INHIBITORS OF NLRP3

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of, and priority to PCT application number PCT/US2022/075421, filed August 24, 2022, and U.S. Provisional Patent Application No. 63/311,463 filed on February 18, 2022, the contents of which are herein incorporated by reference in their entirety and for all purposes.

FIELD OF THE INVENTION

The present invention relates to compounds that are useful as inhibitors of NOD-like receptor protein 3 (NLRP3) inflammasome pathway. The present invention also relates to processes for the preparation of said compounds, pharmaceutical compositions comprising said compounds, methods of using said compounds in the treatment of various diseases and disorders, and medicaments containing them, and their use in diseases and disorders mediated by NLRP3.

BACKGROUND

The term of inflammasome was coined by Martinon et al. to describe the molecular platform triggering activation of inflammatory caspases and processing of interleukin 1 (IL-1) family cytokines (Fabio Martinon et al., *Mol Cell* 10(2):417-26, 2002). Inflammasomes are part of the innate immune system. Inflammasome activation is initiated by assembling of a multiprotein complex, including nucleotide binding oligomerization domain (NOD)-like receptor (NLR), the adapter apoptosis-associated speck-like protein containing a caspase recruitment domain (ASC), and the effector protease caspase-1. The assemble of the complex results in the activation of caspase-1 and the release of the mature proinflammatory cytokines, such as IL-1β and IL-18.

Among inflammasomes, the NLR family NACHT, LRR and PYD domains-containing protein 3 (NLRP3) inflammasome has been studied extensively and was found to be activated by a wide spectrum of stimuli. The regulatory mechanisms of NLRP3 activation are summarized in a recent review paper (Seungwha Paik et al., *Cell Mol Immunol* 18(5):1141-1160, 2021).

NLRP3 activation is triggered by various infectious, non- infectious molecules, including molecular byproducts of aging, physical inactivity and overnutrition. Once activated, it boosts

the downstream production of the inflammatory cytokines IL-1β and IL-18. Gain-of function mutations of NLRP3 are associated with several genetic disorders including cryopyrin-associated periodic syndromes (CAPS). Additionally, NLRP3 is implicated in numerous common I) autoimmune, II) autoinflammatory, III) neurodegenerative, IV) cardiovascular and V) neuromuscular and muscular degenerative diseases e.g. (Matthew S J Mangan et al., *Nat Rev Drug Discov* 17(8):588-606, 2018; Corcoran et al., *Pharmacol Rev* 73(3):968-1000, 2021; Dubuisson et al., *Cells* 10(11):3023, 2021). Inflammasome activation has also been identified in retinal pigment epithelium (RPE) cells and proposed to be a causal factor for RPE dysfunction and degeneration (Gao et al., *Mediators Inflamm* 2015:690243, 2015). Further, NLRP3 activation is associated with severe COVID-19 cases and cytokine release syndrome (CRS) caused by cell-based therapeutics and biologic treatments (Tracey L Freeman and Talia H Swartz *Front Immunol* 11:1518, 2020; Lin et al., *PLoS Pathog* 6;15(6):e1007795, 2019).

Therefore, an NLRP3 inflammasome inhibitor could be used as a single or combination of agents clinically as novel therapies for these diseases. Thus, there is a need for inhibitors of the NLRP3 inflammasome pathway to provide new and/or alternative treatments for these inflammasome-related diseases, disorders , such as autoinflammatory fever syndrome cryopyrin-associated periodic syndrome (CAPS), sickle cell disease, chronic liver disease, nonalcoholic steatohepatitis (NASH), gout, hyperoxaluria, pseudogout (chondrocalcinosis), Type I/Type II diabetes and related complications (e.g. nephropathy, retinopathy), fibrosis, rheumatoid arthritis, inflammatory bowel diseases, asthma and allergic airway inflammation, neuroinflammation-related disorders (e.g. multiple sclerosis, brain infection, acute injury, Alzheimer's disease, Parkinson's disease, Huntington's disease), neuromuscular and muscular degenerative diseases, atherosclerosis and cardiovascular risk (e.g. cardiovascular risk reduction (CvRR), hypertension), hidradenitis suppurativa, wound healing and scar formation, and cancer (e.g. colon cancer, lung cancer, myeloproliferative neoplasms, leukemias, myelodysplastic syndromes (MDS), myelofibrosis).

