHz, DMSO) δ 13.97 (s, 1H), 12.65 (s, 1H), 8.42 (s, 1H), 8.11 (d, $J = 8.1$ Hz, 1H), 7.32 – 7.25 (m, 1H), 6.99 – 6.91 (m, 2H), 6.85 (dd, $J = 16.7, 10.5$ Hz, 1H), 6.26 (dd, $J = 16.7, 2.6$ Hz, 1H), 5.81 – 5.74 (m, 2H), 5.39 (s, 1H), 5.11 (s, 1H), 4.72 – 4.63 (m, 1H), 4.56 (s, 1H), 4.30 (s, 1H), 4.00 (dd, $J = 11.5, 6.6$ Hz, 2H), 3.69 (dd, $J = 18.0, 11.4$ Hz, 2H), 2.29 – 2.18 (m, 2H), 2.25 (s, 3H), 2.08 – 2.00 (m, 2H).

[0579] Additional conditions used for chiral separation of the compounds in Table 1 are provided below in Table 3A:

Table 3A

Condition	Column	Mobile phase
A	DAICEL CHIRALCEL OJ 250mm×30mm, 10 μ m	[CO ₂ -MeOH (0.1%NH ₃ H ₂ O)]; B%: 45%, isocratic elution mode
B	DAICEL CHIRALCEL OJ 250mm×30mm, 10 μ m	[CO ₂ -MeOH]; B%: 46%, isocratic elution mode
C	DAICEL CHIRALPAK IH 250mm×50mm I.D. 10 μ m	[CO ₂ -IPA(0.1%NH ₃ H ₂ O)]; B%: 30%, isocratic elution mode
D	Chiralpak ID -3, 50×4.6mm, 3 μ m	CO ₂ B: IPA[0.2%NH ₃ (7M in MeOH)]
E	DAICEL CHIRALCEL OJ (250mm×30mm, 10 μ m);	[CO ₂ -MeOH]; B%:50%, isocratic elution mode
F	REGIS (s,s) WHELK- O1 (250mm×30mm, 5 μ m);	CO ₂ -MeOH(0.1%NH ₃ H ₂ O); B%: 50%, isocratic elution mode.
G	DAICEL CHIRALCEL OZ 250×25 mm, 10 μ m	[CO ₂ -EtOH: ACN=1:1 (0.1% NH ₃ H ₂ O)]; B%:65%, isocratic elution mode
H	CHIRALPAK IH 250mm×30mm, 10 μ m	[CO ₂ -EtOH (0.1%NH ₃ ·H ₂ O)]; B%: 40%, isocratic elution mode.
I	ChiralPak IH , 250*30mm, 10 μ m	[CO ₂ -IPA];B%:50%, isocratic elution mode
J	ChiralPak IH , 250*30mm, 10 μ m	[CO ₂ -EtOH(0.1%NH ₃ H ₂ O)]; B%:45%, isocratic elution mode
K	DAICEL CHIRALCEL OJ (250mm*30mm,10 μ m)	[CO ₂ -MeOH(0.1%NH ₃ H ₂ O)]; B%:55%, isocratic elution mode
L	REGIS(S,S)WHELK- O1 (250mm*25mm,10 μ m)	[CO ₂ -MeOH(0.1%NH ₃ H ₂ O)]; B%:50%, isocratic elution mode

Condition	Column	Mobile phase
M	DAICEL CHIRALCEL OJ (250mm*30mm,10um)	[CO ₂ -MeOH(0.1%NH ₃ H ₂ O)]; gradient:50%-5% B over 10.0 min
N	DAICEL CHIRALPAK AD-H (250mm*30mm,5um)	[Heptane-EtOH];B%:60%, isocratic elution mode
O	DAICEL CHIRALPAK IG (250mm*30mm,10um)	[CO ₂ -IPA];B%:50%, isocratic elution mode
P	ChiralPak IH , 250*30mm, 10um	[CO ₂ -MeOH(0.1%NH ₃ H ₂ O)]; B%:35%, isocratic elution mode
Q	DAICEL CHIRALCEL OJ (250mm*30mm,10um)	[CO ₂ -MeOH(0.1%NH ₃ H ₂ O)]; B%:53%, isocratic elution mode
R	DAICEL CHIRALCEL OJ (250mm*30mm,10um)	[CO ₂ -MeOH];B%:40%, isocratic elution mode
S	DAICEL CHIRALCEL OD (250mm*30mm,10um)	[CO ₂ -EtOH(0.1%NH ₃ H ₂ O)]; B%:45%, isocratic elution mode
T	CHIRALPAK AD (250mm*50mm,10um)	[CO ₂ -IPA(0.1% NH ₃ H ₂ O)]; B%:20%, isocratic elution mode
U	ChiralPak IH , 250*30mm, 10um	[CO ₂ -EtOH:ACN=1:1 (0.1% NH ₃ H ₂ O)]; B%:42%, isocratic elution mode
V	DAICEL CHIRALPAK IK (250mm*25mm,10um)	[CO ₂ -EtOH];B%:57%, isocratic elution mode
W	REGIS (s,s) WHELK- O1 (250mm*30mm,5um)	[CO ₂ -EtOH];B%:50%, isocratic elution mode
X	REGIS (s,s) WHELK- O1 (250mm*30mm,5um)	[CO ₂ -EtOH(0.1% NH ₃ H ₂ O)]; B%:50%, isocratic elution mode
Y	DAICEL CHIRALCEL OJ (250mm*30mm,10um)	[CO ₂ -MeOH(0.1%NH ₃ H ₂ O)]; B%:40%, isocratic elution mode
Z	DAICEL CHIRALCEL OJ (250mm*30mm,10um)	[CO ₂ -MeOH(0.1%NH ₃ H ₂ O)]; B%:35%, isocratic elution mode
A1	ChiralPak IH , 250*30mm, 10um;mobile	[CO ₂ -MeOH]; B%:35%, isocratic elution mode

Condition	Column	Mobile phase
A2	ChiralPak IH , 250*30mm, 10um	[CO ₂ -MeOH(0.1%NH ₃ H ₂ O)];B%:50%, isocratic elution mode
A3	DAICEL CHIRALCEL OD (250mm*30mm,10um)	[CO ₂ -EtOH:ACN=1:1];B%:38%, isocratic elution mode
A4	DAICEL CHIRALPAK AD (250 mm × 30 mm, 10 um)	[CO ₂ -EtOH]; B%:50%, isocratic elution mode
A5	DAICEL CHIRALPAK AD (250mm × 30 mm, 10um)	[CO ₂ -EtOH (0.1%NH ₃ H ₂ O)]; B%:35%, isocratic elution mode
A6	DAICEL CHIRALPAK IK (250 mm ×25mm, 10 um)	[CO ₂ -EtOH: ACN=1:1]; B%: 60%, isocratic elution mode
A7	DAICEL CHIRALPAK AD (250mm*30mm,10um)	[CO ₂ -MeOH(0.1%NH ₃ H ₂ O)];B%:40%, isocratic elution mode
A8	DAICEL CHIRALCEL OJ 250mm*30mm I.D. 10um	[CO ₂ -MeOH (0.1%NH ₃ H ₂ O)]; B%: 50%, isocratic elution mode
A9	DAICEL CHIRALPAK IG (250mm*50mm,10um)	[CO ₂ -IPA(0.1% NH ₃ H ₂ O)];B%:60%, isocratic elution mode
A10	DAICEL CHIRALCEL OZ 250 × 25 mm I.D. 10 um	[CO ₂ -EtOH (0.1% NH ₃ H ₂ O)]; B%: 60%, isocratic elution mode
A11	DAICEL CHIRALPAK AD (250mm*30mm,10um)	[CO ₂ -IPA (0.1%NH ₃ H ₂ O)]; B%:50%, isocratic elution mode
A12	DAICEL CHIRALCEL OJ 250mm*30mm I.D. 10um	CO ₂ -IPA (0.1%NH ₃ H ₂ O); B%: 50%, isocratic elution mode
A13	REGIS DAICEL CHIRALCEL OZ 250*25 mm I.D. 10um	[CO ₂ -EtOH:ACN=1:1 (0.1% NH ₃ H ₂ O)];B%:60%, isocratic elution mode
A14	DAICEL CHIRALCEL OJ (250mm*30mm,10um)	[CO ₂ -EtOH(0.1%NH ₃ H ₂ O)];B%:50%, isocratic elution mode
A15	DAICEL CHIRALPAK IG (250 mm×30 mm,10 um)	[CO ₂ -IPA (0.1%NH ₃ H ₂ O)]; B%: 50%, isocratic elution mode
A16	ChiralPak IH , 250*30mm, 10um	CO ₂ -EtOH(0.1% NH ₃ H ₂ O)];B%:50%, isocratic elution mode

Condition	Column	Mobile phase
A17	DAICEL CHIRALPAK IF (250mm*30mm,10um)	[CO ₂ -EtOH:ACN=1:1 (0.1% NH ₃ H ₂ O)];B%:46%, isocratic elution mode
A18	ChiralPak IH , 250*30mm, 10um	CO ₂ -IPA (0.1% NH ₃ H ₂ O) B: 50%, isocratic elution mode
A19	DAICEL CHIRALPAK AD (250 mm * 30mm, 10um)	[CO ₂ -EtOH (0.1%NH ₃ H ₂ O)]; B%:40%, isocratic elution mode
A20	ChiralPak IH , 250*30mm, 10um	[CO ₂ -IPA(0.1%NH ₃ H ₂ O)]; B%:40%, isocratic elution mode
A21	DAICEL CHIRALCEL OZ 250*25 mm I.D. 10um	[CO ₂ -EtOH(0.1% NH ₃ H ₂ O)];B%:50%, isocratic elution mode
A22	DAICEL CHIRALCEL OJ (250mm*30mm,10um)	[CO ₂ -EtOH(0.1%NH ₃ H ₂ O)];B%:40%, isocratic elution mode
A23	DAICEL CHIRALCEL OJ (250mm×30mm,10um)	[CO ₂ -EtOH (0.1% NH ₃ H ₂ O)]; B%:35%, isocratic elution mode
A24	ChiralPak IH , 250*30 mm, 10um	[CO ₂ -EtOH (0.1%NH ₃ H ₂ O)]; B%:35%, isocratic elution mode
A25	DAICEL CHIRALCEL OJ 250mm*30mm I.D. 10um	CO ₂ -EtOH: ACN=1:1 (0.1% NH ₃ H ₂ O); B%: 60%, isocratic elution mode
A26	DAICEL CHIRALPAK IG (250mm*30mm,10um)	[CO ₂ -MeOH(0.1%NH ₃ H ₂ O)];B%:45%, isocratic elution mode
A27	ChiralPak IH , 250*30mm, 10um	[CO ₂ -MeOH(0.1%NH ₃ H ₂ O)];B%:45%, isocratic elution mode
A28	DAICEL CHIRALCEL OJ (250mm*30mm,10um)	[CO ₂ -EtOH(0.1% NH ₃ H ₂ O)];B%:45%, isocratic elution mode
A29	Chiralcel OD -3, 50×4.6mm I.D., 3um	CO ₂ B: EtOH[0.2%NH ₃ (7M in MeOH)]
A30	DAICEL CHIRALCEL OJ (250 mm×30 mm, 10 um)	[CO ₂ -MeOH(0.1%NH ₃ H ₂ O)]; B%: 40%, isocratic elution mode)
A31	DAICEL CHIRALCEL OJ (250mm*30mm,10um)	[CO ₂ -EtOH];B%:40%, isocratic elution mode

Condition	Column	Mobile phase
A32	REGIS (s,s) WHELK- O1 (250mm*30mm,5um)	[CO ₂ -IPA (0.1%NH ₃ H ₂ O)]; B%:50%, isocratic elution mode
A33	REGIS (s,s) WHELK- O1 (250 mm×30 mm,5 um)	[CO ₂ -EtOH (0.1% NH ₃ H ₂ O)]; B%: 45%, isocratic elution mode)
A34	DAICEL CHIRALPAK IG (250mm*30mm, 10um)	[CO ₂ -EtOH (0.1% NH ₃ H ₂ O)]; B%:50%, isocratic elution mode
A35	DAICEL CHIRALPAK IG (250mm*30mm,10um)	CO ₂ -MeOH: THF=1:1 ; B%: 50%, isocratic elution mode
A36	DAICEL CHIRALPAK IC (250mm*30mm,10um)	[Hexane-EtOH (0.1% IPAm)]; B%: 40%, isocratic elution mode)
A37	DAICEL CHIRALCEL OX (250mm*30mm*10um)	[CO ₂ -ACN/EtOH (0.1% NH ₃ ·H ₂ O)]; B%:60%, isocratic elution mode)
A38	Silica Gel Flash Column	
A39	DAICEL CHIRALPAK IG (250mm*30mm,10um)	[CO ₂ -MeOH(0.1%NH ₃ H ₂ O)]; B%:50%, isocratic elution mode
A40	DAICEL CHIRALCEL OD 250mm*30mm, 10um	[CO ₂ -IPA (0.1% NH ₃ H ₂ O)]; B%: 50.00%-50.00%, 15.00min
A41	DAICEL CHIRALCEL OX (250mm*30mm,10um);mobile phase	[CO ₂ -EtOH:ACN=4:1(0.1% IPAm)];B%:60%, isocratic elution mode
A42	DAICEL CHIRALCEL OX (250mm*30mm,10um);mobile phase	[CO ₂ -EtOH(0.1% NH ₃ H ₂ O)];B%:65%, isocratic elution mode
A43	DAICEL CHIRALCEL OJ 250mm*30mm I.D. 10um	[CO ₂ -IPA: ACN = 1:1 (0.1% NH ₃ H ₂ O)]; B%: 50%, isocratic elution mode
A44	DAICEL CHIRALCEL OJ (250 mm×30 mm, 10 um)	[CO ₂ -MeOH: ACN = 1:1 (0.1% NH ₃ H ₂ O)]; B%: 50%, isocratic elution mode
A45	DAICEL CHIRALCEL OZ 250*25 mm I.D. 10um	[CO ₂ -MeOH: ACN=1:1 (0.1% NH ₃ H ₂ O)]; B%:55%, isocratic elution mode
A46	DAICEL CHIRALCEL OJ 250mm*30mm I.D. 10um	[CO ₂ -EtOH (0.1% NH ₃ H ₂ O)]; B%: 65%, isocratic elution mode

Condition	Column	Mobile phase
A47	DAICEL CHIRALCEL OD (250mm*30mm,10um)	[CO ₂ -MeOH(0.1%NH ₃ H ₂ O)]; B%:50%, isocratic elution mode
A48	DAICEL CHIRALPAK ID (250mm*30mm,10um)	[CO ₂ -IPA(0.1%NH ₃ H ₂ O)]; B%:56%, isocratic elution mode
A49	DAICEL CHIRALPAK IG (250mm*30mm,10um)	[CO ₂ -THF(0.1%NH ₃ H ₂ O)];B%:50%, isocratic elution mode
A50	DAICEL CHIRALPAK AD (250mm*30mm,10um)	[CO ₂ -IPA (0.1% NH ₃ H ₂ O)]; B%:45%, isocratic elution mode
A51	DAICEL CHIRALCEL OZ 250*25 mm I.D. 10um	[CO ₂ -MeOH (0.1%NH ₃ H ₂ O)]; B%:65%, isocratic elution mode
A52	DAICEL CHIRALCEL OD (250mm*30mm,10um)	[CO ₂ -EtOH(0.1% NH ₃ H ₂ O)];B%:50%, isocratic elution mode
A53	DAICEL CHIRALPAK AD (250mm*30mm, 10um)	[CO ₂ -EtOH (0.1%NH ₃ H ₂ O)]; B%:45%, isocratic elution mode)
A54	DAICEL CHIRALPAK AD (250mm*30mm, 10um)	[CO ₂ -IPA (0.1%NH ₃ H ₂ O)]; B%:30%, isocratic elution mode
A55	DAICEL CHIRALPAK IE (250 mm×30 mm,10 um)	[CO ₂ -EtOH (0.1% NH ₃ H ₂ O)]; B%: 65%, isocratic elution mode
A56	DAICEL CHIRALCEL OD (250mm*30mm,10um)	[CO ₂ -MeOH (0.1%NH ₃ H ₂ O)]; B%:45%, isocratic elution mode
A57	Waters Xbridge BEH C18 100*30mm*10um	[H ₂ O (10mM NH ₄ HCO ₃)-ACN]; gradient: 30%-70% B over 8.0 min
A58	ChiralPak IH , 250×30mm, 10um	[CO ₂ -EtOH (0.1% NH ₃ H ₂ O)]; gradient: 50%-5% B over 17.0 min
A59	DAICEL CHIRALPAK ID (250mm*30mm, 10um)	[CO ₂ -IPA (0.1%NH ₃ H ₂ O)]; B%:38%, isocratic elution mode
A60	DAICEL CHIRALCEL OJ (250mm*30mm,10um)	[CO ₂ -IPA(0.1%NH ₃ H ₂ O)]; B%:40%, isocratic elution mode
A61	DAICEL CHIRALPAK IG (250mm*30mm,10um)	[CO ₂ -EtOH:ACN=1:1 (0.1% NH ₃ H ₂ O)];B%:60%, isocratic elution mode

Condition	Column	Mobile phase
A62	Agilent Poroshell SB -C18 150*21.2*2.7	[Heptane-EtOH:ACN=4:1 (0.1% NH ₃ H ₂ O)];B%:20%, isocratic elution mode
A63	DAICEL CHIRALPAK IC (250 mm×30 mm, 10 um)	[CO ₂ -MeOH (0.1% NH ₃ H ₂ O)]; B%:30%, isocratic elution mode
A64	DAICEL CHIRALCEL OD (250mm*30mm*10um)	[CO ₂ -MeOH(0.1%NH ₃ H ₂ O)];gradient:30%-50% B over 14.0 min

[0580] The compounds set forth in Table 3B were prepared following the procedures set forth above, with the exception that the amine was replaced in the example above with an amine depicted in the final product. Compounds denoted as “1st eluting isomer”, “2nd eluting isomer”, etc., were separated via SFC using the conditions provided in Table 3A to yield single unknown stereoisomers whose stereochemistry is unknown at the stereocenter depicted as racemic. Some compounds were separated via preparative TLC instead of SFC, and are denoted as such in Table 3B.

Table 3B

Cmpd #	MS	¹ H NMR	SFC Conditions
1	<i>m/z</i> (ESI ⁺): 415 (M+H) ⁺		
2	<i>m/z</i> (ESI ⁺): 419.1 (M+H) ⁺	(400 MHz, 400 MHz, CD ₃ OD) δ 8.58 (s, 1H), 8.45 - 8.33 (m, 1H), 7.93 (d, <i>J</i> = 8.0 Hz, 1H), 7.85 (s, 1H), 7.34 - 7.24 (m, 1H), 7.03 - 6.93 (m, 2H), 6.72 (s, 1H), 6.68 - 6.61 (m, 1H), 6.41 - 6.30 (m, 1H), 5.88 - 5.76 (m, 1H), 5.67 - 5.57 (m, 0.5H), 5.53 - 5.44 (m, 0.5H), 4.38 - 4.33 (m, 1H), 4.28 - 4.19 (m, 1H), 4.14 - 4.10 (m, 1H), 4.07 - 3.88 (m, 2H).	
3	<i>m/z</i> (ESI ⁺): 469 (M+H) ⁺	(499 MHz, d ₆ -DMSO) δ 13.54 (s, 1H), 13.04 (s, 1H), 8.35 (s, 1H), 8.12 (dd, <i>J</i> = 8.0, 1.7 Hz, 1H), 7.30 (ddd, <i>J</i> = 8.5, 7.1, 1.6 Hz, 1H), 7.00 - 6.92 (m, 2H), 6.86 (dd, <i>J</i> = 16.7, 10.5 Hz, 1H), 6.25 (dd, <i>J</i> = 16.7, 2.5 Hz, 1H), 5.78 (dd, <i>J</i> = 10.4, 2.5 Hz, 1H), 4.66 - 4.55 (m, 2H), 4.33 (s, 1H), 4.04 (dd, <i>J</i> = 11.4, 7.3 Hz, 2H), 3.71 (ddt, <i>J</i> = 19.9, 11.5, 2.5 Hz, 2H), 2.29 - 2.01 (m, 4H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
4	<i>m/z</i> (ESI ⁺): 349.1 (M+H) ⁺	(400 MHz, 400 MHz, CD ₃ OD) δ 8.40 (s, 1H), 7.96 - 7.92 (m, 1H), 7.31 - 7.25 (m, 1H), 7.01 - 6.93 (m, 2H), 6.50 - 6.46 (m, 1H), 6.33 - 6.20 (m, 2H), 5.70 - 5.64 (m, 1H), 4.52 - 4.41 (m, 1H), 3.64 - 3.52 (m, 1H), 2.43 - 2.23 (m, 3H), 2.19 - 2.10 (m, 1H), 1.98 - 1.86 (m, 1H), 1.80 - 1.69 (m, 1H).	R 1st eluting isomer
5	<i>m/z</i> (ESI ⁺): 349 (M+H) ⁺		
6	<i>m/z</i> (ESI ⁺): 349.1 (M+H) ⁺		S 1st eluting isomer
7	<i>m/z</i> (ESI ⁺): 381.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.12 (s, 1H), 12.42 (d, <i>J</i> = 2.0 Hz, 1H), 8.67 (d, <i>J</i> = 2.0 Hz, 1H), 8.16 (d, <i>J</i> = 7.6 Hz, 1H), 7.30 (t, <i>J</i> = 7.2 Hz, 1H), 7.03 - 6.93 (m, 2H), 6.67 (d, <i>J</i> = 2.8, 10.4, 16.9 Hz, 1H), 6.23 (d, <i>J</i> = 1.6, 16.8 Hz, 1H), 5.83 - 5.70 (m, 1H), 5.63 - 5.38 (m, 1H), 4.35 - 3.85 (m, 4H), 3.78 - 3.65 (m, 1H), 2.91 - 2.79 (m, 2H), 1.26 - 1.21 (m, 3H).	
8	<i>m/z</i> (ESI ⁺): 391.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.18 (s, 1H), 12.54 (s, 1H), 8.53 (s, 1H), 8.02 (d, <i>J</i> = 6.8 Hz, 1H), 7.31 - 7.25 (m, 1H), 6.98 - 6.91 (m, 2H), 6.89 - 6.79 (m, 1H), 6.44 (s, 1H), 6.25 - 6.18 (m, 1H), 5.78 - 5.72 (m, 1H), 4.57 (s, 1H), 4.41 - 4.30 (m, 2H), 4.07 - 3.97 (m, 2H), 3.76 - 3.66 (m, 2H), 2.36 - 2.24 (m, 2H), 2.05 - 1.92 (m, 2H).	
9	<i>m/z</i> (ESI ⁺): 414 (M+H) ⁺		
10	<i>m/z</i> (ESI ⁺): 365.2 (M+H) ⁺	(400 MHz, 400 MHz, CD ₃ OD) δ 8.51 (s, 1H), 7.94 (d, <i>J</i> = 8.4 Hz, 1H), 7.34 - 7.23 (m, 1H), 7.01 - 6.93 (m, 2H), 6.87 - 6.79 (m, 1H), 6.72 (dd, <i>J</i> = 10.8, 16.8 Hz, 1H), 6.32 - 6.18 (m, 1H), 5.91 - 5.77 (m, 1H), 5.75 (s, 1H), 4.40 - 4.13 (m, 1H), 4.08 - 3.87 (m, 2H), 3.85 - 3.73 (m, 1H), 3.71 - 3.60 (m, 1H), 1.23 - 1.07 (m, 3H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
11	<i>m/z</i> (ESI ⁺): 365.2 (M+H) ⁺	(400 MHz, 400 MHz, CD ₃ OD) δ 8.49 (s, 1H), 7.94 (d, <i>J</i> = 8.4 Hz, 1H), 7.34 - 7.22 (m, 1H), 7.04 - 6.93 (m, 2H), 6.86 (dd, <i>J</i> = 10.4, 16.8 Hz, 1H), 6.72 (s, 1H), 6.35 (dd, <i>J</i> = 1.6, 16.8 Hz, 1H), 5.85 (dd, <i>J</i> = 2.0, 10.4 Hz, 1H), 5.54 (s, 1H), 4.67 (dq, <i>J</i> = 2.0, 6.4 Hz, 1H), 4.14 - 4.05 (m, 1H), 4.04 - 3.95 (m, 1H), 3.71 (dd, <i>J</i> = 2.8, 11.6 Hz, 1H), 3.52 - 3.39 (m, 1H), 1.45 (d, <i>J</i> = 6.4 Hz, 3H).	
12	<i>m/z</i> (ESI ⁺): 389.2 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.10 (br s, 1H), 12.50 (br s, 1H), 8.53 (s, 1H), 8.01 (d, <i>J</i> = 7.2 Hz, 1H), 7.33 - 7.24 (m, 1H), 6.99 - 6.90 (m, 2H), 6.62 - 6.39 (m, 2H), 6.09 (ddd, <i>J</i> = 2.4, 8.8, 16.8 Hz, 1H), 5.71 - 5.54 (m, 1H), 3.60 (q, <i>J</i> = 10.4 Hz, 1H), 3.45 - 3.38 (m, 2H), 3.28 (s, 1H), 3.21 (dd, <i>J</i> = 5.6, 8.4 Hz, 1H), 2.21 - 2.14 (m, 2H), 1.91 (dd, <i>J</i> = 6.4, 11.6 Hz, 1H), 1.85 - 1.68 (m, 3H), 1.67 - 1.51 (m, 1H), 1.51 - 1.35 (m, 1H).	
13	<i>m/z</i> (ESI ⁺): 389.2 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.10 (br s, 1H), 12.50 (br s, 1H), 8.53 (s, 1H), 8.02 (d, <i>J</i> = 7.2 Hz, 1H), 7.33 - 7.25 (m, 1H), 6.99 - 6.91 (m, 2H), 6.63 - 6.39 (m, 2H), 6.09 (ddd, <i>J</i> = 2.4, 8.8, 16.8 Hz, 1H), 5.71 - 5.55 (m, 1H), 3.61 (q, <i>J</i> = 10.4 Hz, 1H), 3.45 - 3.38 (m, 2H), 3.29 (d, <i>J</i> = 1.2 Hz, 1H), 3.21 (dd, <i>J</i> = 5.6, 8.4 Hz, 1H), 2.22 - 2.13 (m, 2H), 1.98 - 1.87 (m, 1H), 1.86 - 1.69 (m, 3H), 1.67 - 1.52 (m, 1H), 1.51 - 1.35 (m, 1H).	
14	<i>m/z</i> (ESI ⁺): 389.2 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.13 (d, <i>J</i> = 9.2 Hz, 1H), 12.52 (br s, 1H), 8.51 (d, <i>J</i> = 9.2 Hz, 1H), 8.01 (d, <i>J</i> = 7.6 Hz, 1H), 7.32 - 7.24 (m, 1H), 6.99 - 6.91 (m, 2H), 6.50 (d, <i>J</i> = 2.8 Hz, 1H), 6.45 - 6.26 (m, 1H), 5.99 - 5.85 (m, 1H), 5.55 - 5.43 (m, 1H), 3.58 - 3.47 (m, 1H), 3.38 (s, 0.5H), 3.28 - 3.22 (m, 2.5H), 3.20 (d, <i>J</i> = 12.0 Hz, 0.5H), 2.97 (d, <i>J</i> = 12.4 Hz, 0.5H), 2.22 - 2.12 (m, 2H), 2.10 - 2.00 (m, 1H), 1.97 - 1.85 (m, 2H), 1.85 - 1.71 (m, 3H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
15	<i>m/z</i> (ESI ⁺): 389.2 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.12 (d, <i>J</i> = 9.2 Hz, 1H), 12.52 (d, <i>J</i> = 19.6 Hz, 1H), 8.50 (d, <i>J</i> = 8.8 Hz, 1H), 8.01 (d, <i>J</i> = 7.2 Hz, 1H), 7.31 - 7.25 (m, 1H), 6.98 - 6.92 (m, 2H), 6.50 (s, 1H), 6.45 - 6.27 (m, 1H), 5.99 - 5.83 (m, 1H), 5.53 - 5.45 (m, 1H), 3.59 - 3.46 (m, 1H), 3.37 (s, 0.5H), 3.28 - 3.22 (m, 2.5H), 3.19 (d, <i>J</i> = 12.4 Hz, 0.5H), 2.97 (d, <i>J</i> = 12.4 Hz, 0.5H), 2.23 - 2.13 (m, 2H), 2.10 - 1.99 (m, 1H), 1.98 - 1.86 (m, 2H), 1.85 - 1.70 (m, 3H).	
16	<i>m/z</i> (ESI ⁺): 405.2 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.08 (br s, 1H), 12.44 (br s, 1H), 8.47 (s, 1H), 8.02 (d, <i>J</i> = 8.0 Hz, 1H), 7.28 (t, <i>J</i> = 8.0 Hz, 1H), 6.99 - 6.93 (m, 2H), 6.65 (dt, <i>J</i> = 10.4, 16.0 Hz, 1H), 6.18 (td, <i>J</i> = 2.8, 16.8 Hz, 1H), 5.74 - 5.66 (m, 1H), 4.15 (dt, <i>J</i> = 4.0, 8.0 Hz, 1H), 4.10 - 4.01 (m, 1H), 4.00 - 3.85 (m, 4H), 3.85 - 3.76 (m, 2H), 3.76 - 3.61 (m, 1H), 3.58 - 3.40 (m, 1H), 2.37 - 2.28 (m, 2H), 2.28 - 2.20 (m, 1H), 2.20 - 2.11 (m, 1H).	
17	<i>m/z</i> (ESI ⁺): 389.2 (M+H) ⁺	(400 MHz, 400 MHz, CD ₃ OD) δ 8.45 - 8.40 (m, 1H), 7.94 (d, <i>J</i> = 8.0 Hz, 1H), 7.32 - 7.25 (m, 1H), 7.03 - 6.94 (m, 2H), 6.76 - 6.61 (m, 1H), 6.33 (dd, <i>J</i> = 2.0, 16.8 Hz, 1H), 5.80 (ddd, <i>J</i> = 1.6, 8.0, 10.4 Hz, 1H), 4.32 - 4.19 (m, 1H), 4.08 (d, <i>J</i> = 12.4 Hz, 1H), 3.91 - 3.83 (m, 1H), 3.78 - 3.68 (m, 1H), 2.69 - 2.53 (m, 2H), 1.96 - 1.91 (m, 1H), 1.56 (d, <i>J</i> = 4.0 Hz, 3H), 1.19 - 1.11 (m, 2H), 0.87 - 0.79 (m, 2H).	
18	<i>m/z</i> (ESI ⁺): 389.2 (M+H) ⁺	(400 MHz, 400 MHz, CD ₃ OD) δ 8.42 (s, 1H), 7.94 (d, <i>J</i> = 7.6 Hz, 1H), 7.31 - 7.25 (m, 1H), 7.00 - 6.96 (m, 2H), 6.75 - 6.62 (m, 1H), 6.33 (dd, <i>J</i> = 1.6, 16.8 Hz, 1H), 5.80 (ddd, <i>J</i> = 2.0, 8.4, 10.4 Hz, 1H), 4.29 - 4.17 (m, 1H), 4.08 (d, <i>J</i> = 12.0 Hz, 1H), 3.91 - 3.83 (m, 1H), 3.79 - 3.65 (m, 1H), 2.70 - 2.50 (m, 2H), 1.97 - 1.89 (m, 1H), 1.56 (d, <i>J</i> = 3.6 Hz, 3H), 1.17 - 1.13 (m, 2H), 0.86 - 0.79 (m, 2H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
19	<i>m/z</i> (ESI ⁺): 363.2 (M+H) ⁺	(400 MHz, 400 MHz, CD ₃ OD) δ 8.43 (s, 1H), 8.01 (d, <i>J</i> = 8.4 Hz, 1H), 7.32 - 7.23 (m, 1H), 7.01 - 6.94 (m, 2H), 6.76 - 6.59 (m, 1H), 6.33 (td, <i>J</i> = 0.8, 16.8 Hz, 1H), 5.80 (ddd, <i>J</i> = 2.0, 6.4, 10.4 Hz, 1H), 4.18 - 4.05 (m, 1H), 3.92 - 3.84 (m, 2H), 3.80 - 3.66 (m, 1H), 2.65 - 2.47 (m, 2H), 2.45 (d, <i>J</i> = 2.0 Hz, 3H), 1.54 (d, <i>J</i> = 3.6 Hz, 3H).	
20	<i>m/z</i> (ESI ⁺): 363.2 (M+H) ⁺	(400 MHz, 400 MHz, CD ₃ OD) δ 8.44 (s, 1H), 8.01 (d, <i>J</i> = 8.0 Hz, 1H), 7.33 - 7.24 (m, 1H), 7.01 - 6.95 (m, 2H), 6.75 - 6.61 (m, 1H), 6.36 - 6.29 (m, 1H), 5.80 (ddd, <i>J</i> = 2.0, 6.4, 10.4 Hz, 1H), 4.18 - 4.04 (m, 1.5H), 3.92 - 3.85 (m, 1.5H), 3.79 - 3.66 (m, 1H), 2.67 - 2.47 (m, 2H), 2.45 (d, <i>J</i> = 2.4 Hz, 3H), 1.54 (d, <i>J</i> = 4.0 Hz, 3H).	
21	<i>m/z</i> (ESI ⁺): 375 (M+H) ⁺		K 2 nd eluting isomer
22	<i>m/z</i> (ESI ⁺): 375 (M+H) ⁺		K 1 st eluting isomer
23	<i>m/z</i> (ESI ⁺): 407 (M+H) ⁺	(499 MHz, d ₆ -DMSO) δ 14.21 (s, 1H), 12.37 (s, 1H), 8.58 (d, <i>J</i> = 4.9 Hz, 1H), 8.12 (dt, <i>J</i> = 8.3, 1.5 Hz, 1H), 7.29 (td, <i>J</i> = 7.6, 1.6 Hz, 1H), 7.00 - 6.93 (m, 2H), 6.64 (ddd, <i>J</i> = 20.9, 16.7, 10.3 Hz, 1H), 6.19 (ddd, <i>J</i> = 16.7, 4.3, 2.4 Hz, 1H), 5.70 (ddd, <i>J</i> = 19.0, 10.3, 2.4 Hz, 1H), 4.06 (dd, <i>J</i> = 9.8, 8.0 Hz, 0H), 3.98 - 3.86 (m, 2H), 3.86 - 3.75 (m, 1H), 3.77 - 3.62 (m, 1H), 3.56 - 3.40 (m, 1H), 3.32 (d, <i>J</i> = 6.3 Hz, 1H), 3.23 (d, <i>J</i> = 2.8 Hz, 3H), 2.85 (td, <i>J</i> = 7.5, 2.9 Hz, 2H), 2.43 - 2.21 (m, 2H), 1.84 (pd, <i>J</i> = 6.5, 2.6 Hz, 2H).	
24	<i>m/z</i> (ESI ⁺): 375 (M+H) ⁺	(499 MHz, d ₆ -DMSO) δ 14.08 (s, 1H), 12.34 (s, 1H), 8.58 (d, <i>J</i> = 5.0 Hz, 1H), 8.17 (dt, <i>J</i> = 8.3, 1.8 Hz, 1H), 7.29 (td, <i>J</i> = 7.6, 1.6 Hz, 1H), 6.99 - 6.92 (m, 2H), 6.64 (ddd, <i>J</i> = 17.9, 16.7, 10.3 Hz, 1H), 6.18 (ddd, <i>J</i> = 16.7, 4.8, 2.4 Hz, 1H), 5.70 (ddd, <i>J</i> = 19.4, 10.3, 2.5 Hz, 1H), 4.09 - 3.62 (m, 4H), 3.55 - 3.40 (m, 1H), 2.36 - 2.20 (m, 2H), 1.43 (dd, <i>J</i> = 7.1, 2.4 Hz, 6H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
25	<i>m/z</i> (ESI ⁺): 375 (M+H) ⁺	(499 MHz, d ₆ -DMSO) δ 14.08 (s, 1H), 12.34 (s, 1H), 8.58 (d, <i>J</i> = 5.0 Hz, 1H), 8.17 (dt, <i>J</i> = 8.3, 1.8 Hz, 1H), 7.29 (td, <i>J</i> = 7.6, 1.6 Hz, 1H), 6.99 – 6.92 (m, 2H), 6.64 (ddd, <i>J</i> = 17.9, 16.7, 10.3 Hz, 1H), 6.18 (ddd, <i>J</i> = 16.7, 4.8, 2.4 Hz, 1H), 5.70 (ddd, <i>J</i> = 19.4, 10.3, 2.5 Hz, 1H), 4.09 – 3.62 (m, 4H), 3.55 – 3.40 (m, 1H), 2.36 – 2.20 (m, 2H), 1.43 (dd, <i>J</i> = 7.1, 2.4 Hz, 6H).	
26	<i>m/z</i> (ESI ⁺): 389.2 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.10 (d, <i>J</i> = 4.0 Hz, 1H), 12.51 (br s, 1H), 8.53 (s, 1H), 8.02 (d, <i>J</i> = 8.0 Hz, 1H), 7.28 (t, <i>J</i> = 7.6 Hz, 1H), 7.00 - 6.90 (m, 2H), 6.63 - 6.39 (m, 2H), 6.09 (ddd, <i>J</i> = 2.4, 8.8, 16.8 Hz, 1H), 5.70 - 5.56 (m, 1H), 3.61 (q, <i>J</i> = 10.4 Hz, 1H), 3.47 - 3.38 (m, 2H), 3.30 (s, 1H), 3.21 (dd, <i>J</i> = 5.6, 8.4 Hz, 1H), 2.22 - 2.13 (m, 2H), 1.91 (dd, <i>J</i> = 6.4, 11.6 Hz, 1H), 1.85 - 1.68 (m, 3H), 1.68 - 1.51 (m, 1H), 1.51 - 1.35 (m, 1H).	A 2 nd eluting isomer
27	<i>m/z</i> (ESI ⁺): 389.2 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.17 - 14.10 (m, 1H), 12.54 (br s, 1H), 8.51 (d, <i>J</i> = 9.2 Hz, 1H), 8.01 (dd, <i>J</i> = 1.2, 8.0 Hz, 1H), 7.33 - 7.23 (m, 1H), 7.00 - 6.89 (m, 2H), 6.50 (d, <i>J</i> = 2.8 Hz, 1H), 6.43 - 6.27 (m, 1H), 5.99 - 5.85 (m, 1H), 5.56 - 5.43 (m, 1H), 3.59 - 3.46 (m, 1H), 3.41 - 3.34 (m, 0.5H), 3.31 - 3.22 (m, 2.5H), 3.20 (d, <i>J</i> = 12.4 Hz, 0.5H), 2.97 (d, <i>J</i> = 12.4 Hz, 0.5H), 2.22 - 2.12 (m, 2H), 2.11 - 2.00 (m, 1H), 1.99 - 1.85 (m, 2H), 1.85 - 1.70 (m, 3H).	U 1 st eluting isomer
28	<i>m/z</i> (ESI ⁺): 349.1 (M+H) ⁺		
29	<i>m/z</i> (ESI ⁺): 389.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.25 (s, 1H), 12.52 (s, 1H), 8.57 - 8.48 (m, 1H), 8.08 - 7.98 (m, 1H), 7.35 - 7.24 (m, 1H), 7.01 - 6.90 (m, 2H), 6.65 - 6.54 (m, 1H), 6.44 (s, 1H), 6.22 - 6.10 (m, 1H), 5.71 - 5.61 (m, 1H), 3.96 (dd, <i>J</i> = 6.4, 11.2 Hz, 1H), 3.69 - 3.62 (m, 1H), 3.59 - 3.50 (m, 1H), 2.80 (dd, <i>J</i> = 9.2, 12.8 Hz, 1H), 2.43 - 2.37 (m, 1H), 2.31 - 2.23 (m, 1H), 2.04 - 1.95 (m, 1H), 1.92 - 1.75 (m, 5H), 1.67 - 1.60 (m, 1H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
30	<i>m/z</i> (ESI ⁺): 425.2 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 13.69 (s, 1H), 12.66 (s, 1H), 8.04 (s, 1H), 7.91 (d, <i>J</i> = 8.0 Hz, 1H), 7.55 - 7.43 (m, 5H), 7.29 - 7.22 (m, 1H), 6.94 (d, <i>J</i> = 8.4 Hz, 1H), 6.88 (t, <i>J</i> = 7.6 Hz, 1H), 6.52 (dd, <i>J</i> = 10.4, 16.8 Hz, 1H), 6.17 - 6.03 (m, 1H), 5.64 (ddd, <i>J</i> = 2.4, 8.0, 10.4 Hz, 1H), 3.80 - 3.66 (m, 1H), 3.65 - 3.57 (m, 1H), 3.46 - 3.36 (m, 1H), 3.35 (s, 1H), 2.24 - 2.14 (m, 1H), 2.14 - 2.04 (m, 1H), 1.54 (d, <i>J</i> = 4.4 Hz, 3H).	
31	<i>m/z</i> (ESI ⁺): 389.2 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.43 (s, 1H), 7.93 (d, <i>J</i> = 8.0 Hz, 1H), 7.33 - 7.25 (m, 1H), 7.02 - 6.95 (m, 2H), 6.75 - 6.62 (m, 1H), 6.33 (dd, <i>J</i> = 1.6, 16.8 Hz, 1H), 5.80 (ddd, <i>J</i> = 1.6, 8.0, 10.4 Hz, 1H), 4.32 - 4.05 (m, 2H), 3.87 (dd, <i>J</i> = 6.4, 10.0 Hz, 1H), 3.78 - 3.68 (m, 1H), 2.69 - 2.59 (m, 1H), 2.58 - 2.51 (m, 1H), 1.99 - 1.90 (m, 1H), 1.56 (d, <i>J</i> = 4.0 Hz, 3H), 1.19 - 1.13 (m, 2H), 0.87 - 0.80 (m, 2H).	
32	<i>m/z</i> (ESI ⁺): 363.2 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.44 (s, 1H), 7.99 (dd, <i>J</i> = 1.6, 8.4 Hz, 1H), 7.28 (dt, <i>J</i> = 1.6, 7.2 Hz, 1H), 7.01 - 6.95 (m, 2H), 6.74 - 6.63 (m, 1H), 6.33 (dd, <i>J</i> = 1.6, 17.6 Hz, 1H), 5.80 (ddd, <i>J</i> = 2.0, 6.4, 10.4 Hz, 1H), 4.16 - 4.05 (m, 1H), 3.93 - 3.84 (m, 2H), 3.78 - 3.67 (m, 1H), 2.62 - 2.49 (m, 2H), 2.45 (d, <i>J</i> = 1.6 Hz, 3H), 1.54 (d, <i>J</i> = 3.6 Hz, 3H).	
33	<i>m/z</i> (ESI ⁺): 377.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.08 (s, 1H), 12.61 (s, 1H), 8.57 (s, 1H), 8.04 (d, <i>J</i> = 6.8 Hz, 1H), 7.37 - 7.23 (m, 1H), 7.02 - 6.92 (m, 2H), 6.55 (d, <i>J</i> = 1.6 Hz, 1H), 6.32 (d, <i>J</i> = 5.6, 10.4, 16.7 Hz, 1H), 6.17 - 6.05 (m, 1H), 5.68 (t, <i>J</i> = 2.0, 10.0 Hz, 1H), 4.36 (d, <i>J</i> = 9.2 Hz, 1H), 4.30 - 4.21 (m, 2H), 4.12 - 4.05 (m, 1H), 4.03 - 3.92 (m, 2H), 3.86 - 3.76 (m, 1H), 2.76 - 2.67 (m, 1H), 2.60 - 2.57 (m, 1H).	V 2 nd eluting isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
34	<i>m/z</i> (ESI ⁺): 377.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.15 - 14.04 (m, 1H), 12.61 (s, 1H), 8.56 (s, 1H), 8.03 (d, <i>J</i> = 7.2 Hz, 1H), 7.35 - 7.22 (m, 1H), 7.03 - 6.90 (m, 2H), 6.54 (d, <i>J</i> = 2.0 Hz, 1H), 6.40 - 6.25 (m, 1H), 6.16 - 6.05 (m, 1H), 5.74 - 5.59 (m, 1H), 4.38 - 4.33 (m, 1H), 4.30 - 4.21 (m, 2H), 4.08 (d, <i>J</i> = 10.8 Hz, 1H), 4.02 - 3.91 (m, 2H), 3.85 - 3.73 (m, 1H), 2.76 - 2.67 (m, 1H), 2.58 - 2.53 (m, 1H).	V 1 st eluting isomer
35	<i>m/z</i> (ESI ⁺): 361 (M+H) ⁺		
36	<i>m/z</i> (ESI ⁺): 349 (M+H) ⁺		
37	<i>m/z</i> (ESI ⁺): 426 (M+H) ⁺	(499 MHz, d ₆ -DMSO) δ 13.35 (s, 1H), 13.12 (s, 1H), 8.41 (d, <i>J</i> = 3.3 Hz, 1H), 8.14 (dd, <i>J</i> = 8.0, 1.6 Hz, 1H), 7.32 (td, <i>J</i> = 7.1, 1.6 Hz, 1H), 7.02 - 6.94 (m, 2H), 6.83 - 6.50 (m, 1H), 6.22 (dd, <i>J</i> = 16.7, 1.1 Hz, 1H), 5.73 (ddd, <i>J</i> = 18.1, 10.3, 2.3 Hz, 1H), 4.86 (dt, <i>J</i> = 57.1, 1.9 Hz, 1H), 3.90 (d, <i>J</i> = 76.8 Hz, 2H), 2.63 - 2.57 (m, 1H), 2.54 - 2.51 (m, 1H), 2.11 (dd, <i>J</i> = 4.5, 1.9 Hz, 1H), 2.05 (dd, <i>J</i> = 4.5, 1.9 Hz, 1H).	
38	<i>m/z</i> (ESI ⁺): 413 (M+H) ⁺	(499 MHz, d ₆ -DMSO) δ 8.32 (s, 1H), 8.10 (dd, <i>J</i> = 8.0, 1.6 Hz, 1H), 7.29 (ddd, <i>J</i> = 8.5, 7.1, 1.6 Hz, 1H), 6.97 (dd, <i>J</i> = 6.5, 1.5 Hz, 1H), 6.98 - 6.90 (m, 1H), 6.56 (s, 0H), 6.37 (dd, <i>J</i> = 17.0, 10.3 Hz, 1H), 6.13 (dd, <i>J</i> = 17.0, 2.2 Hz, 1H), 5.70 (dd, <i>J</i> = 10.4, 2.2 Hz, 1H), 4.82 (d, <i>J</i> = 8.6 Hz, 1H), 4.55 (d, <i>J</i> = 10.0 Hz, 1H), 4.36 (d, <i>J</i> = 8.6 Hz, 1H), 4.03 (d, <i>J</i> = 10.0 Hz, 1H), 1.73 (s, 3H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
39	<i>m/z</i> (ESI ⁺): 401 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 8.21 (s, 1H), 7.58 (dd, <i>J</i> = 7.6, 1.8 Hz, 1H), 7.45 (ddd, <i>J</i> = 9.0, 7.5, 1.8 Hz, 1H), 7.28 (dd, <i>J</i> = 8.4, 1.1 Hz, 1H), 7.15 (td, <i>J</i> = 7.5, 1.1 Hz, 1H), 6.19 – 6.02 (m, 2H), 5.23 (s, 2H), 4.03 (q, <i>J</i> = 7.1 Hz, 2H), 3.78 (dq, <i>J</i> = 43.5, 8.6 Hz, 3H), 3.66 – 3.49 (m, 2H), 3.32 (s, 3H), 3.27 (t, <i>J</i> = 6.3 Hz, 2H), 3.19 (s, 3H), 3.22 – 3.14 (m, 1H), 2.80 (t, <i>J</i> = 7.4 Hz, 2H), 2.29 – 2.16 (m, 1H), 2.14 (s, 1H), 1.99 (s, 2H), 1.83 – 1.73 (m, 3H), 1.42 (d, <i>J</i> = 14.7 Hz, 8H), 1.35 (s, 1H), 1.25 (d, <i>J</i> = 9.8 Hz, 3H), 1.21 – 1.10 (m, 3H), 0.88 (s, 2H), 0.91 – 0.82 (m, 1H), -0.06 – -0.16 (m, 1H), -0.13 (s, 7H).	
40	<i>m/z</i> (ESI ⁺): 433 (M+H) ⁺		
41	<i>m/z</i> (ESI ⁺): 363.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.25 (s, 1H), 12.24 (s, 1H), 8.62 (s, 1H), 8.16 - 8.11 (m, 1H), 7.32 - 7.26 (m, 1H), 6.98 - 6.92 (m, 2H), 6.91 - 6.85 (m, 1H), 6.21 - 6.14 (m, 1H), 5.94 (s, 1H), 5.77 - 5.69 (m, 1H), 4.20 - 4.09 (m, 1H), 3.13 - 3.00 (m, 1H), 2.21 (s, 3H), 1.88 - 1.77 (m, 1H), 1.75 - 1.56 (m, 3H), 1.56 - 1.42 (m, 2H).	W 2 nd eluting isomer
42	<i>m/z</i> (ESI ⁺): 363.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.30 - 14.19 (m, 1H), 12.25 (s, 1H), 8.62 (s, 1H), 8.13 (d, <i>J</i> = 8.0 Hz, 1H), 7.32 - 7.26 (m, 1H), 6.98 - 6.93 (m, 2H), 6.92 - 6.84 (m, 1H), 6.20 - 6.13 (m, 1H), 5.94 (d, <i>J</i> = 1.2 Hz, 1H), 5.77 - 5.69 (m, 1H), 4.22 - 4.01 (m, 1H), 3.15 - 2.99 (m, 1H), 2.21 (s, 3H), 1.86 - 1.78 (m, 1H), 1.75 - 1.61 (m, 3H), 1.58 - 1.47 (m, 2H).	W 1 st eluting isomer
43	<i>m/z</i> (ESI ⁺): 349.2 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 13.91 (br s, 1H), 12.20 (br s, 1H), 8.44 (s, 1H), 8.02 - 7.91 (m, 1H), 7.35 - 7.21 (m, 1H), 7.02 - 6.89 (m, 2H), 6.75 - 6.54 (m, 1H), 6.42 (s, 1H), 6.06 (dd, <i>J</i> = 1.6, 16.8 Hz, 1H), 5.73 - 5.57 (m, 1H), 4.08 - 3.90 (m, 1H), 3.83 - 3.73 (m, 1H), 2.29 - 2.16 (m, 1H), 2.15 - 2.06 (m, 1H), 2.04 - 1.94 (m, 2H), 1.90 (s, 3H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
44	<i>m/z</i> (ESI ⁺): 349.2 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 13.90 (br s, 1H), 12.20 (br s, 1H), 8.44 (s, 1H), 7.97 (dd, <i>J</i> = 1.2, 7.6 Hz, 1H), 7.37 - 7.22 (m, 1H), 7.02 - 6.88 (m, 2H), 6.76 - 6.54 (m, 1H), 6.42 (s, 1H), 6.06 (dd, <i>J</i> = 2.0, 16.8 Hz, 1H), 5.72 - 5.57 (m, 1H), 4.00 (d, <i>J</i> = 5.6 Hz, 1H), 3.86 - 3.73 (m, 1H), 2.30 - 2.16 (m, 1H), 2.15 - 2.07 (m, 1H), 2.03 (d, <i>J</i> = 18.4 Hz, 2H), 1.90 (s, 3H).	
45	<i>m/z</i> (ESI ⁺): 389.1 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.41 (s, 1H), 7.97 - 7.92 (m, 1H), 7.29 (dt, <i>J</i> = 1.6, 8.0 Hz, 1H), 7.02 - 6.96 (m, 2H), 6.88 (dd, <i>J</i> = 10.8, 16.8 Hz, 1H), 6.26 (dd, <i>J</i> = 2.0, 16.8 Hz, 1H), 6.09 (br s, 1H), 5.79 (dd, <i>J</i> = 2.0, 10.8 Hz, 1H), 4.23 (dd, <i>J</i> = 2.0, 5.6 Hz, 1H), 2.66 (dd, <i>J</i> = 3.2, 14.0 Hz, 1H), 2.09 - 1.98 (m, 1H), 1.88 - 1.74 (m, 4H), 1.74 - 1.61 (m, 2H), 1.06 - 0.96 (m, 2H), 0.81 - 0.70 (m, 2H).	X 2 nd eluting isomer
46	<i>m/z</i> (ESI ⁺): 389.1 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.41 (s, 1H), 7.94 (d, <i>J</i> = 7.2 Hz, 1H), 7.29 (dt, <i>J</i> = 1.6, 7.6 Hz, 1H), 7.02 - 6.95 (m, 2H), 6.88 (dd, <i>J</i> = 10.8, 16.8 Hz, 1H), 6.26 (dd, <i>J</i> = 1.6, 16.8 Hz, 1H), 6.09 (br s, 1H), 5.79 (dd, <i>J</i> = 1.6, 10.8 Hz, 1H), 4.32 - 4.15 (m, 1H), 2.74 - 2.60 (m, 1H), 2.12 - 1.94 (m, 1H), 1.88 - 1.74 (m, 4H), 1.74 - 1.58 (m, 2H), 1.08 - 0.96 (m, 2H), 0.80 - 0.72 (m, 2H).	X 1 st eluting isomer
47	<i>m/z</i> (ESI ⁺): 383.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 13.38 - 13.30 (m, 1H), 12.89 (s, 1H), 8.50 (s, 1H), 8.13 (d, <i>J</i> = 7.6 Hz, 1H), 7.35 - 7.28 (m, 1H), 7.02 - 6.93 (m, 2H), 6.62 (dd, <i>J</i> = 10.4, 16.8 Hz, 1H), 6.17 (td, <i>J</i> = 2.4, 16.8 Hz, 1H), 5.72 (dt, <i>J</i> = 2.4, 9.6 Hz, 1H), 4.15 (d, <i>J</i> = 10.4 Hz, 0.5H), 4.03 (d, <i>J</i> = 12.0 Hz, 1H), 3.87 (d, <i>J</i> = 12.0 Hz, 0.5H), 3.77 (dd, <i>J</i> = 5.2, 8.8 Hz, 1H), 3.61 - 3.53 (m, 1H), 2.64 - 2.55 (m, 1H), 2.45 - 2.34 (m, 1H), 1.49 (d, <i>J</i> = 11.2 Hz, 3H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
48	<i>m/z</i> (ESI ⁺): 383.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 13.40 (br s, 1H), 12.86 (br s, 1H), 8.48 (s, 1H), 8.12 (d, <i>J</i> = 7.2 Hz, 1H), 7.31 (t, <i>J</i> = 7.2 Hz, 1H), 7.02 - 6.93 (m, 2H), 6.62 (dd, <i>J</i> = 10.4, 16.8 Hz, 1H), 6.17 (d, <i>J</i> = 16.8 Hz, 1H), 5.72 (t, <i>J</i> = 9.6 Hz, 1H), 4.16 (d, <i>J</i> = 10.0 Hz, 0.5H), 4.02 (d, <i>J</i> = 11.6 Hz, 1H), 3.87 (d, <i>J</i> = 12.0 Hz, 0.5H), 3.77 (s, 1H), 3.56 (d, <i>J</i> = 5.6 Hz, 1H), 2.68 - 2.57 (m, 1H), 2.42 - 2.29 (m, 1H), 1.49 (d, <i>J</i> = 10.8 Hz, 3H).	
49	<i>m/z</i> (ESI ⁺): 375.2 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.40 (s, 1H), 7.93 (d, <i>J</i> = 7.6 Hz, 1H), 7.32 - 7.25 (m, 1H), 7.01 - 6.94 (m, 2H), 6.48 (s, 1H), 6.41 - 6.30 (m, 1H), 6.28 - 6.21 (m, 1H), 5.74 (ddd, <i>J</i> = 2.0, 5.6, 10.0 Hz, 1H), 4.30 - 4.20 (m, 2H), 4.06 - 3.96 (m, 2H), 3.54 - 3.44 (m, 1H), 2.52 (dd, <i>J</i> = 8.0, 13.2 Hz, 1H), 2.38 - 2.26 (m, 1H), 2.23 - 2.14 (m, 2H), 2.13 - 2.07 (m, 1H), 2.05 - 1.93 (m, 1H).	Y 2 nd eluting isomer
50	<i>m/z</i> (ESI ⁺): 375.2 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.40 (s, 1H), 7.93 (d, <i>J</i> = 8.0 Hz, 1H), 7.31 - 7.25 (m, 1H), 7.01 - 6.94 (m, 2H), 6.48 (s, 1H), 6.41 - 6.30 (m, 1H), 6.28 - 6.21 (m, 1H), 5.74 (ddd, <i>J</i> = 2.0, 5.2, 10.4 Hz, 1H), 4.29 - 4.21 (m, 2H), 4.06 - 3.96 (m, 2H), 3.54 - 3.45 (m, 1H), 2.52 (dd, <i>J</i> = 7.6, 13.2 Hz, 1H), 2.37 - 2.27 (m, 1H), 2.23 - 2.15 (m, 2H), 2.14 - 2.07 (m, 1H), 2.05 - 1.95 (m, 1H).	Y 1 st eluting isomer
51	<i>m/z</i> (ESI ⁺): 363.1 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.44 (s, 1H), 8.03 - 7.98 (m, 1H), 7.32 - 7.25 (m, 1H), 7.01 - 6.94 (m, 2H), 6.92 - 6.82 (m, 1H), 6.32 - 6.25 (m, 1H), 6.10 - 5.98 (m, 1H), 5.84 - 5.78 (m, 1H), 4.30 - 4.13 (m, 1H), 3.26 - 3.10 (m, 1H), 2.59 - 2.48 (m, 1H), 2.29 (s, 3H), 2.04 - 1.96 (m, 1H), 1.88 - 1.82 (m, 1H), 1.81 - 1.72 (m, 2H), 1.71 - 1.63 (m, 1H).	
52	<i>m/z</i> (ESI ⁺): 383.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 13.39 (br s, 1H), 12.81 (br s, 1H), 8.49 (s, 1H), 8.12 (d, <i>J</i> = 8.0 Hz, 1H), 7.37 - 7.26 (m, 1H), 7.02 - 6.94 (m, 2H), 6.62 (dd, <i>J</i> = 10.4, 16.8 Hz, 1H), 6.17 (td, <i>J</i> = 2.4, 16.8 Hz, 1H), 5.78 - 5.67 (m, 1H), 4.16 (d, <i>J</i> = 10.4 Hz, 0.5H), 4.03 (d, <i>J</i> = 12.0 Hz, 1H), 3.87 (d, <i>J</i> = 12.0 Hz, 0.5H), 3.77 (dd, <i>J</i> = 5.6, 8.8 Hz, 1H), 3.57 (dd, <i>J</i> = 6.0, 8.4 Hz, 1H), 2.63 - 2.54 (m, 1H), 2.44 - 2.34 (m, 1H), 1.54 - 1.47 (m, 3H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
53	<i>m/z</i> (ESI ⁺): 393.1 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.44 (s, 1H), 7.96 (d, <i>J</i> = 7.6 Hz, 1H), 7.39 - 7.20 (m, 1H), 7.06 - 6.92 (m, 2H), 6.79 - 6.59 (m, 1H), 6.37 (dd, <i>J</i> = 2.0, 16.8 Hz, 1H), 5.83 (ddd, <i>J</i> = 1.6, 5.6, 10.4 Hz, 1H), 5.65 - 5.38 (m, 1H), 4.63 - 4.31 (m, 2H), 4.30 - 4.17 (m, 1H), 4.10 - 4.00 (m, 1H), 3.98 - 3.84 (m, 1H), 1.91 (ddd, <i>J</i> = 3.2, 5.2, 8.4 Hz, 1H), 1.11 (dd, <i>J</i> = 1.6, 8.4 Hz, 2H), 0.90 - 0.69 (m, 2H).	
54	<i>m/z</i> (ESI ⁺): 367.1 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.53 (s, 1H), 8.46 (s, 1H), 8.00 (dd, <i>J</i> = 1.2, 8.4 Hz, 1H), 7.37 - 7.21 (m, 1H), 7.08 - 6.92 (m, 2H), 6.69 (ddd, <i>J</i> = 10.4, 13.6, 16.8 Hz, 1H), 6.37 (dd, <i>J</i> = 2.0, 16.8 Hz, 1H), 5.94 - 5.76 (m, 1H), 5.60 - 5.21 (m, 1H), 4.38 - 4.27 (m, 1H), 4.25 - 4.10 (m, 2H), 4.09 - 3.98 (m, 1H), 3.98 - 3.87 (m, 1H), 2.40 (d, <i>J</i> = 1.2 Hz, 3H).	
55	<i>m/z</i> (ESI ⁺): 389.1 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.55 - 8.39 (m, 1H), 7.95 (d, <i>J</i> = 7.6 Hz, 1H), 7.34 - 7.25 (m, 1H), 7.05 - 6.95 (m, 2H), 6.88 (dd, <i>J</i> = 10.8, 16.8 Hz, 1H), 6.26 (dd, <i>J</i> = 1.6, 16.8 Hz, 1H), 6.16 - 6.04 (m, 1H), 5.79 (dd, <i>J</i> = 1.6, 10.8 Hz, 1H), 4.34 - 4.14 (m, 1H), 2.75 - 2.59 (m, 1H), 2.10 - 1.97 (m, 1H), 1.90 - 1.63 (m, 6H), 1.05 - 0.97 (m, 2H), 0.80 - 0.73 (m, 2H).	
56	<i>m/z</i> (ESI ⁺): 363.1 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.44 (s, 1H), 7.94 (d, <i>J</i> = 7.6 Hz, 1H), 7.34 - 7.24 (m, 1H), 7.01 - 6.94 (m, 2H), 6.92 - 6.78 (m, 1H), 6.55 (s, 1H), 6.23 (br d, <i>J</i> = 16.8 Hz, 1H), 5.78 (br d, <i>J</i> = 10.4 Hz, 1H), 5.05 - 4.97 (m, 0.5H), 4.62 - 4.50 (m, 1H), 4.34 - 4.21 (m, 0.5H), 3.55 - 3.39 (m, 0.5H), 3.16 - 2.96 (m, 1.5H), 2.19 - 2.05 (m, 2H), 1.98 - 1.80 (m, 2H), 1.41 - 1.28 (m, 3H).	
57	<i>m/z</i> (ESI ⁺): 418.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 13.99 (br s, 1H), 12.55 (br s, 1H), 8.58 (s, 1H), 8.15 (dd, <i>J</i> = 1.2, 8.4 Hz, 1H), 7.33 - 7.26 (m, 1H), 7.00 - 6.93 (m, 2H), 6.37 (dd, <i>J</i> = 10.0, 16.4 Hz, 1H), 6.15 (dd, <i>J</i> = 1.6, 16.8 Hz, 1H), 5.71 (dd, <i>J</i> = 2.4, 10.4 Hz, 1H), 4.66 (s, 1H), 4.57 - 4.49 (m, 1H), 4.38 - 4.29 (m, 1H), 4.26 (q, <i>J</i> = 6.0 Hz, 2H), 3.23 - 3.18 (m, 2H), 2.99 - 2.89 (m, 3H), 1.78 - 1.68 (m, 3H), 1.66 - 1.55 (m, 1H), 0.91 (d, <i>J</i> = 6.4 Hz, 3H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
58	<i>m/z</i> (ESI ⁺): 360.0 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.05 (s, 1H), 12.72 (s, 1H), 8.75 - 8.60 (m, 1H), 8.17 - 8.04 (m, 1H), 7.44 - 7.25 (m, 1H), 7.09 - 6.94 (m, 2H), 6.78 - 6.64 (m, 2H), 6.41 - 6.32 (m, 1H), 6.01 - 5.88 (m, 1H), 5.15 (d, <i>J</i> = 1.6, 8.4 Hz, 1H), 4.42 - 4.30 (m, 1H), 4.21 - 4.03 (m, 1H), 3.99 - 3.87 (m, 1H), 2.83 - 2.76 (m, 1H), 2.67 - 2.60 (m, 1H).	Preparative TLC 1 st eluting isomer
59	<i>m/z</i> (ESI ⁺): 385 (M+H) ⁺		
60	<i>m/z</i> (ESI ⁺): 385 (M+H) ⁺		
61	<i>m/z</i> (ESI ⁺): 365 (M+H) ⁺	(499 MHz, d ₆ -DMSO) δ 14.09 (s, 1H), 12.51 (s, 1H), 8.54 (s, 1H), 8.01 (dd, 1H), 7.29 (td, <i>J</i> = 7.2, 1.6 Hz, 1H), 6.99 - 6.92 (m, 2H), 6.79 - 6.64 (m, 1H), 6.50 (s, 1H), 5.99 (dd, <i>J</i> = 16.7, 2.2 Hz, 1H), 5.63 (d, <i>J</i> = 10.4 Hz, 1H), 4.01 - 3.95 (m, 2H), 3.88 - 3.81 (m, 1H), 3.76 (d, <i>J</i> = 11.7 Hz, 1H), 3.64 (d, <i>J</i> = 11.6 Hz, 1H), 3.61 - 3.50 (m, 1H), 1.81 (s, 3H).	
62	<i>m/z</i> (ESI ⁺): 481 (M+H) ⁺		
63	<i>m/z</i> (ESI ⁺): 335.1 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.46 - 8.44 (m, 1H), 7.93 - 7.88 (m, 1H), 7.30 (t, <i>J</i> = 7.6 Hz, 1H), 7.01 - 6.96 (m, 2H), 6.56 - 6.52 (m, 1H), 6.34 - 6.24 (m, 2H), 5.79 - 5.58 (m, 1H), 4.99 - 4.95 (m, 0.5H), 4.84 - 4.81 (m, 0.5H), 4.22 - 4.17 (m, 1H), 4.00 (t, <i>J</i> = 6.8 Hz, 0.5H), 3.65 - 3.60 (m, 1H), 3.48 (d, <i>J</i> = 4.8 Hz, 0.5H), 3.42 - 3.34 (m, 1H), 2.63 - 2.47 (m, 1H), 2.22 - 2.09 (m, 1H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
64	<i>m/z</i> (ESI ⁺): 389.2 (M+H) ⁺	(400 MHz, CHLOROFORM- <i>d</i>) δ 13.12 - 12.55 (m, 1H), 8.35 - 8.16 (m, 1H), 7.87 - 7.69 (m, 1H), 7.41 - 7.33 (m, 1H), 7.30 (s, 0.5H), 7.24 (s, 0.5H), 7.06 - 6.96 (m, 1H), 6.45 - 6.35 (m, 2H), 6.31 - 6.20 (m, 1H), 5.66 - 5.47 (m, 1H), 3.76 (dd, <i>J</i> = 5.6, 10.4 Hz, 1H), 3.58 - 3.52 (m, 1H), 3.49 - 3.39 (m, 2H), 3.23 (dd, <i>J</i> = 4.8, 9.6 Hz, 1H), 2.68 - 2.51 (m, 1H), 2.15 - 2.09 (m, 1H), 1.97 - 1.89 (m, 1H), 1.85 - 1.79 (m, 1H), 1.58 (d, <i>J</i> = 13.2 Hz, 2H), 1.41 - 1.26 (m, 2H).	
65	<i>m/z</i> (ESI ⁺): 389.2 (M+H) ⁺	(400 MHz, CHLOROFORM- <i>d</i>) δ 13.12 - 12.68 (m, 1H), 8.36 - 8.16 (m, 1H), 7.88 - 7.71 (m, 1H), 7.41 - 7.31 (m, 1H), 7.25 - 7.15 (m, 1H), 7.06 - 6.94 (m, 1H), 6.47 - 6.31 (m, 2H), 6.30 - 6.22 (m, 1H), 5.68 - 5.43 (m, 1H), 3.78 - 3.62 (m, 1H), 3.55 (dd, <i>J</i> = 5.2, 12.4 Hz, 1H), 3.49 - 3.36 (m, 2H), 3.26 - 3.17 (m, 1H), 2.70 - 2.55 (m, 1H), 2.19 - 2.10 (m, 1H), 1.93 (ddd, <i>J</i> = 3.2, 13.6, 16.8 Hz, 1H), 1.86 - 1.80 (m, 1H), 1.67 - 1.51 (m, 2H), 1.43 - 1.24 (m, 2H).	
66	<i>m/z</i> (ESI ⁺): 365 (M+H) ⁺	(499 MHz, d ₆ -DMSO) δ 14.22 (s, 1H), 12.16 (s, 1H), 8.65 (s, 1H), 8.16 - 8.10 (m, 1H), 7.29 (td, <i>J</i> = 7.6, 1.6 Hz, 1H), 7.00 - 6.92 (m, 2H), 6.87 (dd, <i>J</i> = 16.6, 10.4 Hz, 1H), 6.21 (dd, <i>J</i> = 16.7, 2.3 Hz, 1H), 5.82 - 5.74 (m, 2H), 4.45 (d, <i>J</i> = 12.2 Hz, 1H), 4.07 (s, 1H), 3.94 (dd, <i>J</i> = 11.3, 3.5 Hz, 1H), 3.82 (dd, <i>J</i> = 12.3, 3.6 Hz, 1H), 3.57 (td, <i>J</i> = 11.3, 3.0 Hz, 1H), 2.29 (s, 2H).	
67	<i>m/z</i> (ESI ⁺): 349.2 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 13.92 (br s, 1H), 12.10 (br s, 1H), 8.44 (s, 1H), 7.96 (dd, <i>J</i> = 1.6, 8.0 Hz, 1H), 7.28 (ddd, <i>J</i> = 1.6, 7.2, 8.4 Hz, 1H), 7.02 - 6.91 (m, 2H), 6.74 - 6.54 (m, 1H), 6.42 (s, 1H), 6.05 (d, <i>J</i> = 16.8 Hz, 1H), 5.74 - 5.58 (m, 1H), 4.11 - 3.87 (m, 1H), 3.84 - 3.72 (m, 1H), 2.22 (d, <i>J</i> = 2.8 Hz, 1H), 2.16 - 2.07 (m, 1H), 2.06 - 1.93 (m, 2H), 1.90 (s, 3H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
68	<i>m/z</i> (ESI ⁺): 335.1 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.45 - 8.42 (m, 1H), 7.93 (d, <i>J</i> = 7.2 Hz, 1H), 7.31 - 7.24 (m, 1H), 7.02 - 6.94 (m, 2H), 6.53 - 6.48 (m, 1H), 6.34 - 6.22 (m, 2H), 5.79 - 5.55 (m, 1H), 4.59 (s, 1H), 4.26 - 3.93 (m, 2H), 3.66 - 3.45 (m, 1H), 3.44 - 3.34 (m, 1H), 2.64 - 2.43 (m, 1H), 2.26 - 2.07 (m, 1H).	
69	<i>m/z</i> (ESI ⁺): 375.1 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.40 (s, 1H), 7.93 (d, <i>J</i> = 7.6 Hz, 1H), 7.32 - 7.24 (m, 1H), 7.00 - 6.94 (m, 2H), 6.48 (s, 1H), 6.40 - 6.30 (m, 1H), 6.28 - 6.21 (m, 1H), 5.74 (ddd, <i>J</i> = 2.0, 5.6, 10.0 Hz, 1H), 4.30 - 4.21 (m, 2H), 4.05 - 3.96 (m, 2H), 3.55 - 3.43 (m, 1H), 2.52 (dd, <i>J</i> = 7.6, 13.2 Hz, 1H), 2.39 - 2.26 (m, 1H), 2.23 - 2.14 (m, 2H), 2.14 - 2.07 (m, 1H), 2.05 - 1.95 (m, 1H).	
70	<i>m/z</i> (ESI ⁺): 361.1 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.44 (s, 1H), 7.93 (d, <i>J</i> = 8.0 Hz, 1H), 7.35 - 7.23 (m, 1H), 7.03 - 6.94 (m, 2H), 6.89 (dd, <i>J</i> = 10.4, 16.8 Hz, 0.5H), 6.57 (d, <i>J</i> = 10.4 Hz, 0.5H), 6.53 (d, <i>J</i> = 9.2 Hz, 1H), 6.46 - 6.29 (m, 1H), 5.81 (dd, <i>J</i> = 2.0, 10.4 Hz, 1H), 4.57 (s, 1H), 3.67 (td, <i>J</i> = 2.8, 9.2 Hz, 1H), 3.52 - 3.40 (m, 2H), 2.92 - 2.81 (m, 1H), 2.26 - 2.07 (m, 2H), 1.85 - 1.76 (m, 1H), 1.75 - 1.66 (m, 1H).	Z 2 nd eluting isomer
71	<i>m/z</i> (ESI ⁺): 361.1 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.41 (s, 1H), 7.91 (d, <i>J</i> = 8.0 Hz, 1H), 7.33 - 7.24 (m, 1H), 7.01 - 6.93 (m, 2H), 6.88 (dd, <i>J</i> = 10.4, 16.8 Hz, 0.5H), 6.58 - 6.53 (m, 0.5H), 6.52 - 6.48 (m, 1H), 6.40 - 6.29 (m, 1H), 5.81 (dd, <i>J</i> = 2.0, 10.4 Hz, 1H), 4.75 (s, 1H), 3.65 (td, <i>J</i> = 2.8, 9.2 Hz, 1H), 3.51 - 3.36 (m, 2H), 2.91 - 2.80 (m, 1H), 2.24 - 2.06 (m, 2H), 1.84 - 1.72 (m, 1H), 1.72 - 1.64 (m, 1H).	Z 1 st eluting isomer
72	<i>m/z</i> (ESI ⁺): 335.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.05 (s, 1H), 12.75 (br s, 1H), 8.58 (s, 1H), 8.04 (d, <i>J</i> = 7.6 Hz, 1H), 7.29 (t, <i>J</i> = 7.6 Hz, 1H), 7.02 - 6.88 (m, 2H), 6.66 (s, 1H), 6.44 - 6.27 (m, 1H), 6.25 - 6.08 (m, 1H), 5.71 (d, <i>J</i> = 10.4 Hz, 1H), 4.76 (s, 0.5H), 4.67 - 4.57 (m, 0.5H), 4.56 - 4.49 (m, 0.5H), 4.44 - 4.36 (m, 0.5H), 4.35 - 4.26 (m, 0.5H), 4.16 - 4.06 (m, 0.5H), 3.79 - 3.68 (m, 1H), 1.66 - 1.52 (m, 3H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
73	<i>m/z</i> (ESI ⁺): 349.1 (M+H) ⁺	(400 MHz, CHLOROFORM- <i>d</i>) δ 12.13 (t, <i>J</i> = 12.0 Hz, 1H), 8.15 (s, 1H), 7.79 (d, <i>J</i> = 8.0 Hz, 1H), 7.36 - 7.28 (m, 1H), 7.12 (dd, <i>J</i> = 0.8, 8.0 Hz, 1H), 6.96 (t, <i>J</i> = 7.6 Hz, 1H), 6.47 - 6.41 (m, 1H), 6.40 - 6.32 (m, 2H), 6.22 (d, <i>J</i> = 6.8 Hz, 1H), 6.15 (dd, <i>J</i> = 10.4, 16.8 Hz, 1H), 5.76 - 5.67 (m, 1H), 4.52 - 4.45 (m, 1H), 3.44 - 3.35 (m, 1H), 2.35 (dt, <i>J</i> = 6.0, 13.6 Hz, 1H), 2.30 - 2.20 (m, 1H), 2.17 - 2.07 (m, 1H), 1.93 (td, <i>J</i> = 6.8, 13.6 Hz, 2H), 1.71 (dd, <i>J</i> = 6.4, 13.2 Hz, 1H).	
74	<i>m/z</i> (ESI ⁺): 410 (M+H) ⁺		
75	<i>m/z</i> (ESI ⁺): 401 (M+H) ⁺		
76	<i>m/z</i> (ESI ⁺): 391 (M+H) ⁺		
77	<i>m/z</i> (ESI ⁺): 431 (M+H) ⁺	(499 MHz, d ₆ -DMSO) δ 13.31 (s, 1H), 12.97 (s, 1H), 8.38 (s, 1H), 8.16 - 8.09 (m, 1H), 7.31 (ddd, <i>J</i> = 8.5, 7.1, 1.6 Hz, 1H), 7.02 - 6.93 (m, 2H), 6.86 (dd, <i>J</i> = 16.6, 10.4 Hz, 1H), 6.20 (dd, <i>J</i> = 16.7, 2.3 Hz, 1H), 5.77 (dd, <i>J</i> = 10.4, 2.3 Hz, 1H), 5.73 (s, 1H), 4.54 (d, <i>J</i> = 12.2 Hz, 1H), 4.10 (s, 1H), 3.94 (d, <i>J</i> = 8.3 Hz, 1H), 3.86 (dd, <i>J</i> = 12.3, 3.9 Hz, 1H), 3.59 (t, <i>J</i> = 10.2 Hz, 1H), 3.27 (s, 1H).	
78	<i>m/z</i> (ESI ⁺): 385 (M+H) ⁺	(499 MHz, d ₆ -DMSO) δ 13.36 (s, 1H), 8.49 (s, 1H), 8.19 - 8.08 (m, 1H), 7.31 (ddd, <i>J</i> = 8.4, 7.1, 1.6 Hz, 1H), 6.98 (pd, <i>J</i> = 7.8, 1.3 Hz, 2H), 6.87 (dd, <i>J</i> = 16.7, 10.5 Hz, 1H), 6.21 (dd, <i>J</i> = 16.7, 2.3 Hz, 1H), 5.78 (dd, <i>J</i> = 10.8, 2.5 Hz, 2H), 4.57 (d, <i>J</i> = 12.3 Hz, 1H), 4.21 - 4.00 (m, 1H), 3.92 (d, <i>J</i> = 8.2 Hz, 1H), 3.84 (dd, <i>J</i> = 12.3, 3.7 Hz, 1H), 3.58 (dt, <i>J</i> = 12.0, 6.2 Hz, 1H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
79	<i>m/z</i> (ESI ⁺): 401 (M+H) ⁺	(499 MHz, d ₆ -DMSO) δ 13.85 (d, <i>J</i> = 47.3 Hz, 1H), 8.65 (d, <i>J</i> = 34.6 Hz, 1H), 8.01 (dddd, <i>J</i> = 13.4, 8.6, 5.9, 3.2 Hz, 2H), 7.44 (t, <i>J</i> = 8.7 Hz, 1H), 7.38 – 7.23 (m, 1H), 7.04 – 6.94 (m, 2H), 6.93 – 6.73 (m, 1H), 6.28 (dt, <i>J</i> = 16.8, 1.8 Hz, 1H), 5.81 (ddd, <i>J</i> = 10.3, 5.6, 2.2 Hz, 1H), 5.37 (s, 1H), 5.12 (d, <i>J</i> = 14.0 Hz, 2H), 4.86 (s, 1H).	
80	<i>m/z</i> (ESI ⁺): 349.1 (M+H) ⁺		
81	<i>m/z</i> (ESI ⁺): 385.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 13.78 (br s, 1H), 12.67 (br s, 1H), 8.49 (s, 1H), 7.90 (d, <i>J</i> = 7.6 Hz, 1H), 7.27 - 7.19 (m, 1H), 6.94 - 6.86 (m, 3H), 6.36 (s, 1H), 6.17 (dd, <i>J</i> = 2.4, 16.8 Hz, 2H), 5.73 (br d, <i>J</i> = 9.6 Hz, 1H), 4.44 - 4.21 (m, 1H), 3.04 (s, 2H), 2.58 - 2.48 (m, 1H), 2.36 (s, 1H), 2.02 (m, 2H).	A1 2 nd eluting isomer
82	<i>m/z</i> (ESI ⁺): 385.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.12 (br s, 1H), 12.76 (br s, 1H), 8.69 (s, 1H), 8.14 (d, <i>J</i> = 8.0 Hz, 1H), 7.48 - 7.39 (m, 1H), 7.17 - 7.02 (m, 3H), 6.53 (s, 1H), 6.38 (dd, <i>J</i> = 2.4, 16.8 Hz, 1H), 5.94 (br d, <i>J</i> = 10.0 Hz, 1H), 4.84 - 4.41 (m, 1H), 3.25 (s, 2H), 2.80 - 2.68 (m, 1H), 2.61 - 2.51 (m, 1H), 2.23 (m, 2H).	A1 1 st eluting isomer
83	<i>m/z</i> (ESI ⁺): 349.2 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.45 (s, 1H), 7.92 (d, <i>J</i> = 7.6 Hz, 1H), 7.32 - 7.25 (m, 1H), 7.01 - 6.94 (m, 2H), 6.92 - 6.86 (m, 0.5H), 6.55 (s, 1H), 6.35 - 6.25 (m, 1H), 6.17 (d, <i>J</i> = 2.0 Hz, 0.5H), 5.82 (s, 1H), 4.60 (s, 1H), 4.27 - 3.93 (m, 1H), 3.21 (s, 1H), 2.52 (d, <i>J</i> = 12.4 Hz, 1H), 2.01 (s, 1H), 1.80 (s, 1H), 1.74 (d, <i>J</i> = 11.2 Hz, 1H), 1.68 - 1.51 (m, 2H).	
84	<i>m/z</i> (ESI ⁺): 349.2 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.44 (s, 1H), 7.95 - 7.90 (m, 1H), 7.31 - 7.25 (m, 1H), 7.02 - 6.94 (m, 2H), 6.92 - 6.85 (m, 0.5H), 6.53 (s, 1H), 6.30 (d, <i>J</i> = 16.8 Hz, 1H), 6.17 (s, 0.5H), 5.82 (s, 1H), 4.93 (s, 1H), 4.31 - 3.94 (m, 1H), 3.27 - 2.81 (m, 1H), 2.52 (d, <i>J</i> = 12.8 Hz, 1H), 2.00 (s, 1H), 1.79 (s, 1H), 1.72 (s, 1H), 1.68 - 1.50 (m, 2H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
85	<i>m/z</i> (ESI ⁺): 423.2 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.51 (d, <i>J</i> = 1.6 Hz, 1H), 8.07 - 7.93 (m, 1H), 7.62 (d, <i>J</i> = 3.6 Hz, 1H), 7.59 - 7.52 (m, 2H), 7.31 (t, <i>J</i> = 7.2 Hz, 1H), 7.06 - 6.94 (m, 2H), 6.84 - 6.56 (m, 1H), 6.36 (dd, <i>J</i> = 9.6, 16.4 Hz, 1H), 5.91 - 5.71 (m, 1H), 5.14 (d, <i>J</i> = 6.8 Hz, 2H), 4.96 (s, 2H), 2.08 - 1.95 (m, 1H), 0.91 (d, <i>J</i> = 3.2 Hz, 2H), 0.54 (s, 2H).	
86	<i>m/z</i> (ESI ⁺): 347.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 8.47 (d, <i>J</i> = 9.2 Hz, 1H), 8.00 (d, <i>J</i> = 6.0 Hz, 1H), 7.24 (d, <i>J</i> = 4.4 Hz, 1H), 6.92 (s, 2H), 6.78 (dd, <i>J</i> = 10.8, 16.4 Hz, 0.5H), 6.62 - 6.53 (m, 0.5H), 6.49 (d, <i>J</i> = 16.8 Hz, 1H), 6.21 (d, <i>J</i> = 16.4 Hz, 1H), 5.72 (dd, <i>J</i> = 10.4, 18.8 Hz, 1H), 4.93 - 4.74 (m, 1H), 3.95 (s, 1H), 3.77 (s, 1H), 2.42 (s, 2H), 1.91 - 1.75 (m, 2H).	
87	<i>m/z</i> (ESI ⁺): 335.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.21 - 13.88 (m, 1H), 12.83 - 12.43 (m, 1H), 8.60 - 8.51 (m, 1H), 8.05 - 7.97 (m, 1H), 7.36 - 7.25 (m, 1H), 7.02 - 6.93 (m, 2H), 6.72 (dd, <i>J</i> = 10.4, 16.8 Hz, 1H), 6.43 - 6.33 (m, 1H), 6.24 - 6.09 (m, 1H), 5.80 - 5.53 (m, 1H), 5.51 - 5.29 (m, 1H), 4.02 - 3.95 (m, 0.5H), 3.84 - 3.75 (m, 0.5H), 3.73 - 3.67 (m, 0.5H), 3.60 - 3.56 (m, 0.5H), 2.36 - 2.30 (m, 0.5H), 2.22 - 2.12 (m, 0.5H), 2.07 - 1.96 (m, 2H), 1.96 - 1.78 (m, 1H).	
88	<i>m/z</i> (ESI ⁺): 335.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.11 (s, 1H), 12.70 - 12.29 (m, 1H), 8.56 - 8.50 (m, 1H), 8.03 - 7.96 (m, 1H), 7.32 - 7.25 (m, 1H), 6.99 - 6.92 (m, 2H), 6.71 (dd, <i>J</i> = 10.4, 16.8 Hz, 0.5H), 6.41 - 6.31 (m, 1.5H), 6.18 - 6.09 (m, 1H), 5.76 - 5.51 (m, 1H), 5.48 - 5.29 (m, 1H), 4.01 - 3.94 (m, 0.5H), 3.81 - 3.74 (m, 0.5H), 3.72 - 3.64 (m, 0.5H), 3.59 - 3.54 (m, 0.5H), 2.47 - 2.38 (m, 0.5H), 2.23 - 2.11 (m, 0.5H), 2.05 - 1.97 (m, 2H), 1.95 - 1.76 (m, 1H).	
89	<i>m/z</i> (ESI ⁺): 353 (M+H) ⁺		