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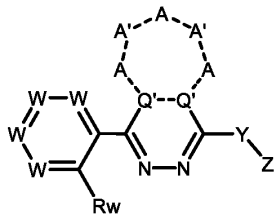
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SUMMARY OF THE INVENTION

The invention provides compounds or pharmaceu-tically acceptable salts thereof, pharmaceutical compositions thereof, which compounds inhibit the NLRP3 inflammasome pathway. The invention further provides methods of treating, or preventing, disease and/or disorders related to NLRP3, comprising administering to a subject in need thereof an effective amount of the compounds of the invention, or a pharmaceutically acceptable salt thereof.

Various aspects of the invention are described herein.

The instant application discloses a compound of Formula I:



I

wherein:

R_w is hydrogen, $C_{1\text{-}6}$alkyl (e.g., CH_3), $C_{2\text{-}8}$alkynyl, halogen (e.g., F, Cl), $C_{1\text{-}6}$alkoxy (e.g., OCH_3), halo-$C_{1\text{-}4}$alkyl (e.g., CHF_2, CF_3), halo-$C_{1\text{-}4}$alkoxy (e.g., $OCHF_2$, OCF_3), cyano, $-NH_2$, $-N(C_{1\text{-}6}alkyl)_2$, thiol, $-SO_2NH_2$, $-SO_2N(C_{1\text{-}6}alkyl)_2$, $-S(=O)(C_{1\text{-}6}alkyl)$, cycloalkyl, CHR_{1a}, $(C=O)R_{1a}$, OR_{1a}, NR_{1b}, $S(=O)R_{1a}$, $S(=O)_2R_{1a}$, $O(C=O)R_{1a}$, $(C=O)OR_{1a}$, $NR_{1b}(C=O)R_{1b}$, $(C=O)NR_{1b}$, $(C=O)N(R_{1b})_2$ $NR_{1b}(C=O)OR_{1a}$, $O(C=O)NR_{1b}$, $ONR_{1b}(C=NR_{1b})NR_{1b}$, $NR_{1b}S(=O)_2$ or $S(=O)_2NR_{1b}$, wherein each $C_{1\text{-}6}$alkyl, heterocycle (e.g., 2, 5-dihydrofuran-3-yl), heteroaryl and aryl are optionally substituted with 1 or 2 substituents each selected from R_5;

each W is independently CH, CR' or N;

each Q' is independently N, C or CH;

each A is independently CH, CH_2, CR_a, CHR_a, CR_4, CHR_4, N, NH, NR_a, NR_4, S, or O;

each A' is independently absent, CH, CH_2, CR_a, CHR_a, CR_4, CHR_4, N, NH, NR_a, NR_4, S, or O;

each R_a is independently hydrogen, deuterium, halogen, -CN, -OH, -OR_2, =O, =N-OR_2, -SR_2, -S(=O)R_2, -$S(=O)_2R_2$, -$N(R_2)_2$, -$NR_2S(=O)(=NR_2)R_2$, -$NR_2S(=O)_2R_2$, -$S(=O)_2N(R_2)_2$, -C(=O)R_2, -OC(=O)R_2, -C(=O)OR_2, -OC(=O)OR_2, -C(=O)$N(R_2)_2$, -OC(=O)$N(R_2)_2$, -$NR_2C(=O)R_2$, -$P(=O)(R_2)_2$, C_{1-4}alkyl, $(C_{1-4}alkyl)_2$, halo-C_{1-6}alkyl, C_{1-6}heteroalkyl, C_{3-8}cycloalkyl, C_{2-7}heterocycloalkyl, aryl or monocyclic heteroaryl;

each--represents either an absent, single, or double bond;