Cmpd #	MS	¹ H NMR	SFC Conditions
90	<i>m/z</i> (ESI ⁺): 351.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.13 (s, 1H), 12.77 (s, 1H), 8.62 (s, 1H), 8.03 (d, <i>J</i> = 7.6 Hz, 1H), 7.32 - 7.25 (m, 1H), 7.01 - 6.81 (m, 3H), 6.63 (s, 1H), 6.21 (d, <i>J</i> = 16.4 Hz, 1H), 5.81 - 5.72 (m, 1H), 4.82 (d, <i>J</i> = 8.0 Hz, 1H), 4.64 - 4.55 (m, 0.5H), 4.45 - 4.42 (m, 0.5H), 4.31 (d, <i>J</i> = 13.2 Hz, 0.5H), 4.10 - 3.93 (m, 1.5H), 3.74 - 3.61 (m, 1H), 3.47 - 3.39 (m, 1H), 3.23 - 3.16 (m, 0.5H), 3.04 - 2.94 (m, 0.5H).	
91	<i>m/z</i> (ESI ⁺): 351.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.10 (s, 1H), 12.79 (s, 1H), 8.62 (s, 1H), 8.03 (d, <i>J</i> = 7.6 Hz, 1H), 7.34 - 7.23 (m, 1H), 7.00 - 6.81 (m, 3H), 6.63 (s, 1H), 6.21 (d, <i>J</i> = 16.4 Hz, 1H), 5.82 - 5.71 (m, 1H), 4.82 (dd, <i>J</i> = 1.6, 10.0 Hz, 1H), 4.64 - 4.56 (m, 0.5H), 4.44 (d, <i>J</i> = 12.8 Hz, 0.5H), 4.31 (d, <i>J</i> = 13.6 Hz, 0.5H), 4.10 - 3.94 (m, 1.5H), 3.76 - 3.62 (m, 1H), 3.47 - 3.39 (m, 1H), 3.23 - 3.16 (m, 0.5H), 3.06 - 2.94 (m, 0.5H).	
92	<i>m/z</i> (ESI ⁺): 375.2 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 13.97 (s, 1H), 12.53 (s, 1H), 8.66 - 8.42 (m, 1H), 7.99 (d, <i>J</i> = 7.2 Hz, 1H), 7.42 - 7.22 (m, 1H), 7.00 - 6.75 (m, 3H), 6.38 (s, 1H), 6.18 (dd, <i>J</i> = 2.4, 16.8 Hz, 1H), 5.85 - 5.63 (m, 1H), 4.77 - 3.97 (m, 1H), 3.54 - 3.34 (m, 1H), 3.29 - 2.97 (m, 1H), 2.39 - 2.24 (m, 1H), 2.05 - 1.79 (m, 2H), 0.93 (d, <i>J</i> = 13.2 Hz, 1H), 0.39 - 0.23 (m, 2H), 0.18 - 0.04 (m, 2H).	
93	<i>m/z</i> (ESI ⁺): 375.2 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 13.97 (br s, 1H), 12.52 (br s, 1H), 8.60 (s, 1H), 7.99 (d, <i>J</i> = 6.8 Hz, 1H), 7.35 - 7.23 (m, 1H), 7.04 - 6.69 (m, 3H), 6.38 (s, 1H), 6.18 (dd, <i>J</i> = 2.4, 16.8 Hz, 1H), 5.85 - 5.64 (m, 1H), 4.81 - 4.02 (m, 1H), 3.54 - 3.34 (m, 1H), 3.30 - 2.98 (m, 1H), 2.31 (dd, <i>J</i> = 1.6, 8.0 Hz, 1H), 2.04 - 1.80 (m, 2H), 0.93 (d, <i>J</i> = 13.0 Hz, 1H), 0.42 - 0.23 (m, 2H), 0.19 - 0.01 (m, 2H).	
94	<i>m/z</i> (ESI ⁺): 335.1 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.48 - 8.44 (m, 1H), 7.96 - 7.92 (m, 1H), 7.31 - 7.26 (m, 1H), 7.00 - 6.90 (m, 2H), 6.63 (s, 1H), 6.43 - 6.33 (m, 1H), 6.26 - 6.20 (m, 1H), 5.73 - 5.66 (m, 1H), 2.82 - 2.74 (m, 2H), 2.68 - 2.60 (m, 2H), 2.21 - 2.10 (m, 2H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
95	<i>m/z</i> (ESI ⁺): 375.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.23 (s, 1H), 12.55 - 12.40 (m, 1H), 8.58 - 8.48 (m, 1H), 8.04 (d, <i>J</i> = 7.6 Hz, 1H), 7.36 - 7.19 (m, 1H), 7.02 - 6.89 (m, 2H), 6.67 - 6.55 (m, 2H), 6.21 (d, <i>J</i> = 2.4, 16.8 Hz, 1H), 5.70 (d, <i>J</i> = 2.4, 10.4 Hz, 1H), 4.00 (t, <i>J</i> = 5.6, 10.4 Hz, 1H), 3.55 (t, <i>J</i> = 6.4 Hz, 2H), 3.47 (d, <i>J</i> = 10.8, 12.4 Hz, 2H), 2.31 (d, <i>J</i> = 5.2, 12.8 Hz, 2H), 2.00 (t, <i>J</i> = 6.8 Hz, 2H), 1.74 (t, <i>J</i> = 6.4 Hz, 2H).	
96	<i>m/z</i> (ESI ⁺): 397.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.14 (s, 1H), 12.53 (s, 1H), 8.74 (s, 1H), 8.16 (d, <i>J</i> = 7.2 Hz, 1H), 7.65 - 7.49 (m, 3H), 7.37 - 7.23 (m, 1H), 7.07 - 6.92 (m, 2H), 6.78 - 6.58 (m, 1H), 6.30 - 6.15 (m, 1H), 5.85 - 5.63 (m, 1H), 5.09 (d, <i>J</i> = 10.8 Hz, 2H), 4.85 (s, 2H), 2.34 (s, 3H).	
97	<i>m/z</i> (ESI ⁺): 406 (M+H) ⁺		
98	<i>m/z</i> (ESI ⁺): 384 (M+H) ⁺	(499 MHz, d ₆ -DMSO) δ 8.79 - 8.59 (m, 2H), 8.06 - 7.92 (m, 2H), 7.36 - 7.25 (m, 1H), 7.05 - 6.93 (m, 2H), 6.79 (dd, <i>J</i> = 16.7, 10.3 Hz, 1H), 6.30 (dt, <i>J</i> = 16.8, 1.8 Hz, 1H), 5.82 (ddt, <i>J</i> = 16.7, 8.8, 4.4 Hz, 1H), 5.43 (s, 1H), 5.18 (d, <i>J</i> = 23.7 Hz, 1H), 5.08 (s, 1H), 4.78 (d, <i>J</i> = 14.4 Hz, 1H).	
99	<i>m/z</i> (ESI ⁺): 375 (M+H) ⁺		
100	<i>m/z</i> (ESI ⁺): 387 (M+H) ⁺		
101	<i>m/z</i> (ESI ⁺): 351 (M+H) ⁺		
102	<i>m/z</i> (ESI ⁺): 406.2 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 13.99 (s, 1H), 12.66 (s, 1H), 8.67 (s, 1H), 8.22 (d, <i>J</i> = 7.6 Hz, 1H), 7.29 (t, <i>J</i> = 7.2 Hz, 1H), 6.99 - 6.91 (m, 2H), 6.44 - 6.34 (m, 1H), 6.17 (dd, <i>J</i> = 2.0, 17.2 Hz, 1H), 5.72 (dd, <i>J</i> = 2.4, 10.4 Hz, 1H), 4.71 - 4.63 (m, 1H), 4.57 - 4.50 (m, 1H), 4.40 - 4.22 (m, 3H), 3.72 (s, 4H), 3.17 (s, 4H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
103	<i>m/z</i> (ESI ⁺): 375.2 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 13.97 (br s, 1H), 12.53 (s, 1H), 8.61 - 8.47 (m, 1H), 7.99 (d, <i>J</i> = 7.6 Hz, 1H), 7.29 (t, <i>J</i> = 7.6 Hz, 1H), 7.12 - 6.75 (m, 3H), 6.38 (s, 1H), 6.18 (dd, <i>J</i> = 2.0, 16.8 Hz, 1H), 5.74 (s, 1H), 4.71 - 3.98 (m, 1H), 3.50 (s, 1H), 3.24 - 2.94 (m, 1H), 2.31 (dd, <i>J</i> = 2.4, 6.8 Hz, 1H), 2.06 - 1.79 (m, 2H), 0.93 (d, <i>J</i> = 13.2 Hz, 1H), 0.37 - 0.22 (m, 2H), 0.19 - 0.03 (m, 2H).	
104	<i>m/z</i> (ESI ⁺): 418.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 13.98 (s, 1H), 12.54 (d, <i>J</i> = 2.0 Hz, 1H), 8.58 (s, 1H), 8.15 (d, <i>J</i> = 7.2 Hz, 1H), 7.30 (t, <i>J</i> = 7.6 Hz, 1H), 6.96 (d, <i>J</i> = 8.0 Hz, 2H), 6.43 - 6.30 (m, 1H), 6.19 - 6.10 (m, 1H), 5.76 - 5.66 (m, 1H), 4.73 - 4.59 (m, 1H), 4.58 - 4.47 (m, 1H), 4.38 - 4.22 (m, 3H), 3.22 (s, 1H), 3.01 - 2.87 (m, 3H), 1.78 - 1.68 (m, 3H), 1.66 - 1.55 (m, 1H), 1.25 - 1.13 (m, 1H), 0.91 (d, <i>J</i> = 6.4 Hz, 3H).	
105	<i>m/z</i> (ESI ⁺): 397.2 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 13.98 (s, 1H), 13.22 - 12.55 (m, 1H), 8.66 (s, 1H), 8.47 (s, 1H), 8.05 (d, <i>J</i> = 6.8 Hz, 1H), 7.50 (d, <i>J</i> = 7.2 Hz, 1H), 7.42 (t, <i>J</i> = 7.6 Hz, 1H), 7.35 - 7.25 (m, 2H), 7.02 - 6.94 (m, 2H), 6.78 (s, 1H), 6.59 - 6.52 (m, 1H), 6.30 - 6.25 (m, 1H), 5.83 - 5.70 (m, 1H), 3.78 (t, <i>J</i> = 6.8 Hz, 2H), 2.87 (t, <i>J</i> = 6.4 Hz, 2H), 1.88 (t, <i>J</i> = 6.4 Hz, 2H).	
106	<i>m/z</i> (ESI ⁺): 337.0 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.12 (s, 1H), 12.76 (d, <i>J</i> = 2.0 Hz, 1H), 9.41 (s, 1H), 8.58 (s, 1H), 8.01 (d, <i>J</i> = 7.6 Hz, 1H), 7.31 - 7.25 (m, 1H), 7.00 - 6.92 (m, 2H), 6.61 (s, 1H), 6.38 (dd, <i>J</i> = 10.4, 17.2 Hz, 1H), 6.14 (dd, <i>J</i> = 2.0, 17.2 Hz, 1H), 5.72 (dd, <i>J</i> = 1.6, 10.4 Hz, 1H), 5.02 (d, <i>J</i> = 6.8 Hz, 2H), 4.88 (d, <i>J</i> = 6.8 Hz, 2H).	
107	<i>m/z</i> (ESI ⁺): 351.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 13.95 (br s, 1H), 12.62 (br s, 1H), 8.57 (s, 1H), 8.00 (d, <i>J</i> = 7.2 Hz, 1H), 7.36 - 7.25 (m, 1H), 7.01 - 6.93 (m, 2H), 6.92 - 6.81 (m, 1H), 6.49 (s, 1H), 6.24 (dd, <i>J</i> = 2.0, 16.4 Hz, 1H), 5.78 (s, 1H), 5.75 - 5.43 (m, 1H), 4.68 - 4.47 (m, 1H), 4.39 - 4.16 (m, 0.5H), 4.13 - 3.97 (m, 0.5H), 3.93 - 3.76 (m, 2H), 3.54 - 3.47 (m, 1H), 3.20 - 3.00 (m, 1H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
108	<i>m/z</i> (ESI ⁺): 351.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 13.95 (br s, 1H), 12.62 (br s, 1H), 8.57 (s, 1H), 8.00 (d, <i>J</i> = 7.2 Hz, 1H), 7.36 - 7.25 (m, 1H), 7.01 - 6.93 (m, 2H), 6.92 - 6.81 (m, 1H), 6.49 (s, 1H), 6.24 (dd, <i>J</i> = 2.0, 16.4 Hz, 1H), 5.78 (s, 1H), 5.75 - 5.43 (m, 1H), 4.68 - 4.47 (m, 1H), 4.39 - 4.16 (m, 0.5H), 4.13 - 3.97 (m, 0.5H), 3.93 - 3.76 (m, 2H), 3.54 - 3.47 (m, 1H), 3.20 - 3.00 (m, 1H).	
109	<i>m/z</i> (ESI ⁺): 361.1 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.44 (s, 1H), 7.93 (d, <i>J</i> = 7.2 Hz, 1H), 7.32 - 7.24 (m, 1H), 7.02 - 6.94 (m, 2H), 6.89 (dd, <i>J</i> = 10.4, 16.8 Hz, 0.5H), 6.67 - 6.56 (m, 0.5H), 6.53 (d, <i>J</i> = 10.2 Hz, 1H), 6.42 - 6.30 (m, 1H), 5.81 (dd, <i>J</i> = 1.9, 10.3 Hz, 1H), 4.79 - 4.74 (m, 1H), 3.67 (td, <i>J</i> = 2.8, 9.2 Hz, 1H), 3.52 - 3.39 (m, 2H), 2.94 - 2.80 (m, 1H), 2.31 - 2.07 (m, 2H), 1.84 - 1.75 (m, 1H), 1.73 - 1.67 (m, 1H).	
110	<i>m/z</i> (ESI ⁺): 404.1 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.49 (s, 1H), 7.98 - 7.91 (m, 1H), 7.29 (dt, <i>J</i> = 1.6, 7.6 Hz, 1H), 7.04 - 6.95 (m, 2H), 6.50 - 6.39 (m, 1H), 6.37 - 6.24 (m, 1H), 5.80 (dd, <i>J</i> = 2.0, 10.4 Hz, 1H), 4.79 - 4.76 (m, 1H), 4.71 - 4.65 (m, 1H), 4.56 - 4.49 (m, 1H), 4.46 - 4.32 (m, 2H), 3.21 (t, <i>J</i> = 5.2 Hz, 4H), 1.80 - 1.62 (m, 6H).	
111	<i>m/z</i> (ESI ⁺): 419.2 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.31 - 14.14 (m, 1H), 12.92 - 12.71 (m, 1H), 8.62 (s, 1H), 8.16 (d, <i>J</i> = 8.0 Hz, 1H), 7.39 - 7.23 (m, 1H), 7.04 - 6.89 (m, 2H), 6.40 (d, <i>J</i> = 10.0, 16.8 Hz, 1H), 6.24 - 6.10 (m, 1H), 5.73 (d, <i>J</i> = 2.4, 10.0 Hz, 1H), 4.68 - 4.59 (m, 1H), 4.52 (t, <i>J</i> = 7.6 Hz, 1H), 4.44 - 4.30 (m, 2H), 4.25 - 4.18 (m, 1H), 3.84 - 3.78 (m, 2H), 3.21 (t, <i>J</i> = 11.6 Hz, 2H), 2.72 (d, <i>J</i> = 7.2 Hz, 2H), 1.79 - 1.68 (m, 1H), 1.53 - 1.43 (m, 2H), 1.33 - 1.22 (m, 2H).	
112	<i>m/z</i> (ESI ⁺): 367 (M+H) ⁺		
113	<i>m/z</i> (ESI ⁺): 349 (M+H) ⁺		

Cmpd #	MS	¹ H NMR	SFC Conditions
114	<i>m/z</i> (ESI ⁺): 349 (M+H) ⁺		
115	<i>m/z</i> (ESI ⁺): 361 (M+H) ⁺		
116	<i>m/z</i> (ESI ⁺): 361 (M+H) ⁺		
117	<i>m/z</i> (ESI ⁺): 433 (M+H) ⁺		
118	<i>m/z</i> (ESI ⁺): 349 (M+H) ⁺		
119	<i>m/z</i> (ESI ⁺): 426 (M+H) ⁺	(499 MHz, d ₆ -DMSO) δ 13.54 (s, 1H), 8.36 (d, J = 3.1 Hz, 1H), 8.12 (dd, J = 8.0, 1.6 Hz, 1H), 7.30 (ddd, J = 8.5, 7.1, 1.6 Hz, 1H), 7.04 – 6.89 (m, 2H), 6.60 (td, J = 16.4, 10.4 Hz, 1H), 6.16 (ddd, J = 16.8, 4.9, 2.3 Hz, 1H), 5.71 (ddd, J = 10.7, 8.5, 2.4 Hz, 1H), 4.24 (dd, J = 11.1, 3.4 Hz, 1H), 4.03 – 3.82 (m, 2H), 3.75 – 3.58 (m, 1H), 2.48 – 2.30 (m, 1H), 1.49 (ddd, J = 17.8, 8.5, 5.2 Hz, 1H), 1.03 (td, J = 5.1, 2.5 Hz, 1H).	
120	<i>m/z</i> (ESI ⁺): 380 (M+H) ⁺	(499 MHz, d ₆ -DMSO) δ 13.50 (s, 1H), 8.48 (d, J = 3.9 Hz, 1H), 8.23 – 8.07 (m, 1H), 7.31 (ddd, J = 8.5, 7.2, 1.6 Hz, 1H), 7.05 – 6.87 (m, 2H), 6.60 (ddd, J = 16.7, 10.4, 9.2 Hz, 1H), 6.16 (ddd, J = 16.7, 5.0, 2.3 Hz, 1H), 5.71 (ddd, J = 10.3, 6.4, 2.3 Hz, 1H), 4.26 (dd, J = 11.1, 7.1 Hz, 1H), 3.97 (dd, J = 10.4, 2.2 Hz, 1H), 3.92 – 3.82 (m, 1H), 3.77 – 3.56 (m, 1H), 2.39 (dt, J = 8.8, 4.5 Hz, 1H), 1.50 (ddd, J = 12.8, 8.5, 5.3 Hz, 1H), 1.05 (td, J = 5.1, 3.1 Hz, 1H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
121	<i>m/z</i> (ESI ⁺): 397.2 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.01 (br s, 1H), 12.65 (br s, 1H), 8.41 (s, 1H), 7.91 (t, <i>J</i> = 8.8 Hz, 1H), 7.29 - 7.21 (m, 2H), 7.20 - 7.11 (m, 3H), 7.02 (dd, <i>J</i> = 10.4, 16.4 Hz, 0.5H), 6.96 - 6.88 (m, 2H), 6.86 - 6.75 (m, 0.5H), 6.28 - 6.17 (m, 1.5H), 6.11 (s, 1H), 5.94 - 5.80 (m, 1H), 5.69 (d, <i>J</i> = 10.4 Hz, 0.5H), 5.05 - 4.88 (m, 1H), 4.80 (d, <i>J</i> = 16.4 Hz, 0.5H), 4.57 (d, <i>J</i> = 17.6 Hz, 0.5H), 3.61 - 3.37 (m, 2H).	
122	<i>m/z</i> (ESI ⁺): 397.2 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 13.98 - 13.82 (m, 1H), 12.64 (s, 1H), 8.42 (s, 1H), 7.91 (t, <i>J</i> = 7.6 Hz, 1H), 7.29 - 7.21 (m, 2H), 7.20 - 7.10 (m, 3H), 7.07 - 6.97 (m, 0.5H), 6.97 - 6.89 (m, 2H), 6.80 (dd, <i>J</i> = 11.6, 16.0 Hz, 0.5H), 6.28 - 6.17 (m, 1.5H), 6.12 (s, 1H), 5.95 - 5.79 (m, 1H), 5.73 - 5.61 (m, 0.5H), 5.10 - 4.89 (m, 1H), 4.85 - 4.73 (m, 0.5H), 4.65 - 4.50 (m, 0.5H), 3.55 - 3.35 (m, 2H).	
123	<i>m/z</i> (ESI ⁺): 349.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.08 (s, 1H), 12.62 (s, 1H), 8.56 (s, 1H), 8.01 (d, <i>J</i> = 8.0 Hz, 1H), 7.33 - 7.25 (m, 1H), 6.99 - 6.90 (m, 2H), 6.71 - 6.53 (m, 1H), 6.50 (d, <i>J</i> = 10.4 Hz, 1H), 6.16 (dd, <i>J</i> = 2.4, 16.8 Hz, 1H), 5.74 - 5.64 (m, 1H), 4.10 (d, <i>J</i> = 10.4 Hz, 0.5H), 3.92 (d, <i>J</i> = 12.0 Hz, 0.5H), 3.81 - 3.73 (m, 1H), 3.71 - 3.53 (m, 2H), 3.52 - 3.43 (m, 0.5H), 2.43 - 2.38 (m, 0.5H), 2.26 - 2.06 (m, 1H), 1.52 (d, <i>J</i> = 2.0 Hz, 3H).	
124	<i>m/z</i> (ESI ⁺): 371 (M+H) ⁺		
125	<i>m/z</i> (ESI ⁺): 429 (M+H) ⁺		
126	<i>m/z</i> (ESI ⁺): 351.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 13.95 (br s, 1H), 12.66 (br s, 1H), 8.58 (s, 1H), 7.99 (d, <i>J</i> = 7.2 Hz, 1H), 7.86 - 7.42 (m, 0.5H), 7.36 - 7.25 (m, 1H), 7.01 - 6.93 (m, 2H), 6.93 - 6.81 (m, 1H), 6.58 - 6.35 (m, 1H), 6.24 (dd, <i>J</i> = 2.4, 16.8 Hz, 1H), 5.78 (s, 1H), 5.67 - 5.50 (m, 0.5H), 4.68 - 4.50 (m, 1H), 4.40 - 3.95 (m, 1H), 3.91 - 3.79 (m, 2H), 3.56 - 3.45 (m, 1H), 3.17 - 3.02 (m, 1H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
127	<i>m/z</i> (ESI ⁺): 397.2 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 13.98 - 13.79 (m, 1H), 12.62 (s, 1H), 8.43 (d, <i>J</i> = 5.2 Hz, 1H), 7.91 (t, <i>J</i> = 7.2 Hz, 1H), 7.30 - 7.21 (m, 2H), 7.20 - 7.10 (m, 3H), 7.06 - 6.97 (m, 0.5H), 6.96 - 6.88 (m, 2H), 6.80 (dd, <i>J</i> = 10.3, 16.8 Hz, 0.5H), 6.27 - 6.17 (m, 1.5H), 6.13 (s, 1H), 5.95 - 5.80 (m, 1H), 5.74 - 5.62 (m, 0.5H), 5.08 - 4.88 (m, 1H), 4.80 (d, <i>J</i> = 15.6 Hz, 0.5H), 4.63 - 4.51 (m, 0.5H), 3.56 - 3.40 (m, 2H).	
128	<i>m/z</i> (ESI ⁺): 440.2 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 13.95 (br s, 1H), 8.73 - 8.59 (m, 1H), 8.11 - 8.00 (m, 1H), 7.97 - 7.90 (m, 1H), 7.60 - 7.48 (m, 2H), 7.31 (br t, <i>J</i> = 7.2 Hz, 1H), 6.99 (d, <i>J</i> = 8.0 Hz, 2H), 6.97 - 6.89 (m, 1H), 6.81 - 6.71 (m, 1H), 6.68 - 6.50 (m, 1H), 5.32 (s, 1H), 5.07 (s, 2H), 4.82 (s, 1H), 3.17 (br d, <i>J</i> = 5.2 Hz, 2H), 2.19 (d, <i>J</i> = 2.0 Hz, 6H).	
129	<i>m/z</i> (ESI ⁺): 360.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.51 - 13.40 (m, 1H), 8.71 (s, 1H), 8.06 - 8.00 (m, 1H), 7.30 (t, <i>J</i> = 7.6 Hz, 1H), 7.02 - 6.94 (m, 2H), 6.45 - 6.33 (m, 1H), 6.17 (dd, <i>J</i> = 2.4, 17.2 Hz, 1H), 5.73 (dd, <i>J</i> = 2.4, 10.4 Hz, 1H), 4.65 (d, <i>J</i> = 8.4 Hz, 1H), 4.57 - 4.51 (m, 1H), 4.50 - 4.42 (m, 1H), 4.39 - 4.31 (m, 1H), 4.28 - 4.21 (m, 1H), 4.18 (s, 2H).	
130	<i>m/z</i> (ESI ⁺): 365 (M+H) ⁺	(499 MHz, d ₆ -DMSO) δ 13.99 (s, 1H), 12.73 (s, 1H), 8.57 (d, <i>J</i> = 3.4 Hz, 1H), 8.00 (dt, <i>J</i> = 8.1, 1.7 Hz, 1H), 7.29 (t, <i>J</i> = 1.6 Hz, 1H), 6.99 - 6.92 (m, 2H), 6.65 (ddd, <i>J</i> = 32.0, 16.8, 10.3 Hz, 1H), 6.50 (d, <i>J</i> = 11.0 Hz, 1H), 6.19 (dt, <i>J</i> = 16.8, 2.1 Hz, 1H), 5.76 - 5.69 (m, 1H), 4.29 (ddt, <i>J</i> = 33.2, 5.3, 3.8 Hz, 1H), 4.10 - 3.98 (m, 1H), 3.96 - 3.80 (m, 2H), 3.72 (ddd, <i>J</i> = 13.1, 10.5, 5.1 Hz, 1H), 3.66 - 3.42 (m, 1H), 3.36 (d, <i>J</i> = 7.1 Hz, 3H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
131	<i>m/z</i> (ESI ⁺): 365 (M+H) ⁺	(499 MHz, d ₆ -DMSO) δ 13.99 (s, 1H), 12.73 (s, 1H), 8.57 (d, J = 3.5 Hz, 1H), 8.00 (dt, J = 8.0, 1.6 Hz, 1H), 7.29 (t, J = 1.6 Hz, 1H), 7.00 – 6.92 (m, 2H), 6.72 – 6.55 (m, 1H), 6.50 (d, J = 11.3 Hz, 1H), 6.19 (dt, J = 16.8, 2.1 Hz, 1H), 5.72 (ddd, J = 10.1, 7.1, 2.4 Hz, 1H), 4.29 (dq, J = 33.3, 4.4 Hz, 1H), 4.10 – 3.98 (m, 1H), 3.96 – 3.79 (m, 2H), 3.77 – 3.68 (m, 1H), 3.55 (ddd, J = 91.0, 12.3, 3.6 Hz, 1H), 3.36 (d, J = 6.2 Hz, 3H).	
132	<i>m/z</i> (ESI ⁺): 425 (M+H) ⁺		
133	<i>m/z</i> (ESI ⁺): 361 (M+H) ⁺		
134	<i>m/z</i> (ESI ⁺): 377 (M+H) ⁺		
135	<i>m/z</i> (ESI ⁺): 361 (M+H) ⁺		
136	<i>m/z</i> (ESI ⁺): 363.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.04 (br s, 1 H), 12.67 (br d, J=3.13 Hz, 1 H), 8.57 (s, 1 H), 8.16 (d, J=8.00 Hz, 1 H), 7.33 - 7.24 (m, 1 H), 7.00 - 6.91 (m, 2 H), 6.38 (dd, J=17.01, 10.26 Hz, 1 H), 6.16 (dd, J=17.01, 2.25 Hz, 1 H), 5.72 (dd, J=10.26, 2.25 Hz, 1 H), 4.68 - 4.61 (m, 1 H), 4.56 - 4.29 (m, 4 H), 4.20 (br dd, J=9.32, 6.82 Hz, 1 H), 1.40 (d, J=7.00 Hz, 6 H).	
137	<i>m/z</i> (ESI ⁺): 389.2 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 13.93 (br s, 1 H), 12.71 (br s, 1 H), 8.42 (s, 1 H), 8.12 - 8.07 (m, 1 H), 7.36 - 7.24 (m, 1 H), 7.04 - 6.90 (m, 2 H), 6.38 (dd, J=16.95, 10.32 Hz, 1 H), 6.16 (dd, J=17.01, 2.25 Hz, 1 H), 5.72 (dd, J=10.26, 2.25 Hz, 1 H), 4.68 - 4.61 (m, 1 H), 4.55 - 4.29 (m, 4 H), 4.20 (br dd, J=9.38, 6.75 Hz, 1 H), 2.02 - 1.83 (m, 6 H), 1.70 (br d, J=4.63 Hz, 2 H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
138	<i>m/z</i> (ESI ⁺): 405.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 13.94 (br s, 1 H), 12.79 (br s, 1 H), 8.57 (br s, 1 H), 8.17 (br d, <i>J</i> =8.00 Hz, 1 H), 7.33 - 7.24 (m, 1 H), 6.97 (br d, <i>J</i> =8.00 Hz, 2 H), 6.44 - 6.33 (m, 1 H), 6.16 (br d, <i>J</i> =17.01 Hz, 1 H), 5.72 (br d, <i>J</i> =10.13 Hz, 1 H), 4.49 (br s, 2 H) 4.67 (br s, 1 H), 4.40 - 4.32 (m, 1 H), 4.21 (br d, <i>J</i> =7.50 Hz, 1 H), 3.99 (br d, <i>J</i> =10.63 Hz, 2 H), 3.49 (br t, <i>J</i> =11.26 Hz, 2 H), 3.12 (br dd, <i>J</i> =11.88, 10.13 Hz, 1 H), 2.24 - 2.12 (m, 2 H), 1.59 (br d, <i>J</i> =12.51 Hz, 2 H).	
139	<i>m/z</i> (ESI ⁺): 446.2 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 13.91 (br s, 1H), 12.81 (br s, 1H), 8.53 (s, 1H), 8.12 (br d, <i>J</i> =7.75 Hz, 1H), 7.32-7.25 (m, 1H), 7.00-6.91 (m, 2H), 6.44-6.33 (m, 1H), 6.16 (br d, <i>J</i> =16.88 Hz, 1H), 5.72 (br d, <i>J</i> =10.38 Hz, 1H), 4.68-4.46 (m, 3H), 4.42-4.32 (m, 1H), 4.25-4.15 (m, 1H), 4.01-3.91 (m, 1H), 3.13 (br d, <i>J</i> =13.8 Hz, 2H), 3.00-2.86 (m, 1H), 2.67-2.56 (m, 1H), 2.44-2.31 (m, 1H), 2.09 (s, 3H), 1.94-1.84 (m, 1H), 1.74-1.64 (m, 2H).	
140	<i>m/z</i> (ESI ⁺): 418.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 8.56 (s, 1 H), 8.35 (br s, 2 H), 8.15 (br d, <i>J</i> =8.13 Hz, 1 H), 7.32 - 7.24 (m, 1 H), 6.99 - 6.91 (m, 2 H), 6.38 (dd, <i>J</i> =17.01, 10.26 Hz, 1 H), 6.20 - 6.11 (m, 1 H), 5.72 (dd, <i>J</i> =10.26, 2.25 Hz, 1 H), 4.70 - 4.62 (m, 1 H), 4.50 - 4.31 (m, 3 H), 4.19 (br dd, <i>J</i> =9.19, 6.44 Hz, 1 H), 2.97 (br d, <i>J</i> =9.88 Hz, 2 H), 2.86 - 2.78 (m, 1 H), 2.29 (s, 3 H), 2.23 - 2.07 (m, 4 H), 1.66 (br d, <i>J</i> =12.38 Hz, 2 H).	
141	<i>m/z</i> (ESI ⁺): 335.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.01 (br s, 1H), 12.79 (br s, 1H), 8.58 (s, 1H), 8.05 - 8.01 (m, 1H), 7.32 - 7.27 (m, 1H), 6.99 - 6.93 (m, 2H), 6.63 (s, 1H), 6.40 - 6.32 (m, 1H), 6.17 - 6.11 (m, 1H), 5.73 - 5.68 (m, 1H), 4.60 (d, <i>J</i> = 8.4 Hz, 1H), 4.29 (t, <i>J</i> = 8.8 Hz, 2H), 4.08 - 3.93 (m, 2H), 1.77 (s, 3H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
142	<i>m/z</i> (ESI ⁺): 406 (M+H) ⁺	(499 MHz, d ₆ -DMSO) δ 14.06 (s, 1H), 12.61 (s, 1H), 8.58 (d, J = 7.0 Hz, 1H), 8.03 (dt, J = 8.0, 2.0 Hz, 1H), 7.29 (ddd, J = 8.5, 7.2, 1.6 Hz, 1H), 7.11 – 6.86 (m, 2H), 6.80 – 6.62 (m, 1H), 6.34 – 6.07 (m, 2H), 5.69 (ddd, J = 44.4, 10.2, 2.4 Hz, 1H), 5.06 (dd, J = 8.6, 2.3 Hz, 1H), 4.21 (dd, J = 9.0, 7.1 Hz, 1H), 3.94 (dq, J = 23.2, 8.6 Hz, 2H), 3.78 – 3.62 (m, 1H), 3.11 (d, J = 1.6 Hz, 4H), 2.97 – 2.79 (m, 4H), 2.58 – 2.41 (m, 8H).	
143	<i>m/z</i> (ESI ⁺): 361 (M+H) ⁺		
144	<i>m/z</i> (ESI ⁺): 423 (M+H) ⁺	(499 MHz, d ₆ -DMSO) δ 13.75 (s, 1H), 8.42 (d, J = 10.9 Hz, 1H), 8.05 (t, J = 5.3 Hz, 1H), 7.59 (dt, J = 45.7, 7.5 Hz, 4H), 7.42 (t, J = 7.4 Hz, 1H), 7.28 (t, J = 7.7 Hz, 1H), 7.03 – 6.86 (m, 2H), 6.53 (ddd, J = 43.3, 16.7, 10.2 Hz, 1H), 6.13 (d, J = 16.8 Hz, 1H), 5.68 (t, J = 9.6 Hz, 1H), 4.15 (dd, J = 47.8, 11.2 Hz, 2H), 3.99 – 3.79 (m, 2H), 3.67 – 3.50 (m, 3H), 2.13 (ddt, J = 74.9, 8.5, 4.3 Hz, 1H), 1.23 – 1.10 (m, 1H), 0.87 (dt, J = 15.8, 5.1 Hz, 1H).	
145	<i>m/z</i> (ESI ⁺): 381 (M+H) ⁺	(499 MHz, d ₆ -DMSO) δ 8.44 (s, 1H), 8.17 – 8.04 (m, 1H), 7.29 (t, J = 7.8 Hz, 1H), 6.95 (dt, J = 16.1, 8.1 Hz, 2H), 6.60 (ddd, J = 16.3, 10.3, 5.7 Hz, 1H), 6.16 (dd, J = 17.1, 5.2 Hz, 1H), 5.78 – 5.64 (m, 1H), 4.26 (dd, J = 11.2, 7.2 Hz, 1H), 4.08 – 3.82 (m, 3H), 3.73 (d, J = 12.0 Hz, 1H), 3.61 (dd, J = 12.1, 4.2 Hz, 1H), 2.39 (dt, J = 8.6, 4.5 Hz, 1H), 1.51 (dq, J = 13.2, 6.3 Hz, 1H), 1.03 (t, J = 5.1 Hz, 1H).	
146	<i>m/z</i> (ESI ⁺): 426 (M+H) ⁺	(499 MHz, d ₆ -DMSO) δ 13.46 (s, 1H), 13.06 (s, 1H), 8.38 (d, J = 4.9 Hz, 1H), 8.13 (dd, J = 7.6, 1.6 Hz, 1H), 7.31 (ddd, J = 8.5, 7.1, 1.6 Hz, 1H), 7.01 – 6.93 (m, 2H), 6.60 (td, J = 17.0, 10.3 Hz, 1H), 6.16 (ddd, J = 16.7, 4.9, 2.3 Hz, 1H), 5.71 (ddd, J = 11.0, 8.9, 2.3 Hz, 1H), 4.24 (dd, J = 11.1, 3.3 Hz, 1H), 4.01 – 3.84 (m, 2H), 3.70 – 3.61 (m, 1H), 2.47 (dt, J = 8.6, 4.4 Hz, 1H), 2.33 (dt, J = 8.8, 4.5 Hz, 0H), 1.54 – 1.44 (m, 1H), 1.04 (td, J = 5.1, 3.4 Hz, 1H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
147	<i>m/z</i> (ESI ⁺): 378.1 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.65 (s, 1H), 8.50 - 8.43 (m, 1H), 8.00 (d, <i>J</i> = 7.6 Hz, 1H), 7.34 - 7.28 (m, 1H), 7.03 - 6.97 (m, 2H), 6.49 - 6.39 (m, 1H), 6.35 (d, <i>J</i> = 2.0 Hz, 1H), 5.82 (dd, <i>J</i> = 2.0, 10.0 Hz, 1H), 4.55 - 4.50 (m, 4H), 4.38 - 4.27 (m, 3H), 2.71 (s, 6H).	
148	<i>m/z</i> (ESI ⁺): 347 (M+H) ⁺	(499 MHz, d ₆ -DMSO) δ 14.16 (s, 1H), 12.43 (s, 1H), 8.52 (d, <i>J</i> = 9.0 Hz, 1H), 8.04 (ddd, <i>J</i> = 8.1, 3.9, 1.6 Hz, 1H), 7.38 - 7.20 (m, 2H), 7.02 - 6.89 (m, 2H), 6.75 - 6.54 (m, 3H), 6.25 - 6.13 (m, 1H), 5.72 (td, <i>J</i> = 10.0, 2.3 Hz, 1H), 4.31 - 4.07 (m, 2H), 4.01 - 3.77 (m, 3H), 2.36 (ddt, <i>J</i> = 37.4, 8.8, 4.5 Hz, 1H), 1.64 (q, <i>J</i> = 6.2 Hz, 1H), 1.06 (td, <i>J</i> = 5.1, 2.4 Hz, 1H).	
149	<i>m/z</i> (ESI ⁺): 353 (M+H) ⁺		
150	<i>m/z</i> (ESI ⁺): 402.2 (M+H) ⁺	(499 MHz, d ₆ -DMSO) δ 8.37 - 8.21 (m, 1H), 8.17 - 8.04 (m, 1.5H), 7.28 - 7.09 (m, 1.5H), 6.96 - 6.84 (m, 2.5H), 6.38 (dd, <i>J</i> = 10.4, 17.2 Hz, 1H), 6.14 (dd, <i>J</i> = 2.0, 17.2 Hz, 1H), 5.90 (d, <i>J</i> = 4.4 Hz, 0.5H), 5.75 - 5.66 (m, 1H), 4.68 - 4.61 (m, 1H), 4.56 (dd, <i>J</i> = 5.2, 8.4 Hz, 1H), 4.40 - 4.30 (m, 2H), 4.27 - 4.21 (m, 1H), 3.92 (s, 3H), 3.58 (s, 2H), 3.04 - 2.74 (m, 2H).	
151	<i>m/z</i> (ESI ⁺): 349.1 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.43 (d, <i>J</i> = 0.8 Hz, 1H), 8.01 (d, <i>J</i> = 8.0 Hz, 1H), 7.38 - 7.21 (m, 1H), 7.05 - 6.93 (m, 2H), 6.79 - 6.57 (m, 1H), 6.40 - 6.26 (m, 1H), 5.79 (ddd, <i>J</i> = 2.0, 10.2, 12.4 Hz, 1H), 4.22 - 4.14 (m, 0.5H), 4.13 - 4.08 (m, 0.5H), 4.07 - 3.98 (m, 1H), 3.97 - 3.88 (m, 1H), 3.84 - 3.75 (m, 1H), 3.70 - 3.56 (m, 1H), 2.53 - 2.43 (m, 1H), 2.41 (d, <i>J</i> = 1.2 Hz, 3H), 2.40 - 2.28 (m, 1H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
152	<i>m/z</i> (ESI ⁺): 389.1 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.43 (s, 1H), 7.97 (dd, <i>J</i> = 1.6, 8.4 Hz, 1H), 7.28 (dt, <i>J</i> = 1.6, 7.6 Hz, 1H), 7.02 - 6.95 (m, 2H), 6.49 - 6.39 (m, 1H), 6.35 - 6.28 (m, 1H), 5.80 (dd, <i>J</i> = 2.0, 10.0 Hz, 1H), 4.81 - 4.75 (m, 1H), 4.59 (d, <i>J</i> = 6.8 Hz, 1H), 4.56 (s, 2H), 4.35 - 4.29 (m, 1H), 2.95 (t, <i>J</i> = 7.2 Hz, 2H), 1.56 (q, <i>J</i> = 7.2 Hz, 2H), 0.71 - 0.61 (m, 1H), 0.44 - 0.38 (m, 2H), 0.05 (q, <i>J</i> = 4.8 Hz, 2H).	
153	<i>m/z</i> (ESI ⁺): 393.2 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.46 (s, 1H), 7.99 (dd, <i>J</i> = 1.6, 8.4 Hz, 1H), 7.33 - 7.25 (m, 1H), 7.01 - 6.94 (m, 2H), 6.49 - 6.39 (m, 1H), 6.36 - 6.27 (m, 1H), 5.80 (dd, <i>J</i> = 2.0, 10.4 Hz, 1H), 4.82 - 4.74 (m, 1H), 4.59 - 4.51 (m, 2H), 4.51 - 4.43 (m, 1H), 4.32 (dd, <i>J</i> = 6.4, 9.6 Hz, 1H), 3.38 (t, <i>J</i> = 6.0 Hz, 2H), 3.35 (s, 3H), 2.91 (t, <i>J</i> = 7.2 Hz, 2H), 1.90 (quin, <i>J</i> = 6.8 Hz, 2H).	
154	<i>m/z</i> (ESI ⁺): 347 (M+H) ⁺	(499 MHz, d ₆ -DMSO) δ 14.17 (s, 1H), 12.43 (s, 1H), 8.52 (d, <i>J</i> = 9.1 Hz, 1H), 8.04 (ddd, <i>J</i> = 8.1, 3.9, 1.6 Hz, 1H), 7.29 (ddt, <i>J</i> = 8.4, 7.1, 1.4 Hz, 1H), 7.04 - 6.83 (m, 2H), 6.64 - 6.52 (m, 2H), 6.18 (dt, <i>J</i> = 16.8, 1.9 Hz, 1H), 5.72 (td, <i>J</i> = 10.0, 2.4 Hz, 1H), 4.37 - 4.06 (m, 2H), 3.99 - 3.73 (m, 3H), 2.35 (ddd, <i>J</i> = 37.4, 8.5, 4.4 Hz, 1H), 1.76 - 1.56 (m, 1H), 1.06 (td, <i>J</i> = 5.1, 2.3 Hz, 1H).	
155	<i>m/z</i> (ESI ⁺): 349 (M+H) ⁺		
156	<i>m/z</i> (ESI ⁺): 446.2 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.64 (s, 1H), 8.02 (dd, <i>J</i> = 1.6, 8.0 Hz, 1H), 7.34 - 7.27 (m, 1H), 7.08 - 6.97 (m, 2H), 6.52 - 6.40 (m, 1H), 6.38 - 6.30 (m, 1H), 5.82 (dd, <i>J</i> = 2.4, 10.4 Hz, 1H), 4.56 (dd, <i>J</i> = 2.4, 9.2 Hz, 4H), 4.36 - 4.29 (m, 1H), 3.00 - 2.88 (m, 1H), 2.75 (s, 1H), 2.52 - 2.36 (m, 2H), 2.21 (d, <i>J</i> = 13.6 Hz, 2H), 1.86 - 1.74 (m, 2H), 1.68 (d, <i>J</i> = 12.8 Hz, 2H).	Preparative TLC 2 nd eluting isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
157	<i>m/z</i> (ESI ⁺): 446.2 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.45 (s, 1H), 7.95 (dd, <i>J</i> = 1.6, 8.4 Hz, 1H), 7.34 - 7.25 (m, 1H), 7.03 - 6.95 (m, 2H), 6.49 - 6.39 (m, 1H), 6.36 - 6.27 (m, 1H), 5.80 (dd, <i>J</i> = 2.0, 10.4 Hz, 1H), 4.78 (s, 1H), 4.60 - 4.48 (m, 3H), 4.36 - 4.27 (m, 1H), 2.99 - 2.84 (m, 1H), 2.57 - 2.45 (m, 1H), 2.12 - 1.97 (m, 4H), 1.96 - 1.87 (m, 2H), 1.77 - 1.62 (m, 2H).	Preparative TLC 1 st eluting isomer
158	<i>m/z</i> (ESI ⁺): 361 (M+H) ⁺		
159	<i>m/z</i> (ESI ⁺): 335 (M+H) ⁺		
160	<i>m/z</i> (ESI ⁺): 375 (M+H) ⁺		
161	<i>m/z</i> (ESI ⁺): 403.2 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 13.92 - 12.91 (m, 2H), 8.38 (s, 1H), 8.07 (d, <i>J</i> = 8.0 Hz, 1H), 7.30 (t, <i>J</i> = 7.6 Hz, 1H), 7.04 - 6.91 (m, 2H), 6.46 - 6.31 (m, 1H), 6.22 - 6.09 (m, 1H), 5.72 (dd, <i>J</i> = 2.0, 10.4 Hz, 1H), 5.45 (s, 1H), 4.76 - 4.67 (m, 1H), 4.64 - 4.56 (m, 1H), 4.41 - 4.28 (m, 3H), 1.52 (s, 6H).	
162	<i>m/z</i> (ESI ⁺): 359.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 13.73 (br s, 1H), 13.13 (br s, 1H), 8.44 (s, 1H), 8.12 (d, <i>J</i> = 8.0 Hz, 1H), 7.30 (t, <i>J</i> = 7.6 Hz, 1H), 7.01 - 6.91 (m, 2H), 6.46 - 6.33 (m, 1H), 6.22 - 6.10 (m, 1H), 5.76 - 5.67 (m, 1H), 4.75 - 4.66 (m, 1H), 4.61 - 4.54 (m, 1H), 4.41 - 4.26 (m, 3H), 2.13 (s, 3H).	
163	<i>m/z</i> (ESI ⁺): 375.1 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.45 (s, 1H), 7.97 (d, <i>J</i> = 8.0 Hz, 1H), 7.31 (t, <i>J</i> = 7.2 Hz, 1H), 7.04 - 6.94 (m, 2H), 6.48 - 6.38 (m, 1H), 6.36 - 6.27 (m, 1H), 5.81 (dd, <i>J</i> = 2.0, 10.0 Hz, 1H), 4.83 - 4.80 (m, 2H), 4.76 - 4.68 (m, 1H), 4.62 - 4.54 (m, 2H), 4.53 - 4.49 (m, 1H), 4.47 - 4.39 (m, 1H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
164	<i>m/z</i> (ESI ⁺): 385.1 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.37 (s, 1H), 7.97 (d, <i>J</i> = 7.2 Hz, 1H), 7.35 - 7.23 (m, 1H), 7.04 - 6.93 (m, 2H), 6.50 - 6.37 (m, 1H), 6.36 - 6.27 (m, 1H), 5.81 (dd, <i>J</i> = 2.0, 10.0 Hz, 1H), 4.79 - 4.72 (m, 2H), 4.56 - 4.48 (m, 2H), 4.44 - 4.28 (m, 1H), 1.57 (tt, <i>J</i> = 5.2, 8.4 Hz, 1H), 0.97 - 0.87 (m, 2H), 0.86 - 0.74 (m, 2H).	
165	<i>m/z</i> (ESI ⁺): 353 (M+H) ⁺		
166	<i>m/z</i> (ESI ⁺): 349 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.13 (br s, 1H), 12.63 (br s, 1H), 8.57 (s, 1H), 8.03 (d, <i>J</i> = 7.92 Hz, 1H), 7.29 (t, <i>J</i> = 7.48 Hz, 1H), 7.06-6.75 (m, 3H), 6.51 (s, 1H), 6.13 (dd, <i>J</i> = 16.64, 2.04 Hz, 1H), 5.70 (br d, <i>J</i> = 10.76 Hz, 1H), 4.62-3.93 (m, 2H), 3.22-2.76 (m, 3H), 2.27-2.12 (m, 1H), 1.95-1.74 (m, 2H), 1.57-1.47 (m, 1H).	Y 1 st eluting isomer
167	<i>m/z</i> (ESI ⁺): 349 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.12 (br s, 1H), 13.02 (br s, 1H), 8.57 (s, 1H), 8.02 (d, <i>J</i> = 7.92 Hz, 1H), 7.29 (t, <i>J</i> = 7.67 Hz, 1H), 7.07-6.76 (m, 3H), 6.50 (s, 1H), 6.13 (dd, <i>J</i> = 16.70, 1.98 Hz, 1H), 5.70 (br d, <i>J</i> = 10.76 Hz, 1H), 4.58-3.94 (m, 2H), 3.23-2.77 (m, 3H), 2.26-2.13 (m, 1H), 1.97-1.74 (m, 2H), 1.52 (br d, <i>J</i> = 1.24 Hz, 1H).	Y 2 nd eluting isomer
168	<i>m/z</i> (ESI ⁺): 363 (M+H) ⁺		
169	<i>m/z</i> (ESI ⁺): 349 (M+H) ⁺	(499 MHz, d ₆ -DMSO) δ 14.22 (s, 1H), 12.70 (s, 1H), 8.62 (s, 1H), 8.19 - 8.07 (m, 1H), 7.37 - 7.23 (m, 1H), 7.05 - 6.92 (m, 2H), 6.45 - 6.33 (m, 1H), 6.22 - 6.12 (m, 1H), 5.78 - 5.65 (m, 1H), 4.65 (t, <i>J</i> = 8.5 Hz, 1H), 4.55 - 4.45 (m, 1H), 4.44 - 4.28 (m, 3H), 4.20 (dd, <i>J</i> = 8.8, 6.0 Hz, 1H), 2.78 (q, <i>J</i> = 7.5 Hz, 2H), 1.18 (t, <i>J</i> = 7.5 Hz, 3H).	
170	<i>m/z</i> (ESI ⁺): 447 (M+H) ⁺		

Cmpd #	MS	¹ H NMR	SFC Conditions
171	<i>m/z</i> (ESI ⁺): 349.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.15 (br s, 1H), 12.76-12.40 (m, 1H), 8.57 (s, 1H), 8.03 (d, <i>J</i> =7.13 Hz, 1H), 7.33-7.25 (m, 1H), 7.05-6.82 (m, 3H), 6.50 (s, 1H), 6.14 (dd, <i>J</i> =16.63, 2.38 Hz, 1H), 5.70 (dd, <i>J</i> =10.38, 1.88 Hz, 1H), 4.65-3.93 (m, 2H), 3.25-2.76 (m, 3H), 2.26-2.13 (m, 1H), 1.98-1.74 (m, 2H), 1.53 (br d, <i>J</i> =7.38 Hz, 1H).	
172	<i>m/z</i> (ESI ⁺): 321.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.35 (br s, 1H), 12.01 (br s, 1H), 9.02 (s, 1H), 8.44 (s, 1H), 7.97 (br d, <i>J</i> =7.75 Hz, 1H), 7.30-7.22 (m, 1H), 6.99-6.89 (m, 2H), 6.36-6.24 (m, 2H), 6.19-6.11 (m, 1H), 5.67 (dd, <i>J</i> =10.19, 1.94 Hz, 1H), 1.63-1.56 (m, 2H), 1.39-1.32 (m, 2H).	
173	<i>m/z</i> (ESI ⁺): 411.2 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.10 (s, 1H), 12.87 (s, 1H), 8.54 (s, 1H), 8.02 (d, <i>J</i> = 7.2 Hz, 1H), 7.28 (s, 1H), 7.27 (d, <i>J</i> = 4.4 Hz, 4H), 7.20 - 7.13 (m, 1H), 6.99 - 6.92 (m, 2H), 6.36 (dd, <i>J</i> = 10.4, 16.8 Hz, 1H), 6.15 (dd, <i>J</i> = 2.4, 17.2 Hz, 1H), 5.71 (dd, <i>J</i> = 2.4, 10.4 Hz, 1H), 4.62 - 4.54 (m, 1H), 4.54 - 4.43 (m, 2H), 4.29 - 4.20 (m, 1H), 4.20 - 4.12 (m, 3H).	
174	<i>m/z</i> (ESI ⁺): 411.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 8.29 (d, <i>J</i> = 2.0 Hz, 1H), 7.87 - 7.84 (m, 1H), 7.60 - 7.52 (m, 4H), 7.48 - 7.42 (m, 1H), 7.27 (t, <i>J</i> = 7.6 Hz, 1H), 7.00 - 6.92 (m, 2H), 6.67 - 6.59 (m, 1H), 6.33 - 6.27 (m, 1H), 5.77 (d, <i>J</i> = 1.6 Hz, 1H), 4.20 - 4.12 (m, 1H), 4.12 - 4.05 (m, 1H), 3.94 (d, <i>J</i> = 10.0 Hz, 0.5H), 3.91 - 3.84 (m, 0.5H), 3.76 - 3.67 (m, 1H), 3.58 - 3.46 (m, 1H), 2.51 - 2.45 (m, 1H), 2.44 - 2.37 (m, 1H).	
175	<i>m/z</i> (ESI ⁺): 349.1 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.43 (s, 1H), 8.00 (d, <i>J</i> = 7.6 Hz, 1H), 7.28 (t, <i>J</i> = 7.2 Hz, 1H), 7.04 - 6.93 (m, 2H), 6.67 (dt, <i>J</i> = 10.4, 16.0 Hz, 1H), 6.37 - 6.27 (m, 1H), 5.85 - 5.73 (m, 1H), 4.23 - 4.14 (m, 0.5H), 4.09 (dd, <i>J</i> = 8.0, 12.0 Hz, 0.5H), 4.05 - 3.98 (m, 1H), 3.97 - 3.86 (m, 1H), 3.83 - 3.74 (m, 1H), 3.69 - 3.56 (m, 1H), 2.54 - 2.43 (m, 1H), 2.40 (s, 3H), 2.38 - 2.27 (m, 1H).	
176	<i>m/z</i> (ESI ⁺): 387 (M+H) ⁺		

Cmpd #	MS	¹ H NMR	SFC Conditions
177	<i>m/z</i> (ESI ⁺): 349 (M+H) ⁺		
178	<i>m/z</i> (ESI ⁺): 349 (M+H) ⁺		
179	<i>m/z</i> (ESI ⁺): 411.1 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.29 (d, <i>J</i> = 2.4 Hz, 1H), 7.91 - 7.82 (m, 1H), 7.62 - 7.51 (m, 4H), 7.45 (dd, <i>J</i> = 1.2, 6.8 Hz, 1H), 7.27 (t, <i>J</i> = 7.6 Hz, 1H), 7.01 - 6.89 (m, 2H), 6.62 (dt, <i>J</i> = 10.4, 17.2 Hz, 1H), 6.30 (ddd, <i>J</i> = 1.6, 4.4, 16.8 Hz, 1H), 5.82 - 5.70 (m, 1H), 4.20 - 4.05 (m, 1H), 4.04 - 3.95 (m, 1H), 3.95 - 3.91 (m, 0.5H), 3.90 - 3.82 (m, 0.5H), 3.76 - 3.65 (m, 1H), 3.62 - 3.40 (m, 1H), 2.54 - 2.45 (m, 1H), 2.44 - 2.30 (m, 1H).	
180	<i>m/z</i> (ESI ⁺): 458.2 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.06 (br s, 1H), 12.62 (s, 1H), 8.57 (d, <i>J</i> = 6.8 Hz, 1H), 8.02 (d, <i>J</i> = 7.2 Hz, 1H), 7.29 (t, <i>J</i> = 7.6 Hz, 1H), 7.06 - 6.88 (m, 2H), 6.72 - 6.56 (m, 1H), 6.54 - 6.48 (m, 1H), 6.38 (dd, <i>J</i> = 7.6, 15.2 Hz, 1H), 4.14 - 4.05 (m, 0.5H), 4.01 - 3.93 (m, 0.5H), 3.80 - 3.73 (m, 1H), 3.70 - 3.64 (m, 1H), 3.62 - 3.53 (m, 1H), 3.51 - 3.40 (m, 1H), 3.22 (d, <i>J</i> = 2.4 Hz, 2H), 2.88 - 2.77 (m, 2H), 2.70 - 2.58 (m, 2H), 2.45 - 2.31 (m, 1H), 2.30 - 2.22 (m, 0.5H), 2.20 - 2.05 (m, 0.5H), 1.26 - 1.14 (m, 5H), 0.95 (d, <i>J</i> = 4.0 Hz, 3H).	
181	<i>m/z</i> (ESI ⁺): 458.2 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.06 (br s, 1H), 12.62 (br s, 1H), 8.65 - 8.51 (m, 1H), 8.06 - 7.95 (m, 1H), 7.29 (t, <i>J</i> = 7.6 Hz, 1H), 7.02 - 6.87 (m, 2H), 6.69 - 6.58 (m, 1H), 6.52 (d, <i>J</i> = 7.6 Hz, 1H), 6.38 (dd, <i>J</i> = 7.6, 15.2 Hz, 1H), 4.15 - 4.04 (m, 0.5H), 3.98 (dd, <i>J</i> = 7.2, 11.6 Hz, 0.5H), 3.83 - 3.73 (m, 1H), 3.71 - 3.64 (m, 1H), 3.63 - 3.51 (m, 1H), 3.49 - 3.41 (m, 1H), 3.23 - 3.16 (m, 2H), 2.83 (t, <i>J</i> = 8.8 Hz, 2H), 2.65 - 2.57 (m, 2H), 2.43 - 2.30 (m, 1H), 2.29 - 2.22 (m, 0.5H), 2.21 - 2.10 (m, 0.5H), 1.23 - 1.18 (m, 5H), 0.96 (d, <i>J</i> = 4.0 Hz, 3H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
182	<i>m/z</i> (ESI ⁺): 520.2 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 13.86 (br s, 1H), 13.13 (br s, 1H), 8.41 (s, 1H), 8.08 - 8.02 (m, 1H), 7.57 - 7.53 (m, 2H), 7.53 - 7.50 (m, 2H), 7.45 - 7.38 (m, 1H), 7.32 - 7.24 (m, 1H), 6.99 - 6.89 (m, 2H), 6.61 (td, <i>J</i> = 6.0, 15.6 Hz, 1H), 6.14 (d, <i>J</i> = 15.6 Hz, 1H), 4.65 - 4.56 (m, 1H), 4.54 - 4.47 (m, 1H), 4.45 - 4.36 (m, 1H), 4.36 - 4.29 (m, 1H), 4.22 - 4.13 (m, 1H), 3.10 - 3.04 (m, 2H), 2.62 (d, <i>J</i> = 8.4 Hz, 2H), 2.10 (s, 2H), 2.04 (d, <i>J</i> = 10.4 Hz, 2H), 1.65 - 1.58 (m, 2H), 1.57 - 1.50 (m, 2H), 1.47 - 1.38 (m, 1H), 1.30 (d, <i>J</i> = 10.8 Hz, 1H).	
183	<i>m/z</i> (ESI ⁺): 482.2 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 13.71 (br s, 1H), 13.18 (br s, 1H), 8.43 (s, 1H), 8.13 (s, 1H), 8.05 (d, <i>J</i> = 7.2 Hz, 1H), 7.58 - 7.54 (m, 2H), 7.54 - 7.50 (m, 2H), 7.46 - 7.40 (m, 1H), 7.32 - 7.26 (m, 1H), 7.01 - 6.90 (m, 2H), 6.65 (td, <i>J</i> = 6.4, 15.2 Hz, 1H), 6.22 (d, <i>J</i> = 15.6 Hz, 1H), 4.67 - 4.58 (m, 1H), 4.50 (t, <i>J</i> = 7.6 Hz, 1H), 4.47 - 4.38 (m, 1H), 4.37 - 4.31 (m, 1H), 4.19 (dd, <i>J</i> = 7.2, 9.2 Hz, 1H), 3.40 (d, <i>J</i> = 4.4 Hz, 2H), 2.59 (d, <i>J</i> = 4.0 Hz, 4H), 1.01 (t, <i>J</i> = 7.2 Hz, 6H).	
184	<i>m/z</i> (ESI ⁺): 339.1 (M+H) ⁺		
185	<i>m/z</i> (ESI ⁺): 415.2 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.56 (br s, 1H), 13.26 (br s, 1H), 8.46 (s, 1H), 7.92 (d, <i>J</i> = 8.0 Hz, 1H), 7.58 - 7.54 (m, 2H), 7.51 (s, 2H), 7.46 - 7.40 (m, 1H), 7.28 - 7.21 (m, 1H), 6.89 (dt, <i>J</i> = 5.2, 8.0 Hz, 1H), 6.39 - 6.30 (m, 1H), 6.19 - 6.10 (m, 1H), 5.71 (dd, <i>J</i> = 2.4, 10.4 Hz, 1H), 4.69 - 4.62 (m, 1H), 4.53 (t, <i>J</i> = 7.6 Hz, 1H), 4.48 - 4.38 (m, 1H), 4.38 - 4.32 (m, 1H), 4.25 - 4.18 (m, 1H).	
186	<i>m/z</i> (ESI ⁺): 361.1 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.49 (s, 2H), 8.42 (s, 1H), 7.93 (dd, <i>J</i> = 1.2, 8.0 Hz, 1H), 7.35 - 7.24 (m, 1H), 7.02 - 6.93 (m, 2H), 6.51 (s, 1H), 6.24 (d, <i>J</i> = 3.2 Hz, 1H), 5.69 (dd, <i>J</i> = 2.8, 9.2 Hz, 1H), 4.05 (s, 3H), 2.68 (s, 6H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
187	<i>m/z</i> (ESI ⁺): 383.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.02 - 13.86 (m, 1H), 13.11 - 12.94 (m, 1H), 8.78 - 8.64 (m, 1H), 8.08 (d, <i>J</i> = 2.0, 5.9 Hz, 1H), 7.99 (d, <i>J</i> = 7.2 Hz, 1H), 7.65 - 7.52 (m, 2H), 7.39 - 7.30 (m, 1H), 7.07 - 6.97 (m, 2H), 6.96 (s, 1H), 6.95 - 6.71 (m, 1H), 6.26 (s, 1H), 5.84 (d, <i>J</i> = 10.8 Hz, 1H), 5.39 (s, 1H), 5.13 (s, 2H), 4.87 (s, 1H).	
188	<i>m/z</i> (ESI ⁺): 389.2 (M+H) ⁺		
189	<i>m/z</i> (ESI ⁺): 347 (M+H) ⁺		
190	<i>m/z</i> (ESI ⁺): 349 (M+H) ⁺		
191	<i>m/z</i> (ESI ⁺): 401 (M+H) ⁺		
192	<i>m/z</i> (ESI ⁺): 401 (M+H) ⁺		
193	<i>m/z</i> (ESI ⁺): 349 (M+H) ⁺		
194	<i>m/z</i> (ESI ⁺): 415 (M+H) ⁺		
195	<i>m/z</i> (ESI ⁺): 397.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.10 (br s, 1H), 12.96 (br s, 1H), 8.61 - 8.50 (m, 1H), 8.06 (d, <i>J</i> = 7.6 Hz, 1H), 8.01 - 7.92 (m, 2H), 7.46 - 7.35 (m, 1H), 7.30 (t, <i>J</i> = 8.0 Hz, 1H), 7.12 (s, 1H), 7.00 - 6.95 (m, 2H), 6.95 - 6.87 (m, 1H), 6.17 (dd, <i>J</i> = 2.0, 16.4 Hz, 1H), 5.79 - 5.70 (m, 1H), 4.89 - 4.74 (m, 2H), 3.91 - 3.78 (m, 2H), 3.00 - 2.90 (m, 2H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
196	<i>m/z</i> (ESI ⁺): 383.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.18 - 13.78 (m, 1H), 8.63 (s, 1H), 8.42 (s, 4H), 8.38 - 8.29 (m, 1H), 8.04 (d, <i>J</i> = 7.6 Hz, 1H), 7.64 (d, <i>J</i> = 7.6 Hz, 1H), 7.43 (t, <i>J</i> = 8.0 Hz, 1H), 7.30 (t, <i>J</i> = 7.6 Hz, 1H), 6.98 (d, <i>J</i> = 8.0 Hz, 2H), 6.91 (s, 1H), 6.81 (dd, <i>J</i> = 10.4, 16.8 Hz, 1H), 6.34 (dd, <i>J</i> = 1.6, 16.8 Hz, 1H), 5.86 (dd, <i>J</i> = 2.0, 10.0 Hz, 1H), 4.33 (s, 2H), 3.54 (s, 2H).	
197	<i>m/z</i> (ESI ⁺): 383.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.37 - 13.66 (m, 1H), 13.41 - 12.67 (m, 1H), 8.82 (d, <i>J</i> = 1.6 Hz, 1H), 8.60 (s, 1H), 8.04 (d, <i>J</i> = 7.2 Hz, 1H), 7.77 (dd, <i>J</i> = 1.2, 7.6 Hz, 1H), 7.46 (d, <i>J</i> = 8.0 Hz, 1H), 7.35 - 7.25 (m, 1H), 7.07 - 6.92 (m, 3H), 6.90 - 6.70 (m, 1H), 6.37 (dd, <i>J</i> = 2.0, 16.4 Hz, 1H), 5.89 (dd, <i>J</i> = 1.6, 10.2 Hz, 1H), 4.30 (t, <i>J</i> = 8.4 Hz, 2H), 4.03 (s, 2H).	
198	<i>m/z</i> (ESI ⁺): 363 (M+H) ⁺		
199	<i>m/z</i> (ESI ⁺): 335 (M+H) ⁺		
200	<i>m/z</i> (ESI ⁺): 399 (M+H) ⁺		
201	<i>m/z</i> (ESI ⁺): 398 (M+H) ⁺		
202	<i>m/z</i> (ESI ⁺): 453 (M+H) ⁺		
203	<i>m/z</i> (ESI ⁺): 401 (M+H) ⁺		
204	<i>m/z</i> (ESI ⁺): 427 (M+H) ⁺		

Cmpd #	MS	¹ H NMR	SFC Conditions
205	<i>m/z</i> (ESI ⁺): 362.2 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 12.90 (s, 1H), 10.61 - 10.42 (m, 1H), 8.65 (s, 1H), 7.87 (d, <i>J</i> = 8.0 Hz, 1H), 7.27 (dd, <i>J</i> = 8.4, 10.8 Hz, 1H), 6.94 (dt, <i>J</i> = 5.2, 8.0 Hz, 1H), 6.73 (s, 1H), 6.61 - 6.40 (m, 2H), 4.72 - 4.65 (m, 1H), 4.48 - 4.36 (m, 2H), 4.29 - 4.16 (m, 2H), 4.00 - 3.89 (m, 2H), 3.78 (dt, <i>J</i> = 2.8, 6.4 Hz, 2H), 2.76 - 2.69 (m, 2H), 1.79 - 1.73 (m, 2H), 1.15 - 1.11 (m, 3H), 1.05 - 1.03 (m, 3H).	
206	<i>m/z</i> (ESI ⁺): 345.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 13.61 (br s, 1H), 13.04 (br s, 1H), 8.62 (s, 1H), 8.07 - 7.97 (m, 1H), 7.35 - 7.26 (m, 1H), 7.04 - 6.92 (m, 2H), 6.89 (s, 1H), 6.42 - 6.27 (m, 1H), 6.15 (dd, <i>J</i> = 2.2, 16.8 Hz, 1H), 5.73 (dd, <i>J</i> = 2.2, 10.4 Hz, 1H), 4.63 (t, <i>J</i> = 8.8 Hz, 1H), 4.39 - 4.29 (m, 2H), 4.07 - 3.86 (m, 2H).	
207	<i>m/z</i> (ESI ⁺): 397.1 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.54 (s, 1H), 7.97 (d, <i>J</i> = 7.2 Hz, 1H), 7.59 - 7.54 (m, 1H), 7.46 - 7.37 (m, 2H), 7.33 - 7.28 (m, 1H), 7.18 (s, 1H), 7.02 - 6.97 (m, 2H), 6.93 - 6.83 (m, 1H), 6.74 (s, 1H), 6.33 - 6.26 (m, 1H), 5.85 - 5.76 (m, 1H), 4.94 (s, 1H), 4.77 (d, <i>J</i> = 18.4 Hz, 1H), 3.87 - 3.82 (m, 2H), 3.18 - 3.04 (m, 2H).	
208	<i>m/z</i> (ESI ⁺): 397.1 (M+H) ⁺		
209	<i>m/z</i> (ESI ⁺): 375.1 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.39 (s, 1H), 7.95 - 7.91 (m, 1H), 7.32 - 7.24 (m, 1H), 7.01 - 6.93 (m, 2H), 6.63 (dd, <i>J</i> = 10.4, 16.8 Hz, 1H), 6.48 (s, 1H), 6.26 (dd, <i>J</i> = 2.0, 16.8 Hz, 1H), 5.74 (dd, <i>J</i> = 2.0, 10.4 Hz, 1H), 3.85 (dd, <i>J</i> = 8.0, 11.2 Hz, 1H), 3.74 - 3.60 (m, 3H), 3.55 - 3.47 (m, 1H), 3.07 - 2.88 (m, 2H), 2.56 (td, <i>J</i> = 7.6, 12.8 Hz, 2H), 1.85 - 1.72 (m, 2H).	
210	<i>m/z</i> (ESI ⁺): 397.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.06 - 13.80 (m, 1H), 13.07 - 12.71 (m, 1H), 8.71 (s, 1H), 8.07 (d, <i>J</i> = 7.6 Hz, 1H), 7.55 (d, <i>J</i> = 6.0 Hz, 1H), 7.46 - 7.37 (m, 2H), 7.31 (s, 1H), 7.22 - 7.14 (m, 1H), 7.02 - 6.95 (m, 2H), 6.81 (s, 1H), 6.18 - 6.03 (m, 1H), 5.76 - 5.56 (m, 1H), 4.97 - 4.86 (m, 2H), 3.85 (t, <i>J</i> = 5.6 Hz, 2H), 3.01 (s, 2H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
211	<i>m/z</i> (ESI ⁺): 392.2 (M+H) ⁺		
212	<i>m/z</i> (ESI ⁺): 361.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 13.98 (s, 1H), 13.07 - 12.38 (m, 1H), 8.39 (s, 1H), 8.09 (d, <i>J</i> = 7.2 Hz, 1H), 7.30 (s, 1H), 7.00 - 6.93 (m, 2H), 6.39 (dd, <i>J</i> = 10.0, 17.2 Hz, 1H), 6.17 (dd, <i>J</i> = 2.0, 16.8 Hz, 1H), 5.73 (dd, <i>J</i> = 2.4, 10.2 Hz, 1H), 4.75 - 4.64 (m, 1H), 4.59 - 4.45 (m, 2H), 4.38 (t, <i>J</i> = 9.2 Hz, 1H), 4.28 - 4.21 (m, 1H), 1.90 - 1.80 (m, 1H), 1.03 - 0.93 (m, 2H), 0.77 - 0.67 (m, 2H).	
213	<i>m/z</i> (ESI ⁺): 398 (M+H) ⁺		
214	<i>m/z</i> (ESI ⁺): 427 (M+H) ⁺		
215	<i>m/z</i> (ESI ⁺): 427 (M+H) ⁺		
216	<i>m/z</i> (ESI ⁺): 335.1 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.56 (s, 1H), 7.64 (dd, <i>J</i> = 1.6, 7.6 Hz, 1H), 7.49 (dt, <i>J</i> = 1.6, 8.0 Hz, 1H), 7.15 - 7.07 (m, 2H), 6.49 - 6.39 (m, 1H), 6.36 - 6.28 (m, 1H), 5.82 (dd, <i>J</i> = 2.4, 10.4 Hz, 1H), 4.66 - 4.57 (m, 3H), 4.57 - 4.52 (m, 1H), 4.40 - 4.33 (m, 1H), 2.42 (s, 3H).	
217	<i>m/z</i> (ESI ⁺): 347.1 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.42 (s, 1H), 7.93 (d, <i>J</i> = 8.4 Hz, 1H), 7.28 (t, <i>J</i> = 7.6 Hz, 1H), 7.02 - 6.91 (m, 2H), 6.44 (s, 1H), 6.32 - 6.14 (m, 2H), 5.68 (dd, <i>J</i> = 2.8, 9.2 Hz, 1H), 2.57 (s, 6H).	
218	<i>m/z</i> (ESI ⁺): 347.1 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.35 (s, 1H), 7.91 (d, <i>J</i> = 7.6 Hz, 1H), 7.34 - 7.21 (m, 1H), 7.02 - 6.92 (m, 2H), 6.61 (dd, <i>J</i> = 10.4, 16.8 Hz, 1H), 6.35 (s, 1H), 6.30 (dd, <i>J</i> = 2.0, 16.8 Hz, 1H), 5.78 (dd, <i>J</i> = 2.0, 10.4 Hz, 1H), 4.13 - 4.02 (m, 2H), 3.88 (dd, <i>J</i> = 4.0, 10.8 Hz, 1H), 3.66 (dd, <i>J</i> = 4.4, 13.2 Hz, 1H), 2.39 - 2.27 (m, 2H), 2.01 (t, <i>J</i> = 3.2 Hz, 1H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
219	<i>m/z</i> (ESI ⁺): 377.2 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.52 - 14.21 (m, 1H), 12.30 (s, 1H), 8.64 - 8.56 (m, 1H), 8.13 (d, <i>J</i> = 8.4 Hz, 1H), 7.29 (t, <i>J</i> = 7.6 Hz, 1H), 7.01 - 6.92 (m, 2H), 6.88 - 6.67 (m, 1H), 6.26 - 6.09 (m, 1H), 5.78 - 5.61 (m, 1H), 4.11 - 3.78 (m, 2H), 3.70 - 3.53 (m, 1H), 3.49 - 3.39 (m, 1H), 3.28 - 3.17 (m, 1H), 2.38 - 2.29 (m, 3H), 2.03 - 1.84 (m, 4H), 1.79 - 1.64 (m, 1H), 1.49 - 1.32 (m, 1H).	
220	<i>m/z</i> (ESI ⁺): 333.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.03 (s, 1H), 12.74 (d, <i>J</i> = 2.0 Hz, 1H), 8.59 (s, 1H), 8.04 (d, <i>J</i> = 8 Hz, 1H), 7.30 (t, <i>J</i> = 7.6 Hz, 1H), 7.01 - 6.92 (m, 2H), 6.68 (s, 1H), 4.65 - 4.50 (m, 1H), 4.42 - 4.29 (m, 2H), 4.28 - 4.18 (m, 1H), 4.17 - 4.08 (m, 1H), 2.03 (s, 3H).	
221	<i>m/z</i> (ESI ⁺): 346.0 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.05 (s, 1H), 12.75 (d, <i>J</i> = 1.2 Hz, 1H), 8.60 (s, 1H), 8.05 (dd, <i>J</i> = 1.2, 8.0 Hz, 1H), 7.36 - 7.26 (m, 2H), 7.01 - 6.93 (m, 2H), 6.69 (s, 1H), 6.58 (d, <i>J</i> = 16.0 Hz, 1H), 4.77 (t, <i>J</i> = 8.8 Hz, 1H), 4.53 (dd, <i>J</i> = 6.0, 9.2 Hz, 1H), 4.48 - 4.37 (m, 1H), 4.29 - 4.18 (m, 2H).	
222	<i>m/z</i> (ESI ⁺): 355.0 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 13.44 (s, 1H), 8.50 (s, 1H), 8.13 (d, <i>J</i> = 7.6 Hz, 1H), 7.36 - 7.28 (m, 1H), 7.03 - 6.91 (m, 2H), 6.38 (dd, <i>J</i> = 10.4, 17.2 Hz, 1H), 6.17 (dd, <i>J</i> = 2.4, 17.2 Hz, 1H), 5.73 (dd, <i>J</i> = 2.0, 10.4 Hz, 1H), 4.78 - 4.64 (m, 1H), 4.55 (dd, <i>J</i> = 5.6, 8.8 Hz, 1H), 4.45 - 4.33 (m, 2H), 4.27 (d, <i>J</i> = 2.8 Hz, 1H).	
223	<i>m/z</i> (ESI ⁺): 397.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 13.75 (br s, 1H), 8.42 (s, 1H), 8.05 (d, <i>J</i> = 7.6 Hz, 1H), 7.62 - 7.48 (m, 4H), 7.43 (d, <i>J</i> = 7.2 Hz, 1H), 7.28 (t, <i>J</i> = 7.2 Hz, 1H), 7.02 - 6.88 (m, 2H), 6.40 - 6.28 (m, 1H), 6.14 (dd, <i>J</i> = 2.4, 16.8 Hz, 1H), 5.71 (dd, <i>J</i> = 2.0, 10.4 Hz, 1H), 4.64 (d, <i>J</i> = 8.8 Hz, 1H), 4.53 (s, 1H), 4.45 - 4.31 (m, 2H), 4.27 - 4.16 (m, 1H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
224	<i>m/z</i> (ESI ⁺): 335.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.13 (s, 1H), 12.50 (br s, 1H), 8.54 (s, 1H), 8.14 - 7.97 (m, 1H), 7.31 - 7.19 (m, 1H), 7.05 - 6.84 (m, 2H), 6.45 (s, 1H), 6.31 (dd, <i>J</i> = 10.4, 16.8 Hz, 1H), 6.09 (dd, <i>J</i> = 2.4, 16.8 Hz, 1H), 5.66 (dd, <i>J</i> = 2.4, 10.4 Hz, 1H), 4.43 - 4.30 (m, 1H), 4.13 - 4.04 (m, 1H), 4.00 (dd, <i>J</i> = 5.2, 8.4 Hz, 1H), 3.73 (dd, <i>J</i> = 5.2, 10.0 Hz, 1H), 3.22 - 3.16 (m, 2H), 3.16 - 3.07 (m, 1H)	
225	<i>m/z</i> (ESI ⁺): 444 (M+H) ⁺		
226	<i>m/z</i> (ESI ⁺): 430 (M+H) ⁺		
227	<i>m/z</i> (ESI ⁺): 416 (M+H) ⁺		
228	<i>m/z</i> (ESI ⁺): 444 (M+H) ⁺		
229	<i>m/z</i> (ESI ⁺): 406 (M+H) ⁺		
230	<i>m/z</i> (ESI ⁺): 364.1 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.46 (s, 1H), 7.94 (d, <i>J</i> = 7.2 Hz, 1H), 7.32 - 7.25 (m, 1H), 7.01 - 6.94 (m, 2H), 6.76 (dd, <i>J</i> = 10.4, 16.8 Hz, 1H), 6.60 (s, 1H), 6.20 (dd, <i>J</i> = 2.0, 16.8 Hz, 1H), 5.74 (dd, <i>J</i> = 1.6, 10.4 Hz, 1H), 3.85 (s, 2H), 3.77 - 3.68 (m, 4H), 2.61 - 2.57 (m, 4H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
231	<i>m/z</i> (ESI ⁺): 335.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.07 (s, 1H), 12.64 (s, 1H), 8.58 (d, <i>J</i> = 5.6 Hz, 1H), 8.02 (d, <i>J</i> = 7.6 Hz, 1H), 7.29 (t, <i>J</i> = 7.6 Hz, 1H), 7.01 - 6.91 (m, 2H), 6.64 (td, <i>J</i> = 10.0, 16.8 Hz, 1H), 6.52 (d, <i>J</i> = 8.0 Hz, 1H), 6.18 (dd, <i>J</i> = 2.0, 16.8 Hz, 1H), 5.71 (dd, <i>J</i> = 2.4, 10.4 Hz, 1H), 4.17 - 4.08 (m, 0.5H), 3.99 (dd, <i>J</i> = 7.2, 11.6 Hz, 0.5H), 3.83 - 3.76 (m, 1H), 3.73 - 3.62 (m, 2H), 3.61 - 3.56 (m, 0.5H), 3.50 - 3.45 (m, 0.5H), 2.41 - 2.36 (m, 1H), 2.30 - 2.24 (m, 0.5H), 2.19 - 2.12 (m, 0.5H).	
232	<i>m/z</i> (ESI ⁺): 335.1 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.07 (s, 1H), 12.64 (s, 1H), 8.58 (d, <i>J</i> = 5.6 Hz, 1H), 8.02 (d, <i>J</i> = 7.6 Hz, 1H), 7.29 (t, <i>J</i> = 7.6 Hz, 1H), 7.00 - 6.92 (m, 2H), 6.64 (td, <i>J</i> = 10.0, 16.8 Hz, 1H), 6.53 (d, <i>J</i> = 8.4 Hz, 1H), 6.18 (dd, <i>J</i> = 2.4, 16.8 Hz, 1H), 5.71 (dd, <i>J</i> = 2.4, 10.4 Hz, 1H), 4.18 - 4.08 (m, 0.5H), 3.99 (dd, <i>J</i> = 7.2, 11.6 Hz, 0.5H), 3.84 - 3.77 (m, 1.5H), 3.74 - 3.63 (m, 1.5H), 3.63 - 3.56 (m, 0.5H), 3.47 (td, <i>J</i> = 8.0, 12.4 Hz, 0.5H), 2.45 - 2.36 (m, 1H), 2.30 - 2.24 (m, 0.5H), 2.20 - 2.10 (m, 0.5H).	
233	<i>m/z</i> (ESI ⁺): 339 (M+H) ⁺		
234	<i>m/z</i> (ESI ⁺): 378.1 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.63 (s, 1H), 7.95 (d, <i>J</i> = 6.8 Hz, 1H), 7.34 - 7.27 (m, 1H), 7.02 - 6.97 (m, 2H), 6.95 (s, 1H), 6.87 - 6.74 (m, 1H), 6.26 (dd, <i>J</i> = 1.6, 16.8 Hz, 1H), 5.80 (d, <i>J</i> = 12.0 Hz, 1H), 3.88 - 3.84 (m, 4H), 3.83 - 3.76 (m, 4H).	
235	<i>m/z</i> (ESI ⁺): 349.0 (M+H) ⁺	(400 MHz, CHLOROFORM- <i>d</i>) δ 14.15 - 13.72 (m, 1H), 12.98 - 12.59 (m, 1H), 8.28 (s, 1H), 7.85 (dd, <i>J</i> = 1.2, 8.0 Hz, 1H), 7.39 - 7.30 (m, 1H), 7.11 (dd, <i>J</i> = 1.2, 8.0 Hz, 1H), 7.04 - 6.97 (m, 1H), 6.75 (dd, <i>J</i> = 10.8, 16.8 Hz, 1H), 6.40 (s, 1H), 6.33 (dd, <i>J</i> = 2.0, 16.8 Hz, 1H), 5.71 (dd, <i>J</i> = 2.0, 10.8 Hz, 1H), 4.90 (d, <i>J</i> = 12.4 Hz, 1H), 4.48 - 4.26 (m, 1H), 3.45 (t, <i>J</i> = 12.8 Hz, 1H), 3.32 (tt, <i>J</i> = 3.6, 11.6 Hz, 1H), 3.08 - 2.92 (m, 1H), 2.50 (d, <i>J</i> = 11.6 Hz, 1H), 2.33 (d, <i>J</i> = 12.4 Hz, 1H), 2.00 - 1.80 (m, 2H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
236	<i>m/z</i> (ESI ⁺): 335.0 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 8.45 (s, 1H), 7.97 - 7.91 (m, 1H), 7.32 - 7.25 (m, 1H), 7.01 - 6.93 (m, 2H), 6.74 - 6.60 (m, 1H), 6.55 (d, <i>J</i> = 5.6 Hz, 1H), 6.32 (td, <i>J</i> = 0.8, 16.8 Hz, 1H), 5.79 (dd, <i>J</i> = 2.0, 10.4 Hz, 1H), 4.22 (d, <i>J</i> = 2.8 Hz, 0.5H), 4.15 - 4.06 (m, 0.5H), 3.95 - 3.72 (m, 3.5H), 3.69 - 3.59 (m, 0.5H), 2.63 - 2.47 (m, 1H), 2.41 - 2.23 (m, 1H).	
237	<i>m/z</i> (ESI ⁺): 391 (M+H) ⁺		
238	<i>m/z</i> (ESI ⁺): 455 (M+H) ⁺		
239	<i>m/z</i> (ESI ⁺): 361 (M+H) ⁺		
240	<i>m/z</i> (ESI ⁺): 430.2 (M+H) ⁺		
241	<i>m/z</i> (ESI ⁺): 429.1 (M+H) ⁺		
242	<i>m/z</i> (ESI ⁺): 405.1 (M+H) ⁺		
243	<i>m/z</i> (ESI ⁺): 361.1 (M+H) ⁺		
244	<i>m/z</i> (ESI ⁺): 405.2 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 14.08 (br s, 1H), 12.44 (br s, 1H), 8.47 (s, 1H), 8.02 (d, <i>J</i> = 8.0 Hz, 1H), 7.28 (t, <i>J</i> = 8.0 Hz, 1H), 6.99 - 6.93 (m, 2H), 6.65 (dt, <i>J</i> = 10.4, 16.0 Hz, 1H), 6.18 (td, <i>J</i> = 2.8, 16.8 Hz, 1H), 5.74 - 5.66 (m, 1H), 4.15 (dt, <i>J</i> = 4.0, 8.0 Hz, 1H), 4.10 - 4.01 (m, 1H), 4.00 - 3.85 (m, 4H), 3.85 - 3.76 (m, 2H), 3.76 - 3.61 (m, 1H), 3.58 - 3.40 (m, 1H), 2.37 - 2.28 (m, 2H), 2.28 - 2.20 (m, 1H), 2.20 - 2.11 (m, 1H).	P 2nd eluting isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
245	<i>m/z</i> (ESI ⁺): 405.2 (M+H) ⁺	(400 MHz, d ₆ -DMSO) δ 13.88 (d, <i>J</i> = 5.2 Hz, 1H), 12.46 (br s, 1H), 8.50 (d, <i>J</i> = 2.8 Hz, 1H), 8.03 (d, <i>J</i> = 8.0 Hz, 1H), 7.30 (t, <i>J</i> = 7.6 Hz, 1H), 7.02 - 6.92 (m, 2H), 6.64 (dt, <i>J</i> = 10.4, 17.2 Hz, 1H), 6.18 (td, <i>J</i> = 3.2, 16.8 Hz, 1H), 5.75 - 5.65 (m, 1H), 4.19 - 4.11 (m, 1H), 4.11 - 4.02 (m, 1H), 4.02 - 3.86 (m, 4H), 3.85 - 3.77 (m, 2H), 3.76 - 3.62 (m, 1H), 3.58 - 3.40 (m, 1H), 2.39 - 2.23 (m, 3H), 2.19 - 2.13 (m, 1H).	P 1st eluting isomer
246	<i>m/z</i> (ESI ⁺): 425.1 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 7.97 (d, <i>J</i> = 1.2 Hz, 1H), 7.74 (dd, <i>J</i> = 1.6, 8.0 Hz, 1H), 7.57 - 7.48 (m, 3H), 7.48 - 7.44 (m, 2H), 7.27 - 7.21 (m, 1H), 6.95 (dd, <i>J</i> = 0.8, 8.0 Hz, 1H), 6.91 - 6.86 (m, 1H), 6.56 (dd, <i>J</i> = 10.4, 16.8 Hz, 0.5H), 6.27 - 6.07 (m, 1.5H), 5.75 - 5.61 (m, 1H), 3.81 (t, <i>J</i> = 10.8 Hz, 1H), 3.74 - 3.67 (m, 1H), 3.65 - 3.59 (m, 1H), 3.59 - 3.52 (m, 1H), 2.40 - 2.26 (m, 1H), 2.25 - 2.14 (m, 1H), 1.62 (d, <i>J</i> = 10.8 Hz, 3H).	Q 2nd eluting isomer
247	<i>m/z</i> (ESI ⁺): 425.1 (M+H) ⁺	(400 MHz, CD ₃ OD) δ 7.96 (s, 1H), 7.74 (d, <i>J</i> = 7.6 Hz, 1H), 7.58 - 7.48 (m, 3H), 7.48 - 7.43 (m, 2H), 7.24 (t, <i>J</i> = 7.6 Hz, 1H), 6.95 (d, <i>J</i> = 8.0 Hz, 1H), 6.89 (t, <i>J</i> = 7.6 Hz, 1H), 6.56 (dd, <i>J</i> = 10.4, 16.8 Hz, 0.5H), 6.27 - 6.06 (m, 1.5H), 5.76 - 5.61 (m, 1H), 3.81 (t, <i>J</i> = 10.4 Hz, 1H), 3.75 - 3.68 (m, 1H), 3.66 - 3.59 (m, 1H), 3.59 - 3.52 (m, 1H), 2.39 - 2.27 (m, 1H), 2.24 - 2.14 (m, 1H), 1.62 (d, <i>J</i> = 10.8 Hz, 3H).	Q 1st eluting isomer
248	<i>m/z</i> (ESI ⁺): 361 (M+H) ⁺		
249	<i>m/z</i> (ESI ⁺): 349.1 (M+H) ⁺		I 2nd eluting isomer
250	<i>m/z</i> (ESI ⁺): 349.1 (M+H) ⁺		I 1st eluting isomer
251	<i>m/z</i> (ESI ⁺): 361.1 (M+H) ⁺		Preparative TLC 2nd eluting isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
252	<i>m/z</i> (ESI ⁺): 391.1 (M+H) ⁺		J 3rd eluting isomer
253	<i>m/z</i> (ESI ⁺): 363.1 (M+H) ⁺		
254	<i>m/z</i> (ESI ⁺): 361.1 (M+H) ⁺		Preparative TLC 1st eluting isomer
255	<i>m/z</i> (ESI ⁺): 361.1 (M+H) ⁺		Preparative TLC 2nd eluting isomer
256	<i>m/z</i> (ESI ⁺): 347.1 (M+H) ⁺		F 2nd eluting isomer
257	<i>m/z</i> (ESI ⁺): 347.1 (M+H) ⁺		F 1st eluting isomer
258	<i>m/z</i> (ESI ⁺): 347.1 (M+H) ⁺		E 2nd eluting isomer
259	<i>m/z</i> (ESI ⁺): 347.1 (M+H) ⁺		E 1st eluting isomer
260	<i>m/z</i> (ESI ⁺): 403.1 (M+H) ⁺		
261	<i>m/z</i> (ESI ⁺): 403.1 (M+H) ⁺		
262	<i>m/z</i> (ESI ⁺): 375.1 (M+H) ⁺		K 3rd eluting isomer
263	<i>m/z</i> (ESI ⁺): 375.1 (M+H) ⁺		