Y is $C(R_{1a})_2$, C=O, O, NR_{1b}, or a bond;

each R_{1a} is independently hydrogen, halogen, hydroxyl, cyano, C_{1-4}alkyl, deutero-C_{1-4}alkyl, halo-C_{1-4}alkyl, amino or hydroxy-C_{1-4}alkyl, C_{3-10}cycloalkyl, C_{2-7}heterocycloalkyl or aryl;

each R_{1b} is independently hydrogen, C_{1-4}alkyl, deutero-C_{1-4}alkyl, halo-C_{1-4}alkyl or hydroxy-C_{1-4}alkyl;

each R' is independently heterocyclyl, heteroaryl, aryl, C_{3-8}cycloalkyl, C_{1-4}alkyl, C_{1-4}alkoxy, deutero-C_{1-4}alkyl, halo-C_{1-4}alkyl (e.g., trifluoromethyl, difluoromethyl), halo-C_{1-4}alkoxy (e.g., trifluoromethoxy), hydroxy-C_{1-4}alkyl, halogen, hydroxy or cyano,

each Z is heterocyclyl, heteroaryl, aryl, C_{3-10}cycloalkyl, C_{1-4}alkyl, deutero-C_{1-4}alkyl, halo-C_{1-4}alkyl, hydroxy-C_{1-8}alkyl, C_{1-6}alkoxy, NH(hydroxy-C_{1-6}alkyl), NH(C_{1-6}alkoxy) wherein each Z is optionally substituted with OH, NH_2, -CO_2H, halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6} hydroxyalkyl, C_{2-6}acyl, C_{2-6}alkanoic acid, C_{2-6}alkanoate ester, or heterocyclyl, and wherein heterocyclyl, C_{3-10}cycloalkyl is a saturated or partially unsaturated 3-7 membered monocyclic, 6-10 membered bicyclic or 13-16 membered polycyclic ring system having 1, 2, or 3 heteroatom ring members independently selected from N, O, and S, each optionally substituted with 1, 2, 3, 4, or 5 substituents each selected from R_2;

R_2 is independently selected from halogen, hydroxyl, cyano, C_{1-4}alkyl, hydroxy-C_{1-4}alkyl, deuterium-C_{1-4}alkyl, halo-C_{1-4}alkyl, amino, C_{1-4}alkylamino, $(C_1$-alkyl$)_2$amino, halo-C_{1-4}alkylamino, (halo-C_{1-6}alkyl$)_2$amino, hydroxy-C_{1-4}alkylamino, C_{1-4}alkoxy-C_{1-4}alkyl-amino, aminoC_{1-4}alkyl, C_{1-4}alkylaminoC_{1-4}alkyl, $(C_{1-4}$alkylamino$)_2C_{1-4}$alkyl, C_{1-4}alkoxy, halo-C_{1-4}alkoxy, hydroxy-C_{1-4}alkoxy, C_{1-4}alkyl-C_{1-4}alkoxy, C_{3-10}cycloalkyl, C_{3-10}cycloalkyl-amino, C_{3-10}cycloalkyl-amino-C_{1-4}alkyl, heteroarylC_{1-4}alkyl, heteroarylamino, heteroarylC_{1-4}alkyl-amino, heterocyclyl, heterocyclyl-C_{1-4}alkyl, heterocyclyl-amino, heterocyclyl-amino-C_{1-4}alkyl, heterocyclyl-C_{1-4}alkoxy, heterocyclyl-amino- C_{3-10}cycloalkyl, phenyl, and phenyl-C_{1-4}alkoxy,

wherein heteroaryl is a 5-6 membered monocyclic or 6-10 membered bicyclic ring system having 1, 2, 3, or 4 heteroatom ring members independently selected from N, O, or S,

wherein heterocyclyl is a saturated or partially unsaturated 3-7 membered monocyclic, 6-10 membered bicyclic or 13-16 membered polycyclic ring system having 1, 2, or 3 heteroatom ring members independently selected from N, O, and S,

wherein C_{3-10}cycloalkyl is a saturated or partially unsaturated 3-7 membered monocyclic ring system, and

wherein each instance of phenyl, heteroaryl, heterocyclyl, or C_{3-10}cycloalkyl is optionally substituted with 1 or 2 substituents each selected from R_3;