Cmpd #	MS	¹ H NMR	SFC Conditions
264	<i>m/z</i> (ESI ⁺): 381 (M+H) ⁺	(499 MHz, d ₆ -DMSO) δ 14.20 (s, 2H), 12.47 (s, 2H), 8.64 (s, 2H), 8.16 – 8.10 (m, 2H), 7.33 – 7.26 (m, 2H), 7.00 – 6.93 (m, 4H), 6.89 (t, J = 13.6 Hz, 2H), 6.21 – 6.12 (m, 2H), 5.76 (d, J = 10.5 Hz, 1H), 5.70 (d, J = 10.6 Hz, 1H), 5.26 (s, 1H), 5.16 (s, 1H), 4.65 (s, 1H), 4.57 (s, 1H), 4.29 (d, J = 17.7 Hz, 2H), 3.51 (t, J = 13.1 Hz, 1H), 3.20 (t, J = 13.4 Hz, 1H), 3.09 (t, J = 12.5 Hz, 1H), 2.76 (t, J = 15.2 Hz, 1H), 2.33 (s, 5H), 1.73 (s, 1H).	
265	<i>m/z</i> (ESI ⁺): 461 (M+H) ⁺		
266	<i>m/z</i> (ESI ⁺): 365.1 (M+H) ⁺		H 2nd eluting isomer
267	<i>m/z</i> (ESI ⁺): 365.1 (M+H) ⁺		H 1st eluting isomer
268	<i>m/z</i> (ESI ⁺): 367.1 (M+H) ⁺		Preparative TLC 2nd eluting isomer
269	<i>m/z</i> (ESI ⁺): 367.1 (M+H) ⁺		Preparative TLC 1st eluting isomer
270	<i>m/z</i> (ESI ⁺): 363.2 (M+H) ⁺		Preparative TLC 2nd eluting isomer
271	<i>m/z</i> (ESI ⁺): 425.1 (M+H) ⁺		
272	<i>m/z</i> (ESI ⁺): 365.1 (M+H) ⁺		T 1st eluting isomer
273	<i>m/z</i> (ESI ⁺): 377.1 (M+H) ⁺		L 2nd eluting isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
274	<i>m/z</i> (ESI ⁺): 377.1 (M+H) ⁺		L 1st eluting isomer
275	<i>m/z</i> (ESI ⁺): 379.1 (M+H) ⁺		M 2nd eluting isomer
276	<i>m/z</i> (ESI ⁺): 379.1 (M+H) ⁺		M 1st eluting isomer
277	<i>m/z</i> (ESI ⁺): 415 (M+H) ⁺		
278	<i>m/z</i> (ESI ⁺): 429.0 (M+H) ⁺		
279	<i>m/z</i> (ESI ⁺): 429.0 (M+H) ⁺		
280	<i>m/z</i> (ESI ⁺): 335.1 (M+H) ⁺		
281	<i>m/z</i> (ESI ⁺): 365.1 (M+H) ⁺		Preparative TLC 1st eluting isomer
282	<i>m/z</i> (ESI ⁺): 433.2 (M+H) ⁺		
283	<i>m/z</i> (ESI ⁺): 433.1 (M+H) ⁺		
284	<i>m/z</i> (ESI ⁺): 419.2 (M+H) ⁺		
285	<i>m/z</i> (ESI ⁺): 361.1 (M+H) ⁺		O 2nd eluting isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
286	<i>m/z</i> (ESI ⁺): 361.1 (M+H) ⁺		O 1st eluting isomer
287	<i>m/z</i> (ESI ⁺): 377.1 (M+H) ⁺		
288	<i>m/z</i> (ESI ⁺): 379.1 (M+H) ⁺		
289	<i>m/z</i> (ESI ⁺): 389.1 (M+H) ⁺		
290	<i>m/z</i> (ESI ⁺): 367.1 (M+H) ⁺		Preparative TLC 2nd eluting isomer
291	<i>m/z</i> (ESI ⁺): 367.1 (M+H) ⁺		Preparative TLC 1st eluting isomer
292	<i>m/z</i> (ESI ⁺): 365 (M+H) ⁺	(499 MHz, d ₆ -DMSO) δ 14.14 (s, 1H), 12.53 (s, 1H), 8.53 (d, J = 4.3 Hz, 1H), 8.02 (dd, J = 8.0, 1.6 Hz, 1H), 7.28 (ddd, J = 8.4, 7.1, 1.6 Hz, 1H), 6.99 – 6.91 (m, 2H), 6.66 (dd, J = 16.6, 10.5 Hz, 0H), 6.52 (dd, J = 16.5, 10.4 Hz, 1H), 6.47 (s, 1H), 5.93 (d, J = 16.7 Hz, 0H), 5.71 (d, J = 16.5 Hz, 1H), 5.33 (d, J = 10.3 Hz, 1H), 4.47 (s, 1H), 4.17 (d, J = 13.6 Hz, 1H), 3.92 (dd, J = 29.0, 11.4 Hz, 1H), 3.81 (d, J = 11.5 Hz, 1H), 3.60 (d, J = 12.1 Hz, 1H), 3.53 (d, J = 13.1 Hz, 1H), 3.48 – 3.34 (m, 1H), 3.26 (d, J = 13.3 Hz, 1H), 3.20 (dd, J = 14.6, 5.9 Hz, 1H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
293	<i>m/z</i> (ESI ⁺): 365 (M+H) ⁺	(499 MHz, d ₆ -DMSO) δ 14.16 (s, 1H), 12.58 (s, 1H), 8.53 (s, 1H), 8.02 (dd, J = 8.0, 1.6 Hz, 1H), 7.28 (ddd, J = 8.5, 7.1, 1.6 Hz, 1H), 6.99 – 6.91 (m, 2H), 6.53 (dd, J = 16.5, 10.3 Hz, 1H), 5.93 (d, J = 16.6 Hz, 0H), 5.71 (d, J = 16.5 Hz, 1H), 5.59 (d, J = 10.5 Hz, 0H), 5.36 – 5.30 (m, 1H), 4.48 (s, 1H), 4.17 (d, J = 13.6 Hz, 1H), 3.92 (dd, J = 28.6, 11.6 Hz, 1H), 3.81 (d, J = 11.5 Hz, 1H), 3.60 (d, J = 11.3 Hz, 1H), 3.53 (d, J = 13.6 Hz, 1H), 3.48 – 3.37 (m, 1H), 3.20 (dd, J = 14.6, 5.9 Hz, 2H).	
294	<i>m/z</i> (ESI ⁺): 407 (M+H) ⁺	(499 MHz, d ₆ -DMSO) δ 14.24 (s, 1H), 12.41 (s, 1H), 8.64 (d, J = 4.9 Hz, 1H), 8.11 (dd, J = 8.5, 1.7 Hz, 1H), 7.29 (td, J = 7.6, 1.6 Hz, 1H), 6.99 – 6.92 (m, 2H), 6.64 (ddd, J = 27.1, 16.7, 10.3 Hz, 1H), 6.18 (ddd, J = 16.7, 4.5, 2.4 Hz, 1H), 5.70 (ddd, J = 19.0, 10.3, 2.4 Hz, 1H), 4.05 (dd, J = 9.7, 8.1 Hz, 1H), 4.01 – 3.90 (m, 2H), 3.90 – 3.61 (m, 2H), 3.61 – 3.50 (m, 2H), 3.53 – 3.37 (m, 4H), 3.05 (td, J = 7.0, 4.8 Hz, 2H), 2.43 – 2.28 (m, 1H), 2.26 (s, 1H), 1.07 (td, J = 7.0, 2.1 Hz, 3H).	
295	<i>m/z</i> (ESI ⁺): 349 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.43 - 8.38 (m, 1H), 8.01 - 7.97 (m, 1H), 7.31 - 7.25 (m, 1H), 7.01 - 6.94 (m, 2H), 6.38 - 6.22 (m, 1.4H), 6.16 - 6.08 (m, 0.3H), 6.02 - 5.93 (m, 0.3H), 5.79 - 5.73 (m, 0.7H), 5.39 (d, J = 9.6 Hz, 0.3H), 4.95 - 4.90 (m, 0.3H), 4.83 - 4.77 (m, 0.7H), 4.18 (t, J = 8.0 Hz, 1.4H), 4.07 - 3.98 (m, 0.6H), 3.59 - 3.42 (m, 1H), 3.42 - 3.34 (m, 1H), 2.64 - 2.41 (m, 1H), 2.37 - 2.34 (m, 3H), 2.22 - 2.01 (m, 1H).	
296	<i>m/z</i> (ESI ⁺): 375 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.40 - 8.34 (m, 1H), 7.98 - 7.91 (m, 1H), 7.28 (t, J = 7.2 Hz, 1H), 7.02 - 6.95 (m, 2H), 6.38 - 6.22 (m, 1.4H), 6.18 - 5.97 (m, 0.6H), 5.79 - 5.72 (m, 0.6H), 5.41 (d, J = 8.8 Hz, 0.4H), 4.29 - 4.16 (m, 1.3H), 4.09 - 3.98 (m, 0.7H), 3.72 - 3.64 (m, 0.6H), 3.61 - 3.54 (m, 0.4H), 3.50 - 3.40 (m, 1.4H), 3.35 (s, 0.6H), 2.67 - 2.45 (m, 1H), 2.26 - 2.09 (m, 1H), 1.96 - 1.81 (m, 1H), 1.11 - 1.02 (m, 2H), 0.84 - 0.75 (m, 2H).	A31 1 st isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
297	<i>m/z</i> (ESI ⁺): 375 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.39 - 8.35 (m, 1H), 7.94 (d, J = 8.4 Hz, 1H), 7.29 (t, J = 7.6 Hz, 1H), 7.02 - 6.95 (m, 2H), 6.39 - 6.23 (m, 1.3H), 6.16 - 5.98 (m, 0.7H), 5.79 - 5.73 (m, 0.6H), 5.44 - 5.38 (m, 0.4H), 4.26 - 4.18 (m, 1.3H), 4.10 - 3.98 (m, 1H), 3.73 - 3.64 (m, 0.7H), 3.63 - 3.52 (m, 0.5H), 3.50 - 3.45 (m, 1H), 3.43 (d, J = 7.6 Hz, 0.5H), 2.67 - 2.45 (m, 1H), 2.25 - 2.10 (m, 1H), 1.95 - 1.83 (m, 1H), 1.10 - 1.04 (m, 2H), 0.84 - 0.72 (m, 2H).	A31 2 nd isomer
298	<i>m/z</i> (ESI ⁺): 361 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.24 - 14.01 (m, 1H), 12.74 - 12.48 (m, 1H), 8.63 - 8.49 (m, 1H), 8.02 (d, J = 7.6 Hz, 1H), 7.35 - 7.22 (m, 1H), 7.02 - 6.90 (m, 2H), 6.52 - 6.37 (m, 1H), 6.37 - 6.27 (m, 0.5H), 6.16 (d, J = 17.2 Hz, 0.5H), 6.10 - 6.04 (m, 0.5H), 5.72 (d, J = 10.0 Hz, 0.5H), 4.99 - 4.84 (m, 1H), 4.23 - 4.15 (m, 1H), 4.01 - 3.85 (m, 1H), 3.52 - 3.36 (m, 2H), 1.31 - 1.15 (m, 1H), 0.68 (s, 3H), 0.48 (d, J = 6.0 Hz, 1H).	
299	<i>m/z</i> (ESI ⁺): 361 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.18 - 14.05 (m, 1H), 12.69 - 12.45 (m, 1H), 8.60 - 8.48 (m, 1H), 8.02 (d, J = 7.6 Hz, 1H), 7.34 - 7.23 (m, 1H), 7.01 - 6.88 (m, 2H), 6.49 - 6.38 (m, 1H), 6.37 - 6.28 (m, 0.5H), 6.16 (d, J = 17.2 Hz, 0.5H), 6.11 - 6.00 (m, 1H), 5.80 - 5.35 (m, 1H), 5.00 - 4.83 (m, 1H), 4.19 (s, 1H), 3.92 (s, 1H), 3.52 - 3.35 (m, 2H), 0.78 - 0.58 (m, 3H), 0.48 (d, J = 7.2 Hz, 1H).	A16 2 nd isomer
300	<i>m/z</i> (ESI ⁺): 365 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.23 (d, J = 2.4 Hz, 1H), 12.24 - 12.05 (m, 1H), 8.64 (s, 1H), 8.19 - 8.08 (m, 1H), 7.34 - 7.23 (m, 1H), 7.00 - 6.92 (m, 2H), 6.91 - 6.82 (m, 1H), 6.21 (dd, J = 2.4, 16.8 Hz, 1H), 5.85 - 5.79 (m, 1H), 5.77 (dd, J = 2.4, 10.4 Hz, 1H), 4.49 - 4.41 (m, 1H), 4.15 - 4.01 (m, 1H), 3.94 (dd, J = 2.8, 10.4 Hz, 1H), 3.81 (dd, J = 3.6, 12.4 Hz, 1H), 3.62 - 3.52 (m, 1H), 3.52 - 3.38 (m, 1H), 2.29 (s, 3H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
301	<i>m/z</i> (ESI ⁺): 423 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.12 (s, 1 H), 12.06 (s, 1 H), 8.63 (s, 1 H), 8.11 (d, J = 7.2 Hz, 1 H), 7.28 (t, J = 8.0 Hz, 1 H), 6.98 - 6.95 (m, 2 H), 6.82 (d, J = 10.4 Hz, 1 H), 6.22 - 6.17 (m, 1H), 5.77 - 5.74 (m, 2 H), 4.31 (d, J = 12.4 Hz 1 H), 3.99 - 3.97 (m, 2 H), 3.86 - 3.85 (m, 1 H), 3.83 - 3.82 (m, 2 H), 3.59 - 3.56 (m, 2 H), 3.22 (s, 3 H), 2.85 - 2.80 (m, 2 H), 1.83 - 1.76 (m, 2 H).	
302	<i>m/z</i> (ESI ⁺): 423 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.50 (s, 1 H), 7.98 (t, J = 1.2 Hz, 1 H), 7.30 - 7.26 (m, 1 H), 6.99 - 6.96 (m, 2 H), 6.79 (dd, J = 10.4, 16.4 Hz, 1 H), 6.29 (dd, J = 1.6, 16.8 Hz, 1 H), 5.99 (s, 1 H), 5.81 (dd, J = 1.6, 10.4 Hz, 1 H), 4.36 (d, J = 12.4 Hz, 1 H), 4.14 (dd, J = 2.4, 11.2 Hz, 1 H), 4.05 - 3.95 (m, 2 H), 3.71 - 3.70 (m, 1 H), 3.60 - 3.51 (m, 1 H), 3.42 - 3.39 (m, 2 H), 3.34 (s, 3 H), 3.06 - 2.99 (m, 1 H), 2.95 - 2.87 (m, 1 H), 1.90 - 1.82 (m, 2 H).	
303	<i>m/z</i> (ESI ⁺): 391 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.09 (d, J = 6.0 Hz, 1H), 12.61 (br s, 1H), 8.57 (d, J = 2.8 Hz, 1H), 8.07 - 7.98 (m, 1H), 7.32 - 7.25 (m, 1H), 7.00 - 6.92 (m, 2H), 6.66 - 6.45 (m, 2H), 6.14 (td, J = 2.8, 16.8 Hz, 1H), 5.67 (ddd, J = 2.4, 6.0, 10.4 Hz, 1H), 4.24 (td, J = 7.6, 12.0 Hz, 1H), 3.94 (dt, J = 3.6, 8.4 Hz, 1H), 3.89 - 3.70 (m, 2H), 3.67 - 3.54 (m, 2H), 3.45 - 3.36 (m, 1H), 2.43 - 2.29 (m, 1H), 2.20 - 2.02 (m, 2H), 2.01 - 1.88 (m, 1H).	J 1 st isomer
304	<i>m/z</i> (ESI ⁺): 391 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.09 (d, J = 6.0 Hz, 1H), 12.61 (br s, 1H), 8.57 (d, J = 2.8 Hz, 1H), 8.07 - 7.98 (m, 1H), 7.32 - 7.25 (m, 1H), 7.00 - 6.92 (m, 2H), 6.66 - 6.45 (m, 2H), 6.14 (td, J = 2.8, 16.8 Hz, 1H), 5.67 (ddd, J = 2.4, 6.0, 10.4 Hz, 1H), 4.24 (td, J = 8.0, 11.6 Hz, 1H), 3.94 (dt, J = 3.6, 8.4 Hz, 1H), 3.89 - 3.70 (m, 2H), 3.67 - 3.54 (m, 2H), 3.45 - 3.36 (m, 1H), 2.61 - 2.48 (m, 1H), 2.43 - 2.29 (m, 1H), 2.20 - 2.02 (m, 1H), 2.01 - 1.88 (m, 1H).	J 2 nd isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
305	<i>m/z</i> (ESI ⁺): 391 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.23 - 13.95 (m, 1H), 12.73 - 12.43 (m, 1H), 8.57 (d, J = 2.8 Hz, 1H), 8.45 - 8.32 (m, 0.3H), 8.03 (d, J = 7.2 Hz, 1H), 7.29 (t, J = 7.6 Hz, 1H), 7.01 - 6.89 (m, 2H), 6.65 - 6.46 (m, 2H), 6.14 (td, J = 2.8, 16.8 Hz, 1H), 5.67 (ddd, J = 2.4, 6.4, 10.0 Hz, 1H), 4.24 (td, J = 7.6, 11.6 Hz, 1H), 3.94 (dt, J = 3.2, 8.0 Hz, 1H), 3.88 - 3.80 (m, 1H), 3.79 - 3.69 (m, 1H), 3.68 - 3.55 (m, 3H), 2.44 - 2.28 (m, 1H), 2.21 - 2.01 (m, 2H), 2.01 - 1.85 (m, 1H).	J 4 th isomer
306	<i>m/z</i> (ESI ⁺): 349 (M+H) ⁺	(499 MHz, DMSO-d ₆) δ 14.04 (d, J = 3.5 Hz, 1H), 12.64 (s, 1H), 8.58 (d, J = 6.3 Hz, 1H), 8.03 (dt, J = 8.0, 2.1 Hz, 1H), 7.32 - 7.25 (m, 1H), 7.00 - 6.91 (m, 2H), 6.67 - 6.56 (m, 2H), 6.18 (dd, J = 16.7, 2.4 Hz, 1H), 5.70 (ddd, J = 10.3, 7.8, 2.4 Hz, 1H), 4.15 (dd, J = 10.3, 8.0 Hz, 1H), 4.07 - 3.97 (m, 1H), 3.93 - 3.78 (m, 1H), 3.63 - 3.55 (m, 1H), 3.30 - 3.21 (m, 1H), 3.11 - 3.03 (m, 1H), 1.06 (dd, J = 6.5, 3.6 Hz, 3H).	
307	<i>m/z</i> (ESI ⁺): 457 (M+H) ⁺	(499 MHz, METHANOL-d ₄) δ 8.54 (s, 1H), 8.32 (d, J = 3.6 Hz, 1H), 7.98 (d, J = 7.8 Hz, 1H), 7.31 (t, J = 7.7 Hz, 1H), 7.03 - 6.97 (m, 2H), 6.35 - 6.12 (m, 2H), 5.75 - 5.58 (m, 1H), 4.42 - 3.69 (m, 6H), 3.40 - 3.32 (m, 1H), 2.58 (s, 1H), 2.46 (d, J = 13.4 Hz, 1H).	
308	<i>m/z</i> (ESI ⁺): 361 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.08 (d, J = 8.8 Hz, 1H), 12.77 - 12.45 (m, 1H), 8.52 (d, J = 4.0 Hz, 1H), 8.02 (d, J = 7.6 Hz, 1H), 7.29 (t, J = 7.2 Hz, 1H), 7.03 - 6.90 (m, 2H), 6.61 (dd, J = 10.4, 16.8 Hz, 0.5H), 6.42 (s, 0.5H), 6.37 - 6.27 (m, 1H), 6.16 (d, J = 2.4, 8.8, 16.8 Hz, 1H), 5.70 (d, J = 2.0, 6.0, 10.0 Hz, 1H), 5.24 - 4.93 (m, 1H), 4.41 - 3.99 (m, 1H), 3.83 (dd, J = 4.0, 8.8 Hz, 0.5H), 3.79 - 3.60 (m, 1H), 3.48 (dd, J = 4.0, 10.4 Hz, 0.5H), 3.15 (s, 1H), 2.40 (dt, J = 6.4, 12.4 Hz, 1H), 2.32 - 2.07 (m, 1H), 1.86 - 1.63 (m, 2H).	A30 1 st isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
309	<i>m/z</i> (ESI ⁺): 361 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.11 (s, 1H), 12.77 - 12.49 (m, 1H), 8.53 (d, J = 3.2 Hz, 1H), 8.02 (d, J = 8.0 Hz, 1H), 7.34 - 7.26 (m, 1H), 7.01 - 6.92 (m, 2H), 6.62 (dd, J = 10.4, 16.8 Hz, 0.5H), 6.43 (s, 0.5H), 6.38 - 6.29 (m, 1H), 6.17 (d, J = 2.0, 8.8, 16.8 Hz, 1H), 5.71 (d, J = 2.4, 6.0, 10.4 Hz, 1H), 5.24 - 4.95 (m, 1H), 4.40 - 4.00 (m, 1H), 3.84 (dd, J = 4.0, 8.8 Hz, 0.5H), 3.80 - 3.60 (m, 1H), 3.49 (dd, J = 4.0, 10.4 Hz, 0.5H), 3.22 - 3.10 (m, 1H), 2.41 (dt, J = 6.4, 12.4 Hz, 1H), 2.32 - 2.08 (m, 1H), 1.84 - 1.65 (m, 2H).	A30 2 nd isomer
310	<i>m/z</i> (ESI ⁺): 406 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.27 - 13.96 (m, 1H), 12.85 - 12.37 (m, 1H), 8.59 - 8.53 (m, 1H), 8.03 (d, J = 8.0 Hz, 1H), 7.32 - 7.23 (m, 1H), 7.00 - 6.90 (m, 2H), 6.68 (dd, J = 10.4, 16.8 Hz, 1H), 6.58 - 6.50 (m, 1H), 6.21 - 6.10 (m, 1H), 5.77 - 5.59 (m, 1H), 5.30 - 4.92 (m, 1H), 4.45 - 4.32 (m, 1H), 3.81 - 3.60 (m, 2H), 3.14 - 3.09 (m, 3H), 2.89 - 2.78 (m, 4H), 2.08 - 1.94 (m, 1H).	A29 1 st isomer
311	<i>m/z</i> (ESI ⁺): 406 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.08 (s, 1H), 12.59 (d, J = 1.2 Hz, 1H), 8.60 - 8.55 (m, 1H), 8.03 (d, J = 8.0 Hz, 1H), 7.32 - 7.25 (m, 1H), 6.99 - 6.92 (m, 2H), 6.68 (dd, J = 10.4, 16.8 Hz, 1H), 6.57 (s, 1H), 6.20 - 6.10 (m, 1H), 5.76 - 5.61 (m, 1H), 5.35 - 5.02 (m, 1H), 4.26 - 3.98 (m, 1H), 3.97 - 3.86 (m, 1H), 3.73 - 3.63 (m, 1H), 3.11 (s, 3H), 2.92 - 2.84 (m, 3H), 2.73 - 2.58 (m, 1H), 2.37 - 2.27 (m, 1H).	A29 2 nd isomer
312	<i>m/z</i> (ESI ⁺): 405 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.49 - 14.26 (m, 1H), 12.30 (s, 1H), 8.57 (s, 1H), 8.12 (d, J = 1.6, 8.4 Hz, 1H), 7.35 - 7.25 (m, 1H), 7.04 - 6.91 (m, 2H), 6.88 - 6.75 (m, 1H), 6.25 (d, J = 2.4, 16.8 Hz, 1H), 5.78 (d, J = 2.4, 10.4 Hz, 1H), 4.59 - 4.51 (m, 1H), 4.31 (s, 1H), 4.06 (d, J = 5.2, 11.2 Hz, 2H), 3.71 (d, J = 12.0, 13.6 Hz, 4H), 2.32 (s, 3H), 2.23 - 2.01 (m, 3H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
313	<i>m/z</i> (ESI ⁺): 395 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 13.49 (s, 1H), 13.00 (s, 1H), 8.48 (s, 1H), 8.12 (d, J = 8.0 Hz, 1H), 7.31 (t, J = 7.2 Hz, 1H), 7.01 - 6.94 (m, 2H), 6.25 (dd, J = 10.4, 17.2 Hz, 0.5H), 6.19 - 6.10 (m, 0.5H), 6.05 - 5.94 (m, 1H), 5.62 (dd, J = 2.0, 10.4 Hz, 0.5H), 5.52 (dd, J = 2.0, 10.4 Hz, 0.5H), 4.30 (d, J = 18.8 Hz, 1H), 4.11 (dd, J = 9.6, 16.8 Hz, 2H), 4.00 - 3.93 (m, 0.5H), 3.86 (t, J = 10.4 Hz, 1H), 3.58 (d, J = 10.4 Hz, 0.5H), 2.63 (s, 1H), 2.43 - 2.30 (m, 2H), 2.28 - 2.19 (m, 1H).	A11 1 st isomer
314	<i>m/z</i> (ESI ⁺): 395 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 13.49 (s, 1H), 13.00 (br s, 1H), 8.49 (s, 1H), 8.12 (d, J = 7.6 Hz, 1H), 7.30 (t, J = 7.6 Hz, 1H), 7.02 - 6.92 (m, 2H), 6.30 - 6.20 (m, 0.5H), 6.19 - 6.09 (m, 0.5H), 6.05 - 5.94 (m, 1H), 5.62 (d, J = 10.4 Hz, 0.5H), 5.56 - 5.47 (m, 0.5H), 4.40 - 4.20 (m, 1H), 4.17 - 4.04 (m, 2H), 4.01 - 3.93 (m, 0.5H), 3.92 - 3.79 (m, 1H), 3.58 (d, J = 10.8 Hz, 0.5H), 2.70 - 2.56 (m, 1H), 2.45 - 2.31 (m, 2H), 2.30 - 2.21 (m, 1H).	A11 2 nd isomer
315	<i>m/z</i> (ESI ⁺): 347 (M+H) ⁺	(400 MHz, CHLOROFORM-d) δ 10.79 - 10.23 (m, 1H), 8.22 (s, 1H), 7.78 (d, J = 7.2 Hz, 1H), 7.35 - 7.29 (m, 1H), 7.14 (d, J = 8.0 Hz, 1H), 6.99 - 6.93 (m, 1H), 6.55 (s, 1H), 6.51 - 6.43 (m, 1H), 6.41 - 6.32 (m, 1H), 5.79 (dd, J = 2.0, 10.0 Hz, 1H), 5.62 (s, 1H), 3.86 (d, J = 10.4 Hz, 1H), 3.69 (dd, J = 2.8, 10.4 Hz, 1H), 2.07 - 2.01 (m, 1H), 1.91 (ddd, J = 4.0, 7.6, 10.8 Hz, 1H), 1.04 - 0.96 (m, 1H), 0.52 - 0.44 (m, 1H).	
316	<i>m/z</i> (ESI ⁺): 347 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.06 - 13.92 (m, 1H), 12.72 (d, J = 3.2 Hz, 1H), 8.59 - 8.52 (m, 1H), 7.99 (t, J = 6.8 Hz, 1H), 7.29 (t, J = 7.6 Hz, 1H), 7.00 - 6.91 (m, 2H), 6.67 - 6.48 (m, 1H), 6.42 (d, J = 12.8 Hz, 1H), 6.12 (d, J = 2.4, 5.6, 16.8 Hz, 1H), 5.75 - 5.55 (m, 1H), 5.49 - 5.33 (m, 1H), 4.05 - 3.97 (m, 0.5H), 3.97 - 3.89 (m, 1H), 3.73 (dd, J = 4.0, 11.6 Hz, 0.5H), 1.91 (dt, J = 3.6, 7.2 Hz, 0.5H), 1.80 (dd, J = 3.6, 7.2 Hz, 1H), 1.76 - 1.70 (m, 0.5H), 0.93 - 0.83 (m, 1H), 0.36 (d, J = 4.0, 8.0 Hz, 1H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
317	<i>m/z</i> (ESI ⁺): 441 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 13.43 (s, 1H), 13.07 (s, 1H), 8.37 (s, 1H), 8.12 (d, J = 8.0 Hz, 1H), 7.32 - 7.28 (m, 1H), 7.04 - 6.90 (m, 2H), 6.247 - 6.20 (m, 0.5H), 6.18 - 6.07 (m, 0.5H), 6.05 - 5.93 (m, 1H), 5.63 - 5.60 (m, 0.5H), 5.53 - 5.50 (m, 0.5H), 4.37 - 4.34 (m, 0.5H), 4.28 - 4.25 (m, 0.5H), 4.18 - 4.04 (m, 2H), 3.98 - 3.95 (m, 0.5H), 3.89 - 3.80 (m, 1H), 3.56 (d, J = 10.4 Hz, 0.5H), 2.75 - 2.58 (m, 1H), 2.42 - 2.34 (m, 1H), 2.34 - 2.18 (m, 2H).	A11 1 st isomer
318	<i>m/z</i> (ESI ⁺): 441 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 13.40 (s, 1H), 13.06 (s, 1H), 8.37 (d, J = 1.2 Hz, 1H), 8.12 (d, J = 8.0 Hz, 1H), 7.41 - 7.23 (m, 1H), 7.06 - 6.90 (m, 2H), 6.27 - 6.20 (m, 0.5H), 6.18 - 6.08 (m, 0.5H), 6.05 - 5.93 (m, 1H), 5.63 - 5.60 (m, 0.5H), 5.53 - 5.50 (m, 0.5H), 4.41 - 4.32 (m, 0.5H), 4.31 - 4.23 (m, 0.5H), 4.17 - 4.04 (m, 2H), 4.01 - 3.93 (m, 0.5H), 3.84 (d, J = 10.8 Hz, 1H), 3.56 (d, J = 10.8 Hz, 0.5H), 2.73 - 2.59 (m, 1H), 2.42 - 2.34 (m, 1H), 2.34 - 2.20 (m, 2H).	A11 2 nd isomer
319	<i>m/z</i> (ESI ⁺): 377 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.15 - 14.02 (m, 1H), 12.37 (s, 1H), 8.58 - 8.53 (m, 1H), 8.17 (d, J = 8.4 Hz, 1H), 7.28 (t, J = 7.6 Hz, 1H), 6.99 - 6.92 (m, 2H), 6.34 - 6.24 (m, 0.5H), 6.18 - 6.01 (m, 1.5H), 5.72 - 5.66 (m, 0.6H), 5.47 - 5.39 (m, 0.4H), 4.83 (s, 0.4H), 4.72 - 4.61 (m, 0.6H), 4.15 - 4.05 (m, 1.3H), 3.95 - 3.81 (m, 1H), 3.56 - 3.49 (m, 0.7H), 3.28 - 3.17 (m, 2H), 2.25 (s, 1.4H), 2.15 - 2.03 (m, 1H), 2.01 - 1.91 (m, 0.6H), 1.44 - 1.37 (m, 6H).	
320	<i>m/z</i> (ESI ⁺): 349 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.40 - 14.29 (m, 1H), 12.38 (s, 1H), 8.60 - 8.56 (m, 1H), 8.14 - 8.10 (m, 1H), 7.32 - 7.25 (m, 1H), 6.98 - 6.93 (m, 2H), 6.35 - 6.02 (m, 2H), 5.72 - 5.67 (m, 0.6H), 5.48 (d, J = 9.6 Hz, 0.4H), 4.90 - 4.65 (m, 1H), 4.15 - 4.04 (m, 1H), 3.94 - 3.80 (m, 1H), 3.55 - 3.47 (m, 0.5H), 3.37 - 3.34 (m, 1H), 3.25 - 3.19 (m, 0.5H), 2.44 - 2.33 (m, 1H), 2.32 - 2.29 (m, 3H), 2.10 - 1.90 (m, 1H).	A28 1 st isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
321	<i>m/z</i> (ESI ⁺): 349 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.40 - 14.29 (m, 1H), 12.38 (s, 1H), 8.60 - 8.56 (m, 1H), 8.14 - 8.10 (m, 1H), 7.32 - 7.25 (m, 1H), 6.98 - 6.93 (m, 2H), 6.35 - 6.02 (m, 2H), 5.72 - 5.67 (m, 0.6H), 5.48 (d, J = 9.6 Hz, 0.4H), 4.90 - 4.65 (m, 1H), 4.15 - 4.04 (m, 1H), 3.94 - 3.80 (m, 1H), 3.55 - 3.47 (m, 0.5H), 3.37 - 3.34 (m, 1H), 3.25 - 3.19 (m, 0.5H), 2.44 - 2.33 (m, 1H), 2.32 - 2.29 (m, 3H), 2.10 - 1.90 (m, 1H).	A28 2 nd isomer
322	<i>m/z</i> (ESI ⁺): 419 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.55 - 8.50 (m, 1H), 7.88 (dd, J = 1.2, 8.4 Hz, 1H), 7.33 - 7.25 (m, 1H), 7.02 - 6.93 (m, 2H), 6.77 - 6.63 (m, 1H), 6.38 - 6.29 (m, 1H), 5.85 - 5.77 (m, 1H), 4.34 (dt, J = 3.2, 8.4 Hz, 1H), 4.29 - 4.16 (m, 1H), 4.16 - 4.07 (m, 2H), 4.05 - 3.97 (m, 0.5H), 3.95 - 3.86 (m, 3H), 3.84 - 3.76 (m, 1H), 3.75 - 3.66 (m, 0.5H), 2.63 - 2.54 (m, 1H), 2.54 - 2.42 (m, 2H), 2.25 - 2.14 (m, 1H), 1.56 (d, J = 3.6 Hz, 3H).	
323	<i>m/z</i> (ESI ⁺): 363 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.47 (s, 1H), 7.97 - 7.91 (m, 1H), 7.32 - 7.25 (m, 1H), 7.01 - 6.94 (m, 2H), 6.61 - 6.51 (m, 2H), 6.24 - 6.15 (m, 1H), 5.76 (d, J = 10.4 Hz, 1H), 4.81 (d, J = 2.4 Hz, 1H), 4.50 - 4.38 (m, 2H), 3.99 - 3.94 (m, 1H), 3.84 - 3.78 (m, 1H), 2.59 (d, J = 10.4 Hz, 1H), 2.28 (d, J = 10.4 Hz, 1H).	
324	<i>m/z</i> (ESI ⁺): 425 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 13.77 - 13.49 (m, 1H), 13.13 - 12.94 (m, 1H), 8.52 (s, 1H), 8.18 (d, J = 7.6 Hz, 1H), 7.43 - 7.27 (m, 1H), 7.08 - 6.99 (m, 2H), 6.92 (d, J = 10.4, 16.8 Hz, 1H), 6.32 (d, J = 2.4, 16.4 Hz, 1H), 5.84 (d, J = 2.4, 10.4 Hz, 1H), 4.74 - 4.59 (m, 2H), 4.40 (s, 1H), 4.11 (d, J = 5.6, 11.2 Hz, 2H), 3.86 - 3.68 (m, 2H), 2.34 - 2.05 (m, 4H).	
325	<i>m/z</i> (ESI ⁺): 399 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.26 (s, 1 H), 7.97 - 7.95 (m, 1 H), 7.32 - 7.30 (m, 1 H), 7.01 - 6.97 (m, 2 H), 6.27 - 6.24 (m, 2 H), 5.68 (dd, J = 2.8, 8.8 Hz, 1 H), 1.67 - 1.64 (m, 2 H), 1.43 - 1.39 (m, 2 H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
326	<i>m/z</i> (ESI ⁺): 335 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.40 (s, 1 H), 7.98 (dd, J = 1.6, 8.4 Hz, 1 H), 7.29 - 7.27 (m, 1 H), 6.98 - 6.95 (m, 2 H), 6.23 (d, J = 6.0 Hz, 2 H), 5.67 (t, J = 6.0 Hz, 1 H), 2.45 (s, 3 H), 1.50 - 1.47 (m, 2 H), 1.37 - 1.34 (m, 2 H).	
327	<i>m/z</i> (ESI ⁺): 397 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 13.90 (s, 1 H), 12.58 (s, 1 H), 8.88 (s, 1 H), 8.24 (s, 1 H), 7.96 (d, J = 7.2 Hz, 1 H), 7.71 (d, J = 7.2 Hz, 2 H), 7.49 (t, J = 7.6 Hz, 2 H), 7.39 - 7.28 (m, 1 H), 7.28 - 7.24 (m, 1 H), 6.96 - 6.90 (m, 2 H), 6.01 - 5.96 (m, 2 H), 5.49 (dd, J = 2.8, 9.6 Hz, 1 H), 1.37 - 1.32 (m, 2 H), 1.23 (s, 2 H).	
328	<i>m/z</i> (ESI ⁺): 405 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.51 (s, 1H), 7.93 - 7.88 (m, 1H), 7.32 - 7.25 (m, 1H), 7.01 - 6.95 (m, 2H), 6.67 (dt, J = 10.4, 16.4 Hz, 1H), 6.33 (ddd, J = 2.0, 3.6, 16.8 Hz, 1H), 5.79 (ddd, J = 2.0, 10.4, 12.8 Hz, 1H), 4.28 (dt, J = 4.0, 8.4 Hz, 1H), 4.20 - 4.10 (m, 1H), 4.08 (d, J = 6.8 Hz, 2H), 4.07 - 3.94 (m, 2H), 3.94 - 3.86 (m, 2H), 3.84 - 3.75 (m, 1H), 3.69 - 3.56 (m, 1H), 2.50 - 2.41 (m, 2H), 2.40 - 2.28 (m, 1H), 2.22 - 2.11 (m, 1H).	
329	<i>m/z</i> (ESI ⁺): 405 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.51 (s, 1H), 7.90 (d, J = 8.0 Hz, 1H), 7.29 (t, J = 8.0 Hz, 1H), 7.01 - 6.95 (m, 2H), 6.67 (dt, J = 10.4, 16.4 Hz, 1H), 6.37 - 6.27 (m, 1H), 5.79 (ddd, J = 2.0, 10.4, 12.4 Hz, 1H), 4.28 (dt, J = 3.6, 8.0 Hz, 1H), 4.19 - 4.12 (m, 1H), 4.12 - 4.05 (m, 3H), 4.05 - 3.97 (m, 1H), 3.97 - 3.86 (m, 2H), 3.84 - 3.77 (m, 1H), 3.68 - 3.57 (m, 1H), 2.50 - 2.40 (m, 2H), 2.40 - 2.27 (m, 1H), 2.22 - 2.10 (m, 1H).	
330	<i>m/z</i> (ESI ⁺): 420 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.25 (s, 1H), 12.36 (s, 1H), 8.64 - 8.58 (m, 1H), 8.12 (d, J = 7.2 Hz, 1H), 7.32 - 7.26 (m, 1H), 6.99 - 6.93 (m, 2H), 6.72 - 6.24 (m, 1H), 6.21 - 6.11 (m, 1H), 5.77 - 5.63 (m, 1H), 5.41 - 5.10 (m, 1H), 4.25 - 4.13 (m, 1H), 4.12 - 4.00 (m, 1H), 3.89 - 3.70 (m, 1H), 3.14 - 3.08 (m, 3H), 2.92 - 2.85 (m, 3H), 2.65 - 2.55 (m, 1H), 2.34 - 2.29 (m, 3H), 2.20 (dd, J = 6.4, 12.4 Hz, 1H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
331	<i>m/z</i> (ESI ⁺): 377 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.45 (s, 1H), 7.98 - 7.90 (m, 1H), 7.33 - 7.23 (m, 1H), 7.02 - 6.93 (m, 2H), 6.85 - 6.66 (m, 1H), 6.49 (s, 1H), 6.19 (d, J = 16.8 Hz, 1H), 5.72 (d, J = 2.8 Hz, 1H), 4.71 (s, 1H), 4.32 - 4.19 (m, 2H), 3.80 (dd, J = 1.2, 11.2 Hz, 1H), 3.70 - 3.61 (m, 1H), 2.57 - 2.47 (m, 1H), 2.43 - 2.28 (m, 2H), 2.23 - 2.11 (m, 1H).	A27 1 st isomer
332	<i>m/z</i> (ESI ⁺): 375 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.40 (s, 1H), 7.94 - 7.90 (m, 1H), 7.30 - 7.25 (m, 1H), 6.99 - 6.93 (m, 2H), 6.77 (dd, J = 10.4, 16.8 Hz, 1H), 6.44 (s, 1H), 6.34 (dd, J = 2.0, 16.8 Hz, 1H), 5.80 (dd, J = 2.0, 10.4 Hz, 1H), 4.83 - 4.80 (m, 1H), 4.70 - 4.63 (m, 1H), 3.73 - 3.57 (m, 1H), 2.25 - 2.14 (m, 2H), 2.13 - 2.01 (m, 5H), 1.95 (dt, J = 2.4, 12.4 Hz, 1H).	
333	<i>m/z</i> (ESI ⁺): 361 (M+H) ⁺	(499 MHz, DMSO-d ₆) δ 14.17 (s, 1H), 12.64 (d, J = 12.2 Hz, 1H), 8.56 (d, J = 6.5 Hz, 1H), 8.03 (ddd, J = 8.1, 4.4, 1.6 Hz, 1H), 7.29 (ddt, J = 8.8, 7.2, 1.8 Hz, 1H), 7.03 - 6.91 (m, 2H), 6.56 - 6.39 (m, 2H), 6.12 (dd, J = 16.7, 2.3 Hz, 0H), 5.92 (dd, J = 16.6, 2.3 Hz, 1H), 5.67 (dd, J = 10.4, 2.3 Hz, 0H), 5.37 (dd, J = 10.3, 2.4 Hz, 1H), 4.57 - 4.46 (m, 1H), 3.78 (d, J = 11.9 Hz, 1H), 3.66 (d, J = 10.4 Hz, 0H), 3.20 (dd, J = 14.3, 4.6 Hz, 0H), 3.12 (dt, J = 13.7, 6.3 Hz, 1H), 3.02 (dd, J = 14.2, 6.3 Hz, 1H), 1.53 (ddtd, J = 23.0, 11.3, 7.4, 4.0 Hz, 2H), 0.67 (dtd, J = 12.9, 7.8, 4.9 Hz, 1H), 0.11 - 0.04 (m, 1H).	
334	<i>m/z</i> (ESI ⁺): 455 (M+H) ⁺	(499 MHz, DMSO-d ₆) δ 12.99 (s, 1H), 8.39 (s, 1H), 8.12 (d, J = 7.9 Hz, 1H), 7.31 (t, J = 7.7 Hz, 1H), 7.01 - 6.92 (m, 2H), 6.32 - 6.09 (m, 1H), 6.02 - 5.93 (m, 1H), 5.69 - 5.49 (m, 1H), 4.52 - 4.29 (m, 1H), 4.25 - 4.17 (m, 2H), 4.13 - 3.87 (m, 4H), 3.69 (dd, J = 74.5, 11.3 Hz, 1H), 2.47 (s, 1H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
335	<i>m/z</i> (ESI ⁺): 411 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.01 (s, 1H), 12.58 - 12.40 (m, 1H), 8.44 (d, J = 4.4 Hz, 1H), 8.00 - 7.92 (m, 1H), 7.27 (t, J = 8.0 Hz, 1H), 7.16 - 7.06 (m, 3H), 7.00 (t, J = 7.2 Hz, 2H), 6.97 - 6.90 (m, 2H), 6.79 (dd, J = 10.4, 16.8 Hz, 1H), 6.28 (td, J = 2.4, 16.8 Hz, 1H), 6.11 (d, J = 12.4 Hz, 1H), 5.84 - 5.74 (m, 1H), 4.22 - 3.88 (m, 6H).	A25 2 nd isomer
336	<i>m/z</i> (ESI ⁺): 484 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 13.50 - 13.28 (m, 1H), 13.27 - 12.98 (m, 1H), 8.43 - 8.35 (m, 1H), 8.13 (d, J = 8.0 Hz, 1H), 7.35 - 7.27 (m, 1H), 7.02 - 6.93 (m, 2H), 6.70 - 6.25 (m, 1H), 6.22 - 6.11 (m, 1H), 5.77 - 5.63 (m, 1H), 5.46 - 5.14 (m, 1H), 4.25 - 4.01 (m, 2H), 3.98 - 3.81 (m, 1H), 3.14 - 3.08 (m, 3H), 2.92 - 2.86 (m, 3H), 2.69 - 2.59 (m, 1H), 2.43 - 2.19 (m, 1H).	A38 1 st isomer
337	<i>m/z</i> (ESI ⁺): 484 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 13.37 (s, 1H), 13.25 - 13.08 (m, 1H), 8.42 - 8.37 (m, 1H), 8.14 (d, J = 7.6 Hz, 1H), 7.35 - 7.28 (m, 1H), 7.02 - 6.93 (m, 2H), 6.66 (dd, J = 10.4, 16.8 Hz, 1H), 6.19 - 6.12 (m, 1H), 5.74 - 5.61 (m, 1H), 5.31 - 4.96 (m, 1H), 4.33 - 4.23 (m, 1H), 3.96 - 3.84 (m, 1H), 3.67 - 3.56 (m, 1H), 3.14 - 3.09 (m, 3H), 2.92 - 2.85 (m, 3H), 2.80 - 2.70 (m, 1H), 2.31 - 2.17 (m, 1H).	A38 2 nd isomer
338	<i>m/z</i> (ESI ⁺): 363 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.47 (s, 1H), 7.98 - 7.91 (m, 1H), 7.32 - 7.25 (m, 1H), 7.01 - 6.94 (m, 2H), 6.59 (s, 1H), 6.57 - 6.51 (m, 1H), 6.20 (d, J = 16.4 Hz, 1H), 5.76 (d, J = 10.0 Hz, 1H), 4.81 (d, J = 2.4 Hz, 1H), 4.51 - 4.38 (m, 2H), 3.99 - 3.93 (m, 1H), 3.81 (d, J = 8.8 Hz, 1H), 2.59 (d, J = 10.4 Hz, 1H), 2.29 (d, J = 10.0 Hz, 1H).	A2 1 st isomer
339	<i>m/z</i> (ESI ⁺): 405 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.49 (s, 1H), 7.89 (dd, J = 1.6, 8.4 Hz, 1H), 7.28 (t, J = 7.6 Hz, 1H), 7.01 - 6.94 (m, 2H), 6.73 - 6.60 (m, 1H), 6.37 - 6.28 (m, 1H), 5.78 (ddd, J = 2.0, 10.4, 12.8 Hz, 1H), 4.28 (dt, J = 4.0, 8.4 Hz, 1H), 4.19 - 4.11 (m, 1H), 4.11 - 4.04 (m, 3H), 4.04 - 3.97 (m, 1H), 3.96 - 3.85 (m, 2H), 3.83 - 3.74 (m, 1H), 3.66 - 3.56 (m, 1H), 2.50 - 2.40 (m, 2H), 2.39 - 2.28 (m, 1H), 2.22 - 2.10 (m, 1H).	P 2 nd isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
340	<i>m/z</i> (ESI ⁺): 377 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.16 - 14.04 (m, 1H), 12.36 (s, 1H), 8.59 - 8.53 (m, 1H), 8.17 (d, J = 8.0 Hz, 1H), 7.28 (t, J = 7.6 Hz, 1H), 6.98 - 6.93 (m, 2H), 6.34 - 6.24 (m, 0.5H), 6.17 - 5.99 (m, 1.5H), 5.69 (d, J = 10.8 Hz, 0.5H), 5.44 (d, J = 9.6 Hz, 0.5H), 4.92 - 4.60 (m, 1H), 4.14 - 4.06 (m, 1H), 3.93 - 3.82 (m, 1H), 3.56 - 3.49 (m, 0.5H), 3.29 - 3.16 (m, 2.5H), 2.44 - 2.28 (m, 1H), 2.14 - 2.08 (m, 0.5H), 2.01 - 1.91 (m, 0.5H), 1.40 (t, J = 8.0 Hz, 6H).	A26 1 st isomer
341	<i>m/z</i> (ESI ⁺): 377 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.14 (s, 1H), 12.37 (s, 1H), 8.58 - 8.51 (m, 1H), 8.17 (d, J = 8.4 Hz, 1H), 7.32 - 7.24 (m, 1H), 6.99 - 6.90 (m, 2H), 6.35 - 6.23 (m, 0.5H), 6.18 - 6.01 (m, 1.5H), 5.72 - 5.66 (m, 0.5H), 5.47 - 5.41 (m, 0.5H), 4.88 - 4.60 (m, 1H), 4.16 - 4.05 (m, 1H), 3.95 - 3.80 (m, 1H), 3.57 - 3.48 (m, 0.5H), 3.17 (s, 2.5H), 2.40 - 2.23 (m, 1H), 2.13 - 2.04 (m, 0.5H), 2.01 - 1.90 (m, 0.5H), 1.44 - 1.37 (m, 6H).	A26 2 nd isomer
342	<i>m/z</i> (ESI ⁺): 363 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.11 (s, 1 H), 12.52 (s, 1 H), 8.57 (s, 1 H), 8.03 (d, J = 7.6 Hz, 1 H), 7.29 (t, J = 7.6 Hz, 1 H), 7.11 - 6.88 (m, 2 H), 6.81 (dd, J = 10.4, 16.4 Hz, 1H), 6.50 (d, J = 12.8 Hz, 1 H), 6.11 (d, J = 16.8 Hz, 1H), 5.69 (t, J = 10.0 Hz, 1H), 4.38 (d, J = 13.2 Hz, 1H), 3.89 (s, 1 H), 3.85 - 3.68 (m, 1 H), 3.40 (d, J = 13.6 Hz, 1 H), 2.43 - 2.20 (m, 1 H), 2.01 - 1.72 (m, 1 H), 1.70 - 1.59 (m, 1 H), 1.45 - 1.36 (m, 1 H), 1.34 (s, 3 H).	
343	<i>m/z</i> (ESI ⁺): 363 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.10 - 14.00 (m, 1 H), 12.55 - 12.38 (m, 1 H), 8.52 (s, 1 H), 7.98 (d, J = 7.6 Hz, 1 H), 7.23 (t, J = 7.6 Hz, 1 H), 6.98 - 6.82 (m, 2 H), 6.76 (dd, J = 10.4, 16.4 Hz, 1 H), 6.45 (d, J = 11.2 Hz, 1 H), 6.06 (d, J = 16.4 Hz, 1 H), 5.63 (t, J = 10.4 Hz, 1 H), 4.33 (d, J = 13.2 Hz, 1 H), 3.83 (s, 1 H), 3.76 - 3.61 (m, 1 H), 3.59 - 3.51 (m, 1 H), 3.36 (s, 1 H), 2.37 - 2.13 (m, 1 H), 1.97 - 1.73 (m, 1 H), 1.60 (s, 1 H), 1.28 (s, 3 H).	A23 2 nd isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
344	<i>m/z</i> (ESI ⁺): 375 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.04 (s, 1H), 12.80 - 12.62 (m, 1H), 8.58 (d, J = 8.4 Hz, 1H), 8.03 (d, J = 7.6 Hz, 1H), 7.32 - 7.26 (m, 1H), 7.07 (dd, J = 10.0, 16.4 Hz, 0.5H), 7.02 - 6.94 (m, 2H), 6.79 (dd, J = 10.4, 16.8 Hz, 0.5H), 6.58 - 6.50 (m, 1H), 6.32 - 6.15 (m, 1H), 5.81 - 5.70 (m, 1H), 4.92 - 4.73 (m, 1H), 4.67 - 4.52 (m, 1H), 3.28 - 3.15 (m, 1H), 2.22 - 2.08 (m, 1H), 2.07 - 1.98 (m, 1H), 1.88 - 1.61 (m, 6H).	A8 1 st isomer
345	<i>m/z</i> (ESI ⁺): 375 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.17 - 14.02 (m, 1H), 12.80 - 12.61 (m, 1H), 8.59 (d, J = 8.4 Hz, 1H), 8.05 (d, J = 7.6 Hz, 1H), 7.31 (t, J = 7.6 Hz, 1H), 7.09 (dd, J = 10.0, 16.4 Hz, 0.5H), 7.01 - 6.94 (m, 2H), 6.80 (dd, J = 10.4, 16.8 Hz, 0.5H), 6.59 - 6.51 (m, 1H), 6.34 - 6.19 (m, 1H), 5.84 - 5.72 (m, 1H), 4.92 - 4.73 (m, 1H), 4.67 - 4.55 (m, 1H), 3.30 - 3.18 (m, 1H), 2.20 - 2.01 (m, 2H), 1.92 - 1.63 (m, 6H).	A8 2 nd isomer
346	<i>m/z</i> (ESI ⁺): 411 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 13.96 (s, 1H), 12.67 (s, 1H), 8.51 (d, J = 5.6 Hz, 1H), 7.97 (d, J = 8.0 Hz, 1H), 7.47 - 7.36 (m, 2H), 7.34 - 7.17 (m, 4H), 6.99 - 6.89 (m, 2H), 6.73 - 6.62 (m, 1H), 6.47 (d, J = 13.6 Hz, 1H), 6.27 - 6.17 (m, 1H), 5.73 (d, J = 2.4, 7.6, 10.0 Hz, 1H), 4.35 - 4.19 (m, 1H), 4.16 - 4.03 (m, 1H), 4.02 - 3.93 (m, 1H), 3.93 - 3.81 (m, 1H), 3.78 - 3.60 (m, 1H), 3.60 - 3.47 (m, 1H).	A12 1 st isomer
347	<i>m/z</i> (ESI ⁺): 411 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.13 - 14.00 (m, 1H), 12.56 - 12.39 (m, 1H), 8.43 (d, J = 3.6 Hz, 1H), 8.00 - 7.92 (m, 1H), 7.32 - 7.24 (m, 1H), 7.15 - 7.05 (m, 3H), 7.03 - 6.90 (m, 4H), 6.79 (dd, J = 10.4, 16.8 Hz, 1H), 6.32 - 6.24 (m, 1H), 6.11 (d, J = 12.4 Hz, 1H), 5.82 - 5.74 (m, 1H), 4.20 (t, J = 6.8 Hz, 1H), 4.13 - 4.06 (m, 2H), 4.04 - 3.98 (m, 1H), 3.92 (dt, J = 6.0, 12.0 Hz, 2H).	A12 1 st isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
348	<i>m/z</i> (ESI ⁺): 421 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 13.81 - 13.51 (m, 1 H), 12.14 (s, 1 H), 8.49 (s, 1 H), 8.00 (d, J = 7.6 Hz, 1 H), 7.31 (t, J = 7.2 Hz, 1 H), 7.04 - 6.92 (m, 2 H), 6.83 (d, J = 10.8, 16.8 Hz, 1 H), 6.18 (d, J = 1.2, 16.8 Hz, 1 H), 5.87 (s, 1 H), 5.75 (d, J = 1.6, 10.4 Hz, 1 H), 4.31 - 4.14 (m, 2 H), 4.01 (d, J = 7.6 Hz, 2 H), 3.94 - 3.79 (m, 5 H), 3.61 (d, J = 8.0 Hz, 2 H), 2.34 - 2.15 (m, 2 H).	
349	<i>m/z</i> (ESI ⁺): 419 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 13.94 (s, 1H), 12.22 (s, 1H), 8.42 (d, J = 5.6 Hz, 1H), 8.00 - 7.91 (m, 1H), 7.28 (t, J = 7.6 Hz, 1H), 7.00 - 6.91 (m, 2H), 6.73 - 6.58 (m, 1H), 6.18 (dd, J = 2.0, 16.8 Hz, 1H), 5.72 (ddd, J = 2.4, 8.4, 10.4 Hz, 1H), 4.25 - 4.19 (m, 1H), 4.19 - 4.09 (m, 1H), 3.99 - 3.90 (m, 2H), 3.89 - 3.81 (m, 1H), 3.81 - 3.72 (m, 2H), 3.71 - 3.63 (m, 1H), 3.63 - 3.50 (m, 1H), 2.53 - 2.51 (m, 1H), 2.45 - 2.27 (m, 2H), 2.25 - 2.12 (m, 1H), 1.44 (d, J = 3.2 Hz, 3H).	E 2 nd isomer
350	<i>m/z</i> (ESI ⁺): 419 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.11 (s, 1H), 12.17 (s, 1H), 8.40 (d, J = 4.8 Hz, 1H), 7.94 (d, J = 8.0 Hz, 1H), 7.27 (t, J = 7.6 Hz, 1H), 6.99 - 6.91 (m, 2H), 6.75 - 6.58 (m, 1H), 6.17 (dd, J = 1.8, 16.8 Hz, 1H), 5.75 - 5.65 (m, 1H), 4.25 - 4.16 (m, 1H), 4.16 - 4.04 (m, 1H), 3.98 - 3.94 (m, 2H), 3.89 - 3.78 (m, 2H), 3.78 - 3.70 (m, 2H), 3.63 - 3.48 (m, 1H), 2.47 (s, 1H), 2.42 - 2.36 (m, 1H), 2.36 - 2.25 (m, 1H), 2.22 - 2.09 (m, 1H), 1.44 (d, J = 4.0 Hz, 3H).	E 4 th isomer
351	<i>m/z</i> (ESI ⁺): 375 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.32 (s, 1H), 12.33 (s, 1H), 8.59 (s, 1H), 8.11 (d, J = 8.0 Hz, 1H), 7.28 (t, J = 7.6 Hz, 1H), 6.99 - 6.92 (m, 2H), 6.24 (dd, J = 10.4, 17.2 Hz, 0.5H), 6.17 - 6.08 (m, 0.5H), 6.05 - 5.92 (m, 1H), 5.62 (dd, J = 2.0, 10.4 Hz, 0.5H), 5.50 (dd, J = 2.0, 10.0 Hz, 0.5H), 4.26 (q, J = 9.6 Hz, 1H), 4.13 - 3.99 (m, 2H), 3.99 - 3.91 (m, 0.5H), 3.80 (dd, J = 10.0, 15.6 Hz, 1H), 3.53 (d, J = 10.8 Hz, 0.5H), 2.57 (d, J = 9.6 Hz, 2H), 2.41 - 2.34 (m, 1H), 2.32 (s, 3H), 2.21 (dd, J = 8.4, 10.8 Hz, 1H).	A24 1 st isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
352	<i>m/z</i> (ESI ⁺): 375 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.42 (d, J = 2.8 Hz, 1H), 8.00 (d, J = 7.6 Hz, 1H), 7.28 (t, J = 7.6 Hz, 1H), 7.02 - 6.93 (m, 2H), 6.36 - 6.22 (m, 0.5H), 6.19 - 6.10 (m, 1.5H), 5.70 (d, J = 10.0 Hz, 0.5H), 5.59 (t, J = 6.4 Hz, 0.5H), 4.43 - 4.30 (m, 1H), 4.21 - 4.09 (m, 2.5H), 3.98 - 3.88 (m, 1H), 3.74 (d, J = 11.6 Hz, 0.5H), 2.61 - 2.45 (m, 2H), 2.44 - 2.39 (m, 1H), 2.38 (s, 3H), 2.36 - 2.30 (m, 1H).	A24 2 nd isomer
353	<i>m/z</i> (ESI ⁺): 431 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 13.81 (s, 1H), 12.45 (s, 1H), 8.51 - 8.41 (m, 1H), 8.03 (d, J = 8.0 Hz, 1H), 7.29 (t, J = 7.2 Hz, 1H), 7.03 - 6.93 (m, 2H), 6.28 - 6.21 (m, 0.5H), 6.16 - 6.06 (m, 0.5H), 6.04 - 5.91 (m, 1H), 5.63 - 5.60 (m, 0.5H), 5.50 - 5.47 (m, 0.5H), 4.28 - 4.22 (m, 1H), 4.22 - 4.13 (m, 2H), 4.11 - 3.99 (m, 1H), 3.98 - 3.91 (m, 1H), 3.86 - 3.80 (m, 1H), 3.80 - 3.75 (m, 2H), 3.75 - 3.68 (m, 1H), 3.66 - 3.64 (m, 0.5H), 3.48 - 3.42 (m, 0.5H), 2.60 (d, J = 9.6 Hz, 1.5H), 2.36 - 2.29 (m, 2H), 2.28 - 2.17 (m, 2H), 2.06 - 1.96 (m, 0.5H).	
354	<i>m/z</i> (ESI ⁺): 403 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.02 (s, 1H), 12.32 (s, 1H), 8.55 (s, 1H), 8.17 (d, J = 8.0 Hz, 1H), 7.37 - 7.23 (m, 1H), 7.01 - 6.92 (m, 2H), 6.26 - 6.19 (m, 0.5H), 6.15 - 6.07 (m, 0.5H), 6.03 - 5.91 (m, 1H), 5.62 - 5.59 (m, 0.5H), 5.50 - 5.47 (m, 0.5H), 4.25 - 4.18 (m, 1H), 4.17 - 4.06 (m, 1.5H), 3.97 (d, J = 13.2 Hz, 1H), 3.80 (d, J = 10.8 Hz, 0.5H), 3.67 (d, J = 9.2 Hz, 0.5H), 3.44 (d, J = 11.2 Hz, 0.5H), 3.27 (d, J = 6.4 Hz, 0.5H), 2.64 - 2.57 (m, 1.5H), 2.37 - 2.26 (m, 2H), 2.25 - 2.16 (m, 1H), 1.42 (d, J = 7.2 Hz, 3H), 1.37 - 1.31 (m, 3H).	
355	<i>m/z</i> (ESI ⁺): 385 (M+H) ⁺	(499 MHz, DMSO-d ₆) δ 12.78 (s, 1H), 8.57 (d, J = 12.4 Hz, 1H), 8.05 - 7.87 (m, 1H), 7.32 (s, 1H), 6.98 (q, J = 7.3 Hz, 2H), 6.57 (ddd, J = 18.1, 11.0, 3.2 Hz, 2H), 6.12 (ddd, J = 90.1, 16.6, 2.2 Hz, 1H), 5.85 - 5.39 (m, 1H), 4.92 - 4.72 (m, 1H), 4.26 - 3.80 (m, 2H), 3.50 (dd, J = 14.9, 4.6 Hz, 1H), 3.18 (d, J = 7.6 Hz, 1H), 3.12 - 3.02 (m, 1H), 2.87 - 2.56 (m, 1H), 2.46 - 2.23 (m, 1H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
356	<i>m/z</i> (ESI ⁺): 419 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 13.76 (s, 1H), 12.23 (s, 1H), 8.45 (s, 1H), 7.95 (d, J = 7.6 Hz, 1H), 7.34 - 7.25 (m, 1H), 7.02 - 6.93 (m, 2H), 6.75 - 6.58 (m, 1H), 6.18 (dd, J = 2.0, 16.8 Hz, 1H), 5.72 (ddd, J = 2.4, 7.6, 10.0 Hz, 1H), 4.25 - 4.18 (m, 1.5H), 4.12 (d, J = 12.0 Hz, 0.5H), 3.97 (d, J = 7.2 Hz, 2H), 3.92 (d, J = 10.4 Hz, 0.5H), 3.84 (q, J = 8.0 Hz, 1.5H), 3.80 - 3.67 (m, 2H), 3.65 - 3.47 (m, 1H), 2.46 - 2.38 (m, 1H), 2.38 - 2.26 (m, 2H), 2.21 - 2.09 (m, 1H), 1.44 (d, J = 4.0 Hz, 3H).	E 1 st isomer
357	<i>m/z</i> (ESI ⁺): 419 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 13.79 (s, 1H), 12.24 (s, 1H), 8.49 - 8.40 (m, 1H), 7.97 (t, J = 6.8 Hz, 1H), 7.29 (t, J = 6.8 Hz, 1H), 7.01 - 6.93 (m, 2H), 6.74 - 6.59 (m, 1H), 6.18 (dd, J = 2.4, 16.8 Hz, 1H), 5.76 - 5.68 (m, 1H), 4.25 - 4.16 (m, 1.5H), 4.13 (d, J = 12.0 Hz, 0.5H), 4.00 - 3.93 (m, 2H), 3.90 (d, J = 10.4 Hz, 0.5H), 3.86 - 3.83 (m, 1H), 3.82 - 3.71 (m, 2H), 3.66 (d, J = 12.0 Hz, 0.5H), 3.63 - 3.48 (m, 1H), 2.46 - 2.39 (m, 1H), 2.37 - 2.27 (m, 2H), 2.24 - 2.13 (m, 1H), 1.45 (d, J = 3.6 Hz, 3H).	E 3 rd isomer
358	<i>m/z</i> (ESI ⁺): 482 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 13.65 (s, 1H), 13.06 (s, 1H), 8.56 (d, J = 4.8 Hz, 1H), 8.47 (s, 1H), 8.07 (d, J = 7.2 Hz, 1H), 7.45 - 7.38 (m, 2H), 7.31 - 7.26 (m, 1H), 6.99 - 6.83 (m, 3H), 6.29 - 6.22 (m, 1H), 5.81 - 5.74 (m, 1H), 4.76 - 4.66 (m, 1H), 4.56 (s, 1H), 4.31 (s, 1H), 4.00 (t, J = 11.6 Hz, 2H), 3.66 (t, J = 10.4 Hz, 2H), 2.57 (s, 3H), 2.40 - 2.22 (m, 2H), 2.19 - 2.10 (m, 2H).	
359	<i>m/z</i> (ESI ⁺): 371 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.45 (s, 1H), 7.94 (d, J = 7.6 Hz, 1H), 7.32 - 7.23 (m, 1H), 7.01 - 6.94 (m, 2H), 6.55 (s, 1H), 6.32 (s, 2H), 5.93 - 5.68 (m, 1H), 5.30 - 5.10 (m, 1H), 4.74 - 4.51 (m, 2H), 3.72 - 3.41 (m, 2H).	A22 1 st isomer
360	<i>m/z</i> (ESI ⁺): 371 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.45 (s, 1H), 7.93 (dd, J = 1.2, 8.0 Hz, 1H), 7.32 - 7.24 (m, 1H), 7.02 - 6.93 (m, 2H), 6.55 (s, 1H), 6.32 (s, 2H), 5.91 - 5.73 (m, 1H), 5.28 - 5.10 (m, 1H), 4.72 - 4.53 (m, 2H), 3.72 - 3.43 (m, 2H).	A22 2 nd isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
361	<i>m/z</i> (ESI ⁺): 363 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 13.91 (s, 1H), 12.73 - 12.63 (m, 1H), 8.63 - 8.50 (m, 1H), 8.09 - 7.96 (m, 1H), 7.36 - 7.23 (m, 1H), 7.02 - 6.92 (m, 2H), 6.56 - 6.42 (m, 0.5H), 6.40 - 6.25 (m, 0.5H), 6.21 - 5.98 (m, 1H), 5.87 (d, J = 4.8 Hz, 0.5H), 5.74 - 5.69 (m, 0.5H), 4.61 - 4.48 (m, 1H), 3.96 - 3.82 (m, 1H), 3.75 - 3.56 (m, 1H), 3.30 (s, 2H), 1.34 - 1.22 (m, 3H), 1.13 (s, 3H).	A21 1 st isomer
362	<i>m/z</i> (ESI ⁺): 375 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.18 (s, 1H), 12.68 (s, 1H), 8.57 (s, 1H), 8.04 (d, J = 6.4 Hz, 1H), 7.33 - 7.25 (m, 1H), 7.03 - 6.88 (m, 2H), 6.56 (s, 1H), 6.36 - 6.25 (m, 0.5H), 6.12 (d, J = 17.2 Hz, 0.5H), 5.99 (d, J = 8.0 Hz, 1H), 5.77 - 5.66 (m, 0.6H), 5.33 (d, J = 4.4 Hz, 0.4H), 4.82 - 4.66 (m, 1H), 4.26 - 4.14 (m, 1H), 3.94 (s, 1H), 3.61 - 3.49 (m, 1H), 3.19 (s, 1H), 2.26 - 2.18 (m, 1H), 2.14 (t, J = 7.2 Hz, 2H), 1.96 - 1.83 (m, 1H), 1.81 - 1.63 (m, 1H), 1.59 - 1.34 (m, 1H).	A21 1 st isomer
363	<i>m/z</i> (ESI ⁺): 403 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.03 (s, 1H), 12.31 (s, 1H), 8.55 (s, 1H), 8.17 (d, J = 8.0 Hz, 1H), 7.39 - 7.20 (m, 1H), 7.05 - 6.88 (m, 2H), 6.26 - 6.19 (m, 0.5H), 6.16 - 6.06 (m, 0.5H), 6.03 - 5.90 (m, 1H), 5.62 - 5.59 (m, 0.5H), 5.50 - 5.47 (m, 0.5H), 4.25 - 4.18 (m, 1H), 4.17 - 4.05 (m, 2H), 4.03 - 3.90 (m, 1H), 3.80 (d, J = 10.8 Hz, 0.5H), 3.67 (d, J = 8.8 Hz, 0.5H), 3.44 (d, J = 10.8 Hz, 0.5H), 3.27 - 3.23 (m, 0.5H), 2.65 - 2.57 (m, 1H), 2.38 - 2.28 (m, 2H), 2.25 - 2.13 (m, 1H), 1.42 (d, J = 7.2 Hz, 3H), 1.33 (d, J = 5.6 Hz, 3H).	A20 1 st isomer
364	<i>m/z</i> (ESI ⁺): 403 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.04 (s, 1H), 12.32 (s, 1H), 8.55 (s, 1H), 8.16 (d, J = 7.6 Hz, 1H), 7.30 - 7.26 (m, 1H), 7.05 - 6.87 (m, 2H), 6.26 - 6.19 (m, 0.5H), 6.16 - 6.06 (m, 0.5H), 6.04 - 5.90 (m, 1H), 5.62 - 5.59 (m, 0.5H), 5.50 - 5.47 (m, 0.5H), 4.28 - 4.18 (m, 1H), 4.17 - 4.05 (m, 2H), 4.03 - 3.90 (m, 1H), 3.79 (d, J = 10.4 Hz, 0.5H), 3.67 (d, J = 8.8 Hz, 0.5H), 3.44 (d, J = 10.0 Hz, 0.5H), 3.27 - 3.22 (m, 0.5H), 2.63 - 2.57 (m, 1H), 2.37 - 2.28 (m, 2H), 2.25 - 2.13 (m, 1H), 1.42 (d, J = 6.8 Hz, 3H), 1.33 (d, J = 6.4 Hz, 3H).	A20 2 nd isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
365	<i>m/z</i> (ESI ⁺): 421 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.12 (s, 1 H), 12.02 (s, 1 H), 8.57 (s, 1 H), 8.02 (d, J = 7.2 Hz, 1 H), 7.31 - 7.27 (m, 1 H), 6.98 - 6.93 (m, 2 H), 6.58 (s, 1 H), 5.27 - 5.24 (m, 1 H), 5.15 - 5.14 (m, 1 H), 4.81 - 4.74 (m, 1 H), 4.29 - 3.93 (m, 1 H), 3.86 (s, 3 H), 3.30 - 3.17 (m, 2 H), 3.07 - 3.01 (m, 1 H), 2.90 - 2.83 (m, 2 H), 2.34 - 2.32 (m, 1 H), 2.12 - 2.11 (m, 1 H).	
366	<i>m/z</i> (ESI ⁺): 378 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.45 (s, 1H), 7.96 - 7.91 (m, 1H), 7.28 (t, J = 1.6, 7.6 Hz, 1H), 6.98 (d, J = 7.6 Hz, 2H), 6.75 (dd, J = 11.2, 16.8 Hz, 1H), 6.59 (s, 1H), 6.19 (d, J = 17.2 Hz, 1H), 5.73 (dd, J = 1.6, 10.4 Hz, 1H), 4.80 - 4.69 (m, 0.5H), 4.44 - 4.25 (m, 1H), 3.98 - 3.88 (m, 0.5H), 3.87 - 3.71 (m, 2H), 3.60 - 3.44 (m, 0.5H), 3.23 - 3.11 (m, 0.5H), 3.03 - 2.94 (m, 1H), 2.83 (d, J = 11.2 Hz, 1H), 2.30 (d, J = 10.4 Hz, 1H), 2.17 (t, J = 10.8 Hz, 1H), 1.44 - 1.32 (m, 3H).	
367	<i>m/z</i> (ESI ⁺): 378 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.45 (s, 1H), 7.97 - 7.91 (m, 1H), 7.28 (t, J = 1.6, 7.6 Hz, 1H), 7.01 - 6.94 (m, 2H), 6.75 (dd, J = 11.2, 16.4 Hz, 1H), 6.59 (s, 1H), 6.19 (d, J = 16.4 Hz, 1H), 5.73 (dd, J = 2.0, 10.8 Hz, 1H), 4.81 - 4.69 (m, 0.5H), 4.44 - 4.27 (m, 1H), 3.97 - 3.89 (m, 0.5H), 3.87 - 3.72 (m, 2H), 3.58 - 3.44 (m, 0.5H), 3.25 - 3.10 (m, 0.5H), 2.98 (d, J = 9.6 Hz, 1H), 2.83 (d, J = 11.2 Hz, 1H), 2.30 (d, J = 9.2 Hz, 1H), 2.17 (t, J = 11.2 Hz, 1H), 1.43 - 1.34 (m, 3H).	
368	<i>m/z</i> (ESI ⁺): 471 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.07 (s, 1H), 12.78 - 12.55 (m, 1H), 8.48 - 8.38 (m, 1H), 8.17 (s, 1H), 8.15 - 8.08 (m, 1H), 7.76 (s, 1H), 7.32 - 7.23 (m, 1H), 6.99 - 6.92 (m, 2H), 6.87 (dd, J = 10.0, 16.4 Hz, 1H), 6.26 (dd, J = 2.4, 16.8 Hz, 1H), 5.78 (dd, J = 2.4, 10.4 Hz, 1H), 4.79 - 4.61 (m, 1H), 4.59 - 4.53 (m, 1H), 4.31 (m, 1H), 4.07 (t, J = 10.4 Hz, 2H), 3.96 (s, 3H), 3.75 - 3.62 (m, 2H), 2.31 - 2.05 (m, 4H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
369	<i>m/z</i> (ESI ⁺): 431 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 13.82 (s, 1H), 12.42 (s, 1H), 8.47 (s, 1H), 7.99 (d, J = 8.0 Hz, 1H), 7.35 - 7.24 (m, 1H), 7.03 - 6.92 (m, 2H), 6.28 - 6.21 (m, 0.5H), 6.17 - 6.06 (m, 0.5H), 6.03 - 5.91 (m, 1H), 5.63 - 5.60 (m, 0.5H), 5.50 - 5.47 (m, 0.5H), 4.26 (s, 1H), 4.22 - 4.11 (m, 2H), 4.11 - 4.01 (m, 1H), 3.94 (d, J = 7.2 Hz, 2H), 3.84 - 3.80 (m, 1H), 3.79 - 3.70 (m, 2H), 3.68 (d, J = 9.2 Hz, 0.5H), 3.44 (s, 0.5H), 2.66 - 2.59 (m, 1H), 2.37 - 2.26 (m, 2H), 2.25 - 2.08 (m, 2H), 2.07 - 1.95 (m, 1H).	A19 2 nd isomer
370	<i>m/z</i> (ESI ⁺): 431 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 13.88 (s, 1H), 12.44 (s, 1H), 8.44 (s, 1H), 8.09 - 7.99 (m, 1H), 7.34 - 7.24 (m, 1H), 7.04 - 6.89 (m, 2H), 6.28 - 6.21 (m, 0.5H), 6.16 - 6.05 (m, 0.5H), 6.04 - 5.92 (m, 1H), 5.63 - 5.60 (m, 0.5H), 5.50 - 5.47 (m, 0.5H), 4.23 (s, 1H), 4.22 - 4.15 (m, 2H), 4.11 - 3.99 (m, 1H), 3.98 - 3.90 (m, 0.5H), 3.88 - 3.84 (m, 0.5H), 3.81 (d, J = 7.6 Hz, 1H), 3.80 - 3.75 (m, 2H), 3.74 - 3.67 (m, 1H), 3.65 (d, J = 9.2 Hz, 0.5H), 3.43 (d, J = 10.4 Hz, 0.5H), 2.63 - 2.59 (m, 1H), 2.39 - 2.14 (m, 5H).	A19 4 th isomer
371	<i>m/z</i> (ESI ⁺): 431 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 13.79 (s, 1H), 12.45 (s, 1H), 8.44 (s, 1H), 8.03 (d, J = 8.0 Hz, 1H), 7.34 - 7.24 (m, 1H), 7.02 - 6.92 (m, 2H), 6.28 - 6.21 (m, 0.5H), 6.16 - 6.05 (m, 0.5H), 6.04 - 5.91 (m, 1H), 5.63 - 5.60 (m, 0.5H), 5.50 - 5.47 (m, 0.5H), 4.23 (s, 1H), 4.22 - 4.15 (m, 2H), 4.12 - 3.99 (m, 1H), 3.98 - 3.91 (m, 0.5H), 3.87 - 3.84 (m, 0.5H), 3.82 (d, J = 5.6 Hz, 1H), 3.78 - 3.75 (m, 2H), 3.74 - 3.68 (m, 1H), 3.65 (d, J = 9.6 Hz, 0.5H), 3.45 (s, 0.5H), 2.60 (d, J = 9.6 Hz, 1H), 2.39 - 2.14 (m, 5H).	A19 1 st isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
372	<i>m/z</i> (ESI ⁺): 363 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.05 - 13.81 (m, 1 H), 13.30 - 12.01 (m, 1 H), 8.62 (s, 1 H), 8.04 (d, J = 8.0 Hz, 1 H), 7.34 - 7.25 (m, 1 H), 7.02 - 6.93 (m, 2 H), 6.74 (s, 1 H), 6.39 - 6.12 (m, 1 H), 6.11 - 5.98 (m, 1 H), 5.74 - 5.49 (m, 1 H), 4.97 - 4.89 (m, 1 H), 4.88 - 4.81 (m, 1 H), 4.70 - 4.63 (m, 1 H), 4.51 - 4.41 (m, 1 H), 4.13 (d, J = 11.6 Hz, 1 H), 3.96 - 3.78 (m, 1 H), 3.62 (d, J = 12.0 Hz, 1 H).	A16 1 st isomer
373	<i>m/z</i> (ESI ⁺): 363 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 13.90 (s, 1 H), 12.92 - 12.60 (m, 1 H), 8.63 (s, 1 H), 8.04 (d, J = 7.2 Hz, 1 H), 7.34 - 7.25 (m, 1 H), 7.00 - 6.94 (m, 2 H), 6.75 (s, 1 H), 6.38 - 6.12 (m, 1 H), 6.11 - 5.98 (m, 1 H), 5.73 - 5.50 (m, 1 H), 4.97 - 4.89 (m, 1 H), 4.87 - 4.81 (m, 1 H), 4.70 - 4.64 (m, 1 H), 4.46 (t, J = 11.2 Hz, 1 H), 4.13 (d, J = 11.6 Hz, 1 H), 3.95 - 3.79 (m, 1 H), 3.62 (d, J = 12.0 Hz, 1 H).	A16 2 nd isomer
374	<i>m/z</i> (ESI ⁺): 377 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.17 (s, 1 H), 12.76 - 12.49 (m, 1 H), 8.65 (s, 1 H), 8.12 (d, J = 7.6 Hz, 1 H), 7.33 - 7.26 (m, 1 H), 7.01 - 6.93 (m, 2 H), 6.34 - 6.12 (m, 1 H), 6.08 - 5.97 (m, 1 H), 5.69 - 5.51 (m, 1 H), 5.03 (d, J = 4.8 Hz, 1 H), 4.90 - 4.80 (m, 2 H), 4.65 (d, J = 10.4 Hz, 0.5 H), 4.48 (d, J = 10.4 Hz, 0.5 H), 4.39 (d, J = 11.6 Hz, 0.5 H), 4.24 (d, J = 10.8 Hz, 0.5 H), 4.15 (d, J = 12.0 Hz, 0.5 H), 3.95 (d, J = 11.2 Hz, 1 H), 3.64 (d, J = 12.0 Hz, 0.5 H), 2.32 (s, 3 H).	A18 1 st isomer
375	<i>m/z</i> (ESI ⁺): 377 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.17 (s, 1 H), 12.71 - 12.51 (m, 1 H), 8.65 (s, 1 H), 8.12 (d, J = 8.0 Hz, 1 H), 7.32 - 7.26 (m, 1 H), 7.01 - 6.93 (m, 2 H), 6.35 - 6.12 (m, 1 H), 6.09 - 5.97 (m, 1 H), 5.70 - 5.49 (m, 1 H), 5.06 - 4.99 (m, 1 H), 4.91 - 4.79 (m, 2 H), 4.65 (d, J = 10.4 Hz, 0.5 H), 4.48 (d, J = 10.4 Hz, 0.5 H), 4.39 (d, J = 12.4 Hz, 0.5 H), 4.24 (d, J = 11.2 Hz, 0.5 H), 4.15 (d, J = 12.0 Hz, 0.5 H), 3.95 (d, J = 11.2 Hz, 1 H), 3.64 (d, J = 12.0 Hz, 0.5 H), 2.32 (s, 3 H).	A18 2 nd isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
376	<i>m/z</i> (ESI ⁺): 419 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.02 (s, 1H), 12.50 (s, 1H), 8.62 (d, J = 4.4 Hz, 1H), 8.21 (d, J = 8.0 Hz, 1H), 7.33 - 7.27 (m, 1H), 7.00 - 6.95 (m, 2H), 6.71 - 6.58 (m, 1H), 6.22 - 6.14 (m, 1H), 5.75 - 5.66 (m, 1H), 4.10 - 4.01 (m, 1H), 3.97 - 3.88 (m, 3H), 3.79 - 3.65 (m, 4H), 3.53 - 3.45 (m, 1H), 3.23 (d, J = 11.2 Hz, 1H), 2.36 - 2.21 (m, 3H), 1.93 - 1.85 (m, 1H), 1.77 - 1.67 (m, 2H).	A17 1 st isomer
377	<i>m/z</i> (ESI ⁺): 419 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.06 (s, 1H), 12.50 (s, 1H), 8.62 (d, J = 3.2 Hz, 1H), 8.20 (d, J = 8.0 Hz, 1H), 7.33 - 7.26 (m, 1H), 7.01 - 6.94 (m, 2H), 6.71 - 6.58 (m, 1H), 6.22 - 6.14 (m, 1H), 5.75 - 5.64 (m, 1H), 4.12 - 3.99 (m, 1H), 3.96 - 3.85 (m, 3H), 3.83 - 3.64 (m, 4H), 3.52 - 3.43 (m, 1H), 3.27 - 3.19 (m, 1H), 2.41 - 2.16 (m, 3H), 1.94 - 1.85 (m, 1H), 1.78 - 1.66 (m, 2H).	A17 2 nd isomer
378	<i>m/z</i> (ESI ⁺): 381 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.99 (s, 1H), 12.35 (s, 1H), 8.68 (s, 1H), 7.99 (d, J = 8.4 Hz, 1H), 7.25 (dd, J = 8.0, 9.6 Hz, 1H), 6.96 - 6.85 (m, 2H), 6.17 (dd, J = 2.4, 16.8 Hz, 1H), 5.95 (m, 1H), 5.73 (dd, J = 2.4, 10.4 Hz, 1H), 4.28 - 4.05 (m, 1H), 3.14 - 2.97 (m, 1H), 2.22 (s, 3H), 1.92 - 1.77 (m, 1H), 1.75 - 1.62 (m, 2H), 1.60 - 1.45 (m, 2H), 1.23 (s, 1H).	O 1 st isomer
379	<i>m/z</i> (ESI ⁺): 381 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 15.06 - 14.92 (m, 1H), 12.47 - 12.24 (m, 1H), 8.69 (s, 1H), 7.99 (d, J = 8.0 Hz, 1H), 7.30 - 7.19 (m, 1H), 6.96 - 6.85 (m, 2H), 6.17 (dd, J = 2.4, 16.8 Hz, 1H), 6.00 - 5.91 (m, 1H), 5.73 (dd, J = 2.0, 10.4 Hz, 1H), 4.28 - 4.03 (m, 1H), 3.12 - 3.02 (m, 1H), 2.22 (s, 3H), 1.87 - 1.79 (m, 1H), 1.72 - 1.64 (m, 2H), 1.59 - 1.49 (m, 2H), 1.26 - 1.21 (m, 1H).	O 2 nd isomer
380	<i>m/z</i> (ESI ⁺): 367 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 15.05 - 14.49 (m, 1H), 12.91 - 12.43 (m, 1H), 8.60 (s, 1H), 7.85 (d, J = 6.8 Hz, 1H), 7.30 - 7.19 (m, 1H), 6.86 (m, 2H), 6.53 - 6.41 (m, 1H), 6.22 - 6.12 (m, 1H), 6.11 - 5.92 (m, 1H), 5.83 - 5.61 (m, 1H), 4.21 - 3.94 (m, 1H), 3.14 - 3.07 (m, 1H), 1.90 - 1.83 (m, 1H), 1.72 - 1.62 (m, 2H), 1.49 - 1.39 (m, 2H), 1.23 (s, 1H).	O 3 rd isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
381	<i>m/z</i> (ESI ⁺): 376 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.46 (s, 1H), 7.96 - 7.89 (m, 1H), 7.32 - 7.24 (m, 1H), 7.01 - 6.93 (m, 2H), 6.56 (s, 1H), 6.37 - 6.28 (m, 1H), 6.26 - 6.18 (m, 1H), 5.72 (dd, J = 2.0, 10.0 Hz, 1H), 4.41 (s, 2H), 4.16 (s, 2H), 3.89 (s, 2H), 3.56 (d, J = 0.8 Hz, 4H).	
382	<i>m/z</i> (ESI ⁺): 502.3 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.59 (d, J = 1.6 Hz, 1H), 7.99 - 7.94 (m, 1H), 7.35 - 7.28 (m, 1H), 7.03 - 6.96 (m, 2H), 6.67 (t, J = 10.4, 16.8 Hz, 1H), 6.38 - 6.28 (m, 1H), 5.79 (d, J = 2.0, 10.4, 14.0 Hz, 1H), 4.18 - 4.08 (m, 1H), 4.08 - 3.93 (m, 2H), 3.89 (t, J = 4.8 Hz, 4H), 3.85 - 3.75 (m, 1H), 3.68 - 3.56 (m, 1H), 3.16 - 3.03 (m, 1H), 2.60 (s, 4H), 2.48 - 2.29 (m, 5H), 2.27 - 2.16 (m, 2H), 1.63 (t, J = 13.6 Hz, 2H), 1.58 - 1.47 (m, 2H).	
383	<i>m/z</i> (ESI ⁺): 421.1 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.69 (s, 1 H), 7.79 (d, J = 7.2 Hz, 1 H), 7.46 - 7.37 (m, 1 H), 7.12 - 7.01 (m, 2 H), 6.88 - 6.72 (m, 1 H), 6.33 (d, J = 2.0, 16.8 Hz, 1 H), 6.11 (s, 1 H), 5.85 (d, J = 2.0, 10.8 Hz, 1 H), 4.43 - 4.37 (m, 1 H), 4.29 - 4.22 (m, 1 H), 4.18 - 4.11 (m, 2 H), 4.07 - 3.98 (m, 4 H), 3.87 (q, J = 8.4 Hz, 1 H), 3.81 - 3.69 (m, 1 H), 3.62 - 3.51 (m, 1 H), 2.38 - 2.26 (m, 1 H), 2.09 - 1.97 (m, 1 H).	A14 2 nd isomer
384	<i>m/z</i> (ESI ⁺): 409.1 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.11 - 14.03 (m, 1H), 12.62 - 12.52 (m, 1H), 8.62 - 8.52 (m, 1H), 8.02 (d, J = 8.0 Hz, 1H), 7.29 (t, J = 8.0 Hz, 1H), 6.99 - 6.91 (m, 2H), 6.76 (dd, J = 10.4, 16.8 Hz, 1H), 6.54 - 6.49 (m, 1H), 6.26 - 6.17 (m, 1H), 5.82 - 5.70 (m, 1H), 5.45 - 5.20 (m, 1H), 4.66 - 4.56 (m, 1H), 4.46 - 4.36 (m, 1H), 4.35 - 4.25 (m, 1H), 4.09 - 3.97 (m, 2H), 3.83 - 3.70 (m, 2H), 2.38 - 2.14 (m, 2H).	A12
	<i>m/z</i> (ESI ⁺): 414.05 (M+H) ⁺		

Cmpd #	MS	¹ H NMR	SFC Conditions
386	<i>m/z</i> (ESI ⁺): 390.1 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.13 - 13.74 (m, 1H), 12.55 (s, 1H), 8.64 - 8.54 (m, 1H), 8.05 - 7.98 (m, 1H), 7.33 - 7.26 (m, 1H), 7.00 - 6.93 (m, 2H), 6.73 - 6.64 (m, 1H), 6.54 (s, 0.5H), 6.21 - 6.11 (m, 1H), 5.94 (d, J = 6.4 Hz, 0.5H), 5.73 - 5.63 (m, 1H), 4.54 - 4.40 (m, 2H), 3.94 - 3.73 (m, 2H), 2.81 - 2.72 (m, 2H), 2.35 - 2.19 (m, 2H), 2.05 - 1.91 (m, 2H), 1.88 - 1.81 (m, 1H), 1.79 - 1.68 (m, 1H).	
387	<i>m/z</i> (ESI ⁺): 375.1 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.43 (s, 1H), 7.97 - 7.88 (m, 1H), 7.34 - 7.22 (m, 1H), 7.03 - 6.91 (m, 2H), 6.62 (dd, J = 10.4, 16.8 Hz, 0.5H), 6.58 (d, J = 2.8 Hz, 1H), 6.48 (dd, J = 10.4, 16.8 Hz, 0.5H), 6.26 (d, J = 2.0, 7.6, 16.8 Hz, 1H), 5.84 - 5.64 (m, 1H), 3.89 - 3.81 (m, 1.5H), 3.80 - 3.69 (m, 1H), 3.68 - 3.63 (m, 0.5H), 3.56 - 3.47 (m, 0.5H), 3.40 - 3.34 (m, 0.5H), 3.29 - 3.24 (m, 0.5H), 3.23 - 3.13 (m, 0.5H), 2.62 - 2.47 (m, 1H), 2.44 - 2.31 (m, 1H), 2.29 - 2.16 (m, 1H), 2.11 - 2.01 (m, 1H), 1.99 - 1.68 (m, 2H).	X 3 rd isomer
388	<i>m/z</i> (ESI ⁺): 375.1 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.43 (s, 1H), 7.99 - 7.87 (m, 1H), 7.34 - 7.23 (m, 1H), 7.02 - 6.93 (m, 2H), 6.62 (dd, J = 10.4, 16.8 Hz, 0.5H), 6.58 (d, J = 2.8 Hz, 1H), 6.48 (dd, J = 10.4, 16.8 Hz, 0.5H), 6.26 (d, J = 2.0, 7.2, 16.8 Hz, 1H), 5.80 - 5.65 (m, 1H), 3.89 - 3.81 (m, 1.5H), 3.80 - 3.69 (m, 1H), 3.69 - 3.62 (m, 0.5H), 3.51 (d, J = 7.6, 10.4 Hz, 0.5H), 3.41 - 3.34 (m, 0.5H), 3.29 - 3.24 (m, 0.5H), 3.18 (ddd, J = 5.2, 7.6, 12.8 Hz, 0.5H), 2.63 - 2.47 (m, 1H), 2.44 - 2.31 (m, 1H), 2.29 - 2.15 (m, 1H), 2.09 - 2.01 (m, 1H), 2.00 - 1.68 (m, 2H).	X 4 th isomer
389	<i>m/z</i> (ESI ⁺): 387.1 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.54 (s, 1 H), 7.69 (s, 1 H), 7.47 (s, 1 H), 7.16 - 7.03 (m, 3 H), 6.92 (s, 1 H), 6.36 (d, J = 17.2 Hz, 1 H), 5.90 (dd, J = 1.6, 10.8 Hz, 1 H), 5.02 (s, 2 H), 4.50 (s, 2 H), 4.23 (t, J = 5.2 Hz, 2 H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
390	<i>m/z</i> (ESI ⁺): 421.1 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 13.97 - 13.52 (m, 1 H), 12.30 - 11.88 (m, 1 H), 8.47 (s, 1 H), 7.99 (dd, J = 1.6, 8.4 Hz, 1 H), 7.32 - 7.26 (m, 1 H), 7.01 - 6.94 (m, 2 H), 6.82 (dd, J = 10.4, 16.8 Hz, 1 H), 6.17 (dd, J = 2.4, 16.8 Hz, 1 H), 5.85 (s, 1 H), 5.74 (dd, J = 2.4, 10.4 Hz, 1 H), 4.24 (d, J = 11.2 Hz, 1 H), 4.17 (dt, J = 4.4, 8.4 Hz, 1 H), 4.00 (d, J = 8.0 Hz, 2 H), 3.90 (d, J = 4.0 Hz, 1 H), 3.88 - 3.85 (m, 2 H), 3.83 (s, 1 H), 3.82 - 3.78 (m, 1 H), 3.61 (d, J = 7.6 Hz, 2 H), 2.31 - 2.22 (m, 1 H), 2.22 - 2.15 (m, 1 H).	A15 1 st isomer
391	<i>m/z</i> (ESI ⁺): 421.1 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 13.68 (s, 1 H), 12.12 (s, 1 H), 8.51 (s, 1 H), 8.00 (dd, J = 1.6, 8.4 Hz, 1 H), 7.34 - 7.27 (m, 1 H), 7.02 - 6.95 (m, 2 H), 6.85 (dd, J = 10.4, 16.8 Hz, 1 H), 6.20 (dd, J = 2.4, 16.8 Hz, 1 H), 5.89 (s, 1 H), 5.76 (dd, J = 2.4, 10.4 Hz, 1 H), 4.26 (d, J = 12.4 Hz, 1 H), 4.16 (t, J = 4.4, 8.4 Hz, 1 H), 4.02 (s, 1 H), 4.01 - 3.97 (m, 1 H), 3.94 (t, J = 7.6 Hz, 2 H), 3.88 (dd, J = 4.0, 12.4 Hz, 1 H), 3.80 (q, J = 8.0 Hz, 2 H), 3.66 - 3.54 (m, 2 H), 2.17 (d, J = 4.4, 8.4, 12.4 Hz, 1 H), 2.12 - 2.06 (m, 1 H).	A15 2 nd isomer
392	<i>m/z</i> (ESI ⁺): 389.1 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.50 - 14.28 (m, 1H), 12.49 - 12.23 (m, 1H), 8.55 (s, 1H), 8.11 (d, J = 8.0 Hz, 1H), 7.33 - 7.22 (m, 1H), 7.01 - 6.87 (m, 2H), 6.63 - 6.33 (m, 1H), 6.10 (d, J = 2.4, 5.6, 16.8 Hz, 1H), 5.71 - 5.50 (m, 1H), 4.05 - 3.90 (m, 1H), 3.78 - 3.61 (m, 1H), 3.59 - 3.46 (m, 1H), 3.44 - 3.38 (m, 0.5H), 3.22 - 3.14 (m, 0.5H), 3.08 - 3.00 (m, 0.5H), 2.89 - 2.81 (m, 0.5H), 2.81 - 2.74 (m, 1H), 2.20 (d, J = 3.2 Hz, 3H), 2.19 - 2.12 (m, 2H), 2.02 - 1.87 (m, 2H), 1.76 - 1.63 (m, 1H).	A13 4 th isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
393	<i>m/z</i> (ESI ⁺): 389.1 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.37 (d, J = 2.4 Hz, 1H), 8.02 - 7.94 (m, 1H), 7.31 - 7.23 (m, 1H), 7.01 - 6.92 (m, 2H), 6.69 - 6.39 (m, 1H), 6.25 (d, J = 2.0, 7.6, 16.8 Hz, 1H), 5.80 - 5.65 (m, 1H), 4.05 (dt, J = 4.8, 9.2 Hz, 1H), 3.87 - 3.80 (m, 0.5H), 3.76 - 3.69 (m, 1H), 3.59 (d, J = 12.8 Hz, 0.5H), 3.54 - 3.47 (m, 0.5H), 3.37 - 3.34 (m, 0.5H), 3.17 - 3.11 (m, 0.5H), 3.06 - 2.94 (m, 0.5H), 2.78 - 2.64 (m, 0.5H), 2.39 - 2.28 (m, 2H), 2.26 (d, J = 5.2 Hz, 3H), 2.10 - 2.04 (m, 1H), 2.01 - 1.82 (m, 2H).	A13 3 rd isomer
394	<i>m/z</i> (ESI ⁺): 390.2 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.43 (s, 1H), 7.92 (d, J = 8.0 Hz, 1H), 7.34 - 7.21 (m, 1H), 7.03 - 6.91 (m, 2H), 6.62 (dd, J = 10.4, 16.8 Hz, 1H), 6.55 (s, 1H), 6.26 (dd, J = 2.0, 16.8 Hz, 1H), 5.73 (dd, J = 2.0, 10.4 Hz, 1H), 3.93 - 3.83 (m, 3H), 3.76 (dd, J = 8.8, 12.8 Hz, 1H), 3.62 - 3.49 (m, 2H), 3.08 - 2.84 (m, 2H), 2.79 - 2.70 (m, 2H), 2.70 - 2.61 (m, 2H).	
395	<i>m/z</i> (ESI ⁺): 390.1 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.23 - 14.05 (m, 1H), 12.56 (s, 1H), 8.58 (s, 1H), 8.03 (d, J = 7.2 Hz, 1H), 7.29 (t, J = 7.6 Hz, 1H), 6.99 - 6.91 (m, 2H), 6.75 (dd, J = 10.4, 16.8 Hz, 1H), 6.61 (s, 1H), 6.11 (dd, J = 2.4, 16.8 Hz, 1H), 5.67 (dd, J = 2.0, 10.4 Hz, 1H), 4.11 (d, J = 13.2 Hz, 1H), 3.78 (s, 2H), 3.75 (s, 1H), 3.31 - 3.25 (m, 3H), 2.90 (d, J = 12.0 Hz, 1H), 2.06 - 1.85 (m, 2H), 1.59 - 1.40 (m, 2H).	
397	<i>m/z</i> (ESI ⁺): 379.1 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.68 - 13.94 (m, 1 H), 13.01 - 12.36 (m, 1 H), 8.54 (s, 1 H), 8.03 (d, J = 7.6 Hz, 1 H), 7.28 (t, J = 8.0 Hz, 1 H), 7.01 - 6.91 (m, 2 H), 6.80 - 6.62 (m, 1 H), 6.58 - 6.50 (m, 1 H), 6.14 (d, J = 1.6 Hz, 1 H), 5.78 - 5.69 (m, 1 H), 4.44 (d, J = 7.6, 11.6 Hz, 1 H), 4.34 - 4.21 (m, 2 H), 3.69 - 3.61 (m, 4 H), 3.47 (s, 3 H), 2.24 - 2.09 (m, 1 H).	A11 1 st isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
398	<i>m/z</i> (ESI ⁺): 379.1 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.34 - 13.95 (m, 1 H), 12.80 - 12.38 (m, 1 H), 8.56 (d, J = 3.6 Hz, 1 H), 8.03 (d, J = 8.0 Hz, 1 H), 7.33 - 7.24 (m, 1 H), 7.03 - 6.92 (m, 2 H), 6.79 - 6.62 (m, 1 H), 6.53 (d, J = 5.2 Hz, 1 H), 6.20 (d, J = 2.4, 16.8 Hz, 1 H), 5.77 - 5.67 (m, 1 H), 4.49 - 4.31 (m, 1 H), 4.17 - 4.06 (m, 1 H), 4.03 - 3.86 (m, 2 H), 3.84 - 3.61 (m, 2 H), 3.54 - 3.43 (m, 3 H), 2.44 - 2.22 (m, 2 H).	A11 2 nd isomer
399	<i>m/z</i> (ESI ⁺): 379.1 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.29 - 13.79 (m, 1H), 12.67 (s, 1H), 8.61 - 8.53 (m, 1H), 8.02 (d, J = 8.0 Hz, 1H), 7.30 (t, J = 7.6 Hz, 1H), 7.01 - 6.91 (m, 2H), 6.78 - 6.61 (m, 1H), 6.57 (s, 1H), 6.18 (d, J = 16.8 Hz, 1H), 5.77 - 5.66 (m, 1H), 4.51 - 4.38 (m, 1H), 4.34 - 4.20 (m, 1H), 3.69 - 3.60 (m, 2H), 3.50 - 3.43 (m, 1H), 3.25 (s, 3H), 3.14 - 3.04 (m, 0.5H), 2.71 (m, 0.5H), 2.65 - 2.54 (m, 1H), 2.25 - 2.07 (m, 1H).	A10 1 st isomer
400	<i>m/z</i> (ESI ⁺): 379.1 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.09 (s, 1H), 12.58 (s, 1H), 8.57 (d, J = 5.6 Hz, 1H), 8.03 (d, J = 8.0 Hz, 1H), 7.34 - 7.24 (m, 1H), 7.01 - 6.90 (m, 2H), 6.78 - 6.60 (m, 1H), 6.53 (d, J = 6.4 Hz, 1H), 6.19 (dd, J = 2.4, 16.8 Hz, 1H), 5.77 - 5.65 (m, 1H), 4.48 - 4.30 (m, 1H), 4.18 - 4.03 (m, 1H), 3.99 - 3.87 (m, 1H), 3.84 - 3.75 (m, 1H), 3.57 - 3.43 (m, 2H), 3.32 (d, J = 2.4 Hz, 3H), 2.44 - 2.18 (m, 2H).	A10 2 nd isomer
401	<i>m/z</i> (ESI ⁺): 421.1 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 13.81 - 13.51 (m, 1 H), 12.14 (s, 1 H), 8.49 (s, 1 H), 8.00 (d, J = 7.6 Hz, 1 H), 7.31 (t, J = 7.2 Hz, 1 H), 7.04 - 6.92 (m, 2 H), 6.83 (d, J = 10.8, 16.8 Hz, 1 H), 6.18 (d, J = 1.2, 16.8 Hz, 1 H), 5.87 (s, 1 H), 5.75 (d, J = 1.6, 10.4 Hz, 1 H), 4.31 - 4.14 (m, 2 H), 4.01 (d, J = 7.6 Hz, 2 H), 3.94 - 3.79 (m, 5 H), 3.61 (d, J = 8.0 Hz, 2 H), 2.34 - 2.15 (m, 2 H).	A14 1 st isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
402	<i>m/z</i> (ESI ⁺): 419.2 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 12.94 - 12.29 (m, 1 H), 8.07 (s, 1 H), 7.79 - 7.77 (m, 1H), 7.56 (s, 1 H), 7.50 - 7.47 (m, 1 H), 6.65 - 6.27 (m, 1 H), 6.21 - 6.19 (m, 1 H), 6.17 - 6.16 (m, 1 H), 5.73 - 5.70 (m, 1 H), 3.78 - 3.71 (m, 2 H), 3.52 - 3.49 (m, 2 H), 3.47 - 3.40 (m, 1 H), 2.69 - 2.64 (m, 1 H), 2.37 - 2.35 (m, 1 H), 2.35 (s, 3 H), 2.29 (s, 1 H), 1.10 - 1.02 (m, 6 H).	
403	<i>m/z</i> (ESI ⁺): 420.2 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.03 (s, 1H), 12.68 (s, 1H), 8.65 - 8.53 (m, 1H), 8.02 (d, J = 7.6 Hz, 1H), 7.34 - 7.23 (m, 1H), 7.01 - 6.90 (m, 2H), 6.79 - 6.55 (m, 2H), 6.18 (d, J = 16.8 Hz, 1H), 5.77 - 5.66 (m, 1H), 4.20 - 4.11 (m, 0.5H), 4.09 - 3.84 (m, 2H), 3.84 - 3.70 (m, 2H), 3.69 - 3.59 (m, 1H), 3.53 - 3.46 (m, 4H), 3.46 - 3.41 (m, 0.5H), 2.53 (s, 4H).	X
404	<i>m/z</i> (ESI ⁺): 409.1 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.16 (s, 1H), 12.80 - 12.42 (m, 1H), 8.59 - 8.54 (m, 1H), 8.02 (d, J = 8.0 Hz, 1H), 7.28 (t, J = 8.0 Hz, 1H), 6.99 - 6.91 (m, 2H), 6.90 - 6.71 (m, 1H), 6.53 - 6.48 (m, 1H), 6.27 - 6.17 (m, 1H), 5.81 - 5.70 (m, 1H), 5.40 - 5.22 (m, 1H), 4.88 (d, J = 11.2 Hz, 1H), 4.65 - 4.56 (m, 1H), 4.45 - 4.25 (m, 1H), 4.09 - 3.96 (m, 2H), 3.84 - 3.64 (m, 2H), 2.40 - 2.15 (m, 2H).	A12 1 st isomer
405	<i>m/z</i> (ESI ⁺): 409.1 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.11 - 14.05 (m, 1H), 12.58 (s, 1H), 8.61 - 8.54 (m, 1H), 8.03 (d, J = 7.6 Hz, 1H), 7.29 (t, J = 8.0 Hz, 1H), 7.00 - 6.92 (m, 2H), 6.91 - 6.71 (m, 1H), 6.55 - 6.49 (m, 1H), 6.26 - 6.17 (m, 1H), 5.81 - 5.70 (m, 1H), 5.40 - 5.21 (m, 1H), 4.89 (d, J = 11.2 Hz, 0.3H), 4.66 - 4.54 (m, 1.3H), 4.46 - 4.25 (m, 1.4H), 4.10 - 3.96 (m, 2H), 3.88 - 3.63 (m, 2H), 2.39 - 2.15 (m, 2H).	A12 2 nd isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
406	<i>m/z</i> (ESI ⁺): 418.2 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.04 (s, 1H), 12.83 - 12.10 (m, 1H), 8.57 (s, 1H), 8.03 (d, J = 7.6 Hz, 1H), 7.33 - 7.25 (m, 1H), 7.00 - 6.92 (m, 2H), 6.55 (s, 1H), 6.52 - 6.40 (m, 1H), 6.08 - 5.84 (m, 1H), 4.45 (d, J = 9.2 Hz, 0.5H), 4.21 (d, J = 8.8 Hz, 1H), 4.00 (d, J = 9.2 Hz, 0.5H), 3.92 (d, J = 10.8 Hz, 0.5H), 3.84 (t, J = 7.2 Hz, 1H), 3.72 (dd, J = 6.0, 9.6 Hz, 1H), 3.48 (d, J = 10.4 Hz, 0.5H), 2.99 (d, J = 5.6 Hz, 1H), 2.85 (d, J = 6.0 Hz, 1H), 2.38 - 2.28 (m, 2H), 2.27 - 2.18 (m, 2H), 2.13 (s, 3H), 1.99 (s, 3H).	A11 1 st isomer
407	<i>m/z</i> (ESI ⁺): 418.2 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.04 (s, 1H), 12.86 - 12.07 (m, 1H), 8.57 (s, 1H), 8.03 (d, J = 7.6 Hz, 1H), 7.29 (t, J = 7.6 Hz, 1H), 7.02 - 6.90 (m, 2H), 6.54 (s, 1H), 6.53 - 6.40 (m, 1H), 6.10 - 5.83 (m, 1H), 4.45 (d, J = 9.2 Hz, 0.5H), 4.21 (d, J = 8.4 Hz, 1H), 4.00 (d, J = 9.2 Hz, 0.5H), 3.92 (d, J = 10.4 Hz, 0.5H), 3.88 - 3.80 (m, 1H), 3.77 - 3.68 (m, 1H), 3.48 (d, J = 10.4 Hz, 0.5H), 2.99 (d, J = 6.0 Hz, 1H), 2.85 (d, J = 6.0 Hz, 1H), 2.38 - 2.28 (m, 2H), 2.28 - 2.19 (m, 2H), 2.13 (s, 3H), 1.99 (s, 3H).	All 2 nd isomer
408	<i>m/z</i> (ESI ⁺): 459 (M+H) ⁺	(499 MHz, DMSO-d ₆) δ 12.66 (s, 1H), 8.28 (s, 1H), 7.65 (ddd, J = 7.6, 2.8, 1.7 Hz, 1H), 7.55 - 7.47 (m, 1H), 7.42 (d, J = 8.4 Hz, 1H), 7.21 (t, J = 7.5 Hz, 1H), 6.64 (ddd, J = 21.2, 16.8, 10.3 Hz, 1H), 6.19 (ddd, J = 16.7, 4.3, 2.4 Hz, 1H), 5.71 (ddd, J = 14.3, 10.3, 2.4 Hz, 1H), 5.63 (d, J = 14.1 Hz, 2H), 4.11-3.41 (m, 4H), 2.40-2.19 (m, 6H).	
409	<i>m/z</i> (ESI ⁺): 509.5 (M+H) ⁺	(499 MHz, DMSO-d ₆) δ 13.98 (s, 1H), 12.94 (s, 1H), 8.24 (s, 1H), 7.94 (s, 1H), 7.30 (d, J = 7.4 Hz, 2H), 7.25 (dd, J = 7.7, 1.3 Hz, 1H), 7.03 - 6.89 (m, 3H), 6.85 (dd, J = 16.7, 10.5 Hz, 1H), 6.26 (dd, J = 16.7, 2.5 Hz, 1H), 5.77 (dd, J = 10.4, 2.6 Hz, 1H), 4.61 - 4.53 (m, 2H), 4.50 (s, 1H), 4.29 (s, 1H), 3.93 (t, J = 11.0 Hz, 1H), 3.64 (ddt, J = 16.8, 11.5, 2.4 Hz, 2H), 3.30 (t, J = 8.7 Hz, 2H), 2.94 (s, 2H), 2.78 (s, 2H), 2.25 (dtdd, J = 33.5, 13.1, 5.0, 2.0 Hz, 2H), 2.10 (dt, J = 13.2, 6.1 Hz, 2H), 1.96 (s, 2H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
410	<i>m/z</i> (ESI ⁺): 525.2 (M+H) ⁺	(499 MHz, DMSO-d ₆) δ 13.98 (s, 1H), 12.81 (s, 1H), 8.21 (s, 1H), 8.02 (dd, J = 8.1, 1.6 Hz, 1H), 7.26 (ddd, J = 8.4, 7.1, 1.6 Hz, 1H), 7.01 – 6.92 (m, 4H), 6.95 – 6.79 (m, 2H), 6.25 (dd, J = 16.6, 2.6 Hz, 1H), 5.80 – 5.74 (m, 1H), 4.56 (s, 1H), 4.53 (s, 1H), 4.42 (tt, J = 12.2, 5.2 Hz, 1H), 4.34 (s, 2H), 4.26 (s, 3H), 3.92 (d, J = 11.8 Hz, 2H), 3.64 (s, 2H), 2.24 (s, 2H), 2.12 (s, 1H), 1.99 (s, 1H), 1.14 (d, J = 13.2 Hz, 1H).	
411	<i>m/z</i> (ESI ⁺): 420.2 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.46 (s, 1H), 7.93 (d, J = 7.2 Hz, 1H), 7.34 - 7.24 (m, 1H), 7.01 - 6.94 (m, 2H), 6.74 - 6.58 (m, 2H), 6.37 - 6.27 (m, 1H), 5.84 - 5.76 (m, 1H), 4.31 - 4.24 (m, 0.5H), 4.20 - 4.14 (m, 0.5H), 4.09 - 4.03 (m, 0.5H), 3.99 - 3.91 (m, 1H), 3.89 - 3.82 (m, 1H), 3.81 - 3.66 (m, 2H), 3.64 (t, J = 4.4 Hz, 4H), 3.62 (s, 0.5H), 2.68 - 2.58 (m, 4H).	X 2 nd isomer
412	<i>m/z</i> (ESI ⁺): 515.3 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.28 - 13.85 (m, 1 H), 12.39 (d, J = 4.4 Hz, 1 H), 8.47 (d, J = 2.0 Hz, 1 H), 7.97 (d, J = 7.6 Hz, 1 H), 7.33 (t, J = 7.6 Hz, 1 H), 7.03 - 6.94 (m, 2 H), 6.65 (m, 1 H), 6.25 - 6.13 (m, 1 H), 5.78 - 5.65 (m, 1 H), 4.10 - 4.01 (m, 1 H), 4.01 - 3.88 (m, 2 H), 3.84 - 3.74 (m, 1 H), 3.74 - 3.63 (m, 2 H), 3.48 (d, J = 15.2 Hz, 5 H), 3.14 - 3.00 (m, 2 H), 2.48 - 2.39 (m, 2 H), 2.38 - 2.27 (m, 2 H), 2.24 (s, 3 H), 2.22 - 2.17 (m, 2 H), 2.09 (d, J = 14.4 Hz, 2 H), 1.60 - 1.47 (m, 2 H), 1.46 - 1.36 (m, 2 H).	
413	<i>m/z</i> (ESI ⁺): 502.3 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.46 (s, 0.4H), 8.39 (s, 1H), 8.07 - 7.93 (m, 1H), 7.34 - 7.22 (m, 1H), 7.02 - 6.93 (m, 2H), 6.87 (s, 2H), 4.75 - 4.61 (m, 2H), 4.31 (s, 1H), 4.15 (d, J = 11.6 Hz, 2H), 3.85 (t, J = 11.6 Hz, 2H), 3.66 (s, 2H), 2.96 (s, 3H), 2.37 (s, 3H), 2.27 - 2.18 (m, 3H), 2.16 (s, 3H), 1.83 - 1.76 (m, 3H), 1.63 (d, J = 4.0 Hz, 2H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
414	<i>m/z</i> (ESI ⁺): 462.3 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.39 (s, 1H), 7.98 (dd, J = 1.2, 8.4 Hz, 1H), 7.33 - 7.22 (m, 1H), 7.02 - 6.93 (m, 2H), 6.91 - 6.80 (m, 2H), 4.76 - 4.61 (m, 2H), 4.31 (s, 1H), 4.15 (d, J = 11.6 Hz, 2H), 3.86 (t, J = 11.6 Hz, 2H), 3.67 (d, J = 5.2 Hz, 2H), 2.69 (s, 3H), 2.37 (s, 3H), 2.31 - 2.17 (m, 4H), 2.16 (s, 3H).	
415	<i>m/z</i> (ESI ⁺): 486.3 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.68 (d, J = 4.8 Hz, 1H), 8.01 (d, J = 7.6 Hz, 1H), 7.34 - 7.25 (m, 1H), 7.03 - 6.96 (m, 2H), 6.67 (dt, J = 10.4, 17.2 Hz, 1H), 6.33 (d, J = 2.0, 4.0, 16.8 Hz, 1H), 5.79 (d, J = 1.6, 10.4, 14.4 Hz, 1H), 4.20 - 4.09 (m, 1H), 4.09 - 3.94 (m, 2H), 3.86 - 3.75 (m, 1H), 3.68 - 3.56 (m, 1H), 3.35 (s, 2H), 3.24 - 3.01 (m, 4H), 2.49 - 2.41 (m, 1H), 2.40 - 2.34 (m, 1H), 2.34 - 2.22 (m, 4H), 2.15 - 2.04 (m, 4H), 2.01 - 1.88 (m, 2H), 1.82 - 1.70 (m, 2H).	
416	<i>m/z</i> (ESI ⁺): 390.1 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.48 - 8.43 (m, 1H), 7.98 - 7.90 (m, 1H), 7.29 (t, J = 7.6 Hz, 1H), 7.01 - 6.94 (m, 2H), 6.72 - 6.59 (m, 1H), 6.57 - 6.52 (m, 1H), 6.40 - 6.29 (m, 1H), 5.85 - 5.76 (m, 1H), 4.24 - 4.17 (m, 0.5H), 4.09 - 3.99 (m, 1H), 3.98 - 3.90 (m, 0.5H), 3.85 (dd, J = 5.6, 11.2 Hz, 0.5H), 3.74 - 3.67 (m, 0.5H), 3.65 - 3.59 (m, 0.5H), 3.56 - 3.51 (m, 1H), 3.48 (s, 0.5H), 3.48 - 3.40 (m, 1H), 3.39 - 3.34 (m, 4H), 2.17 - 2.06 (m, 2H).	A9 1 st isomer
417	<i>m/z</i> (ESI ⁺): 390.1 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.45 (s, 1H), 7.93 (d, J = 7.6 Hz, 1H), 7.28 (t, J = 7.2 Hz, 1H), 7.01 - 6.94 (m, 2H), 6.70 - 6.60 (m, 1H), 6.53 (s, 1H), 6.33 (d, J = 16.4 Hz, 1H), 5.80 (d, J = 2.4, 10.4 Hz, 1H), 4.20 (dd, J = 7.6, 10.8 Hz, 0.5H), 4.10 - 3.98 (m, 1H), 3.96 - 3.90 (m, 0.5H), 3.85 (dd, J = 6.0, 11.2 Hz, 0.5H), 3.69 (dd, J = 6.0, 13.2 Hz, 0.5H), 3.65 - 3.58 (m, 0.5H), 3.58 - 3.50 (m, 1H), 3.49 (d, J = 3.6 Hz, 0.5H), 3.47 - 3.40 (m, 1H), 3.38 - 3.33 (m, 4H), 2.15 - 2.06 (m, 2H).	A9 2 nd isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
418	<i>m/z</i> (ESI ⁺): 375.1 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.26 (s, 1H), 12.56 (s, 1H), 8.53 (s, 1H), 8.03 (d, J = 7.6 Hz, 1H), 7.28 (t, J = 7.2 Hz, 1H), 6.99 - 6.91 (m, 2H), 6.63 (dd, J = 11.2, 15.6 Hz, 1H), 6.51 (d, J = 7.6 Hz, 1H), 6.14 (d, J = 17.2 Hz, 1H), 5.67 (s, 1H), 3.86 - 3.76 (m, 0.5H), 3.75 - 3.70 (m, 0.5H), 3.69 - 3.61 (m, 1H), 3.55 (d, J = 4.0 Hz, 1H), 3.51 - 3.43 (m, 1H), 3.15 (d, J = 1.6 Hz, 1H), 2.99 - 2.84 (m, 2H), 2.33 - 2.23 (m, 1H), 2.11 (d, J = 5.2 Hz, 1H), 2.03 - 1.92 (m, 1H), 1.63 - 1.52 (m, 1H).	A8 2 nd isomer
419	<i>m/z</i> (ESI ⁺): 445.2 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.48 (s, 1 H), 7.88 (d, J = 8.4 Hz, 1 H), 7.29 (t, J = 7.2 Hz, 1 H), 7.05 - 6.91 (m, 2 H), 6.68 - 6.65 (m, 1 H), 6.40 - 6.24 (m, 1 H), 5.88 - 5.69 (m, 1 H), 4.18 - 4.07 (m, 3 H), 4.06 - 3.86 (m, 3 H), 3.80 (dt, J = 2.8, 6.8 Hz, 1 H), 3.68 - 3.57 (m, 1 H), 2.67 - 2.49 (m, 2 H), 2.48 - 2.31 (m, 2 H), 2.29 - 2.16 (m, 4 H), 1.89 - 1.76 (m, 1 H), 1.74 - 1.58 (m, 1 H).	A7 1 st isomer
420	<i>m/z</i> (ESI ⁺): 445.1 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.52 (s, 1 H), 7.91 - 7.75 (m, 1 H), 7.41 - 7.23 (m, 1 H), 7.12 - 6.91 (m, 2 H), 6.69 - 6.65 (m, 1 H), 6.42 - 6.23 (m, 1 H), 5.93 - 5.66 (m, 1 H), 4.23 - 4.04 (m, 4 H), 4.03 - 3.88 (m, 2 H), 3.85 - 3.73 (m, 1 H), 3.62 (t, J = 10.4 Hz, 1 H), 2.64 (dd, J = 8.4, 12.4 Hz, 1 H), 2.57 - 2.29 (m, 3 H), 2.27 - 2.14 (m, 4 H), 1.89 - 1.75 (m, 1 H), 1.72 - 1.58 (m, 1 H).	A7 2 nd isomer
421	<i>m/z</i> (ESI ⁺): 360.1 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 13.66 - 12.67 (m, 1H), 8.73 - 8.65 (m, 1H), 7.92 - 7.78 (m, 1H), 7.45 - 7.33 (m, 1H), 7.08 - 6.98 (m, 2H), 6.89 (s, 1H), 6.63 (m, 1H), 6.22 (dd, J = 1.6, 16.4 Hz, 1H), 5.77 (d, J = 2.0, 10.4 Hz, 1H), 4.30 - 4.23 (m, 1H), 4.19 - 3.88 (m, 4H), 3.75 - 3.67 (m, 1H).	A6 1 st isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
422	<i>m/z</i> (ESI ⁺): 462.2 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.50 (s, 1 H), 8.47 - 8.39 (m, 1 H), 7.89 (d, J = 8.0 Hz, 1 H), 7.28 (t, J = 7.6 Hz, 1 H), 7.03 - 6.93 (m, 2 H), 6.89 - 6.77 (m, 1 H), 6.73 (d, J = 15.2 Hz, 1 H), 4.28 (dt, J = 3.6, 8.4 Hz, 1 H), 4.20 - 4.10 (m, 1 H), 4.10 - 4.03 (m, 3 H), 4.03 - 3.96 (m, 1 H), 3.95 - 3.85 (m, 2 H), 3.84 - 3.76 (m, 1 H), 3.75 - 3.66 (m, 2 H), 3.66 - 3.57 (m, 1 H), 2.72 (s, 3 H), 2.69 (s, 3 H), 2.53 - 2.29 (m, 3 H), 2.22 - 2.10 (m, 1 H).	
423	<i>m/z</i> (ESI ⁺): 517.1 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.31 (s, 1H), 7.64 (dd, J = 1.6, 8.0 Hz, 1H), 7.53 - 7.48 (m, 1H), 7.16 - 7.08 (m, 2H), 6.84 (dd, J = 10.8, 16.8 Hz, 1H), 6.36 (dd, J = 2.0, 16.8 Hz, 1H), 5.86 (dd, J = 2.0, 10.8 Hz, 1H), 4.93 (dd, J = 6.0, 12.0 Hz, 1H), 4.74 (s, 1H), 4.40 (s, 1H), 4.15 (dd, J = 2.8, 11.2 Hz, 2H), 3.88 (t, J = 11.6 Hz, 2H), 2.37 - 2.21 (m, 4H).	
424	<i>m/z</i> (ESI ⁺): 467.2 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 13.83 (s, 1H), 12.85 (s, 1H), 8.36 (s, 1H), 8.02 (d, J = 7.2 Hz, 1H), 7.57 (s, 4H), 7.42 (d, J = 5.6 Hz, 1H), 7.28 (t, J = 7.6 Hz, 1H), 6.99 - 6.81 (m, 3H), 6.26 (d, J = 16.8 Hz, 1H), 5.78 (d, J = 10.0 Hz, 1H), 4.66 (s, 1H), 4.56 (s, 1H), 4.30 (s, 1H), 3.96 (t, J = 10.8 Hz, 2H), 3.64 (t, J = 11.2 Hz, 2H), 2.39 - 2.21 (m, 2H), 2.17 - 2.03 (m, 2H).	
425	<i>m/z</i> (ESI ⁺): 435.2 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.50 (s, 1H), 7.91 (d, J = 7.2 Hz, 1H), 7.30 - 7.26 (m, 1H), 7.03 - 6.94 (m, 2H), 6.71 - 6.62 (m, 1H), 6.34 (d, J = 16.8 Hz, 1H), 5.86 - 5.75 (m, 1H), 4.38 - 4.34 (m, 0.5H), 4.33 - 4.25 (m, 2H), 4.24 - 4.14 (m, 1H), 4.13 - 4.09 (m, 1H), 4.08 - 4.03 (m, 2H), 4.03 - 3.94 (m, 1H), 3.94 - 3.84 (m, 2H), 3.76 - 3.70 (m, 0.5H), 3.63 - 3.59 (m, 0.5H), 3.49 - 3.44 (m, 0.5H), 3.32 (d, J = 1.6 Hz, 3H), 2.52 - 2.39 (m, 1H), 2.29 - 2.14 (m, 1H).	A5 1 st isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
426	<i>m/z</i> (ESI ⁺): 435.2 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.52 (s, 1H), 7.90 (d, J = 8.0 Hz, 1H), 7.30 - 7.26 (m, 1H), 7.04 - 6.93 (m, 2H), 6.75 - 6.58 (m, 1H), 6.34 (d, J = 16.8 Hz, 1H), 5.83 - 5.78 (m, 1H), 4.35 (d, J = 7.6 Hz, 0.5H), 4.33 - 4.24 (m, 2H), 4.23 - 4.15 (m, 1H), 4.15 - 4.08 (m, 2H), 4.07 (s, 1H), 4.03 - 3.94 (m, 1H), 3.93 - 3.86 (m, 2H), 3.79 - 3.70 (m, 0.5H), 3.64 - 3.59 (m, 0.5H), 3.50 - 3.45 (m, 0.5H), 3.33 (s, 3H), 2.52 - 2.38 (m, 1H), 2.17 - 2.12 (m, 1H).	A5 2 nd isomer
427	<i>m/z</i> (ESI ⁺): 345 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 8.62 (s, 1 H), 8.01 (d, J=7.52 Hz, 1 H), 7.29 (t, J=7.82 Hz, 1 H), 7.01 - 6.87 (m, 3 H), 6.56 - 6.45 (m, 1 H), 6.34 (dd, J=17.52, 9.76 Hz, 1 H), 6.26 - 6.13 (m, 1 H), 5.77 (t, J=10.20 Hz, 1 H), 5.62 - 5.54 (m, 1 H), 5.22 (t, J=7.56 Hz, 1 H), 4.37 - 4.15 (m, 1 H), 4.06 - 3.90 (m, 1 H), 2.83 - 2.70 (m, 2 H).	X 1 st isomer
428	<i>m/z</i> (ESI ⁺): 345 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 8.62 (s, 1 H), 8.02 (d, J=7.64 Hz, 1 H), 7.30 (t, J=7.36 Hz, 1 H), 7.03 - 6.88 (m, 3 H), 6.51 (dd, J=16.88, 10.52 Hz, 1 H), 6.40 - 6.29 (m, 1 H), 6.27 - 6.11 (m, 1 H), 5.78 (t, J=9.76 Hz, 1 H), 5.59 (dd, J=7.64, 6.00 Hz, 1 H), 5.23 (dd, J=8.68, 6.32 Hz, 1 H), 4.36 - 4.13 (m, 1 H), 4.09 - 3.89 (m, 1 H), 2.83 - 2.70 (m, 1 H), 2.47 - 2.37 (m, 1 H).	X 2 nd isomer
429	<i>m/z</i> (ESI ⁺): 359 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 13.88 (s, 1 H), 12.81 - 12.49 (m, 1 H), 8.68 (s, 1 H), 8.16 - 8.04 (m, 1 H), 7.36 - 7.22 (m, 1 H), 7.01 - 6.90 (m, 2 H), 6.41 - 6.27 (m, 1 H), 6.14 (dd, J=17.00, 2.13 Hz, 1 H), 5.79 - 5.66 (m, 1 H), 4.64 (t, J=8.44 Hz, 1 H), 4.40 - 4.29 (m, 2 H), 4.09 - 3.89 (m, 2 H), 2.39 (s, 3 H).	
430	<i>m/z</i> (ESI ⁺): 391.1 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.38 (s, 1 H), 7.98 (d, J = 7.6 Hz, 1 H), 7.37 - 7.18 (m, 1 H), 7.05 - 6.91 (m, 2 H), 6.43 - 6.32 (m, 1 H), 6.30 - 6.22 (m, 1 H), 5.76 (d, J = 10.4 Hz, 1 H), 4.54 - 4.32 (m, 2 H), 4.32 - 4.22 (m, 2 H), 4.15 (d, J = 16.4 Hz, 1 H), 4.08 - 3.94 (m, 2 H), 2.83 - 2.72 (m, 1 H), 2.58 - 2.46 (m, 1 H), 2.37 (s, 3 H).	A1 1 st isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
431	<i>m/z</i> (ESI ⁺): 391.1 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.38 (s, 1 H), 7.98 (d, J = 7.2 Hz, 1 H), 7.36 - 7.19 (m, 1 H), 7.04 - 6.91 (m, 2 H), 6.44 - 6.32 (m, 1 H), 6.31 - 6.21 (m, 1 H), 5.76 (d, J = 10.4 Hz, 1 H), 4.54 - 4.33 (m, 2 H), 4.32 - 4.23 (m, 2 H), 4.21 - 4.10 (m, 1 H), 4.08 - 3.94 (m, 2 H), 2.84 - 2.72 (m, 1 H), 2.57 - 2.45 (m, 1 H), 2.37 (s, 3 H).	A1 2 nd isomer
432	<i>m/z</i> (ESI ⁺): 404.2 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.29 (s, 1H), 12.27 (s, 1H), 8.60 (s, 1H), 8.11 (d, J = 7.2 Hz, 1H), 7.33 - 7.24 (m, 1H), 7.00 - 6.91 (m, 2H), 6.68 (dd, J = 10.4, 16.8 Hz, 1H), 6.15 (dd, J = 2.4, 16.4Hz, 1H), 5.67 (dd, J = 2.0, 10.0 Hz, 1H), 4.54 - 4.40 (m, 2H), 3.72 (s, 2H), 2.68 (t, J = 12.0 Hz, 2H), 2.33 (s, 3H), 2.28 (d, J = 10.4 Hz, 1H), 2.19 (d, J = 10.4 Hz, 1H), 1.99 - 1.86 (m, 2H), 1.84 - 1.74 (m, 1H), 1.73 - 1.62 (m, 1H).	
433	<i>m/z</i> (ESI ⁺): 430.2 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ = 13.93 (s, 1H), 12.35 (s, 1H), 8.38 (s, 1H), 8.07 (d, J = 7.2 Hz, 1H), 7.33 - 7.25 (m, 1H), 7.01 - 6.89 (m, 2H), 6.69 (dd, J = 10.0, 16.4 Hz, 1H), 6.16 (dd, J = 2.0, 16.4 Hz, 1H), 5.72 - 5.62 (m, 1H), 4.54 - 4.40 (m, 2H), 3.78 (s, 2H), 2.76 - 2.62 (m, 2H), 2.34 - 2.18 (m, 2H), 2.03 - 1.87 (m, 3H), 1.86 - 1.75 (m, 1H), 1.75 - 1.62 (m, 1H), 1.00 - 0.92 (m, 2H), 0.86 - 0.78 (m, 2H).	
434	<i>m/z</i> (ESI ⁺): 510.3 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.51 (s, 1H), 7.63 (dd, J = 1.6, 7.6 Hz, 1H), 7.52 - 7.44 (m, 1H), 7.15 - 7.04 (m, 2H), 6.87 - 6.72 (m, 2H), 4.86 - 4.78 (m, 1H), 4.72 (s, 1H), 4.38 - 4.27 (m, 5H), 4.16 (d, J = 11.6 Hz, 2H), 3.92 - 3.80 (m, 4H), 2.46 (s, 3H), 2.36 - 2.19 (m, 4H).	
435	<i>m/z</i> (ESI ⁺): 375.2 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.18 (s, 1 H), 12.62 (d, J = 0.8 Hz, 1 H), 8.67 - 8.56 (m, 1 H), 8.08 (d, J = 8.0 Hz, 1 H), 7.40 - 7.31 (m, 1 H), 7.07 - 6.97 (m, 2 H), 6.75 - 6.61 (m, 1 H), 6.55 - 6.41 (m, 1 H), 6.22 - 6.12 (m, 1 H), 5.74 - 5.61 (m, 1 H), 4.51 (d, J = 18.4 Hz, 1 H), 3.59 - 3.48 (m, 1 H), 3.43 (s, 1 H), 3.34 - 3.28 (m, 1 H), 3.24 (s, 2 H), 1.90 - 1.44 (m, 6 H).	A2 1 st isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
436	<i>m/z</i> (ESI ⁺): 435.1 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.52 (s, 1H), 7.90 (d, J = 8.4 Hz, 1H), 7.30 - 7.26 (m, 1H), 7.04 - 6.93 (m, 2H), 6.71 - 6.61 (m, 1H), 6.34 (d, J = 16.8 Hz, 1H), 5.89 - 5.75 (m, 1H), 4.39 - 4.31 (m, 1H), 4.31 - 4.22 (m, 2H), 4.16 (s, 0.5H), 4.15 - 4.06 (m, 3H), 4.03 - 3.94 (m, 1H), 3.94 - 3.86 (m, 2H), 3.77 - 3.71 (m, 0.5H), 3.64 - 3.60 (m, 0.5H), 3.50 - 3.45 (m, 0.5H), 3.33 (s, 3H), 2.54 - 2.35 (m, 1H), 2.18 - 2.12 (m, 1H).	A1 3 rd isomer
437	<i>m/z</i> (ESI ⁺): 387.1 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 8.54 - 8.45 (m, 1 H), 8.22 (s, 1 H), 8.02 - 8.0 (m, 1 H), 7.30 - 7.26 (m, 1 H), 6.96 (d, J = 7.6 Hz, 3 H), 6.54 (s, 1 H), 6.26 - 6.21 (m, 1 H), 5.82 (d, J = 12.0 Hz, 1 H), 5.23 - 5.19 (m, 1H), 5.10 (s, 1 H), 4.34 - 4.24 (m, 2 H), 4.16 - 4.09 (m, 2 H).	
438	<i>m/z</i> (ESI ⁺): 401.1 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.28 (s, 1 H), 12.60 (s, 1 H), 8.50 (s, 1 H), 8.00 (d, J = 7.2 Hz, 1 H), 7.46 (s, 1 H), 7.27 (t, J = 7.6 Hz, 1H), 6.96 - 6.91 (m, 3 H), 6.34 (s, 1 H), 6.17 (d, J = 16.4 Hz, 1 H), 5.75 (d, J = 8.4 Hz, 1 H), 4.87 (s, 1 H), 4.71 (s, 1 H), 4.15 - 4.04 (m, 6 H).	
439	<i>m/z</i> (ESI ⁺): 405.1 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.41 (s, 1 H), 12.36 (s, 1 H), 8.58 (s, 1 H), 8.12 (d, J = 7.2 Hz, 1 H), 7.28 (t, J = 7.6 Hz, 1 H), 6.98 - 6.92 (m, 2 H), 6.92 - 6.85 (m, 1 H), 6.29 - 6.21 (m, 1 H), 5.79 (dd, J = 2.4, 10.0 Hz, 1 H), 4.72 (d, J = 8.0 Hz, 1 H), 4.44 (d, J = 10.0 Hz, 1 H), 3.69 (t, J = 11.2 Hz, 2 H), 3.51 (t, J = 10.0 Hz, 2 H), 3.39 (s, 1 H), 2.72 (dt, J = 6.4, 12.4 Hz, 1 H), 2.27 (s, 3 H), 2.20 - 2.09 (m, 3 H).	A1 1 st isomer
440	<i>m/z</i> (ESI ⁺): 401.1 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.42 (s, 1H), 7.94 - 7.88 (m, 1H), 7.72 (dd, J = 2.4, 5.6 Hz, 1H), 7.59 (d, J = 1.6 Hz, 1H), 7.32 - 7.24 (m, 1H), 7.01 - 6.92 (m, 2H), 6.77 - 6.61 (m, 1H), 6.52 (d, J = 3.6 Hz, 1H), 6.37 (d, J = 1.6, 16.8 Hz, 1H), 6.29 (d, J = 2.0 Hz, 1H), 5.83 (d, J = 2.0, 6.0, 10.4 Hz, 1H), 5.49 - 5.32 (m, 1H), 4.52 - 4.45 (m, 0.5H), 4.42 - 4.39 (m, 0.5H), 4.39 - 4.34 (m, 1H), 4.34 - 4.24 (m, 1H), 4.17 (dd, J = 8.4, 10.8 Hz, 0.5H), 4.12 - 4.04 (m, 0.5H), 4.04 - 3.86 (m, 1H).	A33 1 st isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
441	<i>m/z</i> (ESI ⁺): 419.2 (M+H) ⁺	(499 MHz, DMSO-d ₆) δ 14.34 (s, 1H), 12.33 (s, 1H), 8.59 (s, 1H), 8.13 (dd, J = 8.4, 1.7 Hz, 1H), 7.28 (td, J = 7.6, 1.6 Hz, 1H), 6.98 – 6.91 (m, 2H), 6.85 (dd, J = 16.7, 10.5 Hz, 1H), 6.25 (dd, J = 16.7, 2.5 Hz, 1H), 5.77 (dd, J = 10.4, 2.6 Hz, 1H), 4.56 (s, 1H), 4.47 (td, J = 12.7, 6.2 Hz, 1H), 4.31 (s, 1H), 4.04 (dd, J = 11.4, 6.7 Hz, 2H), 3.70 (ddt, J = 16.9, 11.5, 2.5 Hz, 2H), 2.79 (q, J = 7.5 Hz, 2H), 2.30 – 2.12 (m, 2H), 2.01 (ddd, J = 18.5, 13.0, 5.5 Hz, 2H), 1.23 (t, J = 7.5 Hz, 3H).	
442	<i>m/z</i> (ESI ⁺): 463.5 (M+H) ⁺	(499 MHz, DMSO-d ₆) δ 14.31 (s, 1H), 12.36 (s, 1H), 8.54 (s, 1H), 8.11 (dd, J = 8.4, 1.7 Hz, 1H), 7.34 – 7.25 (m, 1H), 6.95 (ddd, J = 8.4, 3.6, 1.4 Hz, 2H), 6.84 (ddd, J = 15.5, 10.5, 4.9 Hz, 1H), 6.30 – 6.20 (m, 1H), 5.77 (ddd, J = 10.4, 4.2, 2.6 Hz, 1H), 4.56 (s, 1H), 4.48 (tq, J = 11.3, 5.6 Hz, 1H), 4.31 (s, 1H), 4.02 (dd, J = 11.4, 7.1 Hz, 2H), 3.89 – 3.78 (m, 1H), 3.75 – 3.65 (m, 2H), 3.34 – 3.17 (m, 6H), 2.82 (t, J = 7.3 Hz, 2H), 2.29 – 2.20 (m, 1H), 2.17 (td, J = 13.6, 4.8 Hz, 1H), 2.06 – 1.95 (m, 2H), 1.85 (p, J = 6.7 Hz, 2H).	
443	<i>m/z</i> (ESI ⁺): 389.1 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.45 (s, 1 H), 7.94 (d, J = 8.4 Hz, 1 H), 7.37 - 7.18 (m, 1 H), 7.03 - 6.92 (m, 2 H), 6.81 - 6.58 (m, 1 H), 6.48 (d, J = 2.4 Hz, 1 H), 6.40 - 6.24 (m, 1 H), 5.81 (d, J = 2.4, 10.4 Hz, 1 H), 4.25 - 4.07 (m, 1 H), 4.01 (dd, J = 7.6, 10.8 Hz, 1 H), 3.79 - 3.62 (m, 2 H), 3.53 - 3.46 (m, 1 H), 1.95 - 1.77 (m, 2 H), 1.76 - 1.53 (m, 5 H), 1.45 - 1.34 (m, 1 H).	
444	<i>m/z</i> (ESI ⁺): 502.2 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.39 (s, 1 H), 7.99 (dd, J = 1.2, 8.4 Hz, 1 H), 7.31 - 7.24 (m, 1 H), 7.00 - 6.95 (m, 2 H), 6.81 - 6.73 (m, 1 H), 6.66 - 6.59 (m, 1 H), 4.74 - 4.62 (m, 2 H), 4.31 (s, 1 H), 4.15 (s, 1 H), 4.13 - 4.09 (m, 3 H), 3.90 - 3.81 (m, 2 H), 3.53 - 3.48 (m, 3 H), 2.44 (t, J = 8.0 Hz, 2 H), 2.38 (s, 3 H), 2.28 - 2.18 (m, 3 H), 2.15 - 2.08 (m, 2 H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
445	<i>m/z</i> (ESI ⁺): 403 (M+H) ⁺	(400 MHz, ACETONITRILE-d ₃) δ 14.71 - 14.09 (m, 1 H), 10.59 - 9.60 (m, 1 H), 8.49 - 8.37 (m, 1 H), 8.13 - 7.98 (m, 1 H), 7.40 - 7.25 (m, 1 H), 7.06 - 6.94 (m, 2 H), 6.42 - 6.16 (m, 2 H), 5.75 - 5.57 (m, 1 H), 4.82 (d, J=6.24 Hz, 1 H), 4.44 - 4.09 (m, 1 H), 3.99 (d, J=7.24 Hz, 1 H), 3.93 - 3.84 (m, 1 H), 3.67 - 3.47 (m, 1 H), 3.46 - 3.17 (m, 1 H), 2.71 - 2.51 (m, 1 H), 2.15 - 2.02 (m, 3 H), 1.42 - 1.58 (m, 6 H).	A11 1 st isomer
446	<i>m/z</i> (ESI ⁺): 403 (M+H) ⁺	(400 MHz, ACETONITRILE-d ₃) δ 14.53 - 14.01 (m, 1 H), 10.25 - 9.66 (m, 1 H), 8.44 - 8.38 (m, 1 H), 8.02 (dd, J=7.88, 1.36 Hz, 1 H), 7.35 - 7.26 (m, 1 H), 7.02 - 6.93 (m, 2 H), 6.37 - 6.14 (m, 2 H), 5.74 - 5.54 (m, 1 H), 5.08 - 4.75 (m, 1 H), 4.39 - 4.06 (m, 1 H), 3.97 (d, J=7.00 Hz, 1 H), 3.84 (dd, J=8.56, 4.20 Hz, 1 H), 3.60 - 3.47 (m, 1 H), 3.43 - 3.16 (m, 1 H), 2.64 - 2.48 (m, 1 H), 2.10 - 1.99 (m, 3 H), 1.46 (dd, J=13.12, 7.00 Hz, 6 H).	A11 2 nd isomer
447	<i>m/z</i> (ESI ⁺): 375 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.29 - 14.46 (m, 1 H), 12.02 (s, 1 H), 8.65 - 8.54 (m, 1 H), 8.13 (d, J=7.6 Hz, 1 H), 7.28 (t, J=7.6 Hz, 1 H), 7.07 - 6.90 (m, 2 H), 6.39 - 6.22 (m, 1 H), 6.20 - 6.08 (m, 1 H), 5.75 - 5.60 (m, 1 H), 5.17 - 4.82 (m, 1 H), 4.38 - 4.00 (m, 1 H), 3.91 - 3.80 (m, 1 H), 3.76 - 3.49 (m, 1 H), 3.24 (d, J=4.8 Hz, 1 H), 2.44 (t, J=12.8, 6.43 Hz, 1 H), 2.38 - 2.29 (m, 3 H), 2.19 - 2.02 (m, 1 H), 2.01 - 1.88 (m, 1 H), 1.87 - 1.78 (m, 1 H).	A35 1 st isomer
448	<i>m/z</i> (ESI ⁺): 375 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.49 - 14.25 (m, 1 H), 12.05 (s, 1 H), 8.66 - 8.53 (m, 1 H), 8.13 (d, J=7.6 Hz, 1 H), 7.28 (t, J=7.6 Hz, 1 H), 7.03 - 6.89 (m, 2 H), 6.39 - 6.22 (m, 1 H), 6.20 - 6.08 (m, 1 H), 5.76 - 5.59 (m, 1 H), 5.20 - 4.80 (m, 1 H), 4.38 - 3.98 (m, 1 H), 3.90 - 3.80 (m, 1 H), 3.76 - 3.48 (m, 1 H), 3.23 (s, 1 H), 2.43 (t, J=12.4, 6.27 Hz, 1 H), 2.39 - 2.28 (m, 3 H), 2.19 - 2.02 (m, 1 H), 2.01 - 1.88 (m, 1 H), 1.87 - 1.76 (m, 1 H).	A35 2 nd isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
449	<i>m/z</i> (ESI ⁺): 402.1 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 13.87 (d, J = 5.2 Hz, 1H), 12.85 - 12.55 (m, 1H), 8.59 (d, J = 4.8 Hz, 1H), 8.39 (d, J = 11.6 Hz, 1H), 8.01 (d, J = 8.0 Hz, 1H), 7.80 (d, J = 5.2 Hz, 1H), 7.30 (t, J = 8.0 Hz, 1H), 7.00 - 6.92 (m, 2H), 6.69 (d, J = 10.0, 16.8, 18.4 Hz, 1H), 6.55 (d, J = 17.2 Hz, 1H), 6.25 (d, J = 2.8, 16.8 Hz, 1H), 5.89 - 5.72 (m, 2H), 4.51 - 4.41 (m, 1H), 4.40 - 4.22 (m, 2H), 4.16 - 4.03 (m, 1H), 3.96 - 3.76 (m, 1H).	O 2 nd isomer
450	<i>m/z</i> (ESI ⁺): 503.2 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.49 (s, 1H), 7.97 (d, J = 7.6 Hz, 1H), 7.32 - 7.26 (m, 1H), 7.03 - 6.95 (m, 2H), 6.84 (d, J = 10.4, 16.8 Hz, 1H), 6.36 (d, J = 2.0, 16.8 Hz, 1H), 5.85 (d, J = 2.0, 10.8 Hz, 1H), 4.78 - 4.66 (m, 2H), 4.33 (s, 1H), 4.14 (d, J = 4.4, 11.6 Hz, 2H), 3.91 - 3.80 (m, 2H), 3.69 - 3.62 (m, 1H), 3.48 (s, 3H), 3.04 - 2.93 (m, 1H), 2.35 - 2.21 (m, 4H), 2.21 - 2.10 (m, 4H), 1.71 - 1.57 (m, 4H).	
451	<i>m/z</i> (ESI ⁺): 419.2 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.49 - 8.40 (m, 1H), 7.93 (d, J = 7.2 Hz, 1H), 7.29 (t, J = 7.2 Hz, 1H), 7.01 - 6.95 (m, 2H), 6.67 (dt, J = 10.4, 17.2 Hz, 1H), 6.38 - 6.29 (m, 1H), 5.85 - 5.74 (m, 1H), 4.36 (t, J = 7.6 Hz, 1H), 4.20 - 4.15 (m, 2H), 4.10 - 4.03 (m, 2H), 4.02 - 3.95 (m, 1H), 3.87 - 3.76 (m, 1H), 3.70 - 3.58 (m, 1H), 3.52 (t, J = 8.8 Hz, 1H), 3.42 - 3.35 (m, 1H), 2.64 (td, J = 7.6, 15.2 Hz, 1H), 2.50 - 2.41 (m, 1H), 2.40 - 2.31 (m, 1H), 1.09 (d, J = 6.4 Hz, 3H).	
452	<i>m/z</i> (ESI ⁺): 431 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 13.99 (d, J=2.36 Hz, 1 H), 12.36 - 11.97 (m, 1 H), 8.53 - 8.37 (m, 1 H), 8.01 (d, J=7.12 Hz, 1 H), 7.34 - 7.23 (m, 1 H), 7.02 - 6.91 (m, 2 H), 6.39 - 6.27 (m, 1 H), 6.22 - 6.05 (m, 1 H), 5.76 - 5.56 (m, 1 H), 5.13 - 4.70 (m, 1 H), 4.35 - 4.01 (m, 2 H), 4.01 - 3.80 (m, 5 H), 3.75 - 3.51 (m, 1 H), 3.23 (s, 1 H), 2.47 - 2.38 (m, 1 H), 2.30 (d, J=8.00, 3.76 Hz, 1 H), 2.22 - 2.09 (m, 2 H), 2.05 - 1.94 (m, 1 H), 1.77 - 1.90 (m, 1 H).	A19 1 st isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
453	<i>m/z</i> (ESI ⁺): 431 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.19 - 13.77 (m, 1 H), 12.38 - 11.78 (m, 1 H), 8.51 - 8.40 (m, 1 H), 8.02 (d, J=7.88 Hz, 1 H), 7.29 (t, J=7.52 Hz, 1 H), 7.02 - 6.92 (m, 2 H), 6.40 - 6.26 (m, 1 H), 6.23 - 6.07 (m, 1 H), 5.77 - 5.56 (m, 1 H), 5.13 - 4.74 (m, 1 H), 4.36 - 4.01 (m, 2 H), 4.00 - 3.77 (m, 5 H), 3.74 - 3.50 (m, 1 H), 3.26 - 3.19 (m, 1 H), 2.46 - 2.38 (m, 1 H), 2.36 - 2.12 (m, 3 H), 2.04 - 1.94 (m, 1 H), 1.84 (dd, J=11.24, 5.00 Hz, 1 H).	A19 2 nd isomer
454	<i>m/z</i> (ESI ⁺): 431 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.11 - 13.78 (m, 1 H), 12.35 - 11.94 (m, 1 H), 8.52 - 8.39 (m, 1 H), 8.02 (d, J=7.12 Hz, 1 H), 7.35 - 7.21 (m, 1 H), 7.02 - 6.92 (m, 2 H), 6.40 - 6.06 (m, 2 H), 5.78 - 5.56 (m, 1 H), 5.17 - 4.72 (m, 1 H), 4.37 - 4.01 (m, 2 H), 4.00 - 3.88 (m, 3 H), 3.88 - 3.78 (m, 2 H), 3.74 - 3.50 (m, 1 H), 3.26 - 3.15 (m, 1 H), 2.43 (d, J=6.12 Hz, 1 H), 2.38 - 2.13 (m, 3 H), 2.05 - 1.93 (m, 1 H), 1.91 - 1.76 (m, 1 H).	A19 3 rd isomer
455	<i>m/z</i> (ESI ⁺): 431 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.19 - 13.82 (m, 1 H), 12.31 - 11.90 (m, 1 H), 8.56 - 8.38 (m, 1 H), 8.01 (d, J=7.52 Hz, 1 H), 7.29 (t, J=7.36 Hz, 1 H), 7.04 - 6.90 (m, 2 H), 6.38 - 6.02 (m, 2 H), 5.80 - 5.55 (m, 1 H), 5.14 - 4.70 (m, 1 H), 4.36 - 4.01 (m, 2 H), 4.01 - 3.77 (m, 5 H), 3.76 - 3.51 (m, 1 H), 3.23 (s, 1 H), 3.04 - 3.03 (m, 1 H), 2.47 - 2.39 (m, 1 H), 2.30 (dt, J=8.28, 3.92 Hz, 1 H), 2.23 - 2.08 (m, 2 H), 2.06 - 1.93 (m, 1 H), 1.91 - 1.80 (m, 1 H).	A19 4 th isomer
456	<i>m/z</i> (ESI ⁺): 375.1 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.42 (d, J = 2.0 Hz, 1H), 7.92 (d, J = 7.6 Hz, 1H), 7.28 (t, J = 7.6 Hz, 1H), 7.02 - 6.92 (m, 2H), 6.79 - 6.57 (m, 1H), 6.47 (s, 1H), 6.38 - 6.24 (m, 1H), 5.84 - 5.63 (m, 1H), 4.69 - 4.51 (m, 1H), 4.26 - 3.94 (m, 2H), 3.52 (td, J = 6.0, 17.2 Hz, 1H), 3.20 - 2.98 (m, 1H), 2.30 - 2.14 (m, 1H), 2.05 - 1.69 (m, 5H).	A32 1 st isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
457	<i>m/z</i> (ESI ⁺): 375.1 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.43 (d, J = 2.4 Hz, 1H), 7.92 (d, J = 8.0 Hz, 1H), 7.37 - 7.23 (m, 1H), 6.97 (d, J = 8.0 Hz, 2H), 6.69 (d, J = 10.4, 16.8, 19.6 Hz, 1H), 6.48 (s, 1H), 6.39 - 6.22 (m, 1H), 5.77 (d, J = 2.0, 10.8, 13.2 Hz, 1H), 4.66 - 4.51 (m, 1H), 4.22 - 3.96 (m, 2H), 3.59 - 3.50 (m, 1H), 3.23 - 3.13 (m, 1H), 2.30 - 2.16 (m, 1H), 1.96 - 1.66 (m, 5H)	A32 2 nd isomer
458	<i>m/z</i> (ESI ⁺): 401.1 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.19 (s, 1H), 12.59 (s, 1H), 8.53 (s, 1H), 8.02 - 7.98 (m, 1H), 7.31 - 7.25 (m, 1H), 6.97 - 6.94 (m, 2H), 6.93 - 6.81 (m, 1H), 6.40 (s, 1H), 6.21 - 6.07 (m, 2H), 5.79 - 5.73 (m, 1H), 4.87 (s, 1H), 4.73 (s, 1H), 4.14 (s, 2H), 4.13 - 4.09 (m, 1H), 4.05 (d, J = 4.4 Hz, 2H), 4.00 (d, J = 2.0 Hz, 1H).	
459	<i>m/z</i> (ESI ⁺): 504.3 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.41 (s, 1H), 7.97 (d, J = 8.0 Hz, 1H), 7.34 - 7.20 (m, 1H), 7.01 - 6.95 (m, 2H), 6.95 - 6.84 (m, 1H), 6.80 - 6.69 (m, 1H), 4.73 - 4.66 (m, 2H), 4.33 (d, J = 2.4 Hz, 1H), 4.14 (d, J = 11.6 Hz, 2H), 3.89 - 3.81 (m, 2H), 3.75 (t, J = 4.0 Hz, 4H), 3.36 (s, 2H), 2.61 (s, 4H), 2.38 (s, 3H), 2.28 - 2.17 (m, 4H).	
460	<i>m/z</i> (ESI ⁺): 448.2 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 12.37 - 12.28 (m, 1 H), 8.40 - 8.30 (m, 2 H), 7.98 (d, J = 1.6 Hz, 1 H), 7.78 (d, J = 7.6 Hz, 1 H), 7.65 - 7.57 (m, 1 H), 7.52 (t, J = 7.2 Hz, 2H), 7.35 (d, J = 8.0 Hz, 1 H), 6.64 (dt, J = 10.4, 16.4 Hz, 1 H), 6.18 (d, J = 16.4 Hz, 1 H), 5.76 - 5.65 (m, 1 H), 4.12 - 4.05 (m, 2 H), 4.00 - 3.90 (m, 4 H), 3.53 - 3.47 (m, 1 H), 2.35 (s, 1 H), 2.31 - 2.25 (m, 4 H), 2.21 - 2.12 (m, 2 H), 1.10 (s, 18 H), 0.81 (dd, J = 2.4, 6.8 Hz, 3 H), 0.68 (t, J = 8.0 Hz, 3 H).	
461	<i>m/z</i> (ESI ⁺): 461.2 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.38 (s, 1H), 7.81 (d, J = 7.6 Hz, 1H), 7.23 - 7.10 (m, 1H), 6.92 - 6.82 (m, 2H), 6.74 (d, J = 10.4, 16.8 Hz, 1H), 6.25 (d, J = 2.0, 16.8 Hz, 1H), 5.75 (d, J = 2.0, 10.4 Hz, 1H), 4.61 (s, 1H), 4.24 (s, 1H), 4.19 (t, J = 4.0, 8.4 Hz, 1H), 4.08 - 4.01 (m, 2H), 4.01 - 3.93 (m, 2H), 3.79 - 3.70 (m, 3H), 2.37 (d, J = 4.0, 7.9 Hz, 1H), 2.24 - 2.01 (m, 6H), 1.39 - 1.27 (m, 1H).	H 1 st isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
462	<i>m/z</i> (ESI ⁺): 461.2 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.38 (s, 1 H), 7.81 (d, J = 8.0 Hz, 1 H), 7.21 - 7.15 (m, 1 H), 6.92 - 6.85 (m, 2 H), 6.74 (d, J = 10.4, 16.8 Hz, 1 H), 6.30 - 6.21 (m, 1 H), 5.75 (d, J = 2.0, 10.4 Hz, 1 H), 4.61 (s, 1 H), 4.24 (s, 1 H), 4.19 (t, J = 4.0, 8.4 Hz, 1 H), 4.09 - 4.01 (m, 2 H), 4.01 - 3.92 (m, 2 H), 3.78 - 3.71 (m, 3 H), 2.37 (d, J = 4.4, 8.4, 12.0 Hz, 1 H), 2.22 - 2.01 (m, 6 H), 1.43 - 1.31 (m, 1 H).	H 2 nd isomer
463	<i>m/z</i> (ESI ⁺): 361.1 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.90 (s, 1 H), 12.56 (s, 1 H), 8.55 - 8.34 (m, 1 H), 7.98 (d, J = 8.0 Hz, 1 H), 7.23 (d, J = 7.6 Hz, 1 H), 6.91 (d, J = 7.2, 11.2 Hz, 2 H), 6.83 (d, J = 10.4, 16.8 Hz, 1 H), 6.68 (d, J = 10.4, 16.8 Hz, 1 H), 6.42 (d, J = 10.4 Hz, 1 H), 6.15 (d, J = 2.4, 12.0, 16.8 Hz, 1 H), 5.77 - 5.63 (m, 1 H), 4.82 (q, J = 5.2 Hz, 1 H), 4.64 (d, J = 4.8 Hz, 1 H), 4.46 - 4.32 (m, 1 H), 4.17 (dd, J = 7.6, 12.4 Hz, 1 H), 3.99 (d, J = 6.8, 14.0 Hz, 1 H), 3.85 - 3.69 (m, 1 H), 2.95 - 2.80 (m, 1 H), 2.48 - 2.43 (m, 1 H), 2.27 (td, J = 5.6, 11.6 Hz, 1 H), 1.93 (q, J = 8.8 Hz, 1 H), 1.80 - 1.69 (m, 1 H), 1.64 - 1.55 (m, 1 H).	Z 1 st isomer
464	<i>m/z</i> (ESI ⁺): 361.1 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.66 (s, 1 H), 12.58 (s, 1 H), 8.59 - 8.40 (m, 1 H), 7.99 (d, J = 7.6 Hz, 1 H), 7.35 - 7.16 (m, 1 H), 6.99 - 6.88 (m, 2 H), 6.83 (dd, J = 10.0, 16.8 Hz, 1 H), 6.68 (dd, J = 10.4, 16.8 Hz, 1 H), 6.49 - 6.42 (m, 1 H), 6.21 - 6.08 (m, 1 H), 5.78 - 5.63 (m, 1 H), 4.82 (q, J = 5.2 Hz, 1 H), 4.65 (q, J = 4.8 Hz, 1 H), 4.45 - 4.35 (m, 1 H), 4.15 (dd, J = 8.0, 13.2 Hz, 1 H), 3.99 (dd, J = 6.8, 14.0 Hz, 1 H), 3.83 - 3.73 (m, 1 H), 2.92 - 2.81 (m, 1 H), 2.48 - 2.43 (m, 1 H), 2.31 - 2.20 (m, 1 H), 1.97 - 1.86 (m, 1 H), 1.81 - 1.72 (m, 1 H), 1.64 - 1.57 (m, 1 H).	Z 2 nd isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
465	<i>m/z</i> (ESI ⁺): 519.2 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.30 (d, J = 1.6 Hz, 1 H), 12.35 (s, 1 H), 8.53 (s, 1 H), 8.10 (d, J = 8.0 Hz, 1 H), 7.28 (t, J = 7.2 Hz, 1 H), 7.00 - 6.90 (m, 2 H), 6.85 (d, J = 10.4, 16.8 Hz, 1 H), 6.25 (d, J = 2.4, 16.8 Hz, 1 H), 5.77 (d, J = 2.4, 10.4 Hz, 1 H), 4.61 - 4.41 (m, 2 H), 4.31 (s, 1 H), 4.02 (d, J = 5.6, 12.0 Hz, 3 H), 3.76 - 3.61 (m, 6 H), 3.37 (d, J = 5.2 Hz, 2 H), 2.82 (t, J = 7.2 Hz, 2 H), 2.30 - 2.11 (m, 2 H), 2.06 - 1.95 (m, 2 H), 1.94 - 1.80 (m, 4 H).	
466	<i>m/z</i> (ESI ⁺): 497.2 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.07 (s, 1H), 7.79 (d, J = 1.2, 8.0 Hz, 1H), 7.48 - 7.41 (m, 1H), 7.37 (d, J = 1.2, 7.2 Hz, 1H), 7.28 - 7.22 (m, 1H), 7.19 (d, J = 8.0 Hz, 1H), 7.12 (t, J = 7.2 Hz, 1H), 6.98 - 6.94 (m, 1H), 6.93 - 6.88 (m, 1H), 6.81 (d, J = 10.8, 16.8 Hz, 1H), 6.34 (d, J = 2.0, 17.2 Hz, 1H), 5.83 (d, J = 2.0, 10.8 Hz, 1H), 4.66 (s, 1H), 4.57 (t, J = 6.0, 12.0 Hz, 1H), 4.28 (s, 1H), 3.96 (s, 2H), 3.84 (s, 3H), 3.76 (d, J = 8.4 Hz, 2H), 2.33 - 2.10 (m, 4H).	
467	<i>m/z</i> (ESI ⁺): 431.2 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 13.88 - 13.87 (m, 1 H), 12.42 - 12.34 (m, 1 H), 8.43 (d, J = 4.8 Hz, 1 H), 8.07 (d, J = 8.4 Hz, 1 H), 7.32 - 7.28 (m, 1 H), 6.99 - 6.96 (m, 2 H), 6.67 - 6.61 (m, 1 H), 6.18 (d, J = 2.8 Hz, 1 H), 5.74 - 5.67 (m, 1 H), 4.78 (s, 2 H), 4.60 (d, J = 2.0 Hz, 2 H), 4.06 - 4.02 (m, 1 H), 3.94 - 3.89 (m, 1 H), 3.80 - 3.75 (m, 1 H), 3.74 - 3.57 (m, 3 H), 3.51 - 3.42 (m, 1 H), 2.77 - 2.72 (m, 2 H), 2.73 - 2.71 (m, 2 H), 2.33 - 2.30 (m, 1 H), 2.32 - 2.19 (m, 1 H).	
468	<i>m/z</i> (ESI ⁺): 393.1 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.52 (d, J = 2.8 Hz, 1H), 7.68 (d, J = 7.6 Hz, 1H), 7.46 (t, J = 7.6 Hz, 1H), 7.13 - 7.05 (m, 2H), 6.80 (d, J = 10.4, 16.8 Hz, 0.5H), 6.65 (dd, J = 10.4, 16.8 Hz, 0.5H), 6.34 (d, J = 1.6, 7.6, 16.8 Hz, 1H), 5.79 (d, J = 1.6, 6.8, 10.2 Hz, 1H), 4.64 - 4.54 (m, 1H), 4.38 (d, J = 9.2, 18.8 Hz, 0.5H), 4.32 - 4.20 (m, 1H), 4.07 (d, J = 9.2, 12.8 Hz, 0.5H), 3.88 - 3.79 (m, 1H), 3.78 - 3.73 (m, 0.5H), 3.66 - 3.58 (m, 1.5H), 3.43 (d, J = 2.4 Hz, 3H), 2.55 - 2.48 (m, 1H), 2.45 (s, 3H), 2.44 - 2.39 (m, 1H).	A38 1 st isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
469	<i>m/z</i> (ESI ⁺): 393.1 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.53 (s, 1H), 7.72 (d, J = 7.6 Hz, 1H), 7.46 (t, J = 7.6 Hz, 1H), 7.14 - 7.05 (m, 2H), 6.82 (d, J = 10.4, 16.8 Hz, 0.4H), 6.72 - 6.60 (m, 0.6H), 6.40 - 6.26 (m, 1H), 5.85 - 5.75 (m, 1H), 4.58 - 4.42 (m, 1H), 4.30 (d, J = 7.6, 10.0 Hz, 1H), 4.00 - 3.89 (m, 1H), 3.88 - 3.73 (m, 2H), 3.68 - 3.57 (m, 1H), 3.44 - 3.41 (m, 3H), 2.85 - 2.75 (m, 0.3H), 2.71 - 2.60 (m, 0.7H), 2.46 (s, 3H), 2.42 - 2.24 (m, 1H).	A38 2 nd isomer
470	<i>m/z</i> (ESI ⁺): 433.2 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.44 (s, 1H), 7.99 - 7.91 (m, 1H), 7.32 - 7.24 (m, 1H), 7.03 - 6.93 (m, 2H), 6.84 (d, J = 10.8, 16.8 Hz, 1H), 6.35 (d, J = 2.0, 16.8 Hz, 1H), 5.85 (d, J = 2.0, 10.4 Hz, 1H), 4.81 - 4.73 (m, 1H), 4.72 - 4.68 (m, 1H), 4.34 (s, 1H), 4.13 (d, J = 4.0, 11.6 Hz, 2H), 3.89 - 3.81 (m, 2H), 3.40 - 3.35 (m, 1H), 2.36 - 2.23 (m, 2H), 2.22 - 2.12 (m, 2H), 1.51 (d, J = 7.2 Hz, 6H).	
471	<i>m/z</i> (ESI ⁺): 558.3 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 12.78 (s, 1H), 9.16 (s, 1H), 8.71 (s, 1H), 8.55 (s, 1H), 8.01 - 7.85 (m, 1H), 7.35 (t, J = 7.2 Hz, 1H), 7.05 - 6.97 (m, 2H), 6.86 (d, J = 10.4, 16.4 Hz, 1H), 6.26 (d, J = 2.8, 16.4 Hz, 1H), 5.79 (d, J = 2.0, 10.8 Hz, 1H), 4.61 - 4.55 (m, 2H), 4.33 (s, 1H), 4.09 - 4.00 (m, 4H), 3.83 (t, J = 11.2 Hz, 2H), 3.76 - 3.66 (m, 4H), 3.25 - 3.20 (m, 2H), 3.09 (d, J = 11.2 Hz, 1H), 2.28 - 2.13 (m, 6H), 2.05 - 1.92 (m, 3H), 1.78 (d, J = 11.2 Hz, 2H), 1.51 (d, J = 6.8 Hz, 2H).	
472	<i>m/z</i> (ESI ⁺): 361.2 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.13 (s, 1H), 12.53 (s, 1H), 8.54 (s, 1H), 8.07 - 7.98 (m, 1H), 7.34 - 7.23 (m, 1H), 7.03 - 6.88 (m, 2H), 6.79 - 6.43 (m, 2H), 6.22 - 6.11 (m, 1H), 5.75 - 5.63 (m, 1H), 4.69 - 4.55 (m, 1H), 3.67 - 3.38 (m, 2H), 3.28 - 3.24 (m, 1H), 2.99 - 2.87 (m, 1H), 2.20 - 1.96 (m, 2H), 1.79 - 1.56 (m, 2H).	A36 1 st isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
473	<i>m/z</i> (ESI ⁺): 361.2 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.13 (s, 1H), 12.53 (m, 1H), 8.54 (s, 1H), 8.12 - 7.92 (m, 1H), 7.35 - 7.22 (m, 1H), 7.05 - 6.85 (m, 2H), 6.77 - 6.43 (m, 2H), 6.24 - 6.07 (m, 1H), 5.75 - 5.61 (m, 1H), 4.73 - 4.54 (m, 1H), 3.67 - 3.57 (m, 1H), 3.48 - 3.43 (m, 1H), 3.23 - 3.18 (m, 1H), 2.97 - 2.90 (m, 1H), 2.15 - 2.01 (m, 2H), 1.78 - 1.58 (m, 2H).	A36 2 nd isomer
474	<i>m/z</i> (ESI ⁺): 447.3 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.25 (s, 1 H), 12.41 (s, 1 H), 8.57 (s, 1 H), 8.35 - 8.16 (m, 1 H), 7.34 (t, J = 7.6 Hz, 1 H), 7.05 - 6.97 (m, 2 H), 6.91 (d, J = 10.4, 16.8 Hz, 1 H), 6.31 (d, J = 2.4, 16.4 Hz, 1 H), 5.84 (d, J = 2.0, 10.4 Hz, 1 H), 4.69 - 4.54 (m, 2 H), 4.36 (s, 1 H), 4.09 (t, J = 5.6, 10.4 Hz, 2 H), 3.76 (t, J = 12.4 Hz, 2 H), 3.10 - 2.97 (m, 1 H), 2.40 - 2.19 (m, 2 H), 2.04 (t, J = 5.6, 13.2 Hz, 2 H), 1.94 - 1.83 (m, 2 H), 1.49 (d, J = 7.2 Hz, 3 H), 0.86 (t, J = 7.2 Hz, 3 H).	
475	<i>m/z</i> (ESI ⁺): 431.2 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.36 (s, 1H), 8.04 (d, J = 1.6, 8.4 Hz, 1H), 7.34 - 7.27 (m, 1H), 7.03 - 6.96 (m, 2H), 6.83 (d, J = 10.8, 16.8 Hz, 1H), 6.71 (s, 1H), 6.34 (d, J = 2.0, 16.8 Hz, 1H), 5.83 (d, J = 2.0, 10.4 Hz, 1H), 4.71 (s, 1H), 4.61 - 4.52 (m, 1H), 4.35 (s, 1H), 4.16 (d, J = 3.2, 11.2 Hz, 2H), 3.94 (s, 3H), 3.90 - 3.83 (m, 2H), 2.46 - 2.35 (m, 2H), 2.15 - 2.01 (m, 2H).	
476	<i>m/z</i> (ESI ⁺): 498.2 (M+H) ⁺	(400 MHz, CHLOROFORM-d) δ ppm 8.57 (s, 1 H), 8.50 (d, J=4.88 Hz, 1 H), 8.07 (s, 1 H), 7.74 (d, J=7.24 Hz, 1 H), 7.43 (d, J=4.76 Hz, 1 H), 7.38 - 7.30 (m, 1 H), 7.12 (d, J=7.76 Hz, 1 H), 7.01 - 6.93 (m, 1 H), 6.59 (dd, J=16.76, 10.51 Hz, 1 H), 6.35 - 6.25 (m, 1 H), 5.51 (d, J=10.88 Hz, 1 H), 4.81 - 4.64 (m, 2 H), 4.31 (s, 1 H), 4.02 (s, 3 H), 3.97 - 3.92 (m, 1 H), 3.85 (d, J=11.76 Hz, 2 H), 2.58 - 2.48 (m, 1 H), 2.42 - 2.24 (m, 3 H), 2.20 - 2.12 (m, 1 H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
477	<i>m/z</i> (ESI ⁺): 409.4 (M+H) ⁺	(499 MHz, DMSO-d ₆) δ 13.72 (br-s, 1H), 12.52 (br-s, 1H), 8.56 (s, 1H), 8.10 – 8.05 (m, 1H), 7.28 (t, J = 7.7 Hz, 1H), 6.98 – 6.90 (m, 2H), 6.86 (dd, J = 16.7, 10.5 Hz, 1H), 6.24 (dd, J = 16.7, 2.5 Hz, 1H), 5.77 (dd, J = 10.4, 2.5 Hz, 1H), 4.56 (s, 1H), 4.51 (dd, J = 11.8, 5.8 Hz, 1H), 4.32 (s, 1H), 4.04 (dd, J = 11.4, 6.9 Hz, 2H), 3.70 (dd, J = 19.1, 11.4 Hz, 2H), 2.16 (dd, J = 22.9, 5.3 Hz, 4H).	
478	<i>m/z</i> (ESI ⁺): 435 (M+H) ⁺	(499 MHz, DMSO-d ₆) δ 14.15 (s, 1H), 12.62 (s, 1H), 8.62 (s, 1H), 8.09 (dd, J = 8.4, 1.6 Hz, 1H), 7.29 (ddd, J = 8.5, 7.2, 1.6 Hz, 1H), 7.00 – 6.93 (m, 2H), 6.85 (dd, J = 16.7, 10.5 Hz, 1H), 6.25 (dd, J = 16.7, 2.6 Hz, 1H), 5.78 (dd, J = 10.4, 2.5 Hz, 1H), 4.66 (s, 2H), 4.64 – 4.52 (m, 1H), 4.56 (s, 1H), 4.31 (s, 1H), 4.03 (dd, J = 11.4, 7.4 Hz, 2H), 3.70 (dd, J = 18.6, 11.4 Hz, 2H), 3.30 (s, 3H), 2.29 – 2.13 (m, 2H), 2.04 (ddd, J = 23.8, 18.0, 8.0 Hz, 2H).	
479	<i>m/z</i> (ESI ⁺): 477.2 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.55 (s, 1H), 7.95 (d, J = 7.2 Hz, 1H), 7.32 - 7.26 (m, 1H), 7.02 - 6.95 (m, 2H), 6.84 (m, 1H), 6.36 (d, J = 16.4 Hz, 1H), 5.88 - 5.82 (m, 1H), 5.12 - 5.04 (m, 1H), 4.95 - 4.86 (m, 2H), 4.72 (d, J = 6.4 Hz, 1H), 4.34 (s, 1H), 4.15 (m, 2H), 4.04 - 3.97 (m, 1H), 3.97 - 3.93 (m, 1H), 3.90 (d, J = 10.4 Hz, 2H), 3.87 - 3.81 (m, 3H), 2.38 - 2.13 (m, 4H).	
480	<i>m/z</i> (ESI ⁺): 460.2 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.73 - 8.64 (m, 1H), 8.55 - 8.45 (m, 1H), 8.03 (d, J = 8.0 Hz, 1H), 7.34 - 7.27 (m, 1H), 7.06 - 6.96 (m, 2H), 6.74 - 6.60 (m, 1H), 6.36 - 6.30 (m, 1H), 5.83 - 5.76 (m, 1H), 4.20 - 3.91 (m, 4H), 3.85 - 3.78 (m, 1H), 3.69 - 3.55 (m, 2H), 2.96 - 2.66 (m, 6H), 2.49 - 2.42 (m, 1H), 2.41 - 2.31 (m, 3H), 2.23 - 2.09 (m, 2H), 1.99 - 1.86 (m, 2H), 1.84 - 1.73 (m, 2H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
481	<i>m/z</i> (ESI ⁺): 513.2 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.29 (s, 1H), 7.89 (d, J = 7.6 Hz, 1H), 7.63 (s, 1H), 7.33 - 7.21 (m, 1H), 7.02 - 6.91 (m, 2H), 6.83 (d, J = 10.8, 16.8 Hz, 1H), 6.35 (d, J = 2.0, 16.8 Hz, 1H), 5.85 (d, J = 2.0, 10.4 Hz, 1H), 4.77 - 4.73 (m, 1H), 4.70 (s, 1H), 4.50 - 4.43 (m, 2H), 4.32 (s, 1H), 4.27 (t, J = 6.4 Hz, 2H), 4.07 (d, J = 6.0, 11.6 Hz, 2H), 3.83 (t, J = 10.0 Hz, 2H), 2.42 - 2.33 (m, 2H), 2.32 - 2.15 (m, 4H).	
482	<i>m/z</i> (ESI ⁺): 401.1 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 13.49 - 12.83 (m, 2H), 8.58 (s, 1H), 7.94 - 7.84 (m, 1H), 7.40 - 7.32 (m, 1H), 7.06 - 6.82 (m, 5H), 6.23 - 6.17 (m, 1H), 5.76 - 5.71 (m, 1H), 3.88 - 3.83 (m, 2H), 3.79 - 3.75 (m, 2H), 3.02 - 2.96 (m, 4H).	
483	<i>m/z</i> (ESI ⁺): 447.5 (M+H) ⁺	(499 MHz, DMSO-d ₆) δ 14.31 (s, 1H), 12.34 (s, 1H), 8.55 (s, 1H), 8.13 (dd, J = 8.4, 1.7 Hz, 1H), 7.28 (ddd, J = 8.7, 7.2, 1.6 Hz, 1H), 6.99 - 6.92 (m, 2H), 6.85 (dd, J = 16.7, 10.5 Hz, 1H), 6.25 (dd, J = 16.7, 2.5 Hz, 1H), 5.77 (dd, J = 10.4, 2.6 Hz, 1H), 4.56 (s, 1H), 4.54 - 4.45 (m, 1H), 4.31 (s, 1H), 4.02 (dd, J = 11.3, 7.2 Hz, 2H), 3.71 (dd, J = 18.2, 11.6 Hz, 2H), 2.78 (t, J = 7.4 Hz, 2H), 2.25 (t, J = 12.1 Hz, 1H), 1.99 (s, 1H), 1.60 (p, J = 7.4 Hz, 2H), 1.35 (d, J = 7.5 Hz, 1H), 1.32 (d, J = 7.3 Hz, 1H), 0.93 (t, J = 7.3 Hz, 3H).	
484	<i>m/z</i> (ESI ⁺): 449.2 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.29 (s, 1 H), 12.46 - 12.27 (m, 1 H), 8.59 (s, 1 H), 8.11 (d, J=7.6 Hz, 1 H), 7.38 - 7.23 (m, 2 H), 6.97 - 6.93 (m, 1 H), 6.84 (dd, J=16.8, 10.4 Hz, 1 H), 6.25 (dd, J=16.8, 2.4 Hz, 1 H), 5.77 (dd, J=10.4, 2.4 Hz, 1 H), 4.56 (s, 1 H), 4.30 (s, 1 H), 4.05 - 4.02 (m, 1 H), 3.70 (t, J=12.8 Hz, 2 H), 3.62 - 3.52 (m, 4 H), 3.28 (s, 3 H), 2.06 - 1.98 (m, 2 H), 1.80 - 1.72 (m, 2 H).	
485	<i>m/z</i> (ESI ⁺): 371.1 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 14.07 - 13.94 (m, 1 H), 12.81 - 12.68 (m, 1 H), 9.27 (d, J = 8.4 Hz, 1 H), 8.60 (s, 1 H), 7.99 (d, J = 8.2 Hz, 1 H), 7.42 - 7.35 (m, 6 H), 7.37 - 7.33 (m, 1 H), 7.29 (t, J = 7.6 Hz, 1 H), 6.99 - 6.92 (m, 3 H), 6.47 - 6.38 (m, 4 H), 6.20 (d, J = 2.0 Hz, 1 H), 5.71 - 5.69 (dd, J = 8, 10.4 Hz, 1 H).	