R_3 is independently selected from halogen, hydroxyl, cyano, C_{1-4}alkyl, deutero-C_{1-4}alkyl, halo-C_{1-4}alkyl, amino, C_{1-4}alkoxy, and halo-C_{1-4}alkoxy;

each R_4 is independently selected from halogen, hydroxyl, cyano, C_{1-4}alkyl, deutero-C_{1-4}alkyl, halo-C_{1-4}alkyl, amino, C_{1-4}alkylamino, $(C_{1-4}alkyl)_2$amino, C_{1-4}alkoxy, halo-C_{1-4}alkoxy, heteroaryl, heterocyclyl, and phenyl,

wherein heteroaryl is a 5-6 membered monocyclic or 9-10 membered bicyclic ring system having 1, 2, 3, or 4 heteroatom ring members selected from N, O, and S,

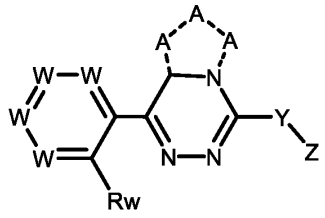
wherein heterocyclyl is a saturated or partially unsaturated 3-7 membered monocyclic or 9-10 membered bicyclic ring system having 1, 2, or 3 heteroatom ring members selected from N, O, and S, and

wherein each instance of phenyl, heteroaryl or heterocyclyl is optionally substituted with 1, or 2 substituents each selected from R_5;

R_5 is independently selected from halogen, hydroxyl, cyano, nitro, C_{1-4}alkyl, deutero-C_{1-4}alkyl, halo-C_{1-4}alkyl, amino, C_{1-4}alkylamino, $(C_{1-4}alkyl)_2$amino, aminoC_{1-4}alkyl, hydroxy-C_{1-4}alkyl, C_{1-4}alkylcarbonyl, C_{1-4}alkoxy, C_{1-4}alkylthio, halo-C_{1-4}alkoxy, and C_{3-10}cycloalkyl;

wherein a form of the compound is selected from the group consisting of a pharmaceutically acceptable salt, hydrate, solvate, racemate, enantiomer, diastereomer, stereoisomer, and tautomer form thereof.

Another aspect of the invention provides a compound having the structure of Formula II:



II

wherein:

each W is independently CH, CR' or N;

each A is independently CH, CH_2, CR_a, CR_4, N, NH or NR_4;

each--represents either a single, or double bond;

Y is NR_{1b} or a bond;

each R_w is hydrogen, halogen, C_{1-4}alkyl, C_{3-10}cycloalkyl, C_{3-10}cycloalkoxy, halo-C_{1-4}alkyl, C_{1-4}alkoxy, or halo-C_{1-4}alkoxy,

each R_{1b} is independently hydrogen, C_{1-4}alkyl, deutero-C_{1-4}alkyl, halo-C_{1-4}alkyl or hydroxy-C_{1-4}alkyl;

each Z is heterocyclyl, heteroaryl, aryl, C_{3-10}cycloalkyl, C_{1-4}alkyl, deutero-C_{1-4}alkyl, halo-C_{1-4}alkyl, hydroxy-C_{1-8}alkyl, NH(hydroxy-C_{1-6}alkyl), NH(C_{1-6}alkoxy) wherein each Z is optionally substituted with OH, NH_2, -CO_2H, halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6} hydroxyalkyl, C_{2-6}acyl, C_{2-6}alkanoic acid, C_{2-6}alkanoate ester, or heterocyclyl, and wherein heterocyclyl is a saturated or partially unsaturated 3-7 membered monocyclic, 6-10 membered bicyclic or 13-16 membered polycyclic ring system having 1, 2, or 3 heteroatom ring members independently selected from N, O, and S, each optionally substituted with 1, 2, 3, 4, or 5 substituents each selected from R_2;