Cmpd #	MS	¹ H NMR	SFC Conditions
486	<i>m/z</i> (ESI ⁺): 376.2 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.15 (s, 1H), 12.49 (s, 1H), 8.74 (t, J = 5.6 Hz, 1H), 8.53 (s, 1H), 8.29 (s, 1H), 8.18 (s, 1H), 8.02 - 7.99 (m, 1H), 7.34 - 7.23 (m, 1H), 7.00 - 6.90 (m, 2H), 6.39 (s, 1H), 6.28 - 6.11 (m, 2H), 5.70 - 5.58 (m, 1H), 4.51 (d, J = 5.6 Hz, 2H), 4.22 - 4.17 (m, 2H).	
487	<i>m/z</i> (ESI ⁺): 375.3 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.21 (s, 1H), 12.51 (s, 1H), 8.53 (s, 1H), 8.07 - 7.98 (m, 1H), 7.35 - 7.22 (m, 1H), 7.02 - 6.88 (m, 2H), 6.46 (s, 1H), 6.37 - 6.25 (m, 1H), 6.16 - 6.01 (m, 1H), 5.72 - 5.58 (m, 1H), 4.30 - 4.19 (m, 1H), 3.99 - 3.88 (m, 2H), 3.67 - 3.59 (m, 2H), 2.77 - 2.69 (m, 2H), 2.65 - 2.62 (m, 1H), 2.29 - 1.87 (m, 3H).	
488	<i>m/z</i> (ESI ⁺): 390.3 (M+H) ⁺	(400 MHz, DMSO-d ₆) δ 14.14 (s, 1H), 12.57 (s, 1H), 8.56 (s, 1H), 8.07 - 8.00 (m, 1H), 7.32 - 7.24 (m, 1H), 7.00 - 6.91 (m, 2H), 6.62 - 6.51 (m, 2H), 6.19 - 6.06 (m, 1H), 5.75 - 5.53 (m, 1H), 3.91 - 3.79 (m, 1H), 3.72 - 3.63 (m, 2H), 3.61 - 3.42 (m, 3H), 3.30 - 3.26 (m, 2H), 3.22 - 3.00 (m, 2H), 1.87 - 1.69 (m, 2H).	A37
489	<i>m/z</i> (ESI ⁺): 363.0 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ 8.57 (s, 1 H), 7.95 (d, J = 7.2 Hz, 1 H), 7.32 - 7.28 (m, 1 H), 6.99 (d, J = 6.8 Hz, 2 H), 6.86 (s, 1 H), 6.42 - 6.40 (m, 2 H), 6.25 - 6.23 (m, 1 H), 5.83 (dd, J = 3.6, 8.0 Hz, 1 H).	
490	<i>m/z</i> (ESI ⁺): 373.0 (M+H) ⁺		
491	<i>m/z</i> (ESI ⁺): 434.1 (M+H) ⁺	(400 MHz, METHANOL-d ₄) δ = 8.43 (s, 1H), 8.00 (d, J = 7.6 Hz, 1H), 7.34 - 7.25 (m, 1H), 7.03 - 6.95 (m, 2H), 6.84 - 6.61 (m, 1H), 6.35 - 6.23 (m, 1H), 5.80 (ddd, J = 2.0, 10.4, 16.8 Hz, 1H), 4.63 (d, J = 1.2 Hz, 0.5H), 4.42 (s, 0.5H), 4.30 (s, 0.5H), 4.15 (dd, J = 4.8, 11.2 Hz, 1H), 4.09 (s, 0.5H), 3.94 (dd, J = 6.4, 11.6 Hz, 1H), 3.90 - 3.84 (m, 1H), 3.78 (dd, J = 2.0, 11.6 Hz, 1H), 3.62 (dd, J = 2.8, 6.8 Hz, 1H), 3.56 (d, J = 10.8 Hz, 1H), 2.83 (dd, J = 5.2, 11.6 Hz, 1H), 2.49 (t, J = 11.6 Hz, 1H), 2.36 (s, 4H), 1.58 - 1.46 (m, 3H)	A64 2 nd eluting isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
492	m/z (ESI+): 434.1 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.40 (s, 1H), 7.98 (d, J = 8.0 Hz, 1H), 7.28 (t, J = 7.6 Hz, 1H), 7.04 - 6.92 (m, 2H), 6.84 - 6.60 (m, 1H), 6.30 (d, J = 16.4 Hz, 1H), 5.87 - 5.74 (m, 1H), 4.63 (s, 0.5H), 4.46 - 4.26 (m, 1H), 4.15 (dd, J = 4.8, 11.6 Hz, 1H), 4.09 (s, 0.5H), 3.94 (dd, J = 7.2, 11.6 Hz, 1H), 3.87 (d, J = 11.2 Hz, 1H), 3.82 - 3.75 (m, 1H), 3.61 (dd, J = 3.2, 6.8 Hz, 1H), 3.55 (d, J = 11.2 Hz, 1H), 2.87 - 2.80 (m, 1H), 2.49 (t, J = 11.6 Hz, 1H), 2.38 (d, J = 2.8 Hz, 1H), 2.35 (s, 3H), 1.51 (d, J = 6.4 Hz, 3H)	A64 1 st eluting isomer
493	m/z (ESI+): 482.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.42 (s, 1H), 7.62 (td, J = 2.4, 10.0 Hz, 1H), 7.04 (ddd, J = 3.2, 8.0, 10.8 Hz, 1H), 6.76 (dd, J = 10.8, 16.8 Hz, 1H), 6.32 (dd, J = 2.0, 16.8 Hz, 1H), 5.82 (dd, J = 2.0, 10.4 Hz, 1H), 4.23 (s, 1H), 4.07 (dd, J = 7.2, 11.6 Hz, 2H), 3.90 - 3.81 (m, 4H), 3.55 - 3.36 (m, 1H), 3.15 (dd, J = 2.4, 10.8 Hz, 2H), 2.61 - 2.50 (m, 2H), 1.93 - 1.82 (m, 1H), 1.10 - 1.00 (m, 2H), 0.81 - 0.69 (m, 2H)	N/A
494	m/z (ESI+): 464.1 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.42 (s, 1H), 7.77 (d, J = 8.0 Hz, 1H), 7.15 (ddd, J = 1.2, 8.0, 10.8 Hz, 1H), 6.94 (dt, J = 5.2, 8.0 Hz, 1H), 6.76 (dd, J = 10.8, 16.8 Hz, 1H), 6.32 (dd, J = 2.0, 16.8 Hz, 1H), 5.82 (dd, J = 2.0, 10.8 Hz, 1H), 4.23 (s, 1H), 4.08 (dd, J = 7.2, 11.6 Hz, 2H), 3.90 - 3.81 (m, 4H), 3.15 (d, J = 11.6 Hz, 2H), 2.87 - 2.72 (m, 1H), 2.61 - 2.51 (m, 2H), 1.93 - 1.81 (m, 1H), 1.09 - 1.01 (m, 2H), 0.77 - 0.71 (m, 2H)	N/A
495	m/z (ESI+): 435.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.40 (s, 1H), 8.00 (dd, J = 1.6, 8.4 Hz, 1H), 7.28 (dt, J = 1.6, 8.4 Hz, 1H), 7.02 - 6.94 (m, 2H), 6.92 - 6.78 (m, 1H), 6.44 - 6.32 (m, 1H), 5.88 (dt, J = 1.6, 9.6 Hz, 1H), 4.64 (s, 1H), 4.53 - 4.42 (m, 1H), 4.39 (s, 0.5H), 4.33 (dd, J = 5.2, 11.6 Hz, 1H), 4.27 (s, 0.5H), 4.11 - 4.03 (m, 1H), 3.92 - 3.78 (m, 2H), 3.73 (dt, J = 1.6, 11.2 Hz, 1H), 3.24 (d, J = 7.6 Hz, 3H), 2.36 (s, 3H), 2.31 - 2.10 (m, 2H)	A39 2 nd eluting isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
496	m/z (ESI+): 435.1 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.40 (s, 1H), 8.00 (dd, J = 1.6, 8.4 Hz, 1H), 7.28 (dt, J = 1.6, 7.6 Hz, 1H), 7.02 - 6.95 (m, 2H), 6.93 - 6.78 (m, 1H), 6.44 - 6.29 (m, 1H), 5.92 - 5.83 (m, 1H), 4.63 - 4.62 (m, 1H), 4.51 - 4.42 (m, 1H), 4.40 (s, 0.5H), 4.33 (dd, J = 5.2, 11.6 Hz, 1H), 4.28 (s, 0.5H), 4.12 - 4.02 (m, 1H), 3.94 - 3.78 (m, 2H), 3.73 (dt, J = 2.0, 12.0 Hz, 1H), 3.24 (d, J = 7.2 Hz, 3H), 2.36 (s, 3H), 2.32 - 2.09 (m, 2H)	A39 1 st eluting isomer
497	m/z (ESI+): 442.1 (M+H)+	(400 MHz, DMSO-d ₆) δ = 8.73 (d, J = 19.2 Hz, 1H), 7.83 (t, J = 8.4 Hz, 1H), 7.42 - 7.29 (m, 1H), 6.83 - 6.77 (m, 1H), 6.76 (s, 1H), 6.62 (s, 0.5H), 6.46 - 6.39 (m, 0.5H), 6.20 (ddd, J = 2.4, 10.4, 16.8 Hz, 1H), 5.92 (d, J = 8.0 Hz, 1H), 5.74 (dt, J = 2.4, 10.4 Hz, 1H), 4.43 (s, 1H), 4.28 - 4.19 (m, 1H), 3.94 - 3.86 (m, 2H), 3.86 - 3.82 (m, 1H), 3.76 (s, 1H), 3.69 - 3.58 (m, 2H), 3.15 - 3.07 (m, 2H), 2.45 - 2.37 (m, 2H)	N/A
498	m/z (ESI+): 424.1 (M+H)+	(400 MHz, DMSO-d ₆) δ = 8.61 (s, 1H), 7.85 (d, J = 8.0 Hz, 1H), 7.26 - 7.19 (m, 1H), 6.93 - 6.85 (m, 1H), 6.82 - 6.74 (m, 1H), 6.58 (s, 1H), 6.22 - 6.14 (m, 1H), 5.75 - 5.69 (m, 1H), 4.42 (s, 1H), 4.21 (s, 1H), 3.95 - 3.88 (m, 2H), 3.74 (s, 2H), 3.64 (t, J = 10.4 Hz, 2H), 3.09 (d, J = 11.2 Hz, 2H), 2.46 - 2.40 (m, 2H)	N/A
499	m/z (ESI+): 474.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.45 (s, 0.5H), 8.39 (s, 1H), 7.99 (dd, J = 1.2, 8.4 Hz, 1H), 7.32 - 7.22 (m, 1H), 7.01 - 6.92 (m, 2H), 6.85 - 6.79 (m, 1H), 6.77 - 6.68 (m, 1H), 4.58 (s, 2H), 4.30 (s, 1H), 4.15 (d, J = 12.0 Hz, 2H), 3.93 - 3.87 (m, 4H), 3.87 - 3.80 (m, 2H), 3.77 (d, J = 6.0 Hz, 2H), 2.47 - 2.39 (m, 2H), 2.38 (s, 3H), 2.27 - 2.14 (m, 4H)	N/A
500	m/z (ESI+): 407.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.42 (d, J = 1.6 Hz, 1H), 7.80 (d, J = 8.0 Hz, 1H), 7.20 - 7.08 (m, 1H), 6.92 (dt, J = 5.2, 8.0 Hz, 1H), 6.34 - 6.00 (m, 2H), 5.72 - 5.50 (m, 1H), 4.33 - 4.21 (m, 1H), 4.11 - 3.86 (m, 2H), 3.79 - 3.64 (m, 2H), 2.41 (s, 3H), 2.30 - 2.08 (m, 4H), 2.05 - 1.95 (m, 1H), 1.93 - 1.71 (m, 1H)	A50 2 nd eluting isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
501	m/z (ESI+): 407.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.38 (s, 1H), 7.77 (d, J = 8.0 Hz, 1H), 7.18 - 7.05 (m, 1H), 6.97 - 6.81 (m, 1H), 6.34 - 6.01 (m, 2H), 5.71 - 5.47 (m, 1H), 4.26 (d, J = 5.6 Hz, 1H), 4.08 - 3.87 (m, 2H), 3.79 - 3.63 (m, 2H), 2.39 (s, 3H), 2.29 - 2.07 (m, 4H), 2.04 - 1.92 (m, 1H), 1.88 - 1.73 (m, 1H)	A50 1 st eluting isomer
502	m/z (ESI+): 425.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.43 (d, J = 2.4 Hz, 1H), 7.64 (d, J = 10.0 Hz, 1H), 7.01 (ddd, J = 2.8, 8.4, 10.8 Hz, 1H), 6.34 - 5.99 (m, 2H), 5.75 - 5.46 (m, 1H), 4.26 (d, J = 3.6 Hz, 1H), 4.07 - 3.86 (m, 2H), 3.79 - 3.59 (m, 2H), 2.41 (s, 3H), 2.31 - 2.08 (m, 4H), 2.05 - 1.96 (m, 1H), 1.91 - 1.73 (m, 1H)	A50 2 nd eluting isomer
503	m/z (ESI+): 425.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.44 (d, J = 2.8 Hz, 1H), 7.65 (d, J = 10.0 Hz, 1H), 7.02 (ddd, J = 2.8, 8.4, 10.8 Hz, 1H), 6.37 - 5.96 (m, 2H), 5.74 - 5.46 (m, 1H), 4.27 (d, J = 3.6 Hz, 1H), 4.09 - 3.85 (m, 2H), 3.78 - 3.62 (m, 2H), 2.42 (s, 3H), 2.31 - 2.09 (m, 4H), 2.05 - 1.94 (m, 1H), 1.90 - 1.74 (m, 1H)	A50 1 st eluting isomer
504	m/z (ESI+): 446.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.39 (s, 1H), 7.94 (dd, J = 1.6, 8.4 Hz, 1H), 7.35 - 7.24 (m, 1H), 7.04 - 6.95 (m, 2H), 6.75 (dd, J = 10.4, 16.8 Hz, 1H), 6.32 (dd, J = 2.0, 16.8 Hz, 1H), 5.81 (dd, J = 2.0, 10.4 Hz, 1H), 4.57 (s, 2H), 4.22 (s, 1H), 4.07 (dd, J = 7.6, 11.6 Hz, 2H), 3.86 (dd, J = 2.4, 4.4 Hz, 1H), 3.83 (s, 2H), 3.15 (d, J = 11.6 Hz, 2H), 2.60 - 2.49 (m, 2H), 1.92 - 1.79 (m, 1H), 1.11 - 0.98 (m, 2H), 0.75 (dd, J = 1.6, 5.6 Hz, 2H)	N/A
505	m/z (ESI+): 364.1 (M+H)+	(400 MHz, DMSO-d ₆) δ = 13.84 (br s, 1H), 8.63 (s, 1H), 8.13 (d, J = 7.2 Hz, 1H), 7.45 (br s, 1H), 7.36 - 7.27 (m, 1H), 7.07 - 6.92 (m, 2H), 6.37 (dd, J = 10.4, 17.2 Hz, 1H), 6.15 (dd, J = 2.4, 17.2 Hz, 1H), 5.71 (dd, J = 2.4, 10.4 Hz, 1H), 4.98 - 4.81 (m, 1H), 4.67 (t, J = 8.8 Hz, 1H), 4.57 - 4.46 (m, 1H), 4.39 - 4.31 (m, 1H), 4.29 - 4.20 (m, 1H)	N/A

Cmpd #	MS	¹ H NMR	SFC Conditions
506	m/z (ESI+): 393.1 (M+H)+	(400 MHz, DMSO-d ₆) δ = 12.83 (br s, 1H), 8.62 - 8.54 (m, 1H), 7.90 (d, J = 6.4 Hz, 1H), 7.34 (t, J = 7.6 Hz, 1H), 7.03 - 6.93 (m, 2H), 6.86 - 6.58 (m, 2H), 6.24 - 6.12 (m, 1H), 5.79 - 5.60 (m, 1H), 5.14 - 4.81 (m, 2H), 4.71 (d, J = 6.0 Hz, 1H), 3.83 - 3.79 (m, 0.5H), 3.72 (dd, J = 2.4, 7.2 Hz, 0.5H), 2.27 (dt, J = 2.8, 12.8 Hz, 1H), 2.14 - 2.06 (m, 1H), 2.01 - 1.88 (m, 4H)	A40 2 nd eluting isomer
507	m/z (ESI+): 393.1 (M+H)+	(400 MHz, DMSO-d ₆) δ = 14.08 (br s, 1H), 12.50 (br s, 1H), 8.60 - 8.50 (m, 1H), 8.02 (d, J = 7.6 Hz, 1H), 7.33 - 7.22 (m, 1H), 7.00 - 6.91 (m, 2H), 6.86 - 6.61 (m, 1H), 6.51 - 6.45 (m, 1H), 6.23 - 6.11 (m, 1H), 5.78 - 5.60 (m, 1H), 5.15 - 4.81 (m, 2H), 4.76 - 4.67 (m, 1H), 3.76 - 3.74 (m, 0.5H), 3.67 (d, J = 1.2 Hz, 0.5H), 2.29 - 2.22 (m, 1H), 2.13 - 2.06 (m, 1H), 2.01 - 1.88 (m, 4H)	A40 1 st eluting isomer
508	m/z (ESI+): 419.2 (M+H)+	(400 MHz, DMSO-d ₆) δ = 14.34 (s, 1H), 12.33 (s, 1H), 8.56 (s, 1H), 8.11 (d, J = 7.6 Hz, 1H), 7.28 (t, J = 7.6 Hz, 1H), 6.99 - 6.92 (m, 2H), 6.92 - 6.82 (m, 1H), 6.32 - 6.19 (m, 1H), 5.84 - 5.73 (m, 1H), 4.70 (s, 0.5H), 4.42 (d, J = 9.6 Hz, 0.5H), 4.32 (s, 0.5H), 3.97 (s, 0.5H), 3.79 (t, J = 11.6 Hz, 1H), 3.73 - 3.62 (m, 1H), 3.56 - 3.45 (m, 2H), 2.48 - 2.36 (m, 2H), 2.35 - 2.28 (m, 0.5H), 2.26 (s, 3H), 2.22 - 2.16 (m, 0.5H), 2.16 - 2.09 (m, 1H), 0.86 (t, J = 6.0 Hz, 3H)	A1 2 nd eluting isomer
509	m/z (ESI+): 419.2 (M+H)+	(400 MHz, CHLOROFORM-d) δ = 13.99 (br s, 1H), 10.55 (br s, 1H), 8.11 (s, 1H), 7.85 (d, J = 7.6 Hz, 1H), 7.35 - 7.29 (m, 1H), 7.10 (d, J = 8.0 Hz, 1H), 6.98 (t, J = 7.6 Hz, 1H), 6.71 - 6.59 (m, 1H), 6.53 - 6.41 (m, 1H), 5.84 (d, J = 10.4 Hz, 1H), 4.94 (d, J = 10.0 Hz, 0.5H), 4.57 (s, 0.5H), 4.33 - 4.24 (m, 0.5H), 3.91 - 3.80 (m, 1.5H), 3.80 - 3.70 (m, 1H), 3.69 - 3.59 (m, 2H), 2.68 - 2.54 (m, 1H), 2.53 - 2.37 (m, 2H), 2.28 (s, 3H), 2.26 - 2.18 (m, 0.5H), 2.15 - 2.06 (m, 0.5H), 1.07 (d, J = 6.4 Hz, 3H)	A1 1 st eluting isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
510	m/z (ESI+): 375.1 (M+H)+	(400 MHz, CHLOROFORM-d) δ = 14.65 - 14.23 (m, 1H), 12.52 (s, 1H), 8.15 (s, 1H), 7.81 (dd, J = 1.6, 8.0 Hz, 1H), 7.32 - 7.28 (m, 1H), 7.11 (dd, J = 1.2, 8.4 Hz, 1H), 6.98 - 6.92 (m, 1H), 6.56 (s, 1H), 6.55 (d, J = 2.4 Hz, 1H), 6.30 (t, J = 1.6 Hz, 1H), 5.83 (dd, J = 4.8, 7.2 Hz, 1H), 4.46 (dd, J = 3.2, 7.6 Hz, 1H), 3.78 (dd, J = 5.6, 8.0 Hz, 2H), 3.41 (dt, J = 3.2, 7.6 Hz, 1H), 2.92 - 2.81 (m, 1H), 2.46 - 2.35 (m, 1H), 2.23 - 2.13 (m, 1H), 2.13 - 2.01 (m, 2H), 1.96 - 1.86 (m, 1H), 1.76 - 1.64 (m, 1H)	A16 2 nd eluting isomer
511	m/z (ESI+): 375.1 (M+H)+	(400 MHz, CHLOROFORM-d) δ = 14.71 - 14.19 (m, 1H), 12.52 (s, 1H), 8.15 (s, 1H), 7.81 (dd, J = 1.6, 8.0 Hz, 1H), 7.33 - 7.28 (m, 1H), 7.11 (dd, J = 1.2, 8.0 Hz, 1H), 6.98 - 6.92 (m, 1H), 6.56 (s, 1H), 6.55 (d, J = 2.4 Hz, 1H), 6.30 (t, J = 1.2 Hz, 1H), 5.83 (dd, J = 4.8, 7.2 Hz, 1H), 4.46 (dd, J = 3.2, 7.6 Hz, 1H), 3.78 (dd, J = 5.6, 8.0 Hz, 2H), 3.41 (dt, J = 3.2, 7.6 Hz, 1H), 2.92 - 2.81 (m, 1H), 2.46 - 2.35 (m, 1H), 2.23 - 2.11 (m, 1H), 2.11 - 2.01 (m, 2H), 1.96 - 1.86 (m, 1H), 1.75 - 1.63 (m, 1H)	A16 1 st eluting isomer
512	m/z (ESI+): 476.3 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.50 (s, 1H), 7.96 - 7.85 (m, 1H), 7.36 - 7.26 (m, 1H), 7.01 - 6.95 (m, 2H), 6.91 (td, J = 6.8, 15.2 Hz, 1H), 6.30 (d, J = 15.6 Hz, 1H), 4.61 - 4.49 (m, 4H), 4.35 - 4.23 (m, 2H), 4.05 (d, J = 7.2 Hz, 2H), 3.96 - 3.87 (m, 1H), 3.78 (quin, J = 7.2 Hz, 1H), 3.35 (d, J = 6.4 Hz, 2H), 2.61 (q, J = 7.2 Hz, 4H), 2.48 - 2.37 (m, 1H), 2.21 - 2.07 (m, 1H), 1.10 (t, J = 7.2 Hz, 6H)	A41 2 nd eluting isomer
513	m/z (ESI+): 476.3 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.51 (s, 1H), 7.91 (dd, J = 1.6, 8.4 Hz, 1H), 7.28 (dd, J = 1.6, 7.2 Hz, 1H), 7.02 - 6.95 (m, 2H), 6.90 (td, J = 6.4, 15.6 Hz, 1H), 6.33 (d, J = 15.6 Hz, 1H), 4.59 - 4.54 (m, 4H), 4.29 (tdd, J = 4.4, 8.0, 12.6 Hz, 2H), 4.08 - 4.02 (m, 2H), 3.95 - 3.88 (m, 1H), 3.82 - 3.75 (m, 1H), 3.41 (d, J = 6.0 Hz, 2H), 2.67 (q, J = 7.2 Hz, 4H), 2.48 - 2.37 (m, 1H), 2.21 - 2.06 (m, 1H), 1.12 (t, J = 7.2 Hz, 6H)	A41 1 st eluting isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
514	m/z (ESI+): 391.1 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.50 (s, 1H), 7.90 (dd, J = 1.6, 8.4 Hz, 1H), 7.35 - 7.24 (m, 1H), 7.05 - 6.94 (m, 2H), 6.52 - 6.20 (m, 2H), 5.80 (dd, J = 2.0, 10.4 Hz, 1H), 4.80 - 4.76 (m, 1H), 4.58 - 4.52 (m, 3H), 4.36 - 4.23 (m, 2H), 4.11 - 4.02 (m, 2H), 3.97 - 3.86 (m, 1H), 3.83 - 3.73 (m, 1H), 2.51 - 2.36 (m, 1H), 2.19 - 2.07 (m, 1H)	A42 2 nd eluting isomer
515	m/z (ESI+): 391.1 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.51 (s, 1H), 7.90 (dd, J = 1.6, 8.4 Hz, 1H), 7.35 - 7.23 (m, 1H), 7.04 - 6.93 (m, 2H), 6.48 - 6.28 (m, 2H), 5.87 - 5.74 (m, 1H), 4.79 - 4.74 (m, 1H), 4.57 - 4.51 (m, 3H), 4.36 - 4.23 (m, 2H), 4.08 - 4.03 (m, 2H), 3.96 - 3.88 (m, 1H), 3.84 - 3.75 (m, 1H), 2.50 - 2.36 (m, 1H), 2.20 - 2.08 (m, 1H)	A42 1 st eluting isomer
516	m/z (ESI+): 391.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.40 (s, 1H), 7.95 - 7.91 (m, 1H), 7.30 - 7.26 (m, 1H), 6.99 - 6.94 (m, 2H), 6.47 (s, 1H), 6.38 - 6.20 (m, 2H), 5.76 - 5.70 (m, 1H), 4.43 - 4.33 (m, 1H), 4.32 - 4.23 (m, 1H), 4.19 - 4.10 (m, 1H), 4.08 - 4.00 (m, 2H), 3.72 - 3.64 (m, 1H), 3.01 - 2.96 (m, 2H), 2.91 - 2.80 (m, 1H), 2.48 - 2.39 (m, 1H), 2.06 - 1.98 (m, 1H)	A11 2 nd eluting isomer
517	m/z (ESI+): 391.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.40 (s, 1H), 7.93 (d, J = 7.2 Hz, 1H), 7.32 - 7.25 (m, 1H), 7.01 - 6.93 (m, 2H), 6.47 (s, 1H), 6.38 - 6.19 (m, 2H), 5.77 - 5.69 (m, 1H), 4.44 - 4.34 (m, 1H), 4.32 - 4.24 (m, 1H), 4.19 - 4.10 (m, 1H), 4.09 - 4.00 (m, 2H), 3.71 - 3.65 (m, 1H), 3.01 - 2.96 (m, 2H), 2.91 - 2.80 (m, 1H), 2.47 - 2.39 (m, 1H), 2.05 - 1.98 (m, 1H)	A11 1 st eluting isomer
518	m/z (ESI+): 367.2 (M+H)+	(400 MHz, CHLOROFORM-d) δ = 14.40 - 13.03 (m, 1H), 12.80 - 12.35 (m, 1H), 8.34 - 8.08 (m, 1H), 7.86 - 7.68 (m, 1H), 7.43 - 7.29 (m, 1H), 7.16 - 7.06 (m, 1H), 7.03 - 6.87 (m, 1H), 6.50 - 6.34 (m, 3H), 5.74 - 5.68 (m, 1H), 5.36 - 4.97 (m, 1H), 4.01 - 3.80 (m, 3H), 3.62 (d, J = 7.2 Hz, 1H), 3.24 - 2.63 (m, 3H)	A51 2 nd eluting isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
519	m/z (ESI+): 367.2 (M+H)+	(400 MHz, CHLOROFORM-d) δ = 14.01 - 13.49 (m, 1H), 12.62 - 12.31 (m, 1H), 8.35 - 8.11 (m, 1H), 7.88 - 7.70 (m, 1H), 7.34 (q, J = 6.8 Hz, 1H), 7.11 (dd, J = 3.6, 8.0 Hz, 1H), 6.98 (td, J = 7.2, 14.4 Hz, 1H), 6.49 - 6.32 (m, 3H), 5.78 - 5.65 (m, 1H), 5.33 - 4.98 (m, 1H), 4.11 - 3.86 (m, 3H), 3.83 - 3.62 (m, 1H), 3.30 - 2.89 (m, 3H)	A51 1 st eluting isomer
520	m/z (ESI+): 375.2 (M+H)+	(400 MHz, CHLOROFORM-d) δ = 10.91 - 10.55 (m, 1H), 8.17 (s, 1H), 7.86 - 7.76 (m, 1H), 7.38 - 7.30 (m, 1H), 7.19 - 7.06 (m, 1H), 7.05 - 6.93 (m, 1H), 6.69 (dd, J = 10.4, 16.8 Hz, 1H), 6.45 - 6.24 (m, 2H), 5.77 (d, J = 10.8 Hz, 1H), 4.82 - 4.44 (m, 1H), 4.17 - 3.81 (m, 1H), 3.53 - 3.26 (m, 2H), 2.93 (d, J = 13.2 Hz, 1H), 2.74 - 2.56 (m, 2H), 2.37 - 2.23 (m, 1H), 2.14 - 1.93 (m, 2H), 1.78 (d, J = 12.0 Hz, 1H)	A52 2 nd eluting isomer
521	m/z (ESI+): 375.2 (M+H)+	400 MHz, CHLOROFORM-d) δ = 11.17 - 10.65 (m, 1H), 8.17 (s, 1H), 7.87 - 7.74 (m, 1H), 7.40 - 7.29 (m, 1H), 7.12 (d, J = 7.6 Hz, 1H), 7.04 - 6.93 (m, 1H), 6.81 - 6.58 (m, 1H), 6.46 - 6.27 (m, 2H), 5.81 - 5.62 (m, 1H), 4.82 - 4.42 (m, 1H), 4.22 - 3.83 (m, 1H), 3.51 - 3.27 (m, 2H), 3.00 - 2.84 (m, 1H), 2.75 - 2.58 (m, 2H), 2.32 - 2.22 (m, 1H), 2.13 - 1.99 (m, 2H), 1.79 (s, 1H)	A52 1 st eluting isomer
522	m/z (ESI+): 347.2 (M+H)+	(400 MHz, METHANOL-d4) δ = 8.46 - 8.36 (m, 1H), 7.93 (d, J = 8.0 Hz, 1H), 7.32 - 7.21 (m, 1H), 7.01 - 6.92 (m, 2H), 6.60 (dd, J = 10.4, 16.8 Hz, 1H), 6.45 - 6.34 (m, 2H), 6.00 - 5.85 (m, 2H), 5.85 - 5.71 (m, 1H), 5.32 - 5.15 (m, 1H), 4.37 (dd, J = 1.6, 14.8 Hz, 1H), 4.21 - 4.10 (m, 1H), 3.45 - 3.37 (m, 2H)	J 2 nd eluting isomer
523	m/z (ESI+): 347.2 (M+H)+	(400 MHz, METHANOL-d4) δ = 8.46 - 8.36 (m, 1H), 7.93 (d, J = 8.0 Hz, 1H), 7.32 - 7.21 (m, 1H), 7.01 - 6.92 (m, 2H), 6.60 (dd, J = 10.4, 16.8 Hz, 1H), 6.45 - 6.34 (m, 2H), 6.00 - 5.85 (m, 2H), 5.85 - 5.71 (m, 1H), 5.32 - 5.15 (m, 1H), 4.37 (dd, J = 1.6, 14.8 Hz, 1H), 4.21 - 4.10 (m, 1H), 3.45 - 3.37 (m, 2H)	J 1 st eluting isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
524	m/z (ESI+): 471.1 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.57 (s, 1H), 7.92 (d, J = 6.8 Hz, 1H), 7.34 - 7.23 (m, 1H), 7.04 - 6.94 (m, 2H), 6.91 - 6.77 (m, 1H), 6.37 - 6.33 (m, 1H), 6.29 - 6.00 (m, 1H), 5.89 - 5.81 (m, 1H), 5.28 - 5.15 (m, 1H), 4.71 (s, 1H), 4.57 (s, 1H), 4.34 (s, 1H), 4.14 - 4.07 (m, 2H), 3.91 - 3.79 (m, 2H), 2.36 - 2.12 (m, 4H)	N/A
525	m/z (ESI+): 393.1 (M+H)+	(400 MHz, DMSO-d ₆) δ = 15.04 (br s, 1H), 12.41 (br s, 1H), 8.65 (s, 1H), 7.96 (d, J = 8.0 Hz, 1H), 7.29 - 7.18 (m, 1H), 6.97 - 6.87 (m, 1H), 6.29 - 6.08 (m, 1H), 6.03 - 5.92 (m, 1H), 5.67 - 5.46 (m, 1H), 4.26 (q, J = 9.6 Hz, 1H), 4.14 - 4.01 (m, 2H), 3.99 - 3.92 (m, 0.5H), 3.80 (dd, J = 10.0, 19.2 Hz, 1H), 3.52 (d, J = 10.8 Hz, 0.5H), 2.63 - 2.54 (m, 1H), 2.35 (s, 1H), 2.32 (s, 3H), 2.30 - 2.15 (m, 2H)	A12 2 nd eluting isomer
526	m/z (ESI+): 393.1 (M+H)+	(400 MHz, DMSO-d ₆) δ = 15.06 (br s, 1H), 12.40 (br s, 1H), 8.65 (s, 1H), 7.96 (d, J = 8.0 Hz, 1H), 7.29 - 7.19 (m, 1H), 6.92 (dt, J = 5.2, 8.0 Hz, 1H), 6.30 - 6.07 (m, 1H), 6.04 - 5.92 (m, 1H), 5.65 - 5.47 (m, 1H), 4.26 (q, J = 9.6 Hz, 1H), 4.13 - 4.00 (m, 2H), 3.99 - 3.91 (m, 0.5H), 3.80 (dd, J = 10.0, 18.8 Hz, 1H), 3.53 (d, J = 10.4 Hz, 0.5H), 2.63 - 2.54 (m, 1H), 2.39 - 2.33 (m, 1H), 2.32 (s, 3H), 2.30 - 2.15 (m, 2H)	A12 1 st eluting isomer
527	m/z (ESI+): 393.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.43 (d, J = 2.4 Hz, 1H), 7.80 (d, J = 7.6 Hz, 1H), 7.21 - 7.08 (m, 1H), 6.91 (dt, J = 4.8, 8.0 Hz, 1H), 6.32 - 6.09 (m, 2H), 5.73 - 5.55 (m, 1H), 4.37 (q, J = 9.6 Hz, 1H), 4.21 - 4.08 (m, 2.5H), 3.94 (t, J = 10.8 Hz, 1H), 3.73 (d, J = 11.2 Hz, 0.5H), 2.62 - 2.39 (m, 3H), 2.37 (s, 3H), 2.36 - 2.27 (m, 1H)	A12
528	m/z (ESI+): 420.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.42 (s, 1H), 8.00 (dd, J = 1.6, 8.4 Hz, 1H), 7.30 (dt, J = 1.6, 7.6 Hz, 1H), 7.03 - 6.96 (m, 2H), 6.76 (dd, J = 10.8, 16.8 Hz, 1H), 6.33 (dd, J = 2.0, 16.8 Hz, 1H), 5.82 (dd, J = 2.0, 10.8 Hz, 1H), 4.56 (s, 1H), 4.22 (s, 1H), 4.07 (dd, J = 8.8, 11.2 Hz, 2H), 3.92 - 3.78 (m, 2H), 3.71 (s, 2H), 3.14 (d, J = 10.8 Hz, 2H), 2.57 - 2.49 (m, 2H), 2.34 (s, 3H)	N/A

Cmpd #	MS	¹ H NMR	SFC Conditions
529	m/z (ESI+): 391.2 (M+H)+	(400 MHz, DMSO-d ₆) δ = 14.14 (s, 1H), 12.49 (br s, 1H), 8.54 (s, 1H), 8.04 - 8.01 (m, 1H), 7.31 - 7.26 (m, 1H), 6.98 - 6.92 (m, 2H), 6.48 (s, 1H), 6.34 - 6.24 (m, 1H), 6.12 - 6.05 (m, 1H), 5.69 - 5.62 (m, 1H), 4.35 (d, J = 9.2 Hz, 0.5H), 4.24 (d, J = 9.6 Hz, 1H), 4.15 (d, J = 9.2 Hz, 0.5H), 4.06 (d, J = 10.8 Hz, 0.5H), 3.99 - 3.91 (m, 2H), 3.87 - 3.83 (m, 0.5H), 3.60 - 3.54 (m, 1H), 2.96 - 2.89 (m, 2H), 2.84 - 2.76 (m, 1H), 2.37 - 2.30 (m, 1H), 1.98 - 1.88 (m, 1H)	A11
530	m/z (ESI+): 377.1 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.45 - 8.42 (m, 1H), 7.92 (d, J = 8.0 Hz, 1H), 7.28 (t, J = 7.6 Hz, 1H), 7.01 - 6.93 (m, 2H), 6.73 - 6.55 (m, 1H), 6.54 - 6.48 (m, 1H), 6.40 - 6.27 (m, 1H), 5.85 - 5.75 (m, 1H), 4.75 (t, J = 6.0 Hz, 1H), 4.27 - 4.13 (m, 1H), 4.08 - 3.99 (m, 2H), 3.99 - 3.92 (m, 2H), 3.87 - 3.81 (m, 1H), 3.73 - 3.63 (m, 1H), 3.30 - 3.23 (m, 1H)	X 2 nd eluting isomer
531	m/z (ESI+): 377.1 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.46 - 8.40 (m, 1H), 7.92 (d, J = 8.0 Hz, 1H), 7.32 - 7.24 (m, 1H), 7.01 - 6.93 (m, 2H), 6.73 - 6.55 (m, 1H), 6.54 - 6.48 (m, 1H), 6.40 - 6.27 (m, 1H), 5.85 - 5.75 (m, 1H), 4.78 - 4.71 (m, 1H), 4.26 - 4.14 (m, 1H), 4.07 - 3.99 (m, 2H), 3.95 (ddd, J = 2.4, 7.2, 11.6 Hz, 2H), 3.87 - 3.81 (m, 1H), 3.73 - 3.63 (m, 1H), 3.29 - 3.24 (m, 1H)	X 1 st eluting isomer
532	m/z (ESI+): 423.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.42 (s, 1H), 7.81 (d, J = 8.4 Hz, 1H), 7.16 - 7.09 (m, 1H), 6.95 - 6.83 (m, 2H), 6.40 - 6.34 (m, 1H), 5.89 - 5.84 (m, 1H), 4.83 (s, 1H), 4.47 (d, J = 9.2 Hz, 1H), 3.86 - 3.79 (m, 2H), 3.69 - 3.62 (m, 2H), 2.96 - 2.84 (m, 1H), 2.44 - 2.34 (m, 2H), 2.32 (s, 3H), 2.28 - 2.17 (m, 2H)	N/A
533	m/z (ESI+): 376.1 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 7.67 (s, 1H), 7.56 - 7.47 (m, 1H), 7.46 - 7.38 (m, 1H), 7.08 - 7.01 (m, 2H), 6.84 - 6.72 (m, 1H), 6.46 - 6.32 (m, 1H), 6.06 (s, 1H), 5.89 - 5.81 (m, 1H), 4.92 - 4.88 (m, 1H), 4.79 - 4.75 (m, 1H), 3.95 - 3.83 (m, 2H), 3.60 - 3.47 (m, 2H), 2.19 (dd, J = 5.2 Hz, 1H), 2.10 - 1.89 (m, 3H)	N/A

Cmpd #	MS	¹ H NMR	SFC Conditions
534	m/z (ESI+): 392.2 (M+H)+	(400 MHz, DMSO-d ₆) δ = 14.37 (br s, 1H), 12.83 (br s, 1H), 10.40 (br s, 1H), 7.56 (s, 1H), 7.48 (d, J = 7.6 Hz, 1H), 7.44 - 7.38 (m, 1H), 7.06 (d, J = 8.0 Hz, 1H), 7.02 - 6.98 (m, 1H), 6.93 - 6.87 (m, 1H), 6.29 - 6.24 (m, 1H), 6.14 (s, 1H), 5.87 - 5.78 (m, 1H), 4.61 (s, 1H), 4.47 (d, J = 1.6 Hz, 1H), 4.31 - 4.28 (m, 2H), 4.02 - 3.97 (m, 2H), 3.74 - 3.59 (m, 4H)	N/A
535	m/z (ESI+): 406.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.46 (s, 1H), 7.94 (d, J = 7.6 Hz, 1H), 7.36 - 7.20 (m, 1H), 7.03 - 6.92 (m, 2H), 6.75 (dd, J = 10.4, 16.8 Hz, 1H), 6.60 (s, 1H), 6.31 (dd, J = 1.6, 16.8 Hz, 1H), 5.81 (dd, J = 2.0, 10.8 Hz, 1H), 4.56 (s, 1H), 4.22 (s, 1H), 4.08 (dd, J = 8.0, 11.6 Hz, 2H), 3.90 - 3.81 (m, 2H), 3.79 - 3.69 (m, 2H), 3.15 (d, J = 11.6 Hz, 2H), 2.57 - 2.45 (m, 2H)	N/A
536	m/z (ESI+): 397.1 (M+H)+	(400 MHz, DMSO-d ₆) δ = 14.12 (br s, 1H), 12.62 (br s, 1H), 8.53 (s, 1H), 8.00 (d, J = 7.6 Hz, 1H), 7.42 - 7.24 (m, 4H), 7.01 - 6.90 (m, 2H), 6.69 (ddd, J = 2.8, 10.4, 16.8 Hz, 1H), 6.37 (s, 1H), 6.22 (dd, J = 2.4, 16.8 Hz, 1H), 5.75 (d, J = 10.8 Hz, 1H), 4.94 (s, 2H), 4.71 (d, J = 4.4 Hz, 2H), 4.24 (s, 2H)	N/A
537	m/z (ESI+): 455.1 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.58 (s, 1H), 7.64 (dd, J = 1.6, 7.6 Hz, 1H), 7.53 - 7.44 (m, 1H), 7.15 - 7.05 (m, 2H), 6.84 (dd, J = 10.4, 16.8 Hz, 1H), 6.40 - 6.05 (m, 2H), 5.86 (dd, J = 2.0, 10.4 Hz, 1H), 4.80 (s, 1H), 4.73 (s, 1H), 4.37 (s, 1H), 4.13 (dd, J = 3.6, 11.6 Hz, 2H), 3.91 - 3.82 (m, 2H), 3.54 (dt, J = 3.2, 18.4 Hz, 2H), 2.31 - 2.20 (m, 4H)	N/A
538	m/z (ESI+): 401.1 (M+H)+	(400 MHz, DMSO-d ₆) δ = 14.27 (br s, 1H), 12.47 (br s, 1H), 8.56 (s, 1H), 8.04 (d, J = 6.8 Hz, 1H), 7.33 - 7.26 (m, 1H), 7.01 - 6.93 (m, 3H), 6.65 - 6.56 (m, 1H), 6.26 - 6.16 (m, 1H), 5.79 (d, J = 12.0 Hz, 1H), 5.25 - 5.08 (m, 1H), 5.02 (s, 1H), 4.22 - 4.02 (m, 4H), 2.42 (s, 3H)	N/A

Cmpd #	MS	¹ H NMR	SFC Conditions
539	m/z (ESI+): 528.3 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.53 (s, 1H), 8.48 (s, 1H), 8.00 (d, J = 7.6 Hz, 1H), 7.35 - 7.23 (m, 1H), 7.04 - 6.93 (m, 2H), 6.84 (ddd, J = 6.8, 10.4, 16.8 Hz, 1H), 6.41 - 6.30 (m, 1H), 5.89 - 5.82 (m, 1H), 4.74 (s, 5H), 4.38 - 4.31 (m, 1H), 4.18 - 4.07 (m, 2H), 3.86 (t, J = 10.0 Hz, 2H), 3.27 - 3.17 (m, 2H), 2.56 - 2.43 (m, 1H), 2.41 - 2.15 (m, 7H), 1.99 (s, 2H), 1.81 - 1.64 (m, 2H), 1.52 (d, J = 6.8 Hz, 3H)	N/A
540	m/z (ESI+): 528.3 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.54 (s, 1H), 8.43 (s, 1H), 7.99 (d, J = 8.0 Hz, 1H), 7.29 (t, J = 7.6 Hz, 1H), 7.05 - 6.95 (m, 2H), 6.84 (ddd, J = 6.0, 10.8, 16.8 Hz, 1H), 6.36 (d, J = 16.8 Hz, 1H), 5.92 - 5.76 (m, 1H), 4.81 - 4.62 (m, 5H), 4.35 (d, J = 12.4 Hz, 1H), 4.15 (dd, J = 4.4, 11.6 Hz, 2H), 3.91 - 3.83 (m, 2H), 3.46 - 3.38 (m, 2H), 2.45 - 2.16 (m, 5H), 2.15 - 2.01 (m, 5H), 1.83 - 1.75 (m, 2H), 1.48 (d, J = 6.8 Hz, 3H)	N/A
541	m/z (ESI+): 389.2 (M+H)+	(400 MHz, DMSO-d ₆) δ = 14.29 (s, 1H), 12.19 (s, 1H), 8.58 (s, 1H), 8.11 (d, J = 8.0 Hz, 1H), 7.28 (t, J = 7.6 Hz, 1H), 7.02 - 6.89 (m, 2H), 6.27 - 6.03 (m, 1H), 6.01 - 5.85 (m, 1H), 5.63 - 5.44 (m, 1H), 4.14 (s, 1H), 3.93 - 3.71 (m, 2H), 3.66 - 3.49 (m, 2H), 2.35 (s, 3H), 2.18 - 2.03 (m, 4H), 1.94 - 1.82 (m, 1H), 1.75 - 1.63 (m, 1H)	A11 2 nd eluting isomer
542	m/z (ESI+): 389.2 (M+H)+	(400 MHz, DMSO-d ₆) δ = 14.28 (s, 1H), 12.18 (s, 1H), 8.58 (s, 1H), 8.11 (d, J = 8.0 Hz, 1H), 7.28 (t, J = 7.6 Hz, 1H), 7.01 - 6.90 (m, 2H), 6.28 - 6.03 (m, 1H), 6.01 - 5.86 (m, 1H), 5.64 - 5.44 (m, 1H), 4.14 (s, 1H), 3.93 - 3.71 (m, 2H), 3.66 - 3.49 (m, 2H), 2.35 (s, 3H), 2.21 - 2.04 (m, 4H), 1.93 - 1.81 (m, 1H), 1.75 - 1.62 (m, 1H)	A11 1 st eluting isomer
543	m/z (ESI+): 411.1 (M+H)+	(400 MHz, DMSO-d ₆) δ = 15.26 - 14.67 (m, 1H), 12.45 (s, 1H), 8.68 (s, 1H), 7.91 (d, J = 10.4 Hz, 1H), 7.37 - 7.25 (m, 1H), 6.85 (dd, J = 10.4, 16.6 Hz, 1H), 6.25 (dd, J = 2.4, 16.8 Hz, 1H), 5.77 (dd, J = 2.4, 10.4 Hz, 1H), 4.56 (s, 1H), 4.53 - 4.42 (m, 1H), 4.31 (s, 1H), 4.05 (dd, J = 5.2, 11.2 Hz, 2H), 3.71 (t, J = 13.2 Hz, 2H), 2.32 (s, 3H), 2.26 - 1.97 (m, 4H)	A53 2 nd eluting isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
544	m/z (ESI+): 411.1 (M+H)+	(400 MHz, DMSO-d ₆) δ = 15.33 - 14.61 (m, 1H), 12.49 (s, 1H), 8.69 (s, 1H), 7.92 (d, J = 10.4 Hz, 1H), 7.31 (s, 1H), 6.89 (dd, J = 10.4, 16.8 Hz, 1H), 6.25 (dd, J = 2.4, 16.8 Hz, 1H), 5.79 (dd, J = 2.4, 10.4 Hz, 1H), 4.72 (d, J = 8.4 Hz, 1H), 4.44 (d, J = 9.6 Hz, 1H), 3.76 - 3.64 (m, 2H), 3.51 (t, J = 10.0 Hz, 2H), 2.74 (s, 1H), 2.34 - 2.23 (m, 4H), 2.22 - 2.08 (m, 3H)	A53 1 st eluting isomer
545	m/z (ESI+): 531.3 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.58 - 8.47 (m, 1H), 8.43 (s, 1H), 7.97 (d, J = 7.2 Hz, 1H), 7.33 - 7.23 (m, 1H), 7.03 - 6.95 (m, 2H), 6.84 (ddd, J = 2.8, 10.8, 16.8 Hz, 1H), 6.36 (dd, J = 1.6, 16.8 Hz, 1H), 5.85 (d, J = 10.8 Hz, 1H), 4.72 (d, J = 5.2 Hz, 3H), 4.57 (s, 4H), 4.35 (s, 1H), 4.18 - 4.05 (m, 2H), 3.92 - 3.81 (m, 2H), 3.52 - 3.39 (m, 2H), 3.35 (s, 3H), 2.93 - 2.85 (m, 1H), 2.81 - 2.76 (m, 1H), 2.44 (d, J = 6.0 Hz, 2H), 2.34 - 2.12 (m, 4H), 1.50 (d, J = 7.2 Hz, 3H)	N/A
546	m/z (ESI+): 488.3 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.49 (s, 1H), 8.47 (s, 1H), 8.02 (d, J = 8.0 Hz, 1H), 7.35 - 7.23 (m, 1H), 7.04 - 6.96 (m, 2H), 6.89 - 6.77 (m, 1H), 6.37 (td, J = 1.6, 16.8 Hz, 1H), 5.86 (dd, J = 2.0, 5.2, 10.4 Hz, 1H), 4.73 (d, J = 17.6 Hz, 2H), 4.58 (s, 1H), 4.36 (d, J = 12.8 Hz, 1H), 4.20 - 4.10 (m, 2H), 4.06 - 3.83 (m, 6H), 3.69 - 3.51 (m, 2H), 2.47 - 2.32 (m, 3H), 2.28 - 2.12 (m, 3H), 1.53 (d, J = 6.8 Hz, 3H)	F 2 nd eluting isomer
547	m/z (ESI+): 488.3 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.52 (s, 1H), 8.47 (s, 1H), 8.01 (d, J = 8.0 Hz, 1H), 7.34 - 7.22 (m, 1H), 7.04 - 6.94 (m, 2H), 6.84 (ddd, J = 7.2, 10.4, 17.2 Hz, 1H), 6.36 (td, J = 1.6, 16.8 Hz, 1H), 5.92 - 5.77 (m, 1H), 4.75 - 4.65 (m, 2H), 4.58 (s, 1H), 4.36 (d, J = 12.8 Hz, 1H), 4.19 - 4.10 (m, 2H), 3.93 - 3.70 (m, 6H), 3.50 - 3.40 (m, 2H), 2.43 - 2.29 (m, 3H), 2.28 - 2.11 (m, 3H), 1.52 (d, J = 6.4 Hz, 3H)	F 1 st eluting isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
548	m/z (ESI+): 518.3 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.44 (s, 1H), 7.96 (d, J = 7.2 Hz, 1H), 7.28 (t, J = 7.2 Hz, 1H), 7.03 - 6.93 (m, 2H), 6.87 - 6.80 (m, 1H), 6.35 (dd, J = 2.0, 16.8 Hz, 1H), 5.87 - 5.83 (m, 1H), 4.75 - 4.66 (m, 2H), 4.34 (s, 1H), 4.17 - 4.02 (m, 2H), 3.92 - 3.80 (m, 2H), 3.64 (t, J = 4.0 Hz, 4H), 3.52 - 3.41 (m, 1H), 2.94 - 2.84 (m, 1H), 2.83 - 2.74 (m, 1H), 2.64 - 2.55 (m, 2H), 2.52 (d, J = 2.8 Hz, 2H), 2.40 - 2.09 (m, 4H), 1.50 (d, J = 7.2 Hz, 3H)	A54 2 nd eluting isomer
549	m/z (ESI+): 518.3 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.44 (s, 1H), 7.96 (d, J = 7.2 Hz, 1H), 7.28 (t, J = 7.2 Hz, 1H), 7.02 - 6.95 (m, 2H), 6.89 - 6.79 (m, 1H), 6.36 (dd, J = 2.0, 16.8 Hz, 1H), 5.87 - 5.83 (m, 1H), 4.75 - 4.68 (m, 2H), 4.35 (s, 1H), 4.18 - 4.03 (m, 2H), 3.93 - 3.79 (m, 2H), 3.71 - 3.59 (m, 4H), 3.47 - 3.43 (m, 1H), 2.93 - 2.84 (m, 1H), 2.83 - 2.74 (m, 1H), 2.63 - 2.55 (m, 2H), 2.52 (d, J = 4.0 Hz, 2H), 2.41 - 2.10 (m, 4H), 1.51 (d, J = 7.2 Hz, 3H)	A54 1 st eluting isomer
550	m/z (ESI+): 524.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.43 (s, 1H), 7.96 (d, J = 7.2 Hz, 1H), 7.33 - 7.23 (m, 1H), 7.02 - 6.93 (m, 2H), 6.83 (ddd, J = 5.6, 10.8, 16.4 Hz, 1H), 6.35 (d, J = 16.4 Hz, 1H), 5.84 (td, J = 1.6, 10.4 Hz, 1H), 4.76 - 4.64 (m, 2H), 4.34 (d, J = 10.4 Hz, 1H), 4.18 - 4.07 (m, 2H), 3.85 (t, J = 9.6 Hz, 2H), 3.66 - 3.48 (m, 4H), 3.26 - 3.16 (m, 1H), 3.09 - 2.90 (m, 2H), 2.34 - 2.10 (m, 4H), 1.50 (d, J = 7.2 Hz, 3H)	N/A
551	m/z (ESI+): 377.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.40 (d, J = 4.4 Hz, 1H), 7.91 (d, J = 7.8 Hz, 1H), 7.31 - 7.24 (m, 1H), 7.00 - 6.92 (m, 2H), 6.82 - 6.49 (m, 1H), 6.45 - 6.23 (m, 2H), 5.87 - 5.67 (m, 1H), 4.69 (d, J = 7.2 Hz, 1H), 4.57 (d, J = 12.8 Hz, 1H), 4.01 - 3.90 (m, 2H), 3.84 - 3.75 (m, 2H), 3.75 - 3.67 (m, 1H), 2.79 - 2.61 (m, 1H), 2.39 - 2.23 (m, 1H)	A55 2 nd eluting isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
552	m/z (ESI+): 377.2 (M+H)+	(400 MHz, DMSO-d ₆) δ = 8.40 (d, J = 4.4 Hz, 1H), 7.91 (d, J = 7.6 Hz, 1H), 7.32 - 7.24 (m, 1H), 7.01 - 6.92 (m, 2H), 6.82 - 6.50 (m, 1H), 6.45 - 6.23 (m, 2H), 5.87 - 5.67 (m, 1H), 4.69 (d, J = 6.8 Hz, 1H), 4.56 (d, J = 12.8 Hz, 1H), 4.02 - 3.91 (m, 2H), 3.84 - 3.75 (m, 2H), 3.73 - 3.67 (m, 1H), 2.78 - 2.61 (m, 1H), 2.38 - 2.23 (m, 1H)	A55 1 st eluting isomer
553	m/z (ESI+): 377.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.40 (d, J = 4.4 Hz, 1H), 7.92 (d, J = 7.6 Hz, 1H), 7.27 (t, J = 7.6 Hz, 1H), 7.00 - 6.92 (m, 2H), 6.81 - 6.49 (m, 1H), 6.45 - 6.36 (m, 1H), 6.29 (dt, J = 1.6, 16.4 Hz, 1H), 5.86 - 5.67 (m, 1H), 4.72 - 4.63 (m, 1H), 4.57 (d, J = 11.6 Hz, 1H), 4.01 - 3.92 (m, 2H), 3.82 - 3.76 (m, 2H), 3.74 - 3.68 (m, 1H), 2.78 - 2.62 (m, 1H), 2.39 - 2.23 (m, 1H)	A55
554	m/z (ESI+): 423.1 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.54 - 8.44 (m, 1H), 8.40 (s, 1H), 7.77 (dd, J = 2.8, 10.4 Hz, 1H), 7.07 - 6.99 (m, 1H), 6.98 - 6.91 (m, 1H), 6.84 (dd, J = 10.8, 16.8 Hz, 1H), 6.35 (dd, J = 2.0, 16.8 Hz, 1H), 5.85 (dd, J = 2.0, 10.8 Hz, 1H), 4.58 (s, 2H), 4.34 (s, 1H), 4.14 (dd, J = 3.2, 11.6 Hz, 2H), 3.91 - 3.81 (m, 2H), 2.38 (s, 3H), 2.33 - 2.12 (m, 4H)	N/A
555	m/z (ESI+): 387.0 (M+H)+	(400 MHz, DMSO-d ₆) δ = 13.81 - 13.30 (m, 1H), 13.29 - 12.97 (m, 1H), 8.49 (s, 1H), 8.11 (d, J = 7.6 Hz, 1H), 7.39 - 7.25 (m, 1H), 7.10 - 6.90 (m, 2H), 6.66 (ddd, J = 3.2, 10.4, 16.8 Hz, 1H), 6.31 - 6.15 (m, 1H), 5.75 (dd, J = 2.4, 10.4 Hz, 1H), 5.67 - 5.41 (m, 1H), 4.32 - 4.21 (m, 1H), 4.20 - 4.04 (m, 2H), 4.01 - 3.72 (m, 2H)	N/A

Cmpd #	MS	¹ H NMR	SFC Conditions
556	m/z (ESI+): 473.2 (M+H)+	(400 MHz, DMSO-d ₆) δ = 14.28 (d, J = 2.4 Hz, 1H), 12.35 (s, 1H), 8.60 - 8.53 (m, 1H), 8.17 - 8.09 (m, 1H), 7.33 - 7.23 (m, 1H), 6.99 - 6.91 (m, 2H), 6.85 (dd, J = 10.4, 16.8 Hz, 1H), 6.25 (dd, J = 2.4, 16.8 Hz, 1H), 5.83 - 5.70 (m, 1H), 4.57 (s, 1H), 4.54 - 4.46 (m, 1H), 4.31 (s, 1H), 4.02 (dd, J = 6.0, 11.2 Hz, 2H), 3.71 (t, J = 12.4 Hz, 2H), 2.94 - 2.79 (m, 2H), 2.44 (d, J = 6.0 Hz, 1H), 2.30 - 2.18 (m, 2H), 2.17 - 2.09 (m, 2H), 1.98 (dt, J = 4.8, 13.6 Hz, 2H), 1.92 - 1.84 (m, 1H), 1.69 - 1.58 (m, 1H), 1.37 - 1.29 (m, 1H), 1.11 - 0.98 (m, 3H)	N/A 2 nd eluting isomer
557	m/z (ESI+): 473.2 (M+H)+	(400 MHz, DMSO-d ₆) δ = 14.30 (s, 1H), 12.39 (s, 1H), 8.56 (d, J = 4.0 Hz, 1H), 8.13 (d, J = 7.6 Hz, 1H), 7.28 (t, J = 7.6 Hz, 1H), 6.95 (d, J = 7.6 Hz, 2H), 6.92 - 6.83 (m, 1H), 6.26 (dd, J = 9.6, 15.2 Hz, 1H), 5.87 - 5.73 (m, 1H), 4.70 (d, J = 8.4 Hz, 1H), 4.44 (s, 1H), 3.70 (dd, J = 11.2, 17.2 Hz, 2H), 3.53 (t, J = 12.0 Hz, 2H), 2.94 - 2.72 (m, 1.5H), 2.67 (dd, J = 7.2, 13.6 Hz, 1.5H), 2.40 - 2.25 (m, 1H), 2.22 - 2.12 (m, 3H), 2.12 - 2.03 (m, 2H), 1.86 - 1.70 (m, 1H), 1.64 - 1.52 (m, 1H), 1.35 - 1.15 (m, 2H), 1.08 - 0.93 (m, 3H)	N/A 1 st eluting isomer
558	m/z (ESI+): 389.2 (M+H)+	(400 MHz, DMSO-d ₆) δ = 14.30 (s, 1H), 12.26 (s, 1H), 8.60 (d, J = 4.4 Hz, 1H), 8.12 (d, J = 7.6 Hz, 1H), 7.34 - 7.22 (m, 1H), 7.02 - 6.88 (m, 2H), 6.78 - 6.52 (m, 1H), 6.18 (ddd, J = 2.4, 9.2, 16.8 Hz, 1H), 5.79 - 5.55 (m, 1H), 4.65 - 4.37 (m, 1H), 4.27 - 3.94 (m, 1H), 3.89 - 3.69 (m, 1H), 3.66 - 3.52 (m, 1H), 3.16 - 2.95 (m, 1H), 2.35 (d, J = 4.0 Hz, 3H), 1.95 (d, J = 5.6 Hz, 2H), 1.75 - 1.49 (m, 4H)	A56 2 nd eluting isomer
559	m/z (ESI+): 389.2 (M+H)+	(400 MHz, DMSO-d ₆) δ = 14.32 (s, 1H), 12.47 - 12.01 (m, 1H), 8.59 (d, J = 4.0 Hz, 1H), 8.12 (d, J = 7.6 Hz, 1H), 7.34 - 7.21 (m, 1H), 7.03 - 6.90 (m, 2H), 6.77 - 6.54 (m, 1H), 6.18 (ddd, J = 1.6, 9.2, 16.8 Hz, 1H), 5.78 - 5.61 (m, 1H), 4.65 - 4.36 (m, 1H), 4.23 - 3.94 (m, 1H), 3.89 - 3.69 (m, 1H), 3.61 (dd, J = 9.2, 19.6 Hz, 1H), 3.14 - 2.92 (m, 1H), 2.35 (d, J = 3.6 Hz, 3H), 2.04 - 1.75 (m, 2H), 1.74 - 1.50 (m, 4H)	A56 1 st eluting isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
560	m/z (ESI+): 375.1 (M+H)+	(400 MHz, DMSO-d ₆) δ = 14.37 (d, J = 13.2 Hz, 1H), 12.23 (s, 1H), 8.61 (d, J = 10.4 Hz, 1H), 8.13 (d, J = 8.0 Hz, 1H), 7.29 (t, J = 7.6 Hz, 1H), 6.96 (d, J = 7.2 Hz, 2H), 6.80 (dd, J = 10.4, 16.8 Hz, 0.5H), 6.58 - 6.43 (m, 0.5H), 6.20 (dd, J = 2.8, 17.2 Hz, 1H), 5.72 (d, J = 11.2 Hz, 1H), 4.67 - 4.46 (m, 1H), 3.56 (d, J = 8.0 Hz, 0.5H), 3.50 - 3.43 (m, 1H), 3.42 (s, 0.5H), 3.26 (s, 0.5H), 3.21 (d, J = 10.8 Hz, 0.5H), 2.76 (d, J = 18.4 Hz, 1H), 2.34 (d, J = 18.4 Hz, 3H), 2.26 - 2.18 (m, 1H), 2.07 - 1.97 (m, 1H), 1.93 (d, J = 10.4 Hz, 0.5H), 1.79 (d, J = 9.6 Hz, 0.5H), 1.70 (d, J = 10.4 Hz, 0.5H), 1.62 (d, J = 10.0 Hz, 0.5H)	A43 2 nd eluting isomer
561	m/z (ESI+): 375.1 (M+H)+	(400 MHz, DMSO-d ₆) δ = 14.37 (d, J = 13.2 Hz, 1H), 12.23 (s, 1H), 8.61 (d, J = 10.4 Hz, 1H), 8.13 (d, J = 8.8 Hz, 1H), 7.29 (t, J = 7.6 Hz, 1H), 6.96 (d, J = 7.2 Hz, 2H), 6.80 (dd, J = 10.4, 16.8 Hz, 0.5H), 6.50 (dd, J = 10.4, 16.8 Hz, 0.5H), 6.20 (ddd, J = 2.4, 5.2, 16.8 Hz, 1H), 5.77 - 5.67 (m, 1H), 4.64 - 4.47 (m, 1H), 3.59 - 3.54 (m, 0.5H), 3.49 - 3.44 (m, 1H), 3.42 (s, 0.5H), 3.26 (d, J = 2.4 Hz, 0.5H), 3.21 (d, J = 11.2 Hz, 0.5H), 2.80 - 2.72 (m, 1H), 2.34 (d, J = 18.4 Hz, 3H), 2.25 - 2.18 (m, 1H), 2.08 - 1.96 (m, 1H), 1.93 (d, J = 11.2 Hz, 0.5H), 1.80 (d, J = 10.4 Hz, 0.5H), 1.73 - 1.67 (m, 0.5H), 1.62 (d, J = 9.6 Hz, 0.5H)	A43 1 st eluting isomer
562	m/z (ESI+): 419.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.38 (s, 1H), 8.02 - 7.94 (m, 1H), 7.31 - 7.23 (m, 1H), 7.00 - 6.94 (m, 2H), 6.81 (dd, J = 10.4, 16.8 Hz, 1H), 6.20 (dd, J = 2.0, 16.8 Hz, 1H), 5.75 (dd, J = 1.6, 10.8 Hz, 1H), 4.28 (s, 1H), 4.18 - 4.09 (m, 1H), 4.08 - 3.99 (m, 2H), 3.91 - 3.80 (m, 1H), 3.70 - 3.57 (m, 1H), 3.50 - 3.36 (m, 1H), 2.37 (s, 4H), 2.18 - 2.09 (m, 1H), 1.97 - 1.87 (m, 2H), 1.87 - 1.77 (m, 1H), 1.76 - 1.63 (m, 1H)	A11 2 nd eluting isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
563	m/z (ESI+): 419.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.34 (s, 1H), 7.96 (d, J = 8.0 Hz, 1H), 7.27 (t, J = 7.6 Hz, 1H), 7.01 - 6.90 (m, 2H), 6.80 (dd, J = 10.4, 16.8 Hz, 1H), 6.20 (d, J = 16.4 Hz, 1H), 5.74 (d, J = 10.8 Hz, 1H), 4.26 (s, 1H), 4.17 - 4.07 (m, 1H), 4.06 - 3.95 (m, 2H), 3.84 (d, J = 13.6 Hz, 1H), 3.70 - 3.53 (m, 1H), 3.50 - 3.35 (m, 1H), 2.34 (s, 4H), 2.11 (t, J = 10.0 Hz, 1H), 1.97 - 1.86 (m, 2H), 1.85 - 1.76 (m, 1H), 1.75 - 1.57 (m, 1H)	A11 1 st eluting isomer
564	m/z (ESI+): 375.1 (M+H)+	(400 MHz, DMSO-d ₆) δ = 14.42 (s, 1H), 12.23 (s, 1H), 8.62 - 8.57 (m, 1H), 8.13 (d, J = 8.4 Hz, 1H), 7.28 (t, J = 7.6 Hz, 1H), 6.99 - 6.91 (m, 2H), 6.80 (dd, J = 10.4, 16.8 Hz, 0.5H), 6.50 (dd, J = 10.4, 16.8 Hz, 0.5H), 6.20 (ddd, J = 2.4, 5.6, 16.8 Hz, 1H), 5.77 - 5.68 (m, 1H), 4.65 - 4.46 (m, 1H), 3.56 (d, J = 8.8 Hz, 0.5H), 3.50 - 3.41 (m, 1H), 3.37 (s, 0.5H), 3.32 (s, 0.5H), 3.21 (d, J = 10.8 Hz, 0.5H), 2.76 (d, J = 18.8 Hz, 1H), 2.34 (d, J = 18.4 Hz, 3H), 2.27 - 2.18 (m, 1H), 2.06 - 1.98 (m, 1H), 1.94 (d, J = 10.0 Hz, 0.5H), 1.80 (d, J = 10.4 Hz, 0.5H), 1.70 (d, J = 10.4 Hz, 0.5H), 1.61 (d, J = 10.4 Hz, 0.5H)	A43
565	m/z (ESI+): 434.2 (M+H)+	(400 MHz, DMSO-d ₆) δ = 14.20 (s, 1H), 12.41 (s, 1H), 8.64 - 8.54 (m, 1H), 8.12 (d, J = 8.8 Hz, 1H), 7.34 - 7.25 (m, 1H), 7.00 - 6.92 (m, 2H), 6.76 - 6.52 (m, 1H), 6.24 - 6.15 (m, 1H), 5.76 - 5.66 (m, 1H), 4.17 - 4.01 (m, 1H), 3.97 (m, 1H), 3.90 - 3.82 (m, 2H), 3.78 - 3.71 (m, 1H), 3.67 - 3.50 (m, 1H), 3.47 (s, 4H), 2.45 - 2.40 (m, 4H), 2.37 (s, 3H)	A44 2 nd eluting isomer
566	m/z (ESI+): 434.2 (M+H)+	(400 MHz, DMSO-d ₆) δ = 14.19 (s, 1H), 12.39 (s, 1H), 8.60 (d, J = 3.6 Hz, 1H), 8.12 (d, J = 7.2 Hz, 1H), 7.29 (t, J = 6.8 Hz, 1H), 7.00 - 6.92 (m, 2H), 6.75 - 6.50 (m, 1H), 6.24 - 6.14 (m, 1H), 5.71 (ddd, J = 2.4, 10.4, 16.0 Hz, 1H), 4.16 - 4.00 (m, 1H), 3.99 - 3.93 (m, 1H), 3.90 - 3.80 (m, 2H), 3.79 - 3.69 (m, 1H), 3.68 - 3.50 (m, 1H), 3.46 (s, 4H), 2.46 - 2.38 (m, 4H), 2.36 (d, J = 1.6 Hz, 3H)	A44 1 st eluting isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
567	m/z (ESI+): 423.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.43 (s, 1H), 7.82 (d, J = 8.4 Hz, 1H), 7.17 - 7.08 (m, 1H), 6.92 (dt, J = 5.2, 8.0 Hz, 1H), 6.84 (dd, J = 10.4, 16.8 Hz, 1H), 6.35 (dd, J = 2.0, 16.8 Hz, 1H), 5.85 (dd, J = 2.0, 10.8 Hz, 1H), 4.74 - 4.65 (m, 2H), 4.34 (s, 1H), 4.14 (dd, J = 3.6, 11.6 Hz, 2H), 3.91 - 3.81 (m, 2H), 2.38 (s, 3H), 2.32 - 2.14 (m, 4H)	N/A
568	m/z (ESI+): 419.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.37 (s, 1H), 7.98 (dd, J = 1.6, 8.4 Hz, 1H), 7.31 - 7.23 (m, 1H), 7.01 - 6.93 (m, 2H), 6.81 (dd, J = 10.4, 16.8 Hz, 1H), 6.20 (dd, J = 2.0, 16.8 Hz, 1H), 5.75 (dd, J = 2.0, 10.4 Hz, 1H), 4.28 (s, 1H), 4.17 - 4.08 (m, 1H), 4.08 - 3.98 (m, 2H), 3.91 - 3.79 (m, 1H), 3.70 - 3.55 (m, 1H), 3.51 - 3.35 (m, 1H), 2.36 (s, 4H), 2.17 - 2.09 (m, 1H), 1.96 - 1.87 (m, 2H), 1.87 - 1.77 (m, 1H), 1.75 - 1.63 (m, 1H)	A11
569	m/z (ESI+): 364.1 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.50 (s, 1H), 7.94 (d, J = 8.0 Hz, 1H), 7.33 - 7.25 (m, 1H), 7.02 - 6.93 (m, 2H), 6.81 (dt, J = 10.6, 17.4 Hz, 1H), 6.68 (s, 1H), 6.26 (dd, J = 6.4, 16.4 Hz, 1H), 5.78 (dd, J = 10.6, 18.0 Hz, 1H), 4.65 - 4.51 (m, 1H), 4.24 - 4.12 (m, 1H), 3.57 - 3.47 (m, 1H), 3.47 - 3.37 (m, 1H), 3.19 - 3.04 (m, 2H), 2.39 - 2.26 (m, 1H), 2.21 (s, 3H)	A57 2 nd eluting isomer
570	m/z (ESI+): 364.1 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.50 (s, 1H), 7.94 (d, J = 7.6 Hz, 1H), 7.32 - 7.25 (m, 1H), 7.02 - 6.94 (m, 2H), 6.80 (m, 1H), 6.68 (s, 1H), 6.26 (dd, J = 5.4, 16.8 Hz, 1H), 5.78 (dd, J = 10.4, 17.6 Hz, 1H), 4.63 - 4.51 (m, 1H), 4.17 (d, J = 11.2 Hz, 1H), 3.57 - 3.47 (m, 1H), 3.47 - 3.37 (m, 1H), 3.19 - 3.05 (m, 2H), 2.40 - 2.27 (m, 1H), 2.21 (s, 3H)	A57 1 st eluting isomer
571	m/z (ESI+): 421.1 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.44 (s, 1H), 7.97 - 7.90 (m, 1H), 7.33 - 7.24 (m, 1H), 7.02 - 6.94 (m, 2H), 6.92 - 6.77 (m, 1H), 6.53 (d, J = 1.6 Hz, 1H), 6.37 (td, J = 2.0, 16.8 Hz, 1H), 5.86 (ddd, J = 2.0, 8.0, 10.4 Hz, 1H), 4.84 (s, 1H), 4.63 (s, 0.5H), 4.41 (s, 0.5H), 4.36 - 4.25 (m, 2H), 4.06 (dd, J = 5.2, 11.6 Hz, 1H), 3.86 - 3.77 (m, 1H), 3.76 - 3.67 (m, 2H), 3.34 (d, J = 5.6 Hz, 3H), 2.41 - 2.28 (m, 1H), 2.25 - 2.12 (m, 1H)	A45 2 nd eluting isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
572	m/z (ESI+): 421.1 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.44 (s, 1H), 7.93 (d, J = 9.2 Hz, 1H), 7.30 - 7.24 (m, 1H), 7.00 - 6.93 (m, 2H), 6.92 - 6.78 (m, 1H), 6.53 (s, 1H), 6.36 (dd, J = 1.2, 16.8 Hz, 1H), 5.90 - 5.82 (m, 1H), 4.85 (s, 1H), 4.63 (s, 0.5H), 4.40 (s, 0.5H), 4.35 - 4.27 (m, 2H), 4.09 - 4.02 (m, 1H), 3.85 - 3.77 (m, 1H), 3.76 - 3.66 (m, 2H), 3.34 (d, J = 5.6 Hz, 3H), 2.41 - 2.27 (m, 1H), 2.23 - 2.13 (m, 1H)	A45 1 st eluting isomer
573	m/z (ESI+): 389.2 (M+H)+	(400 MHz, DMSO-d ₆) δ = 14.11 (s, 1H), 12.53 (s, 1H), 8.55 (d, J = 4.8 Hz, 1H), 8.02 (d, J = 8.0 Hz, 1H), 7.32 - 7.23 (m, 1H), 7.02 - 6.92 (m, 2H), 6.69 - 6.40 (m, 2H), 6.13 - 6.00 (m, 1H), 5.66 - 5.56 (m, 1H), 3.81 - 3.71 (m, 1H), 3.68 - 3.56 (m, 1H), 3.48 (d, J = 11.2 Hz, 1H), 3.39 (dd, J = 4.8, 10.8 Hz, 1H), 3.23 (dd, J = 4.8, 12.8 Hz, 1H), 3.04 - 2.94 (m, 2H), 1.98 - 1.77 (m, 2H), 1.76 - 1.56 (m, 3H), 1.54 - 1.41 (m, 1H)	A58 2 nd eluting isomer
574	m/z (ESI+): 389.1 (M+H)+	(400 MHz, DMSO-d ₆) δ = 14.28 (s, 1H), 12.52 (s, 1H), 8.52 (d, J = 6.0 Hz, 1H), 8.01 (d, J = 7.6 Hz, 1H), 7.28 (t, J = 7.2 Hz, 1H), 7.04 - 6.86 (m, 2H), 6.61 - 6.43 (m, 2H), 6.13 - 5.99 (m, 1H), 5.67 - 5.55 (m, 1H), 3.83 - 3.72 (m, 1H), 3.69 - 3.57 (m, 1H), 3.48 (d, J = 10.8 Hz, 1H), 3.39 (dd, J = 4.4, 10.8 Hz, 1H), 3.25 (d, J = 4.8 Hz, 1H), 3.10 - 2.90 (m, 2H), 1.96 - 1.78 (m, 2H), 1.77 - 1.57 (m, 3H), 1.53 - 1.42 (m, 1H)	A58 1 st eluting isomer
575	m/z (ESI+): 459.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.40 (s, 1H), 7.93 - 7.89 (m, 1H), 7.34 - 7.27 (m, 1H), 7.03 - 6.96 (m, 2H), 6.88 - 6.79 (m, 1H), 6.39 - 6.33 (m, 1H), 5.88 - 5.82 (m, 1H), 4.99 - 4.93 (m, 1H), 4.73 (s, 1H), 4.36 (s, 1H), 4.14 - 4.07 (m, 2H), 3.85 (t, J = 10.8 Hz, 2H), 2.33 - 2.23 (m, 4H)	N/A

Cmpd #	MS	¹ H NMR	SFC Conditions
576	m/z (ESI+): 558.3 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.45 (s, 1H), 7.96 (d, J = 8.0 Hz, 1H), 7.28 (t, J = 6.8 Hz, 1H), 7.05 - 6.92 (m, 2H), 6.90 - 6.74 (m, 1H), 6.35 (dd, J = 2.0, 16.4 Hz, 1H), 5.85 (dd, J = 2.0, 10.4 Hz, 1H), 4.72 (d, J = 5.6 Hz, 2H), 4.33 (d, J = 1.2 Hz, 1H), 4.21 - 4.13 (m, 1H), 4.02 (dd, J = 4.4, 11.6 Hz, 1H), 3.89 - 3.75 (m, 6H), 2.54 (s, 4H), 2.42 (s, 1H), 2.33 - 2.23 (m, 2H), 2.23 - 2.11 (m, 4H), 2.10 - 2.06 (m, 2H), 1.97 - 1.86 (m, 2H), 1.73 - 1.59 (m, 2H), 1.36 - 1.28 (m, 1H)	A15 2 nd eluting isomer
577	m/z (ESI+): 558.3 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.45 (s, 1H), 7.96 (d, J = 8.0 Hz, 1H), 7.28 (t, J = 7.2 Hz, 1H), 7.06 - 6.92 (m, 2H), 6.89 - 6.75 (m, 1H), 6.35 (dd, J = 2.0, 16.8 Hz, 1H), 5.85 (dd, J = 2.0, 10.8 Hz, 1H), 4.74 - 4.66 (m, 2H), 4.33 (s, 1H), 4.23 - 4.10 (m, 1H), 4.03 (dd, J = 4.0, 12.0 Hz, 1H), 3.89 - 3.76 (m, 6H), 2.66 - 2.48 (m, 4H), 2.41 (s, 1H), 2.34 - 2.24 (m, 2H), 2.23 - 2.11 (m, 4H), 2.10 - 2.06 (m, 2H), 1.96 - 1.86 (m, 2H), 1.74 - 1.56 (m, 2H), 1.33 - 1.28 (m, 1H)	A15 1 st eluting isomer
578	m/z (ESI+): 389.2 (M+H)+	(400 MHz, DMSO-d ₆) δ = 14.11 (s, 1H), 12.53 (s, 1H), 8.55 (d, J = 4.6 Hz, 1H), 8.02 (d, J = 8.0 Hz, 1H), 7.29 - 7.26 (m, 1H), 6.97 - 6.93 (m, 2H), 6.56 - 6.48 (m, 2H), 6.09 - 6.04 (m, 1H), 5.63 - 5.60 (m, 1H), 3.78 - 3.75 (m, 1H), 3.65 - 3.62 (m, 1H), 3.48 (d, J = 11.2 Hz, 1H), 3.39 (dd, J = 4.8, 10.8 Hz, 1H), 3.23 (dd, J = 4.8, 12.8 Hz, 1H), 3.01 - 2.99 (m, 2H), 1.81 - 1.79 (m, 2H), 1.73 - 1.63 (m, 3H), 1.48 (s, 1H)	A58
579	m/z (ESI+): 423.1 (M+H)+	(400 MHz, DMSO-d ₆) δ = 13.73 (s, 1H), 12.66 (s, 1H), 8.46 (d, J = 4.4 Hz, 1H), 8.00 (d, J = 7.6 Hz, 1H), 7.30 (t, J = 7.6 Hz, 1H), 7.02 - 6.93 (m, 2H), 6.71 - 6.55 (m, 1H), 6.19 (d, J = 16.8 Hz, 1H), 5.77 - 5.65 (m, 1H), 5.49 (s, 0.5H), 5.35 (s, 0.5H), 4.31 - 4.20 (m, 1.5), 4.17 - 4.11 (m, 1.5H), 4.08 - 4.02 (m, 2H), 4.02 - 3.85 (m, 2.5H), 3.83 - 3.67 (m, 1.5H), 3.60 - 3.43 (m, 1H), 2.39 - 2.25 (m, 2H)	A46 2 nd eluting isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
580	m/z (ESI+): 423.1 (M+H)+	(400 MHz, DMSO-d ₆) δ = 13.72 (s, 1H), 12.66 (d, J = 1.6 Hz, 1H), 8.47 (d, J = 4.4 Hz, 1H), 7.99 (d, J = 6.4 Hz, 1H), 7.30 (t, J = 7.6 Hz, 1H), 7.03 - 6.94 (m, 2H), 6.72 - 6.56 (m, 1H), 6.19 (d, J = 16.8 Hz, 1H), 5.76 - 5.67 (m, 1H), 5.48 (s, 0.5H), 5.38 - 5.30 (m, 0.5H), 4.30 - 4.20 (m, 1.5H), 4.18 - 4.10 (m, 1.5H), 4.10 - 4.03 (m, 2H), 4.02 - 3.87 (m, 2.5H), 3.83 - 3.64 (m, 1.5H), 3.56 - 3.44 (m, 1H), 2.41 - 2.27 (m, 2H)	A46 1 st eluting isomer
581	m/z (ESI+): 415.1 (M+H)+	(400 MHz, CHLOROFORM-d) δ = 13.74 (s, 1H), 12.39 - 12.10 (m, 1H), 8.33 (s, 1H), 7.94 - 7.86 (m, 1H), 7.43 - 7.32 (m, 1H), 7.12 (dd, J = 0.8, 8.0 Hz, 1H), 7.06 - 6.97 (m, 1H), 6.62 (dd, J = 10.4, 16.8 Hz, 1H), 6.27 (dd, J = 2.0, 16.8 Hz, 1H), 5.45 (dd, J = 1.6, 10.4 Hz, 1H), 4.95 (td, J = 6.0, 12.0 Hz, 1H), 4.81 (s, 1H), 4.44 (s, 1H), 4.26 - 4.11 (m, 2H), 3.92 (d, J = 11.6 Hz, 2H), 3.50 (s, 1H), 2.63 - 2.49 (m, 2H), 2.41 (dd, J = 4.4, 13.2 Hz, 1H), 2.28 - 2.13 (m, 1H)	N/A
582	m/z (ESI+): 399.1 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.38 (s, 1H), 7.99 - 7.94 (m, 1H), 7.33 - 7.28 (m, 1H), 7.02 - 6.96 (m, 2H), 6.71 - 6.62 (m, 1H), 6.38 - 6.31 (m, 1H), 5.84 - 5.78 (m, 1H), 4.43 - 4.32 (m, 1H), 4.27 - 4.21 (m, 0.5H), 4.19 - 4.13 (m, 0.5H), 4.13 - 4.05 (m, 1H), 4.04 - 3.96 (m, 1.5H), 3.91 - 3.84 (m, 0.5H), 3.73 - 3.67 (m, 0.5H), 3.64 - 3.58 (m, 0.5H), 3.40 (s, 3H)	A13 2 nd eluting isomer
583	m/z (ESI+): 399.1 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.39 (s, 1H), 7.97 (d, J = 7.2 Hz, 1H), 7.31 (t, J = 7.6 Hz, 1H), 7.02 - 6.97 (m, 2H), 6.71 - 6.62 (m, 1H), 6.38 - 6.31 (m, 1H), 5.85 - 5.77 (m, 1H), 4.43 - 4.32 (m, 1H), 4.27 - 4.22 (m, 0.5H), 4.19 - 4.14 (m, 0.5H), 4.13 - 4.05 (m, 1H), 4.04 - 3.97 (m, 1.5H), 3.91 - 3.84 (m, 0.5H), 3.73 - 3.68 (m, 0.5H), 3.64 - 3.57 (m, 0.5H), 3.40 (s, 3H)	A13 1 st eluting isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
584	m/z (ESI+): 379.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.41 (s, 1H), 8.01 - 7.97 (m, 1H), 7.28 (t, J = 7.6 Hz, 1H), 7.00 - 6.94 (m, 2H), 6.71 - 6.61 (m, 1H), 6.37 - 6.30 (m, 1H), 5.84 - 5.77 (m, 1H), 4.38 - 4.28 (m, 1H), 4.25 - 4.18 (m, 1H), 4.13 - 4.04 (m, 1H), 4.03 - 3.96 (m, 0.5H), 3.96 - 3.88 (m, 1H), 3.80 - 3.73 (m, 0.5H), 3.68 - 3.62 (m, 0.5H), 3.56 - 3.49 (m, 0.5H), 3.34 (d, J = 2.0 Hz, 3H), 2.39 (s, 3H)	A1 2 nd eluting isomer
585	m/z (ESI+): 379.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.41 (s, 1H), 7.99 (d, J = 7.2 Hz, 1H), 7.31 - 7.25 (m, 1H), 7.01 - 6.95 (m, 2H), 6.72 - 6.61 (m, 1H), 6.37 - 6.30 (m, 1H), 5.84 - 5.77 (m, 1H), 4.38 - 4.28 (m, 1H), 4.24 - 4.18 (m, 1H), 4.13 - 4.04 (m, 1H), 4.03 - 3.97 (m, 0.5H), 3.95 - 3.88 (m, 1H), 3.79 - 3.73 (m, 0.5H), 3.67 - 3.62 (m, 0.5H), 3.55 - 3.50 (m, 0.5H), 3.34 (d, J = 2.0 Hz, 3H), 2.39 (s, 3H)	A1 1 st eluting isomer
586	m/z (ESI+): 443.0, 445.0 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.30 (s, 1H), 7.97 (d, J = 7.6 Hz, 1H), 7.31 (t, J = 8.0 Hz, 1H), 7.04 - 6.95 (m, 2H), 6.73 - 6.60 (m, 1H), 6.34 (dd, J = 1.6, 16.8 Hz, 1H), 5.84 - 5.77 (m, 1H), 4.46 - 4.32 (m, 1H), 4.28 - 4.06 (m, 2H), 4.05 - 3.96 (m, 1.5H), 3.89 - 3.82 (m, 0.5H), 3.73 - 3.68 (m, 0.5H), 3.63 - 3.56 (m, 0.5H), 3.40 (s, 3H)	A47 2 nd eluting isomer
587	m/z (ESI+): 443.0, 445.0 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.31 (s, 1H), 8.01 - 7.92 (m, 1H), 7.36 - 7.27 (m, 1H), 7.05 - 6.95 (m, 2H), 6.73 - 6.60 (m, 1H), 6.34 (dd, J = 1.6, 16.8 Hz, 1H), 5.84 - 5.77 (m, 1H), 4.45 - 4.33 (m, 1H), 4.29 - 4.07 (m, 2H), 4.06 - 3.96 (m, 1.5H), 3.90 - 3.81 (m, 0.5H), 3.73 - 3.68 (m, 0.5H), 3.63 - 3.56 (m, 0.5H), 3.40 (s, 3H)	A47 1 st eluting isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
588	m/z (ESI+): 447.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.38 (s, 1H), 7.96 - 7.89 (m, 1H), 7.30 - 7.23 (m, 1H), 7.01 - 6.93 (m, 2H), 6.88 - 6.75 (m, 1H), 6.34 (d, J = 16.8 Hz, 1H), 5.88 - 5.79 (m, 1H), 4.77 - 4.61 (m, 2H), 4.31 (s, 1H), 4.16 - 4.02 (m, 2H), 3.91 - 3.77 (m, 2H), 3.11 - 2.96 (m, 1H), 2.36 - 2.19 (m, 2H), 2.18 - 2.06 (m, 2H), 1.92 - 1.85 (m, 2H), 1.48 (d, J = 7.2 Hz, 3H), 0.87 (t, J = 7.2 Hz, 3H)	A59 2 nd eluting isomer
589	m/z (ESI+): 447.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.39 (s, 1H), 7.97 - 7.91 (m, 1H), 7.31 - 7.24 (m, 1H), 7.02 - 6.93 (m, 2H), 6.83 (dd, J = 10.8, 16.8 Hz, 1H), 6.35 (dd, J = 2.0, 16.8 Hz, 1H), 5.85 (dd, J = 2.0, 10.8 Hz, 1H), 4.72 (d, J = 5.2 Hz, 2H), 4.33 (s, 1H), 4.17 - 4.06 (m, 2H), 3.85 (t, J = 10.4 Hz, 2H), 3.06 (d, J = 7.6 Hz, 1H), 2.29 (t, J = 13.2 Hz, 2H), 2.20 - 2.08 (m, 2H), 1.90 (t, J = 7.6 Hz, 2H), 1.49 (d, J = 7.2 Hz, 3H), 0.88 (t, J = 7.2 Hz, 3H)	A59 1 st eluting isomer
590	m/z (ESI+): 419.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.47 (d, J = 1.6 Hz, 1H), 7.96 - 7.90 (m, 1H), 7.29 (t, J = 7.6 Hz, 1H), 7.02 - 6.95 (m, 2H), 6.67 (dt, J = 10.4, 17.6 Hz, 1H), 6.37 - 6.28 (m, 1H), 5.79 (ddd, J = 1.6, 10.8, 12.8 Hz, 1H), 4.36 (t, J = 7.6 Hz, 1H), 4.20 - 4.15 (m, 2H), 4.14 - 4.04 (m, 2H), 4.03 - 3.94 (m, 1H), 3.89 - 3.75 (m, 1H), 3.68 - 3.57 (m, 1H), 3.52 (t, J = 8.8 Hz, 1H), 3.38 (dd, J = 6.0, 8.4 Hz, 1H), 2.72 - 2.58 (m, 1H), 2.49 - 2.42 (m, 1H), 2.40 - 2.30 (m, 1H), 1.09 (dd, J = 1.6, 6.8 Hz, 3H)	A44 3 rd eluting isomer
591	m/z (ESI+): 390.2 (M+H)+	(400 MHz, DMSO-d ₆) δ = 14.13 (s, 1H), 12.55 (brs, 1H), 8.56 (s, 1H), 8.02 (d, J = 8.0 Hz, 1H), 7.29 (t, J = 7.6 Hz, 1H), 7.03 - 6.89 (m, 2H), 6.53 (s, 1H), 6.44 - 6.32 (m, 1H), 6.17 - 6.08 (m, 1H), 5.69 (d, J = 10.4 Hz, 1H), 4.57 - 4.35 (m, 1H), 4.32 - 4.22 (m, 1H), 4.11 - 3.99 (m, 1H), 3.95 - 3.57 (m, 2H), 2.36 (s, 3H), 2.28 - 2.17 (m, 3H), 1.90 - 1.80 (m, 1H).	N/A

Cmpd #	MS	¹ H NMR	SFC Conditions
592	m/z (ESI+): 519.3 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.42 (s, 1H), 7.96 (dd, J = 1.2, 8.4 Hz, 1H), 7.33 - 7.24 (m, 1H), 7.03 - 6.93 (m, 2H), 6.83 (dd, J = 10.4, 16.8 Hz, 1H), 6.35 (dd, J = 2.0, 16.8 Hz, 1H), 5.85 (dd, J = 2.0, 10.4 Hz, 1H), 4.75 - 4.63 (m, 2H), 4.33 (s, 1H), 4.17 - 4.08 (m, 3H), 3.91 - 3.80 (m, 4H), 3.79 - 3.68 (m, 2H), 3.54 - 3.42 (m, 2H), 2.94 (t, J = 7.2 Hz, 2H), 2.33 - 2.10 (m, 4H), 2.04 - 1.90 (m, 4H)	N/A
593	m/z (ESI+): 399.1 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.40 (s, 1H), 7.98 (d, J = 8.0 Hz, 1H), 7.34 - 7.28 (m, 1H), 7.03 - 6.97 (m, 2H), 6.71 - 6.62 (m, 1H), 6.38 - 6.31 (m, 1H), 5.84 - 5.78 (m, 1H), 4.43 - 4.33 (m, 1H), 4.28 - 4.22 (m, 0.5H), 4.19 - 4.14 (m, 0.5H), 4.13 - 4.06 (m, 1H), 4.05 - 3.97 (m, 1.4H), 3.91 - 3.84 (m, 0.6H), 3.73 - 3.68 (m, 0.5H), 3.64 - 3.57 (m, 0.5H), 3.40 (s, 3H)	A13
594	m/z (ESI+): 379.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.43 (s, 1H), 8.01 - 7.98 (m, 1H), 7.32 - 7.25 (m, 1H), 7.02 - 6.95 (m, 2H), 6.72 - 6.62 (m, 1H), 6.37 - 6.31 (m, 1H), 5.84 - 5.77 (m, 1H), 4.39 - 4.28 (m, 1H), 4.26 - 4.18 (m, 1H), 4.14 - 4.04 (m, 1H), 4.04 - 3.97 (m, 0.5H), 3.96 - 3.89 (m, 1H), 3.80 - 3.73 (m, 0.5H), 3.68 - 3.62 (m, 0.5H), 3.56 - 3.50 (m, 0.5H), 3.35 (d, J = 2.0 Hz, 3H), 2.40 (s, 3H)	A1
595	m/z (ESI+): 411.1 (M+H)+	(400 MHz, DMSO-d ₆) δ = 13.92 (s, 1H), 12.69 (s, 1H), 8.62 - 8.51 (m, 2H), 8.43 (t, J = 3.6 Hz, 1H), 7.97 (d, J = 7.6 Hz, 1H), 7.97 (d, J = 8.4 Hz, 1H), 7.35 (d, J = 4.0, 8.0 Hz, 1H), 7.34 - 7.27 (t, J = 7.6 Hz, 1H), 6.96 - 6.95 (m, 2H), 6.73 - 6.63 (m, 1H), 6.50 (d, J = 12.8 Hz, 1H), 6.22 (d, J = 16.8 Hz, 1H), 5.75 - 5.74 (m, 1H), 5.78 - 5.70 (m, 1H), 4.38 - 4.23 (m, 1H), 4.20 - 4.04 (m, 1H), 4.03 - 3.67 (m, 3H), 3.57 - 3.33 (m, 1H)	A60 2 nd eluting isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
596	m/z (ESI+): 411.1 (M+H)+	(400 MHz, DMSO-d ₆) δ = 13.93 (s, 1H), 12.67 (s, 1H), 8.59 - 8.55 (m, 2H), 8.51 - 8.43 (m, 1H), 7.99 (d, J = 7.2 Hz, 1H), 7.98 - 7.87 (d, J = 7.2 Hz, 1H), 7.35 - 7.33 (m, 1H), 7.27 - 6.94 (m, 1H), 7.03 - 6.85 (m, 2H), 6.67 (d, J = 10.4, 16.0 Hz, 1H), 6.50 (d, J = 12.8 Hz, 1H), 6.22 (d, J = 16.4 Hz, 1H), 5.76 - 5.75 (m, 1H), 4.45 - 4.15 (m, 2H), 4.15 - 4.04 (m, 1H), 4.02 - 3.77 (m, 2H), 3.67 - 3.33 (m, 1H)	A60 1 st eluting isomer
597	m/z (ESI+): 411.1 (M+H)+	(400 MHz, DMSO-d ₆) δ = 14.61 (s, 1H), 8.34 (s, 1H), 8.26 - 8.21 (m, 2H), 7.92 (d, J = 4.0 Hz, 1H), 7.32 - 7.29 (m, 1H), 7.24 - 7.21 (m, 1H), 7.11 - 7.12 (m, 1H), 6.90 - 6.81 (m, 2H), 6.79 - 6.74 (m, 1H), 6.29 - 6.25 (dd, J = 1.6, 15.2 Hz, 1H), 6.08 (d, J = 16, 1H), 5.79 - 5.75 (m, 1H), 4.21 - 4.13 (m, 4H), 4.02 - 3.34 (m, 2H)	A60 1 st eluting isomer
598	m/z (ESI+): 419.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.46 (d, J = 2.0 Hz, 1H), 7.95 - 7.89 (m, 1H), 7.28 (t, J = 7.6 Hz, 1H), 6.97 (d, J = 7.6 Hz, 2H), 6.66 (dt, J = 10.8, 16.8 Hz, 1H), 6.37 - 6.28 (m, 1H), 5.83 - 5.73 (m, 1H), 4.35 (t, J = 7.6 Hz, 1H), 4.20 - 4.15 (m, 2H), 4.14 - 4.02 (m, 2H), 4.00 - 3.93 (m, 1H), 3.86 - 3.77 (m, 1H), 3.69 - 3.59 (m, 1H), 3.51 (t, J = 8.8 Hz, 1H), 3.42 - 3.35 (m, 1H), 2.64 (td, J = 7.6, 15.2 Hz, 1H), 2.49 - 2.41 (m, 1H), 2.39 - 2.30 (m, 1H), 1.09 (d, J = 6.4 Hz, 3H)	A8 2 nd eluting isomer
599	m/z (ESI+): 419.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.47 (d, J = 1.6 Hz, 1H), 7.93 (dd, J = 1.2, 8.4 Hz, 1H), 7.28 (t, J = 7.6 Hz, 1H), 7.02 - 6.95 (m, 2H), 6.67 (dt, J = 10.4, 17.6 Hz, 1H), 6.37 - 6.28 (m, 1H), 5.79 (ddd, J = 2.0, 10.8, 12.8 Hz, 1H), 4.36 (t, J = 8.0 Hz, 1H), 4.21 - 4.15 (m, 2H), 4.14 - 4.03 (m, 2H), 4.02 - 3.93 (m, 1H), 3.85 - 3.75 (m, 1H), 3.67 - 3.58 (m, 1H), 3.52 (t, J = 8.8 Hz, 1H), 3.42 - 3.35 (m, 1H), 2.70 - 2.59 (m, 1H), 2.50 - 2.42 (m, 1H), 2.40 - 2.31 (m, 1H), 1.09 (dd, J = 1.6, 6.8 Hz, 3H)	A8 1 st eluting isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
600	m/z (ESI+): 471.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.50 (s, 1H), 7.92 - 7.89 (m, 1H), 7.44 (s, 1H), 7.32 - 7.24 (m, 1H), 7.01 - 6.94 (m, 2H), 6.90 - 6.76 (m, 0.6H), 6.68 - 6.48 (m, 0.4H), 6.31 - 6.11 (m, 1H), 5.81 (d, J = 10.0 Hz, 0.6H), 5.72 - 5.61 (m, 0.4H), 4.70 (s, 2H), 4.60 (s, 1H), 4.28 (s, 1H), 4.24 - 4.16 (m, 2H), 4.14 (s, 2H), 4.09 - 4.07 (m, 3H), 3.95 - 3.82 (m, 2H), 2.53 - 2.30 (m, 1H), 2.25 - 2.06 (m, 1H)	N/A
601	m/z (ESI+): 475.2 (M+H)+	(400 MHz, DMSO-d ₆) δ = 14.07 (s, 1H), 12.49 (s, 1H), 8.52 (s, 1H), 8.05 (d, J = 8.4 Hz, 1H), 7.34 - 7.24 (m, 1H), 7.03 - 6.92 (m, 2H), 6.85 (ddd, J = 2.4, 10.8, 16.8 Hz, 1H), 6.25 (dd, J = 2.4, 16.8 Hz, 1H), 5.83 - 5.73 (m, 1H), 4.76 - 4.61 (m, 2H), 4.55 (s, 1H), 4.30 (s, 1H), 4.12 - 3.97 (m, 3H), 3.70 (t, J = 12.8 Hz, 2H), 3.62 - 3.52 (m, 1H), 2.31 - 2.13 (m, 2H), 2.12 - 1.89 (m, 5H), 1.77 - 1.70 (m, 2H), 1.59 (d, J = 12.0 Hz, 1H)	A48 2 nd eluting isomer
602	m/z (ESI+): 475.2 (M+H)+	(400 MHz, DMSO-d ₆) δ = 14.04 (s, 1H), 12.49 (s, 1H), 8.52 (s, 1H), 8.05 (d, J = 8.4 Hz, 1H), 7.41 - 7.18 (m, 1H), 7.00 - 6.92 (m, 2H), 6.85 (ddd, J = 2.4, 10.8, 16.8 Hz, 1H), 6.25 (dd, J = 2.4, 16.8 Hz, 1H), 5.77 (td, J = 2.0, 10.4 Hz, 1H), 4.77 - 4.60 (m, 2H), 4.55 (s, 1H), 4.30 (s, 1H), 4.11 - 3.97 (m, 3H), 3.70 (t, J = 12.8 Hz, 2H), 3.61 - 3.50 (m, 1H), 2.31 - 2.13 (m, 2H), 2.13 - 1.90 (m, 5H), 1.76 - 1.70 (m, 2H), 1.59 (d, J = 12.0 Hz, 1H)	A48 1 st eluting isomer
603	m/z (ESI+): 476.2 (M+H)+	(400 MHz, DMSO-d ₆) δ = 14.11 (s, 1H), 12.41 (s, 1H), 8.63 (s, 1H), 8.21 (d, J = 7.2 Hz, 1H), 7.35 - 7.23 (m, 1H), 7.01 - 6.86 (m, 3H), 6.27 (dd, J = 2.4, 16.8 Hz, 1H), 5.89 - 5.65 (m, 1H), 4.69 (d, J = 10.4 Hz, 1H), 4.42 (s, 1H), 3.78 - 3.64 (m, 6H), 3.53 (t, J = 10.4 Hz, 2H), 3.12 (s, 4H), 3.00 - 2.76 (m, 1H), 2.34 - 2.10 (m, 4H)	N/A

Cmpd #	MS	¹ H NMR	SFC Conditions
604	m/z (ESI+): 412.2 (M+H)+	(400 MHz, DMSO-d ₆) δ = 13.95 (s, 1H), 12.53 (s, 1H), 8.46 (d, J = 6.0 Hz, 1H), 8.31 (t, J = 6.0 Hz, 2H), 8.01 - 7.88 (m, 1H), 7.27 (t, J = 7.6 Hz, 1H), 7.00 (dd, J = 6.0, 9.6 Hz, 2H), 6.97 - 6.90 (m, 2H), 6.78 (dd, J = 10.2, 16.8 Hz, 1H), 6.33 - 6.23 (m, 1H), 6.16 (d, J = 11.6 Hz, 1H), 5.80 - 5.78 (m, 1H), 4.24 - 4.13 (m, 2H), 4.13 - 4.11 (m, 2H), 4.10 - 4.04 (m, 1H), 4.03 - 3.93 (m, 1H)	J 4 th eluting isomer
605	m/z (ESI+): 412.1 (M+H)+	(400 MHz, DMSO-d ₆) δ = 13.95 (d, J = 5.6 Hz, 1H), 12.50 (s, 1H), 8.44 (d, J = 6.0 Hz, 1H), 8.29 (t, J = 6.0 Hz, 2H), 8.03 - 7.87 (m, 1H), 7.26 (t, J = 7.6 Hz, 1H), 6.98 (dd, J = 6.0, 9.6 Hz, 2H), 6.95 - 6.88 (m, 2H), 6.76 (dd, J = 10.0, 16.4 Hz, 1H), 6.24 - 6.15 (m, 1H), 6.14 (d, J = 11.6 Hz, 1H), 5.79 - 5.77 (m, 1H), 4.23 - 4.14 (m, 2H), 4.13 - 4.10 (m, 2H), 4.09 - 4.03 (m, 1H), 4.00 - 3.93 (m, 1H)	J 3 rd eluting isomer
606	m/z (ESI+): 412.1 (M+H)+	(400 MHz, DMSO-d ₆) δ = 14.01 (s, 1H), 12.58 - 12.39 (m, 1H), 8.41 (d, J = 2.8 Hz, 1H), 8.35 (t, J = 4.0 Hz, 1H), 7.94 (m, 1H), 7.56 - 7.45 (m, 1H), 7.26 (t, J = 7.6 Hz, 1H), 7.13 - 7.04 (m, 2H), 6.97 - 6.87 (m, 2H), 6.75 (td, J = 10.9, 16.6 Hz, 1H), 6.24 (dd, J = 2.0, 16.8 Hz, 1H), 6.03 (d, J = 5.6 Hz, 1H), 5.78 - 5.71 (m, 1H), 4.24 - 4.14 (m, 5H), 4.03 - 3.99 (m, 2H)	N/A
607	m/z (ESI+): 412.1 (M+H)+	(400 MHz, DMSO-d ₆) δ = 13.99 - 13.95 (d, J = 3.6 Hz, 1H), 12.71 - 12.60 (m, 1H), 8.56 - 8.55 (m, 1H), 8.52 (d, J = 4.6 Hz, 1H), 7.98 (d, J = 8.0 Hz, 1H), 7.71-7.69 (m, 1H), 7.27 - 7.25 (m, 1H), 6.96 - 6.93 (m, 2H), 6.48 (m, 2H), 6.45 (m, 1H), 6.23 (d, J = 10.2, 16.6 Hz, 1H), 5.73 - 5.7 (m, 1H), 6.21 (d, J = 16.8 Hz, 1H), 5.76 - 5.68 (m, 1H), 4.30 - 4.13 (m, 2H), 4.13 - 3.98 (m, 2H), 3.90 (dt, J = 6.6, 9.6 Hz, 1H), 3.69 - 3.66 (m, 1H)	N/A

Cmpd #	MS	¹ H NMR	SFC Conditions
608	m/z (ESI+): 412.2 (M+H)+	(400 MHz, DMSO-d ₆) δ = 13.96 (s, 1H), 12.67 (s, 1H), 8.55 - 8.46 (m, 3H), 7.96 (d, J = 8.0 Hz, 1H), 7.42 (dd, J = 6.0, 13.2 Hz, 2H), 7.28 (t, J = 7.6 Hz, 1H), 6.99 - 6.88 (m, 2H), 6.68 (dd, J = 10.4, 16.8 Hz, 1H), 6.49 (d, J = 13.6 Hz, 1H), 6.28 - 6.18 (m, 1H), 5.77 - 5.75 (m, 1H), 4.34 - 4.32 (m, 2H), 4.31 - 4.30 (m, 1H), 4.13 - 4.12 (m, 1H), 3.99 - 3.96 (m, 1H), 3.93 - 3.79 (m, 1H), 3.56 (t, J = 11.2 Hz, 1H)	A61 2 nd eluting isomer
609	m/z (ESI+): 412.1 (M+H)+	(400 MHz, DMSO-d ₆) δ = 13.98 (s, 1H), 12.72 - 12.60 (m, 1H), 8.52 - 8.46 (m, 3H), 7.97 (d, J = 8.0 Hz, 1H), 7.42 (dd, J = 6.0, 13.2 Hz, 2H), 7.27 (t, J = 7.6 Hz, 1H), 7.02 - 6.86 (m, 2H), 6.67 (dd, J = 10.4, 16.4 Hz, 1H), 6.48 (d, J = 12.8 Hz, 1H), 6.30 - 6.24 (m, 1H), 5.76 - 5.73 (m, 1H), 4.36 - 4.18 (m, 2H), 4.16 - 4.03 (m, 1H), 4.00 - 3.90 (m, 1H), 3.87 - 3.75 (m, 1H), 3.70 - 3.63 (m, 1H), 3.56 (t, J = 11.2 Hz, 1H)	A61 1 st eluting isomer
610	m/z (ESI+): 405.1 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.35 (s, 1H), 7.93 (d, J = 7.6 Hz, 1H), 7.27 (t, J = 7.6 Hz, 1H), 7.00 - 6.94 (m, 2H), 6.81 (dd, J = 10.8, 16.8 Hz, 1H), 6.59 (s, 1H), 6.32 (dd, J = 2.0, 16.8 Hz, 1H), 5.82 (dd, J = 2.0, 10.8 Hz, 1H), 4.66 - 4.60 (m, 1H), 4.29 (s, 1H), 3.79 (dd, J = 5.6, 11.6 Hz, 2H), 3.51 (t, J = 10.8 Hz, 2H), 2.87 (t, J = 16.8 Hz, 2H), 2.13 - 2.02 (m, 2H), 1.38 (s, 3H)	N/A
611	m/z (ESI+): 475.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.50 (s, 1H), 7.93 (d, J = 7.5 Hz, 1H), 7.33 - 7.25 (m, 1H), 7.02 - 6.94 (m, 2H), 6.84 (ddd, J = 2.1, 10.6, 16.8 Hz, 1H), 6.36 (dd, J = 1.9, 16.7 Hz, 1H), 5.92 - 5.79 (m, 1H), 4.81 - 4.81 (m, 1H), 4.85 - 4.79 (m, 1H), 4.71 (br s, 1H), 4.34 (br s, 1H), 4.20 - 4.08 (m, 3H), 3.86 (br t, J = 10.5 Hz, 2H), 3.77 - 3.67 (m, 1H), 2.33 - 2.16 (m, 4H), 2.15 - 1.98 (m, 2H), 1.92 - 1.78 (m, 3H), 1.69 (br d, J = 11.3 Hz, 1H)	A48

Cmpd #	MS	¹ H NMR	SFC Conditions
612	m/z (ESI+): 475.2 (M+H)+	(400 MHz, DMSO-d ₆) δ = 14.09 (s, 1H), 12.48 (s, 1H), 8.59 (s, 1H), 8.19 (d, J = 8.0 Hz, 1H), 7.32 - 7.26 (m, 1H), 6.99 - 6.93 (m, 2H), 6.85 (dd, J = 10.8, 16.8 Hz, 1H), 6.25 (dd, J = 2.4, 16.8 Hz, 1H), 5.80 - 5.74 (m, 1H), 4.56 (s, 2H), 4.31 (s, 1H), 4.07 (td, J = 5.6, 11.2 Hz, 2H), 3.93 (d, J = 10.4 Hz, 1H), 3.86 - 3.79 (m, 1H), 3.77 (d, J = 17.6 Hz, 2H), 3.69 (d, J = 13.2 Hz, 2H), 3.20 - 3.09 (m, 1H), 2.31 - 2.19 (m, 2H), 2.18 - 2.12 (m, 1H), 2.07 - 1.98 (m, 2H), 1.95 - 1.88 (m, 1H), 1.74 (s, 2H)	A12 2 nd eluting isomer
613	m/z (ESI+): 475.2 (M+H)+	(400 MHz, DMSO-d ₆) δ = 14.11 (s, 1H), 12.50 (s, 1H), 8.60 (s, 1H), 8.19 (d, J = 8.0 Hz, 1H), 7.33 - 7.26 (m, 1H), 7.00 - 6.93 (m, 2H), 6.85 (dd, J = 10.4, 16.4 Hz, 1H), 6.25 (dd, J = 2.4, 16.4 Hz, 1H), 5.77 (dd, J = 2.4, 10.4 Hz, 1H), 4.62 - 4.51 (m, 2H), 4.31 (s, 1H), 4.07 (td, J = 5.2, 10.8 Hz, 2H), 3.93 (d, J = 11.6 Hz, 1H), 3.86 - 3.79 (m, 1H), 3.79 - 3.73 (m, 2H), 3.72 - 3.65 (m, 2H), 3.20 - 3.08 (m, 1H), 2.30 - 2.10 (m, 3H), 2.09 - 1.96 (m, 2H), 1.91 (d, J = 11.6 Hz, 1H), 1.78 - 1.68 (m, 2H)	A12 1 st eluting isomer
614	m/z (ESI+): 423.2 (M+H)+	(400 MHz, DMSO-d ₆) δ = 14.33 (br s, 1H), 12.23 (br s, 1H), 8.67 - 8.60 (m, 1H), 8.12 (d, J = 8.4 Hz, 1H), 7.28 (t, J = 7.6 Hz, 1H), 7.01 - 6.92 (m, 2H), 6.91 - 6.76 (m, 1H), 6.29 - 6.20 (m, 1H), 5.85 - 5.71 (m, 1H), 5.18 - 4.98 (m, 1H), 4.65 - 4.47 (m, 2H), 4.42 (s, 1H), 4.16 - 4.01 (m, 2H), 3.82 - 3.64 (m, 2H), 2.84 - 2.68 (m, 1H), 2.35 (s, 3H), 2.06 - 1.94 (m, 1H)	A12 2 nd eluting isomer
615	m/z (ESI+): 423.2 (M+H)+	(400 MHz, DMSO-d ₆) δ = 14.33 (br s, 1H), 12.32 - 12.14 (m, 1H), 8.63 (d, J = 3.2 Hz, 1H), 8.12 (d, J = 8.0 Hz, 1H), 7.28 (t, J = 7.6 Hz, 1H), 7.01 - 6.92 (m, 2H), 6.92 - 6.75 (m, 1H), 6.29 - 6.20 (m, 1H), 5.85 - 5.71 (m, 1H), 5.17 - 4.97 (m, 1H), 4.65 - 4.46 (m, 2H), 4.46 - 4.36 (m, 1H), 4.14 - 4.03 (m, 2H), 3.83 - 3.64 (m, 2H), 2.85 - 2.68 (m, 1H), 2.36 (s, 3H), 2.05 - 1.95 (m, 1H)	A12 1 st eluting isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
616	m/z (ESI+): 542.3 (M+H)+		N/A
617	m/z (ESI+): 519.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.46 - 8.39 (m, 1H), 8.27 (s, 1H), 7.97 (dd, J = 1.2, 8.0 Hz, 1H), 7.32 - 7.23 (m, 1H), 7.02 - 6.94 (m, 2H), 6.83 (dd, J = 10.8, 16.8 Hz, 1H), 6.35 (dd, J = 2.0, 16.8 Hz, 1H), 5.85 (dd, J = 2.0, 10.8 Hz, 1H), 4.74 - 4.63 (m, 2H), 4.33 (s, 1H), 4.17 - 4.09 (m, 3H), 3.91 - 3.79 (m, 4H), 3.78 - 3.70 (m, 2H), 3.53 - 3.44 (m, 2H), 2.99 - 2.91 (m, 2H), 2.27 (d, J = 13.2 Hz, 2H), 2.22 - 2.12 (m, 2H), 2.04 - 1.98 (m, 2H), 1.97 - 1.90 (m, 2H)	N/A
618	m/z (ESI+): 489.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.45 (s, 1H), 7.98 (dd, J = 1.2, 8.3 Hz, 1H), 7.32 - 7.24 (m, 1H), 7.01 - 6.94 (m, 2H), 6.84 (dd, J = 10.4, 16.8 Hz, 1H), 6.35 (dd, J = 2.0, 16.8 Hz, 1H), 5.85 (dd, J = 2.0, 10.8 Hz, 1H), 4.77 - 4.68 (m, 2H), 4.34 (s, 1H), 4.15 - 4.10 (m, 2H), 3.98 - 3.90 (m, 1H), 3.89 - 3.80 (m, 3H), 3.79 - 3.72 (m, 1H), 3.00 - 2.91 (m, 2H), 2.34 - 2.12 (m, 4H), 2.09 - 2.02 (m, 1H), 1.97 - 1.84 (m, 4H), 1.63 - 1.54 (m, 1H)	A55 2 nd eluting isomer
619	m/z (ESI+): 489.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.45 (s, 1H), 7.98 (d, J = 7.6 Hz, 1H), 7.27 (t, J = 7.2 Hz, 1H), 7.00 - 6.94 (m, 2H), 6.83 (dd, J = 10.4, 16.8 Hz, 1H), 6.35 (dd, J = 2.0, 16.8 Hz, 1H), 5.84 (dd, J = 2.0, 10.4 Hz, 1H), 4.75 - 4.67 (m, 2H), 4.33 (s, 1H), 4.12 (d, J = 11.6 Hz, 2H), 3.98 - 3.90 (m, 1H), 3.89 - 3.80 (m, 3H), 3.79 - 3.72 (m, 1H), 2.98 - 2.92 (m, 2H), 2.27 (d, J = 12.4 Hz, 2H), 2.21 - 2.10 (m, 2H), 2.07 - 2.02 (m, 1H), 1.96 - 1.84 (m, 4H), 1.61 - 1.54 (m, 1H)	A55 1 st eluting isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
620	m/z (ESI+): 505.2 (M+H)+	(400 MHz, CHLOROFORM-d) δ = 12.00 (br d, J=5.63 Hz, 1 H), 8.29 (s, 1H), 7.88 (d, J=7.00 Hz, 1H), 7.40 - 7.31 (m, 1H), 7.12 (d, J=8.13 Hz, 1H), 7.05 - 6.97 (m, 1H), 6.58 (dd, J=16.70, 10.44 Hz, 1H), 6.16 (br d, J=16.63 Hz, 1H), 5.23 (br d, J=9.38 Hz, 1H), 4.83 - 4.71 (m, 2H), 4.22 - 4.04 (m, 3H), 4.46 (br s, 1H), 3.94 - 3.65 (m, 8H), 3.11 (br t, J=6.00 Hz, 2H), 2.74 - 2.59 (m, 1H), 2.42 (br dd, J=13.26, 3.88 Hz, 1H), 2.21 - 2.08 (m, 2H), 2.00 - 1.87 (m, 2H)	W
621	m/z (ESI+): 505.2 (M+H)+	(400 MHz, CHLOROFORM-d) δ = 10.62 - 10.36 (m, 1H), 8.24 (s, 1H), 7.85 (d, J=7.13 Hz, 1H), 7.39 - 7.30 (m, 1H), 7.14 (d, J=8.13 Hz, 1 H), 7.05 - 6.94 (m, 1H), 6.66 (dd, J=16.76, 10.51 Hz, 1H), 6.51 - 6.42 (m, 1H), 5.85 (dd, J=10.44, 1.81 Hz, 1H), 4.95 (br d, J=10.26 Hz, 1H), 4.31 (br d, J=9.51 Hz, 1H), 4.10 - 4.02 (m, 1H), 3.90 - 3.69 (m, 8H), 3.65 - 3.53 (m, 2H), 3.16 (td, J=10.88, 5.00 Hz, 1H), 3.05 - 2.92 (m, 2H), 2.51 (br dd, J=11.38, 7.13 Hz, 2H), 2.28 - 2.14 (m, 1H), 2.13 - 2.03 (m, 1H), 1.98 - 1.80 (m, 2H), 1.28 (br d, J=10.76 Hz, 1H)	A62 2 nd eluting isomer
622	m/z (ESI+): 505.2 (M+H)+	(400 MHz, CHLOROFORM-d) δ = 10.75 - 10.09 (m, 1H), 8.24 (s, 1H), 7.84 (d, J=7.00 Hz, 1H), 7.38 - 7.31 (m, 1H), 7.17 (br d, J=7.50 Hz, 1H), 7.02 - 6.96 (m, 1H), 6.65 (dd, J=16.76, 10.51 Hz, 1H), 6.51 - 6.41 (m, 1H), 5.85 (dd, J=10.44, 1.81 Hz, 1H), 4.94 (br d, J=9.63 Hz, 1H), 4.30 (br d, J=9.76 Hz, 1H), 4.11 - 4.00 (m, 1H), 3.92 - 3.68 (m, 8H), 3.66 - 3.53 (m, 2H), 3.24 - 3.09 (m, 1H), 2.99 (br s, 2H), 2.59 - 2.43 (m, 2H), 2.29 - 2.15 (m, 1H), 2.14 - 2.03 (m, 1H), 1.98 - 1.79 (m, 2H), 1.35 - 1.21 (m, 1H)	A62 1 st eluting isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
623	m/z (ESI+): 475.3 (M+H)+	(400 MHz, DMSO-d ₆) δ = 14.46 - 14.08 (m, 1H), 12.38 (br s, 1H), 8.59 (s, 1H), 8.10 (br d, J=7.99 Hz, 1H), 7.28 (br t, J=7.51 Hz, 1H), 7.00 - 6.91 (m, 2H), 6.85 (br dd, J=16.63, 10.43 Hz, 1H), 6.25 (br d, J=16.57 Hz, 1H), 5.77 (br d, J=10.49 Hz, 1H), 4.60 - 4.45 (m, 2H), 4.30 (br s, 1H), 4.02 (td, J=11.44, 6.20 Hz, 3H), 3.80 - 3.62 (m, 4H), 2.98 - 2.91 (m, 2H), 2.26 - 2.14 (m, 2H), 2.10 - 1.98 (m, 2H), 1.95 - 1.76 (m, 3H), 1.55 (br dd, J=10.67, 7.45 Hz, 1H)	A39 2 nd eluting isomer
624	m/z (ESI+): 475.3 (M+H)+	(400 MHz, DMSO-d ₆) δ = 14.68 - 14.08 (m, 1H), 12.71 - 12.18 (m, 1H), 8.61 - 8.51 (m, 1H), 8.09 (br d, J=8.23 Hz, 1H), 7.31 - 7.24 (m, 1H), 6.99 - 6.83 (m, 3H), 6.23 (dt, J=16.63, 2.71 Hz, 1H), 5.81 - 5.74 (m, 1H), 4.70 (br d, J=6.91 Hz, 1H), 4.43 (br d, J=7.15 Hz, 1H), 4.07 - 3.94 (m, 1H), 3.81 - 3.63 (m, 3H), 3.62 - 3.46 (m, 3H), 2.97 - 2.69 (m, 3H), 2.31 - 2.08 (m, 4H), 1.94 - 1.71 (m, 3H), 1.55 - 1.42 (m, 1H)	A39 4 th eluting isomer
625	m/z (ESI+): 475.3 (M+H)+	(400 MHz, DMSO-d ₆) δ = 14.33 (br s, 1H), 12.52 - 12.20 (m, 1H), 8.59 (s, 1H), 8.10 (br d, J=7.99 Hz, 1H), 7.28 (t, J=7.63 Hz, 1H), 6.99 - 6.78 (m, 3H), 6.25 (dd, J=16.69, 2.38 Hz, 1H), 5.77 (dd, J=10.43, 2.44 Hz, 1H), 4.59 - 4.44 (m, 2H), 4.30 (br s, 1H), 4.08 - 3.93 (m, 3H), 3.83 - 3.59 (m, 4H), 3.00 - 2.88 (m, 2H), 2.27 - 2.10 (m, 2H), 2.07 - 1.76 (m, 5H), 1.60 - 1.49 (m, 1H)	A39 3 rd eluting isomer
626	m/z (ESI+): 475.3 (M+H)+	(400 MHz, DMSO-d ₆) δ = 14.36 (br s, 1H), 12.44 (br s, 1H), 8.58 (d, J=2.27 Hz, 1H), 8.10 (dd, J=8.40, 1.49 Hz, 1H), 7.32 - 7.23 (m, 1H), 6.98 - 6.83 (m, 3H), 6.23 (dt, J=16.69, 2.74 Hz, 1H), 5.78 (dd, J=10.43, 2.32 Hz, 1H), 4.70 (br d, J=5.96 Hz, 1H), 4.43 (br d, J=6.80 Hz, 1H), 4.05 - 3.95 (m, 1H), 3.78 - 3.65 (m, 3H), 3.60 - 3.48 (m, 3H), 2.95 - 2.69 (m, 3H), 2.30 - 2.09 (m, 4H), 1.95 - 1.72 (m, 3H), 1.54 - 1.43 (m, 1H)	A39 1 st eluting isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
627	m/z (ESI+): 405.1 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.34 (s, 1H), 8.00 (d, J = 7.2 Hz, 1H), 7.27 (t, J = 7.2 Hz, 1H), 7.02 - 6.92 (m, 2H), 6.80 (dd, J = 10.8, 16.8 Hz, 1H), 6.32 (dd, J = 2.0, 16.8 Hz, 1H), 5.83 (dd, J = 2.0, 10.8 Hz, 1H), 4.72 - 4.58 (m, 1H), 4.30 (s, 1H), 3.81 (t, J = 12.1 Hz, 2H), 3.60 - 3.47 (m, 2H), 3.37 - 3.33 (m, 1H), 3.13 - 3.00 (m, 2H), 2.54 (s, 3H), 2.16 - 1.98 (m, 2H), 1.41 (s, 3H)	N/A
628	m/z (ESI+): 485.2 (M+H)+	(400 MHz, DMSO-d ₆) δ = 13.77 (d, J = 7.6 Hz, 1H), 12.79 - 12.63 (m, 1H), 8.42 - 8.35 (m, 1H), 8.02 (d, J = 8.0 Hz, 1H), 7.63 - 7.52 (m, 4H), 7.46 - 7.40 (m, 1H), 7.28 (t, J = 7.6 Hz, 1H), 7.00 - 6.89 (m, 2H), 6.89 - 6.76 (m, 1H), 6.25 (td, J = 2.4, 16.4 Hz, 1H), 5.84 - 5.73 (m, 1H), 5.31 - 5.04 (m, 1H), 4.86 (d, J = 9.6 Hz, 0.4H), 4.78 - 4.58 (m, 1H), 4.58 - 4.51 (m, 1.2H), 4.38 (s, 0.4H), 4.00 - 3.89 (m, 2H), 3.76 - 3.58 (m, 2H), 2.87 - 2.63 (m, 1H), 2.10 - 1.94 (m, 1H)	A49 2 nd eluting isomer
629	m/z (ESI+): 485.2 (M+H)+	(400 MHz, DMSO-d ₆) δ = 13.77 (d, J = 7.2 Hz, 1H), 12.78 - 12.65 (m, 1H), 8.41 - 8.35 (m, 1H), 8.02 (d, J = 8.0 Hz, 1H), 7.62 - 7.52 (m, 4H), 7.47 - 7.40 (m, 1H), 7.28 (t, J = 7.6 Hz, 1H), 6.99 - 6.89 (m, 2H), 6.89 - 6.76 (m, 1H), 6.25 (td, J = 2.4, 16.4 Hz, 1H), 5.84 - 5.74 (m, 1H), 5.29 - 5.06 (m, 1H), 4.86 (d, J = 11.6 Hz, 0.4H), 4.76 - 4.59 (m, 1H), 4.59 - 4.50 (m, 1.3H), 4.38 (s, 0.3H), 3.99 - 3.89 (m, 2H), 3.75 - 3.57 (m, 2H), 2.86 - 2.64 (m, 1H), 2.09 - 1.94 (m, 1H)	A49 1 st eluting isomer
630	m/z (ESI+): 489.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.31 (s, 1H), 7.89 (d, J = 7.2 Hz, 1H), 7.20 - 7.16 (m, 1H), 6.90 - 6.86 (m, 2H), 6.73 (dd, J = 10.8, 16.8 Hz, 1H), 6.23 (dd, J = 2.0, 16.8 Hz, 1H), 5.74 (dd, J = 2.0, 10.4 Hz, 1H), 4.61 - 4.59 (m, 2H), 4.02 (dd, J = 4.4, 11.6 Hz, 2H), 3.84 - 3.80 (m, 1H), 3.79 - 3.76 (m, 3H), 3.67 - 3.65 (m, 2H), 3.38 - 3.36 (m, 2H), 2.80 - 2.79 (m, 2H), 2.20 - 2.18 (m, 2H), 2.17 - 2.16 (m, 1H), 2.07 - 2.04 (m, 2H), 1.70 - 1.68 (m, 2H), 1.57 - 1.52 (m, 2H)	N/A