R_2 is independently selected from halogen, hydroxyl, cyano, C_{1-4}alkyl, deutero-C_{1-4}alkyl, halo-C_{1-4}alkyl, amino, C_{1-4}alkylamino, (C_{1-6}alkyl)$_2$amino, halo-C_{1-4}alkylamino, (halo-C_{1-6}alkyl)$_2$amino, hydroxy-C_{1-4}alkylamino, C_{1-4}alkoxy-C_{1-4}alkyl-amino, aminoC_{1-4}alkyl, C_{1-4}alkylaminoC_{1-4}alkyl, (C_{1-4}alkylamino)$_2$$C_{1-4}$alkyl, C_{1-4}alkoxy, halo-C_{1-4}alkoxy, , C_{1-4}alkyl-C_{1-4}alkoxy, C_{3-10}cycloalkyl, C_{3-10}cycloalkyl-amino, C_{3-10}cycloalkyl-amino-C_{1-4}alkyl, heteroarylC_{1-4}alkyl, heteroarylamino, heteroarylC_{1-4}alkyl-amino, heterocyclyl, heterocyclyl-C_{1-4}alkyl,

heterocyclyl-amino, heterocyclyl-amino-C_{1-4}alkyl, heterocyclyl-C_{1-4}alkoxy, heterocyclyl-amino-C_{3-10}cycloalkyl, phenyl, and phenyl-C_{1-4}alkoxy,

wherein heteroaryl is a 5-6 membered monocyclic or 6-10 membered bicyclic ring system having 1, 2, 3, or 4 heteroatom ring members independently selected from N, O, and S,

wherein heterocyclyl is a saturated or partially unsaturated 3-7 membered monocyclic, 6-10 membered bicyclic or 13-16 membered polycyclic ring system having 1, 2, or 3 heteroatom ring members independently selected from N, O, and S,

wherein C_{3-10}cycloalkyl is a saturated or partially unsaturated 3-7 membered monocyclic ring system,

wherein each instance of phenyl, heteroaryl, heterocyclyl, or C_{3-10}cycloalkyl is optionally substituted with 1 or 2 substituents each selected from R_3;

R_3 is independently selected from halogen, hydroxyl, cyano, C_{1-4}alkyl, deutero-C_{1-4}alkyl, halo-C_{1-4}alkyl, amino, C_{1-4}alkoxy, and halo-C_{1-4}alkoxy;

R' is selected from H, substituted or unsubstituted cycloalkyl, C_{1-4}alkyl, halo-C_{1-4}alkyl, halo-C_{1-6}alkoxy, halogen, C_{1-6}alkoxy, cyano, hydroxy-C_{1-4}alkyl or aryl optionally substituted by C_{1-4}alkyl;

each R_a is independently H, deuterium, halogen, -CN, -OH, -OR_2, =O, =N-OR_2, -SR_2, -$S(=O)R_2$, -$S(=O)_2R_2$, -$N(R_2)_2$, -$NR_2S(=O)(=NR_2)R_2$, -$NR_2S(=O)_2R_2$, -$S(=O)_2N(R_2)_2$, -$C(=O)R_2$, -$OC(=O)R_2$, -$C(=O)OR_2$, -$OC(=O)OR_2$, -$C(=O)N(R_2)_2$, -$OC(=O)N(R_2)_2$, -$NR_2C(=O)R_2$, -$P(=O)(R_2)_2$, C_{1-4}alkyl, $(C_{1-4}alkyl)_2$, halo- C_{1-6}alkyl, C_{1-6}heteroalkyl, C_{3-8}cycloalkyl, C_{2-7}heterocycloalkyl, aryl or monocyclic heteroaryl; and

R_4 is independently selected from halogen, hydroxyl, cyano, or C_{1-4}alkyl;

wherein a form of the compound is selected from the group consisting of a pharmaceutically acceptable salt, hydrate, solvate, racemate, enantiomer, diastereomer, stereoisomer, tautomer, and isotope enriched form thereof.

The invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound according to the definition of the compound of Formula I or a form thereof, as disclosed herein, or a pharmaceutically acceptable salt thereof, and one or more pharmaceutically acceptable carriers. The pharmaceutical composition is useful in the treatment of diseases and/or disorders related to the NLRP3 activity. In another aspect, the invention

provides a combination, in particular a pharmaceutical combination, comprising a therapeutically effective amount of a compound according to the definition of compounds of Formula I, or sub-Formula thereof, as disclosed herein, or a pharmaceutically acceptable salt thereof, and one or more therapeutic agents. In another aspect, the invention provides a combination, in particular a pharmaceutical combination, as disclosed herein, for use as a medicament.