Cmpd #	MS	¹ H NMR	SFC Conditions
631	m/z (ESI+): 489.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.45 (s, 1H), 7.98 (dd, J = 1.2, 8.3 Hz, 1H), 7.31 - 7.24 (m, 1H), 7.01 - 6.94 (m, 2H), 6.84 (dd, J = 10.4, 16.8 Hz, 1H), 6.35 (dd, J = 2.0, 16.8 Hz, 1H), 5.85 (dd, J = 2.0, 10.4 Hz, 1H), 4.77 - 4.66 (m, 2H), 4.33 (s, 1H), 4.12 (d, J = 11.6 Hz, 2H), 3.98 - 3.90 (m, 1H), 3.89 - 3.79 (m, 3H), 3.78 - 3.72 (m, 1H), 3.02 - 2.89 (m, 2H), 2.31 - 2.21 (m, 2H), 2.20 - 2.09 (m, 2H), 2.08 - 2.00 (m, 1H), 1.99 - 1.93 (m, 1H), 1.92 - 1.81 (m, 3H), 1.62 - 1.52 (m, 1H)	A55
632	m/z (ESI+): 431.5 (M+H)+	¹ H NMR (499 MHz, DMSO-d ₆) δ 13.97 (s, 1H), 12.65 (s, 1H), 8.42 (s, 1H), 8.14 - 8.08 (m, 1H), 7.32 - 7.25 (m, 1H), 6.99 - 6.91 (m, 2H), 6.85 (dd, J = 16.7, 10.5 Hz, 1H), 6.25 (dd, J = 16.7, 2.6 Hz, 1H), 5.78 (dd, J = 10.4, 2.6 Hz, 1H), 5.39 (s, 1H), 5.11 (s, 1H), 4.72 - 4.63 (m, 1H), 4.56 (s, 1H), 4.30 (s, 1H), 4.00 (dd, J = 11.5, 6.6 Hz, 2H), 3.69 (dd, J = 18.1, 11.4 Hz, 2H), 2.33 - 2.15 (m, 4H), 2.08 - 2.00 (m, 2H).	N/A
633	m/z (ESI+): 449.2 (M+H)+		N/A
634	m/z (ESI+): 441.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.39 (s, 1H), 7.95 (d, J = 8.8 Hz, 1H), 7.44 (s, 1H), 7.32 - 7.26 (m, 1H), 7.01 - 6.95 (m, 2H), 6.93 - 6.78 (m, 0.8H), 6.64 - 6.51 (m, 0.2H), 6.32 - 6.12 (m, 1H), 5.86 - 5.63 (m, 1H), 4.75 (s, 2H), 4.23 - 4.19 (m, 2H), 4.18 (s, 2H), 4.12 - 4.08 (m, 2H), 1.94 - 1.86 (m, 1H), 1.11 - 1.05 (m, 2H), 0.83 - 0.79 (m, 2H)	N/A
635	m/z (ESI+): 415.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.42 (s, 1H), 8.01 - 7.98 (m, 1H), 7.44 (s, 1H), 7.31 - 7.25 (m, 1H), 7.01 - 6.95 (m, 2H), 6.91 - 6.80 (m, 0.6H), 6.63 - 6.49 (m, 0.4H), 6.30 - 6.13 (m, 1H), 5.81 (d, J = 10 Hz, 0.6H), 5.70 - 5.62 (m, 0.4H), 4.71 (s, 2H), 4.20 (d, J = 0.8 Hz, 2H), 4.11 - 4.07 (m, 4H), 2.39 (s, 3H)	N/A

Cmpd #	MS	¹ H NMR	SFC Conditions
636	m/z (ESI+): 475.2 (M+H)+	(400 MHz, DMSO-d ₆) δ = 14.11 (s, 1H), 12.50 (s, 1H), 8.60 (s, 1H), 8.19 (d, J = 8.0 Hz, 1H), 7.33 - 7.26 (m, 1H), 7.00 - 6.93 (m, 2H), 6.85 (dd, J = 10.4, 16.4 Hz, 1H), 6.25 (dd, J = 2.4, 16.4 Hz, 1H), 5.77 (dd, J = 2.4, 10.4 Hz, 1H), 4.62 - 4.51 (m, 2H), 4.31 (s, 1H), 4.07 (td, J = 5.2, 10.8 Hz, 2H), 3.93 (d, J = 11.6 Hz, 1H), 3.86 - 3.79 (m, 1H), 3.79 - 3.73 (m, 2H), 3.72 - 3.65 (m, 2H), 3.20 - 3.08 (m, 1H), 2.30 - 2.10 (m, 3H), 2.09 - 1.96 (m, 2H), 1.91 (d, J = 11.6 Hz, 1H), 1.78 - 1.68 (m, 2H)	A12
637	m/z (ESI+): 477.3 (M+H)+	(400 MHz, CHLOROFORM-d) δ = 14.26 - 12.86 (m, 1H), 12.76 - 12.32 (m, 1H), 8.25 - 8.16 (m, 1H), 7.82 - 7.75 (m, 1H), 7.34 (t, J = 7.2 Hz, 1H), 7.08 (d, J = 8.0 Hz, 1H), 6.99 (t, J = 7.2 Hz, 1H), 6.50 - 6.34 (m, 3H), 5.85 - 5.60 (m, 1H), 4.89 - 4.83 (m, 1H), 4.36 - 4.15 (m, 2H), 4.06 - 3.92 (m, 3H), 3.89 (dd, J = 5.6, 9.6 Hz, 1H), 3.74 - 3.62 (m, 1H), 3.52 - 3.22 (m, 1H), 3.03 (s, 1H), 2.96 (s, 1H)	N/A
638	m/z (ESI+): 408.0 (M+H)+	¹ H NMR (499 MHz, DMSO-d ₆) δ 14.38 (s, 1H), 12.30 (s, 1H), 8.57 (s, 1H), 8.11 (dd, J = 8.4, 1.7 Hz, 1H), 7.28 (ddd, J = 8.4, 7.2, 1.6 Hz, 1H), 6.99 - 6.92 (m, 2H), 6.85 (dd, J = 16.7, 10.5 Hz, 1H), 6.25 (dd, J = 16.7, 2.5 Hz, 1H), 5.77 (dd, J = 10.4, 2.5 Hz, 1H), 4.56 (s, 1H), 4.47 (td, J = 12.6, 6.1 Hz, 1H), 4.31 (s, 1H), 4.05 (dd, J = 11.4, 6.6 Hz, 2H), 3.75 - 3.66 (m, 2H), 2.49 (s, 2H), 2.26 - 1.98 (m, 4H).	N/A
639	m/z (ESI+): 475.2 (M+H)+	(400 MHz, DMSO-d ₆) δ = 14.09 (s, 1H), 12.48 (s, 1H), 8.59 (s, 1H), 8.19 (d, J = 8.0 Hz, 1H), 7.32 - 7.26 (m, 1H), 6.99 - 6.93 (m, 2H), 6.85 (dd, J = 10.8, 16.8 Hz, 1H), 6.25 (dd, J = 2.4, 16.8 Hz, 1H), 5.80 - 5.74 (m, 1H), 4.56 (s, 2H), 4.31 (s, 1H), 4.07 (td, J = 5.6, 11.2 Hz, 2H), 3.93 (d, J = 10.4 Hz, 1H), 3.86 - 3.79 (m, 1H), 3.77 (d, J = 17.6 Hz, 2H), 3.69 (d, J = 13.2 Hz, 2H), 3.20 - 3.09 (m, 1H), 2.31 - 2.19 (m, 2H), 2.18 - 2.12 (m, 1H), 2.07 - 1.98 (m, 2H), 1.95 - 1.88 (m, 1H), 1.74 (s, 2H)	A12

Cmpd #	MS	¹ H NMR	SFC Conditions
640	m/z (ESI+): 477.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.55 (s, 1H), 7.95 (d, J = 7.6 Hz, 1H), 7.32 - 7.26 (m, 1H), 7.03 - 6.95 (m, 2H), 6.84 (m, 1H), 6.36 (dd, J = 1.2, 16.8 Hz, 1H), 5.85 (m, 1H), 5.08 (m, 1H), 4.96 - 4.89 (m, 2H), 4.74 - 4.68 (m, 1H), 4.34 (s, 1H), 4.15 (m, 2H), 4.04 - 3.98 (m, 1H), 3.97 - 3.93 (m, 1H), 3.90 (m, 2H), 3.87 - 3.81 (m, 3H), 2.36 - 2.13 (m, 4H)	A34 2 nd eluting isomer
641	m/z (ESI+): 477.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.57 (s, 1H), 7.97 (d, J = 7.6 Hz, 1H), 7.31 (m, 1H), 7.04 - 6.98 (m, 2H), 6.86 (m, 1H), 6.38 (dd, J = 1.2, 16.8 Hz, 1H), 5.87 (m, 1H), 5.10 (m, 1H), 4.98 - 4.91 (m, 2H), 4.73 (m, 1H), 4.36 (s, 1H), 4.17 (m, 2H), 4.05 - 3.99 (m, 1H), 3.99 - 3.95 (m, 1H), 3.94 - 3.90 (m, 2H), 3.89 - 3.82 (m, 3H), 2.37 - 2.17 (m, 4H)	A34 1 st eluting isomer
642	m/z (ESI+): 462.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.50 (s, 1H), 8.45 (s, 1H), 7.90 (d, J = 7.6 Hz, 1H), 7.29 (t, J = 7.6 Hz, 1H), 7.02 - 6.95 (m, 2H), 6.89 - 6.78 (m, 1H), 6.72 - 6.60 (m, 1H), 4.33 - 4.24 (m, 1H), 4.20 - 4.10 (m, 1H), 4.08 (dd, J = 3.2, 6.8 Hz, 2H), 4.05 - 3.98 (m, 1H), 3.98 - 3.85 (m, 3H), 3.84 - 3.77 (m, 1H), 3.68 - 3.60 (m, 1H), 3.56 (dd, J = 6.4, 14.8 Hz, 2H), 2.59 (d, J = 10.8 Hz, 6H), 2.51 - 2.32 (m, 3H), 2.17 (ttt, J = 4.0, 8.0, 16.0 Hz, 1H)	A63 2 nd eluting isomer
643	m/z (ESI+): 462.2 (M+H)+	(400 MHz, METHANOL-d ₄) δ = 8.50 (d, J = 1.2 Hz, 1H), 7.90 (d, J = 7.2 Hz, 1H), 7.29 (t, J = 7.6 Hz, 1H), 7.02 - 6.94 (m, 2H), 6.88 - 6.78 (m, 1H), 6.75 - 6.62 (m, 1H), 4.28 (d, J = 4.0 Hz, 1H), 4.21 - 4.10 (m, 1H), 4.08 (d, J = 6.8 Hz, 2H), 4.06 - 3.96 (m, 2H), 3.95 - 3.85 (m, 2H), 3.85 - 3.75 (m, 1H), 3.63 (dd, J = 6.8, 14.8 Hz, 3H), 2.64 (d, J = 11.2 Hz, 6H), 2.50 - 2.40 (m, 2H), 2.40 - 2.26 (m, 1H), 2.23 - 2.11 (m, 1H)	A63 1 st eluting isomer

Cmpd #	MS	¹ H NMR	SFC Conditions
644	m/z (ESI+): 475.3 (M+H)+	(400 MHz, DMSO-d ₆) δ = 14.05 (s, 1H), 12.41 (s, 1H), 8.55 (s, 1H), 8.16 (dd, J = 1.6, 8.4 Hz, 1H), 7.32 - 7.24 (m, 1H), 6.99 - 6.92 (m, 2H), 6.85 (dd, J = 10.4, 16.8 Hz, 1H), 6.25 (dd, J = 2.4, 16.4 Hz, 1H), 5.82 - 5.72 (m, 1H), 4.63 - 4.51 (m, 2H), 4.31 (s, 1H), 4.09 - 3.98 (m, 4H), 3.78 - 3.65 (m, 2H), 3.51 (t, J = 11.2 Hz, 2H), 3.18 - 3.10 (m, 1H), 2.28 - 2.13 (m, 4H), 2.06 - 1.96 (m, 2H), 1.65 (d, J = 11.6 Hz, 2H)	N/A
645	m/z (ESI+): 463.1 (M+H)+		N/A

Biological Examples

SMARCA2 and SMARCA4 Degradation Assay

[0581] Degradation of protein which is expressed from the SMARCA2 and SMARCA4 genes was monitored using engineered HiBiT-fusion HeLa cell lines from Promega. In brief, 384-well white opaque plates (Greiner) were seeded with SMARCA2-HiBiT or SMARCA4-HiBiT HeLa cells at 8,000 cells/well and incubated overnight at 37 °C to allow cell attachment. After overnight incubation, test compounds were added in a 10-point dilution series (typically 10 μM to 300 pM) using a TECAN D300e Digital Dispenser, and plates were subsequently incubated for 24 hours at 37 °C. 24-hours post-treatment, protein levels were quantified with the addition of HiBiT lytic buffer, LgBiT protein, and HiBiT substrate, according to manufacturer's specifications. Plates were incubated on an orbital plate shaker for 10 minutes at room temperature. Resulting luminescent values were read out using a ClarioStar plate reader and used to construct dose-response curves and calculation of degradation DC_{50s} (GraphPad Prism).

[0582] Table 4 provides data from the assays. Activity of the tested compounds is provided in Table 4 below as follows: A = DC₅₀ < 0.50 μM; B = 0.5 μM < DC₅₀ < 5.0 μM; C = DC₅₀ > 5.0 μM. For SMARCA2 and SMARCA4 degradation activity @ 1 μM, +++ = > 70%; ++ = 30-70%; + = < 30%.

Table 4

Ex.	SMARCA2 DC ₅₀ (μM)	SMARCA2 deg. (%) 1 μM	SMARCA4 DC ₅₀ (μM)	SMARCA4 deg. (%) 1 μM
1	A	++	A	++
2	A	++	A	++

Ex.	SMARCA2 DC ₅₀ (μ M)	SMARCA2 deg. (%) 1 μ M	SMARCA4 DC ₅₀ (μ M)	SMARCA4 deg. (%) 1 μ M
3	A	++	A	+
4	B	+	C	+
5	B	++	C	+
6	A	+	C	+
7	A	++	A	++
8	A	++	A	+
9	B	++	C	+
10	A	++	A	++
11	A	+++	A	++
12	B	++	C	+
13	B	++	B	+
14	B	+	C	+
15	B	+	C	+
16	A	++	A	++
17	A	++	A	++
18	A	++	A	++
19	A	++	A	++
20	A	++	A	++
21	A	++	B	+
22	B	++	B	+
23	A	++	A	++
24	A	++	A	++
25	A	++	A	++
26	B	+	B	+
27	B	+	C	+
28	A	+	C	+
29	B	+	B	+
30	B	++	B	++
31	A	++	A	++
32	A	++	A	++

Ex.	SMARCA2 DC ₅₀ (μ M)	SMARCA2 deg. (%) 1 μ M	SMARCA4 DC ₅₀ (μ M)	SMARCA4 deg. (%) 1 μ M
33	A	++	B	+
34	B	++	B	+
35	A	+++	B	++
36	B	+	B	+
37	A	++	B	++
38	B	++	B	+
39	B	++	B	+
40	B	++	B	+
41	A	+++	A	++
42	A	+++	A	+++
43	B	+	C	+
44	B	+	B	+
45	A	+++	A	++
46	A	+++	A	+++
47	B	++	B	+
48	A	++	B	+
49	A	++	A	+
50	A	++	B	+
51	A	+++	A	+++
52	B	++	B	+
53	A	++	B	++
54	A	++	A	++
55	A	+++	A	+++
56	B	++	B	+
57	A	++	A	++
58	B	+	C	+
59	A	+++	B	++
60	A	++	B	++
61	A	++	C	+
62	B	++	B	+

Ex.	SMARCA2 DC ₅₀ (μ M)	SMARCA2 deg. (%) 1 μ M	SMARCA4 DC ₅₀ (μ M)	SMARCA4 deg. (%) 1 μ M
63	A	++	B	+
64	B	++	B	+
65	B	++	B	+
66	A	+++	A	+++
67	B	+	C	+
68	B	++	B	+
69	A	++	B	+
70	A	++	B	+
71	A	++	B	++
72	A	++	B	+
73	C	+	C	+
74	A	++	B	+
75	B	+	B	+
76	A	++	B	++
77	A	+++	A	++
78	A	+++	B	++
79	A	++	B	++
80	B	+	C	+
81	A	++	B	+
82	A	++	B	++
83	B	++	B	+
84	A	+++	A	+++
85	A	+++	B	++
86	B	++	B	+
87	B	++	B	+
88	A	++	C	+
89	B	++	B	+
90	B	++	B	++
91	A	++	B	++
92	A	++	B	+

Ex.	SMARCA2 DC ₅₀ (μ M)	SMARCA2 deg. (%) 1 μ M	SMARCA4 DC ₅₀ (μ M)	SMARCA4 deg. (%) 1 μ M
93	A	++	A	++
94	B	+	B	+
95	B	+	B	+
96	A	++	B	+
97	A	++	C	+
98	A	+	C	+
99	A	++	A	+
100	A	++	C	+
101	B	++	C	+
102	A	++	A	+
103	A	++	B	++
104	B	++	B	++
105	B	++	B	+
106	A	++	C	+
107	A	+++	A	++
108	A	++	A	++
109	A	++	B	+
110	A	++	B	++
111	B	++	B	+
112	A	++	A	+
113	B	++	B	+
114	B	++	B	+
115	B	++	B	+
116	B	+	C	+
117	A	+++	B	+
118	B	++	B	+
119	A	++	B	++
120	A	++	B	++
121	A	++	B	++
122	B	++	B	+

Ex.	SMARCA2 DC ₅₀ (μ M)	SMARCA2 deg. (%) 1 μ M	SMARCA4 DC ₅₀ (μ M)	SMARCA4 deg. (%) 1 μ M
123	B	++	B	+
124	B	++	C	+
125	B	++	B	++
126	A	++	I	++
127	B	++	B	+
128	B	++	B	++
129	B	+	B	+
130	B	+	B	+
131	B	++	B	++
132	B	+	C	+
133	B	+	B	+
134	B	++	B	+
135	B	++	B	+
136	A	+++	A	+++
137	A	+++	A	++
138	A	++	B	+
139	C	+	C	+
140	B	+	C	+
141	A	++	B	+
142	B	+	B	+
143	B	++	B	+
144	A	++	B	++
145	B	++	B	+
146	A	++	B	++
147	B	+	C	+
148	B	++	B	+
149	B	++	C	+
150	B	+	C	+
151	A	++	A	++
152	A	++	A	++

Ex.	SMARCA2 DC ₅₀ (μ M)	SMARCA2 deg. (%) 1 μ M	SMARCA4 DC ₅₀ (μ M)	SMARCA4 deg. (%) 1 μ M
153	A	++	A	++
154	B	++	B	++
155	A	++	B	+
156	B	+	B	+
157	A	++	B	+
158	A	++	B	+
159	B	++	C	+
160	A	++	B	+
161	B	+	C	+
162	B	++	B	+
163	B	+	C	+
164	B	++	B	+
165	A	++	B	+
166	B	++	B	+
167	B	++	B	+
168	B	+	C	+
169	A	+++	A	++
170	A	+++	A	++
171	B	++	B	+
172	A	++	B	+
173	A	++	B	+
174	A	+++	A	++
175	A	++	B	+
176	B	++	B	+
177	B	+	C	+
178	A	+	B	+
179	A	++	B	+
180	A	++	A	++
181	A	++	A	+
182	A	+++	B	++

Ex.	SMARCA2 DC ₅₀ (μ M)	SMARCA2 deg. (%) 1 μ M	SMARCA4 DC ₅₀ (μ M)	SMARCA4 deg. (%) 1 μ M
183	A	+++	A	++
184	B	+	C	+
185	B	++	B	+
186	B	+	B	+
187	A	++	A	++
188	B	+	C	+
189	A	++	B	++
190	A	++	B	++
191	A	++	B	+
192	B	++	B	++
193	B	++	B	+
194	A	++	C	+
195	A	++	A	+
196	B	++	B	+
197	B	+	B	+
198	A	++	C	+
199	B	++	C	+
200	B	+	C	+
201	B	++	B	++
202	B	++	B	++
203	B	++	B	+
204	B	++	B	+
205	A	++	A	++
206	B	++	B	++
207	B	++	B	+
208	B	+	B	+
209	A	++	C	+
210	C	+	C	+
211	A	+	C	+
212	A	+++	A	++

Ex.	SMARCA2 DC ₅₀ (μ M)	SMARCA2 deg. (%) 1 μ M	SMARCA4 DC ₅₀ (μ M)	SMARCA4 deg. (%) 1 μ M
213	A	++	B	++
214	A	++	B	++
215	B	++	B	+
216	A	+++	A	++
217	B	+	B	+
218	B	++	B	+
219	A	++	B	++
220	B	++	B	+
221	B	++	B	+
222	B	++	C	+
223	B	++	B	++
224	B	++	C	+
225	A	++	A	+
226	B	+	C	+
227	A	+	C	+
228	A	+++	A	+++
229	A	++	C	+
230	B	+	C	+
231	B	++	B	+
232	B	+	C	+
233	B	+	C	+
234	B	+	C	+
235	A	+	C	+
236	B	++	B	+
237	B	++	B	+
238	B	++	B	+
239	B	++	B	+
240	B	++	B	+
241	A	++	B	++
242	A	++	B	++

Ex.	SMARCA2 DC ₅₀ (μ M)	SMARCA2 deg. (%) 1 μ M	SMARCA4 DC ₅₀ (μ M)	SMARCA4 deg. (%) 1 μ M
243	A	++	A	+
244	A	++	A	++
245	B	+	C	+
246	A	++	B	+
247	B	++	B	+
248	B	++	B	+
249	B	+	B	+
250	B	+	C	+
251	B	++	B	+
252	B	+	B	+
253	B	++	B	+
254	B	++	B	+
255	A	++	B	++
256	A	++	B	++
257	A	++	B	+
258	B	++	B	+
259	B	++	B	+
260	A	++	B	++
261	A	++	B	+
262	B	++	B	+
263	B	++	B	+
264	A	+++	A	++
265	A	++	B	+
266	B	+	C	+
267	A	+++	A	++
268	A	++	B	+
269	A	++	B	+
270	B	+	B	+
271	B	++	B	+
272	A	+++	A	++

Ex.	SMARCA2 DC ₅₀ (μ M)	SMARCA2 deg. (%) 1 μ M	SMARCA4 DC ₅₀ (μ M)	SMARCA4 deg. (%) 1 μ M
273	B	++	B	+
274	A	++	B	+
275	A	++	B	+
276	A	+++	A	++
277	A	++	B	+
278	A	+++	A	+++
279	A	+++	A	++
280	A	++	A	++
281	A	++	B	+
282	A	++	A	++
283	B	++	B	+
284	A	++	A	++
285	A	++	B	+
286	A	+++	B	++
287	A	++	B	+
288	A	+++	B	++
289	B	++	B	+
290	A	++	B	+
291	A	++	C	+
292	B	++	C	+
293	A	++	C	+
294	B	+++	B	++
295	A	+++	B	++
296	A	++	B	++
297	B	+++	B	+++
298	B	+++	B	++
299	A	+++	B	++
300	A	+++	A	+++
301	A	+++	A	+++
302	A	+++	A	+++

Ex.	SMARCA2 DC ₅₀ (μ M)	SMARCA2 deg. (%) 1 μ M	SMARCA4 DC ₅₀ (μ M)	SMARCA4 deg. (%) 1 μ M
303	A	++	A	+
304	A	++	C	+
305	B	+	C	+
306	B	++	B	++
307	A	+++	B	+++
308	A	+++	A	++
309	A	++	B	++
310	A	+	C	+
311	A	++	B	+
312	A	+++	A	++
313	A	+++	B	+++
314	B	+++	B	++
315	A	+++	B	+++
316	A	+++	B	+++
317	A	+++	B	++
318	A	+++	A	+++
319	B	+++	B	++
320	A	++	A	+
321	B	+++	B	++
322	A	++	A	++
323	A	+	B	++
324	A	+++	B	++
325	B	+++	B	++
326	B	++	B	++
327	B	++	A	++
328	A	+++	A	++
329	A	++	A	++
330	A	++	B	+
331	B	++	B	++
332	B	++	C	+

Ex.	SMARCA2 DC ₅₀ (μ M)	SMARCA2 deg. (%) 1 μ M	SMARCA4 DC ₅₀ (μ M)	SMARCA4 deg. (%) 1 μ M
333	B	++	B	++
334	B	+++	B	++
335	B	++	C	++
336	A	++	C	++
337	A	++	C	+
338	A	+	B	++
339	A	+++	B	++
340	B	++	B	++
341	B	+++	B	+++
342	B	++	C	+
343	B	++	C	++
344	A	++	A	++
345	A	++	B	++
346	A	+++	A	+++
347	B	++	B	+
348	B	+++	B	++
349	B	++	B	++
350	A	++	A	++
351	A	+++	A	+++
352	A	++	B	++
353	A	+++	A	+++
354	A	+++	A	+++
355	B	++	B	++
356	A	++	B	++
357	A	++	A	++
358	A	++	A	++
359	A	+++	B	++
360	A	++	B	++
361	A	++	B	++
362	A	++	B	++

Ex.	SMARCA2 DC ₅₀ (μ M)	SMARCA2 deg. (%) 1 μ M	SMARCA4 DC ₅₀ (μ M)	SMARCA4 deg. (%) 1 μ M
363	A	+++	A	+++
364	A	++	B	++
365	B	++	C	+
366	A	++	C	+
367	A	++	B	+
368	A	++	A	++
369	A	+++	A	+++
370	A	++	B	+
371	A	+++	A	+++
372	A	+++	B	++
373	B	+++	B	++
374	A	+++	A	+++
375	A	+++	B	++
376	A	+++	A	++
377	A	++	A	++
378	A	+++	A	+++
379	A	++	A	++
380	B	+++	B	+++
381	B	+	C	+
382	A	+++	A	++
383	A	+++	B	++
384	A	++	B	++
385	A	++	C	+
386	A	++	B	+
387	A	++	A	++
388	B	++	B	++
389	A	++	B	++
390	A	+++	A	+++
391	A	+++	A	+++
392	A	+	A	+

Ex.	SMARCA2 DC ₅₀ (μ M)	SMARCA2 deg. (%) 1 μ M	SMARCA4 DC ₅₀ (μ M)	SMARCA4 deg. (%) 1 μ M
393	A	+++	A	+++
394	A	+	B	+
395	A	++	B	+
397	A	++	B	++
398	A	++	B	++
399	A	+++	B	++
400	B	++	B	+
401	A	+++	A	+++
402	A	++	A	++
403	A	+++	B	++
404	A	++	C	++
405	A	+++	C	++
406	A	++	B	+
407	B	++	C	+
408	A	++	B	++
409	A	++	B	++
410	B	++	B	++
411	B	++	B	+
412	A	+++	A	++
413	A	++	B	++
414	A	++	B	++
415	A	++	A	++
416	A	++	B	+
417	A	++	A	+
418	B	++	B	++
419	A	++	B	++
420	A	+++	B	++
421	A	+++	A	+++
422	B	++	C	+
423	A	++	A	++

Ex.	SMARCA2 DC ₅₀ (μ M)	SMARCA2 deg. (%) 1 μ M	SMARCA4 DC ₅₀ (μ M)	SMARCA4 deg. (%) 1 μ M
424	A	++	B	++
425	A	+++	A	++
426	A	+++	B	++
427	B	+++	B	++
428	A	++	A	++
429	A	++	A	++
430	A	+++	A	++
431	A	++	B	+
432	A	+++	B	++
433	A	++	B	+
434	A	++	A	++
435	B	+	C	+
436	A	+	B	+
437	A	++	C	++
438	A	++	B	++
439	A	+++	A	+++
440	A	+++	A	+++
441	A	+++	A	++
442	A	++	B	++
443	B	++	B	++
444	A	++	B	+
445	A	+++	A	+++
446	A	+++	A	+++
447	A	+++	A	+++
448	A	+++	A	+++
449	A	+++	B	+++
450	A	+++	B	++
451	A	++	B	++
452	B	+++	A	+++
453	B	+++	B	+++

Ex.	SMARCA2 DC ₅₀ (μ M)	SMARCA2 deg. (%) 1 μ M	SMARCA4 DC ₅₀ (μ M)	SMARCA4 deg. (%) 1 μ M
454	A	+++	A	+++
455	A	+++	A	+++
456	A	+++	A	++
457	B	+++	B	++
458	A	++	C	++
459	B	+	C	+
460	A	+++	A	++
461	A	+++	C	++
462	A	++	C	++
463	B	++	B	+
464	B	++	C	+
465	A	++	B	++
466	A	++	B	++
467	A	+++	A	++
468	A	++	A	++
469	A	+++	A	+++
470	A	++	A	++
471	A	+++	A	++
472	A	++	B	++
473	B	++	C	+
474	A	+++	B	++
475	A	+++	A	++
476	B	+++	B	++
477	B	++	C	+
478	B	+++	B	+
479	B	+++	B	++
480	A	+++	A	++
481	A	+++	A	++
482	B	++	C	+
483	B	+++	B	++

Ex.	SMARCA2 DC ₅₀ (μ M)	SMARCA2 deg. (%) 1 μ M	SMARCA4 DC ₅₀ (μ M)	SMARCA4 deg. (%) 1 μ M
484	B	++	C	+
485	B	+++	B	+++
486	A	+	C	+
487	B	++	B	+
488	B	+	C	+
489	A	+++	B	+++
490	B	++	C	+
491	A	+++	A	++
492	A	++	C	+
493	A	+++	C	+
494	A	+++	B	++
495	A	++	A	++
496	A	+++	A	+++
497	A	++	C	+
498	A	++	C	+
499	A	++	B	++
500	A	+++	A	+++
501	A	+++	B	++
502	A	+++	A	+++
503	A	++	C	+
504	A	+++	A	++
505	C	++	C	+
506	B	++	C	+
507	A	++	B	++
508	A	+++	A	+++
509	A	++	A	++
510	B	++	C	+
511	B	+++	B	++
512	B	++	A	+
513	B	++	C	++

Ex.	SMARCA2 DC ₅₀ (μ M)	SMARCA2 deg. (%) 1 μ M	SMARCA4 DC ₅₀ (μ M)	SMARCA4 deg. (%) 1 μ M
514	A	++	A	+
515	A	++	A	+
516	A	++	B	++
517	A	++	B	++
518	A	++	B	+
519	A	++	B	++
520	A	++	B	++
521	A	++	A	++
522	B	++	B	++
523	A	++	B	+
524	B	++	C	+
525	A	+++	A	+++
526	A	+++	B	+
527	A	+++	A	+++
528	A	+++	A	++
529	A	++	B	++
530	A	++	A	+
531	A	+++	A	+
532	A	+++	A	++
533	A	+++	A	+++
534	A	+++	A	+++
535	A	+++	A	++
536	A	++	B	+
537	A	++	C	+
538	A	++	C	++
539	B	++	B	+
540	B	++	C	++
541	A	+++	A	+++
542	A	+++	B	++
543	A	+++	A	+

Ex.	SMARCA2 DC ₅₀ (μ M)	SMARCA2 deg. (%) 1 μ M	SMARCA4 DC ₅₀ (μ M)	SMARCA4 deg. (%) 1 μ M
544	A	+++	A	++
545	B	++	C	++
546	C	++	C	+
547	C	++	C	+
548	A	++	B	++
549	B	++	B	++
550	B	++	B	++
551	A	+++	A	++
552	A	++	A	+
553	A	+++	B	++
554	A	+++	A	++
555	B	+++	B	+
556	B	++	B	++
557	A	+++	A	+++
558	A	++	A	++
559	A	+++	A	+++
560	A	++	A	++
561	A	+++	A	+++
562	A	++	B	++
563	A	++	C	+
564	A	++	A	++
565	A	++	A	++
566	A	+	B	+
567	A	+++	B	++
568	A	++	C	+
569	A	++	B	+
570	A	++	A	++
571	A	++	A	++
572	A	+++	A	++
573	B	++	C	+

Ex.	SMARCA2 DC ₅₀ (μ M)	SMARCA2 deg. (%) 1 μ M	SMARCA4 DC ₅₀ (μ M)	SMARCA4 deg. (%) 1 μ M
574	A	++	B	++
575	B	++	C	+
576	A	++	A	++
577	A	++	A	++
578	B	++	B	++
579	A	++	B	+
580	B	+++	B	++
581	B	++	B	++
582	A	++	B	+
583	B	+++	B	++
584	A	+++	A	++
585	A	++	A	++
586	B	+++	B	++
587	B	+++	B	++
588	A	++	B	++
589	A	+++	B	++
590	C	++	C	++
591	A	+++	B	++
592	A	++	B	++
593	B	++	B	++
594	A	+++	A	++
595	B	++	B	++
596	A	+++	A	+++
597	B	++	B	+
598	A	+++	B	++
599	A	+++	B	++
600	B	++	B	++
601	B	+++	B	++
602	A	+++	B	++
603	A	+++	A	+++

Ex.	SMARCA2 DC ₅₀ (μ M)	SMARCA2 deg. (%) 1 μ M	SMARCA4 DC ₅₀ (μ M)	SMARCA4 deg. (%) 1 μ M
604	A	++	B	+
605	A	++	B	+
606	B	++	C	+
607	A	+++	A	+++
608	A	+++	A	+++
609	B	++	C	++
610	A	++	B	++
611	B	+++	B	++
612	A	++	B	++
613	A	++	A	++
614	A	++	A	++
615	A	++	A	++
616	A	++	A	++
617	A	++	A	++
618	A	++	B	++
619	A	++	B	++
620	A	++	C	++
621	A	+++	A	+++
622	B	+++	B	+++
623	B	++	C	+
624	A	+++	B	+++
625	A	++	B	++
626	A	+++	A	+++
627	A	++	A	++
628	A	++	B	++
629	A	++	B	++
630	A	++	B	++
631	A	++	B	++
632	A	++	B	++
633	B	++	C	+

Ex.	SMARCA2 DC ₅₀ (μ M)	SMARCA2 deg. (%) 1 μ M	SMARCA4 DC ₅₀ (μ M)	SMARCA4 deg. (%) 1 μ M
634	A	+++	B	++
635	A	+++	A	++
636	A	++	B	++
637	A	+++	B	+++
638	A	+++	A	++
639	A	++	A	+
640	A	++	B	++
641	A	+++	C	++
642	B	++	C	+
643	B	++	C	+
644	B	+++	B	++
645	B	++	B	++

[0583] Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure belongs.

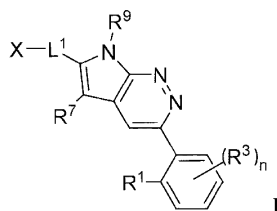
[0584] The disclosure illustratively described herein may suitably be practiced in the absence of any element or elements, limitation or limitations, not specifically disclosed herein. Thus, for example, the terms “comprising,” “including,” “containing,” etc. shall be read expansively and without limitation. Additionally, the terms and expressions employed herein have been used as terms of description and not of limitation, and there is no intention in the use of such terms and expressions of excluding any equivalents of the features shown and described or portions thereof, but it is recognized that various modifications are possible within the scope of the claims.

[0585] All publications, patent applications, patents, and other references mentioned herein are expressly incorporated by reference in their entirety, to the same extent as if each were incorporated by reference individually. In case of conflict, the present specification, including definitions, will control.

[0586] It is to be understood that while the disclosure has been described in conjunction with the above embodiments, that the foregoing description and examples are intended to illustrate and not limit the scope of the disclosure. Other aspects, advantages and modifications within the scope of the disclosure will be apparent to those skilled in the art to which the disclosure pertains.

WHAT IS CLAIMED IS:

1. A compound of Formula I:



or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein:

n is 0, 1, or 2;

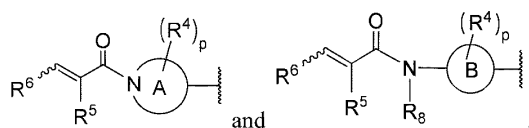
R¹ is OR¹², halo, cyano, C₁-₄ alkoxy, N(R²)₂, or C(O)CH(C₁-₄ alkyl)N(R²)₂;

each R² is independently hydrogen, C₁-₄ alkyl, or C₃-₆ cycloalkyl, wherein each alkyl or cycloalkyl is unsubstituted or substituted with one to three Z¹;

each R³ is independently halo, cyano, C₁-₆ alkyl, or C₁-₃ haloalkyl;

L¹ is a bond, C₁-₄ alkylene, -C₁-₄ alkylene-heteroaryl-, C₂-₃ alkenylene, C₂-₃ alkynylene, or -C(O)-;

X is selected from:



p is 0, 1, or 2;

Ring A is a monocyclic, spirocyclic, fused bicyclic, or bridged bicyclic 4-10 membered heterocyclyl or a monocyclic or fused bicyclic 5-10 membered heteroaryl;

Ring B is a monocyclic, spirocyclic, fused bicyclic, or bridged bicyclic 3-10 membered cycloalkyl, a monocyclic, spirocyclic, fused bicyclic, or bridged bicyclic 4-10 membered heterocyclyl, or a monocyclic or fused bicyclic 5-10 membered heteroaryl; wherein the nitrogen atom and L¹ may be attached anywhere on Ring B, including on the same carbon;

each R⁴ is independently oxo, halo, cyano, -NO₂, -SF₅, C₁-₆ alkyl, C₂-₆ alkenyl, C₂-₆ alkynyl, C₃-₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, -C(O)R¹¹, -C(O)OR¹¹, -S(O)₀-₂R¹¹, -NR¹¹S(O)₀-₂R¹¹, -S(O)₀-₂N(R¹¹)₂, -NR¹¹S(O)₀-₂N(R¹¹)₂, -NR¹¹C(O)N(R¹¹)₂, -C(O)N(R¹¹)₂, -NR¹¹C(O)R¹¹, -OC(O)N(R¹¹)₂, or -NR¹¹C(O)OR¹¹; wherein each C₁-₆ alkyl, C₂-₆ alkenyl, C₂-₆ alkynyl, C₃-₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z¹;

R⁵ is hydrogen, halo, cyano, or C₁-₆ alkyl optionally substituted with one to three Z¹;

R⁶ is hydrogen, halo, cyano, C₁-₆ alkyl, C₂-₆ alkenyl, C₂-₆ alkynyl, C₃-₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, -C(O)R¹¹, -C(O)OR¹¹, -S(O)₀-₂R¹¹, -NR¹¹S(O)₀-₂R¹¹, -S(O)₀-₂N(R¹¹)₂, -NR¹¹S(O)₀-₂N(R¹¹)₂, -NR¹¹C(O)N(R¹¹)₂, -C(O)N(R¹¹)₂, -NR¹¹C(O)R¹¹, -OC(O)N(R¹¹)₂, or

-NR¹¹C(O)OR¹¹; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z¹;

R⁷ is hydrogen, halo, cyano, -NO₂, -SF₅, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, -C(O)R¹¹, -C(O)OR¹¹, -S(O)₀₋₂R¹¹, -NR¹¹S(O)₀₋₂R¹¹, -S(O)₀₋₂N(R¹¹)₂, -NR¹¹S(O)₀₋₂N(R¹¹)₂, -NR¹¹C(O)N(R¹¹)₂, -C(O)N(R¹¹)₂, -NR¹¹C(O)R¹¹, -OC(O)N(R¹¹)₂, or -NR¹¹C(O)OR¹¹; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z¹;

R⁸ is hydrogen or C₁₋₆ alkyl optionally substituted with one to three Z¹;

R⁹ is hydrogen, -C(O)R¹³, -C(R¹³)₂OC(O)R¹⁵, -C(O)OCH₂OC(O)R¹⁵, -C(O)OCH(CH₃)OC(O)R¹⁵, -C(O)OCH₂OC(O)R¹⁵, -C(O)OCH(CH₃)OC(O)R¹⁵, -(CH₂)_mOP(O)(OR¹⁴)₂, -CH(CH₃)OP(O)(OR¹⁴)₂, -(CH₂)_mOP(O)(R¹⁴)(OR¹⁴), -CH(CH₃)OP(O)(R¹⁴)(OR¹⁴), -(CH₂)_mOP(O)(N(R¹⁴)₂)(OR¹⁴), -CH(CH₃)OP(O)(N(R¹⁴)₂)(OR¹⁴), -(CH₂)_mOP(O)(R¹⁴)(N(R¹⁴)₂), -(CH₂)_mOP(O)(N(R¹⁴)₂)₂, or -C(CH₃)OP(O)(N(R¹⁴)₂)₂;

m is 1 or 2;

each Z¹ is independently halo, cyano, -NO₂, -SF₅, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, -P(O)(OR¹¹)₂, -C(O)R¹¹, -C(O)OR¹¹, -S(O)₀₋₂R¹¹, -NR¹¹S(O)₀₋₂R¹¹, -S(O)₀₋₂N(R¹¹)₂, -NR¹¹S(O)₀₋₂N(R¹¹)₂, -NR¹¹C(O)N(R¹¹)₂, -C(O)N(R¹¹)₂, -NR¹¹C(O)R¹¹, -OC(O)N(R¹¹)₂, or -NR¹¹C(O)OR¹¹; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1a};

each R¹¹ is independently hydrogen, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1a};

each Z^{1a} is independently hydroxy, halo, cyano, -NO₂, -SF₅, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹³)₂, -OR¹³, -P(O)(OR¹³)₂, -C(O)R¹³, -C(O)OR¹³, -S(O)₀₋₂R¹³, -NR¹³S(O)₀₋₂R¹³, -S(O)₀₋₂N(R¹³)₂, -NR¹³S(O)₀₋₂N(R¹³)₂, -NR¹³C(O)N(R¹³)₂, -C(O)N(R¹³)₂, -NR¹³C(O)R¹³, -OC(O)N(R¹³)₂, or -NR¹³C(O)OR¹³; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1b};

R¹² is hydrogen, -C(O)R¹³, -C(O)N(R¹⁴)₂, -P(O)(OR¹⁴)₂, -CH₂OP(O)(OR¹⁴)₂, -CH(CH₃)OP(O)(OR¹⁴)₂, -P(O)(R¹⁴)(OR¹⁴), -CH₂OP(O)(R¹⁴)(OR¹⁴), -CH(CH₃)OP(O)(R¹⁴)(OR¹⁴), -P(O)(N(R¹⁴)₂)(OR¹⁴), -CH₂OP(O)(N(R¹⁴)₂)(OR¹⁴), -CH(CH₃)OP(O)(N(R¹⁴)₂)(OR¹⁴), -P(O)(R¹⁴)(N(R¹⁴)₂), -CH₂OP(O)(R¹⁴)(N(R¹⁴)₂), -CH(CH₃)OP(O)(R¹⁴)(N(R¹⁴)₂), -P(O)(N(R¹⁴)₂)₂, -CH₂OP(O)(N(R¹⁴)₂)₂, or -CH(CH₃)OP(O)(N(R¹⁴)₂)₂;

each R¹³ is independently hydrogen, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl; wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl,

C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to five Z^{1b};

each R¹⁴ is independently hydrogen, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, aryl, heteroaryl, or heterocyclyl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, or heterocyclyl is independently optionally substituted with one to five Z^{1b}; or two R¹⁴ together with the atom to which they are attached form a heterocyclyl; wherein said heterocyclyl is independently optionally substituted one to five Z^{1b};

R¹⁵ is independently R¹⁶, -OR¹⁶, -SR¹⁶, or -N(R¹⁶)₂;

each R¹⁶ is independently hydrogen, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, aryl, heteroaryl, or heterocyclyl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, or heterocyclyl is independently optionally substituted with one to five Z^{1b};

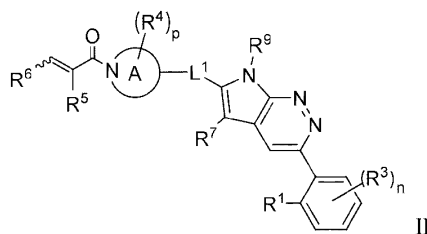
each Z^{1b} is independently halo, cyano, hydroxy, -SH, -NH₂, -NO₂, -SF₅, -P(O)(OH)₂, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -L-C₁₋₆ alkyl, -L-C₂₋₆ alkenyl, -L-C₂₋₆ alkynyl, -L-C₁₋₆ haloalkyl, -L-C₃₋₁₀ cycloalkyl, -L-heterocyclyl, -L-aryl, or -L-heteroaryl; and

each L is independently -O-, -NH-, -S-, -S(O)-, -S(O)₂-, -N(C₁₋₆ alkyl)-, -N(C₂₋₆ alkenyl)-, -N(C₂₋₆ alkynyl)-, -N(C₁₋₆ haloalkyl)-, -N(C₃₋₁₀ cycloalkyl)-, -N(heterocyclyl)-, -N(aryl)-, -N(heteroaryl)-, -C(O)-, -C(O)O-, -C(O)NH-, -C(O)N(C₁₋₆ alkyl)-, -C(O)N(C₂₋₆ alkenyl)-, -C(O)N(C₂₋₆ alkynyl)-, -C(O)N(C₁₋₆ haloalkyl)-, -C(O)N(C₃₋₁₀ cycloalkyl)-, -C(O)N(heterocyclyl)-, -C(O)N(aryl)-, -C(O)N(heteroaryl)-, -NHC(O)-, -NHC(O)O-, -NHC(O)NH-, -NHS(O)-, -S(O)₂NH-, -P(O)(OH)O-, -P(O)(O-C₁₋₆ alkyl)O-, -P(O)(O-C₂₋₆ alkenyl)O-, -P(O)(O-C₂₋₆ alkynyl)O-, -P(O)(OC₁₋₆ haloalkyl)O-, -P(O)(OC₃₋₁₀ cycloalkyl)O-, -P(O)(O-heterocyclyl)O-, -P(O)(O-aryl)O-, or -P(O)(O-heteroaryl)O-;

wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, and heteroaryl of Z^{1b} and L is further independently optionally substituted with one to five hydroxy, halo, cyano, hydroxy, -SH, -NH₂, -NO₂, -SF₅, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkoxy, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl;

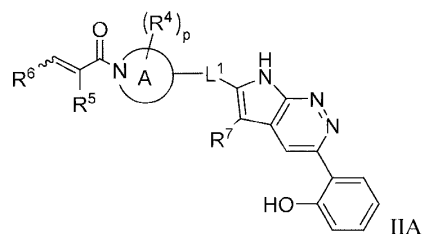
and wherein the compound is not 1-[3-[3-(2-Hydroxyphenyl)-7H-pyrrolo[2,3-c]pyridazin-6-yl]-1-azetidinyl]-2-propen-1-one.

2. The compound of claim 1, of Formula II:



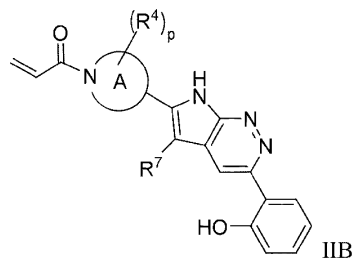
or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof.

3. The compound of claim 2, of Formula IIA:



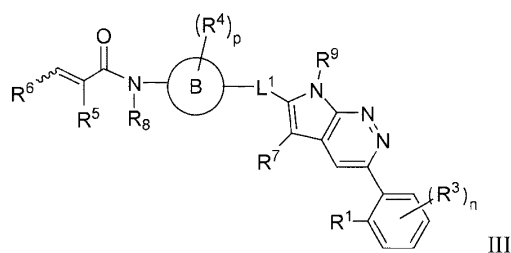
or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof.

4. The compound of claim 3, of Formula IIB:



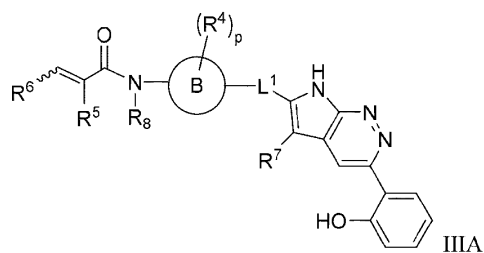
or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof.

5. The compound of claim 1, of Formula III:



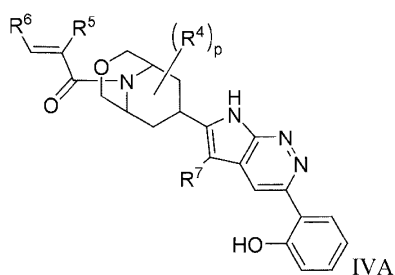
or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof.

6. The compound of claim 5, of Formula IIIA:



or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof.

7. The compound of claim 6, of Formula IVA:



or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof.

8. The compound of any one of claims 1, 2, or 5, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein R¹ is hydroxy.

9. The compound of any one of claims 1, 2, or 5, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein R⁹ is hydrogen.

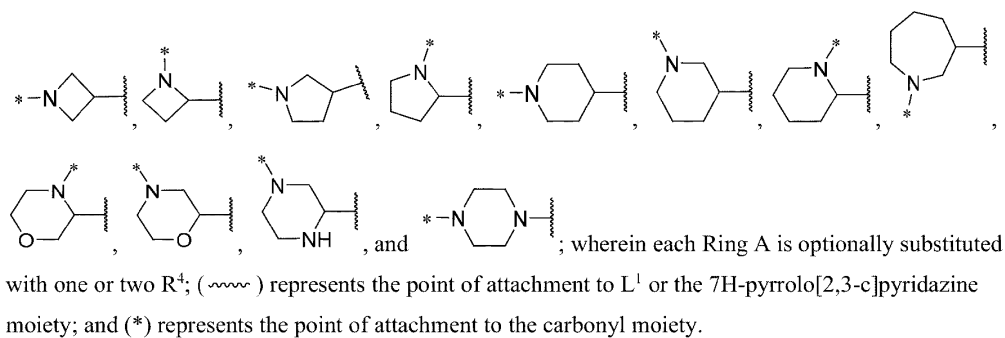
10. The compound of any one of claims 1-3, 5, 6, or 8-9, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein L¹ is a bond.

11. The compound of any one of claims 1-3, 5, 6, or 8-9, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein L¹ is -CH₂-, -C(O)-, -CH₂-heteroaryl, or ethynyl.

12. The compound of claim 11, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein L¹ is -CH₂-.

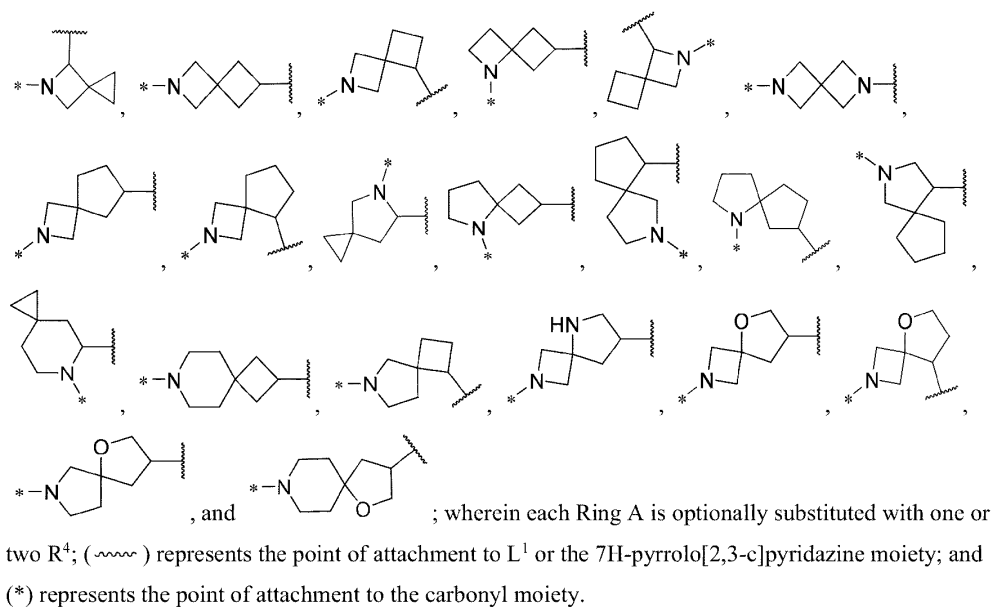
13. The compound of any one of claims 1-4, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein Ring A is a monocyclic 4-10 membered heterocyclyl optionally substituted with one or two R⁴.

14. The compound of claim 13, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein Ring A is selected from:



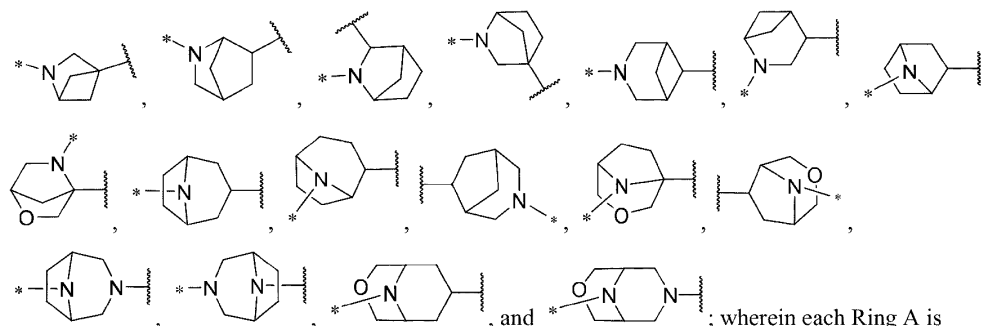
15. The compound of any one of claims 1-4, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein Ring A is a spirocyclic 4-10 membered heterocyclyl optionally substituted with one or two R⁴.

16. The compound of claim 15, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein Ring A is selected from:



17. The compound of any one of claims 1-4, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein Ring A is a bridged bicyclic 4-10 membered heterocyclyl optionally substituted with one or two R⁴.

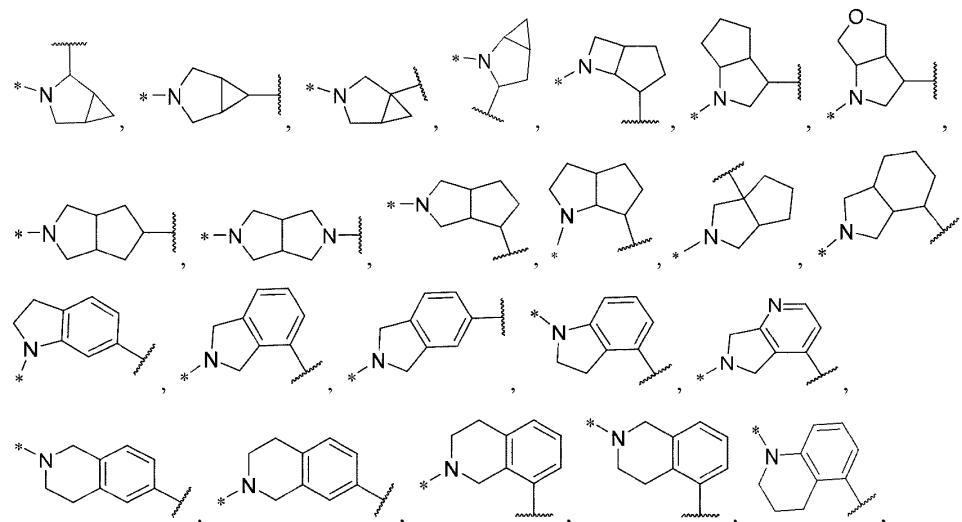
18. The compound of claim 17, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein Ring A is selected from:

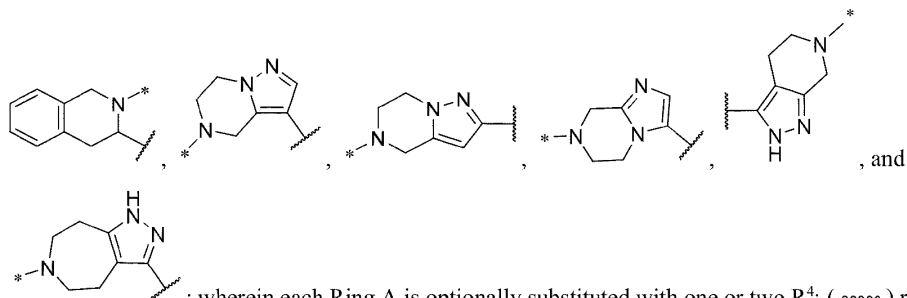


optionally substituted with one or two R⁴; (~~~~~) represents the point of attachment to L¹ or the 7H-pyrrolo[2,3-c]pyridazine moiety; and (*) represents the point of attachment to the carbonyl moiety.

19. The compound of any one of claim 1-4, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein Ring A is a fused bicyclic 4-10 membered heterocyclyl optionally substituted with one or two R⁴.

20. The compound of claim 19, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein Ring A is selected from:

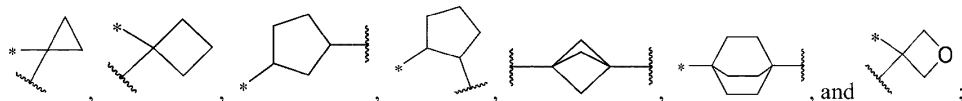




; wherein each Ring A is optionally substituted with one or two R^4 ; (~~~~) represents the point of attachment to L^1 or the 7H-pyrrolo[2,3-c]pyridazine moiety; and (*) represents the point of attachment to the carbonyl moiety.

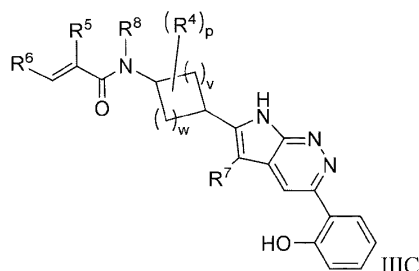
21. The compound of any one of claims 1 or 5-7, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein Ring B is a monocyclic or bridged bicyclic 3-10 membered cycloalkyl or monocyclic 4-10 membered heterocyclyl; wherein each 3-10 membered cycloalkyl or monocyclic 4-10 membered heterocyclyl is optionally substituted with one or two R^4 .

22. The compound of claim 21, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein Ring B is selected from:

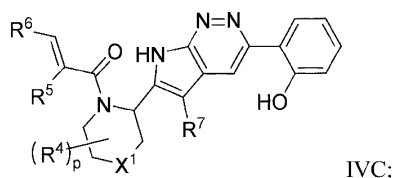
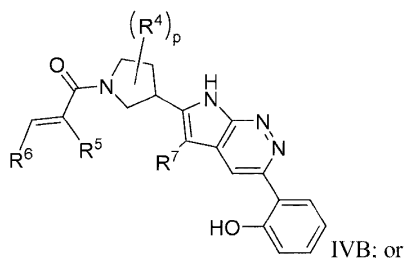
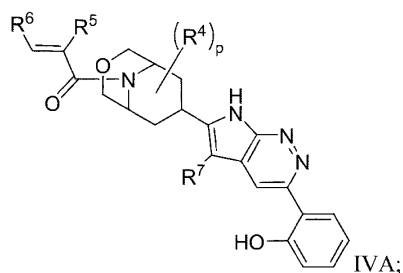


wherein each Ring B is optionally substituted with one or two R^4 ; (~~~~) represents the point of attachment to L^1 or the 7H-pyrrolo[2,3-c]pyridazine moiety; and (*) represents the point of attachment to the nitrogen atom.

23. The compound of claim 1, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein the compound is represented by Formula IIIC, Formula IVA, Formula IVB, or Formula IVC:



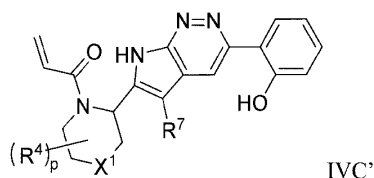
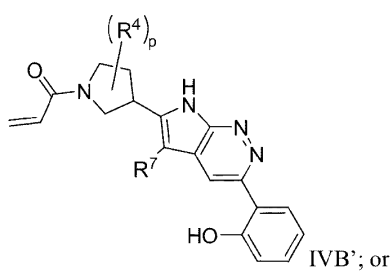
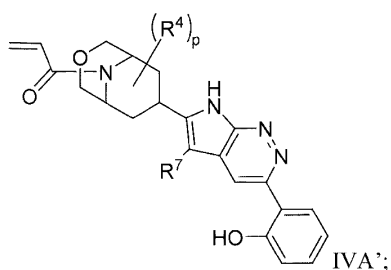
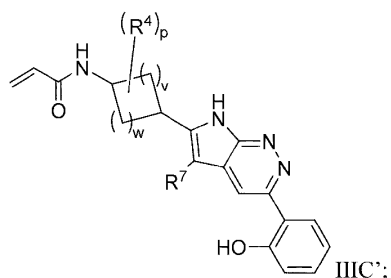
wherein v and w are each independently 0, 1, 2, 3, or 4; provided that the sum of v and w is at least 1;



wherein X^1 is O or CH_2 .

24. The compound of any one of claim 1-23, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein R^5 is hydrogen.
25. The compound of any one of claims 1-24, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein R^6 is hydrogen.
26. The compound of any one of claims 1-24, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein R^6 is halo, cyano, C_{3-10} cycloalkyl, or C_{1-6} alkyl optionally substituted with one to eight Z^1 .
27. The compound of claim 26, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein R^6 is C_{1-6} alkyl optionally substituted with halo, $-N(R^{11})_2$, or heterocyclyl optionally substituted with one to five Z^{1a} .
28. The compound of any one of claims 1-27, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein R^8 is hydrogen.

29. The compound of claim 1, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein the compound is represented by Formula IIIC, Formula IVA', Formula IVB', or Formula IVC':



wherein X¹ is O or CH₂.

30. The compound of any one of claims 1-29, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein p is 1 or 2.

31. The compound of any one of claims 1-30, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein each R⁴ is independently halo, cyano, C₁₋₆ alkyl, -OR¹¹, or -C(O)N(R¹¹)₂, wherein each C₁₋₆ alkyl is independently optionally substituted with one to eight Z¹.

32. The compound of any one of claims 1-29, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein p is 0.
33. The compound of any one of claims 1-32, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein R⁷ is hydrogen, halo, cyano, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, heteroaryl, -N(R¹¹)₂, -OR¹¹, -C(O)R¹¹, or -C(O)N(R¹¹)₂, wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, heterocyclyl, aryl, or heteroaryl is independently optionally substituted with one to eight Z¹.
34. The compound of any one of claims 1-33, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein R⁷ is hydrogen.
35. The compound of any one of claims 1-33, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein R⁷ is halo.
36. The compound of any one of claims 1-33, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein R⁷ is C₁₋₆ alkyl, C₂₋₆ alkenyl, or C₂₋₆ alkynyl, wherein each C₁₋₆ alkyl, C₂₋₆ alkenyl, or C₂₋₆ alkynyl is independently optionally substituted with one to three Z¹.
37. The compound of any one of claims 1-33, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein R⁷ is C₃₋₁₀ cycloalkyl or heterocyclyl, wherein each C₃₋₁₀ cycloalkyl or heterocyclyl is independently optionally substituted with one to three Z¹.
38. The compound of any one of claims 1-33, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, wherein R⁷ is phenyl or 5-6 membered heteroaryl, wherein each phenyl or 5-6 membered heteroaryl is independently optionally substituted with one to three Z¹.
39. A compound, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof, selected from Table 1 or Table 2.
40. A pharmaceutical composition comprising a pharmaceutically acceptable excipient and an effective amount of a compound of any one of claims 1-39, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof.

41. A method for modulating or degrading protein which is expressed from the SMARCA2 gene, which method comprises contacting the protein with an effective amount of a compound according to any one of claims 1-39, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof.

42. A method for modulating or degrading protein which is expressed from the SMARCA4 gene, which method comprises contacting the protein with an effective amount of a compound according to any one of claims 1-39, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof.

43. A method for modulating or degrading protein which is expressed from the SMARCA2 gene in a subject, which method comprises administering to said subject an effective amount of a compound according to any one of claims 1-39, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof.

44. A method for modulating or degrading protein which is expressed from the SMARCA4 gene in a subject, which method comprises administering to said subject an effective amount of a compound according to any one of claims 1-39, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof.

45. A method for modulating or degrading protein which is expressed from the SMARCA2 gene in a subject, which method comprises administering to said subject an effective amount of a pharmaceutical composition according to claim 40.

46. A method for modulating or degrading protein which is expressed from the SMARCA4 gene in a subject, which method comprises administering to said subject an effective amount of a pharmaceutical composition according to claim 40.

47. A method for treating cancer in a subject in need thereof, which method comprises administering to said subject an effective amount of a compound according to any one of claims 1-39, or a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof.

48. A method for treating cancer in a subject in need thereof, which method comprises administering to said subject an effective amount of a pharmaceutical composition according to claim 40.

49. A method for treating hyperplasia in a subject in need thereof, which method comprises administering to said subject an effective amount of a compound according to any one of claims 1-39, or

a pharmaceutically acceptable salt, solvate, stereoisomer, isotopically enriched analog, or tautomer thereof.

50. A method for treating hyperplasia in a subject in need thereof, which method comprises administering to said subject an effective amount of a pharmaceutical composition according to claim 40.