In another aspect, the invention provides a compound of Formula I, or sub-Formula thereof, as disclosed herein, or a pharmaceutically acceptable salt thereof, for use in the treatment of a disease or disorder in which the NLRP3 signaling contributes to the pathology, and/or symptoms, and/or progression, of said disease or disorder. In another aspect, the invention provides a method of treating a disease or disorder in which the NLRP3 signaling contributes to the pathology, and/or symptoms, and/or progression, of said disease or disorder, comprising administering a therapeutically effective amount of a compound of Formula I, or sub-Formula thereof, as disclosed herein, or a pharmaceutically acceptable salt thereof. In another aspect, the invention provides a method of inhibiting the NLRP3 inflammasome activity in a subject in need thereof, the method comprises administering to the subject in need thereof a therapeutically effective amount of a compound of Formula I or form thereof, as disclosed herein, or a pharmaceutically acceptable salt thereof.

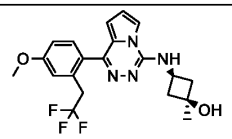
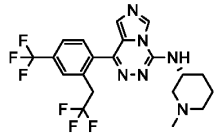
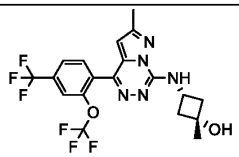
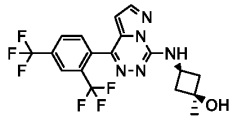
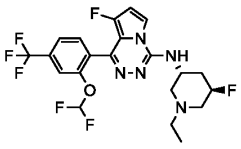
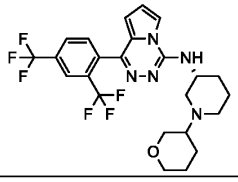
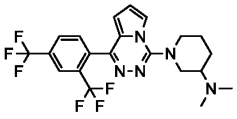
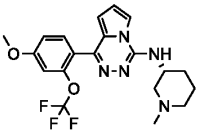
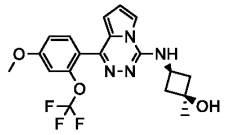
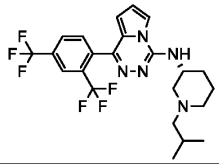
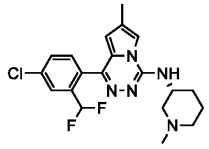
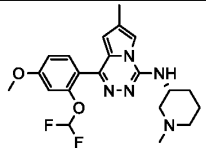
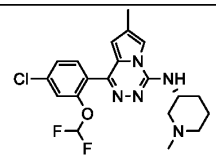
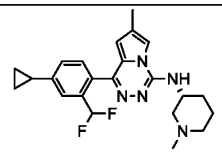
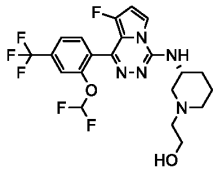
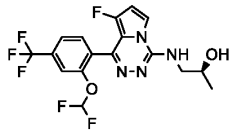
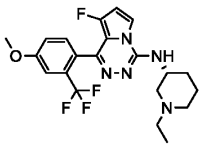
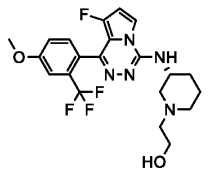
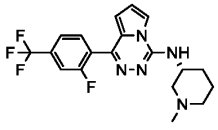
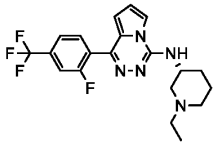
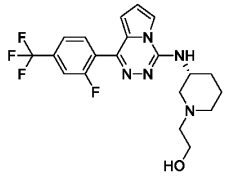
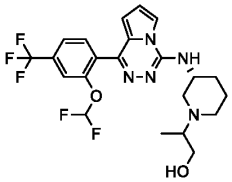
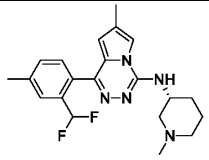
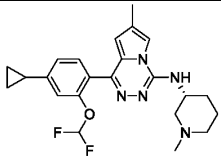
Another aspect of the invention relates to the use of a compound of Formula I, or sub-Formula thereof, as disclosed herein, or a pharmaceutically acceptable salt thereof, as a medicament.

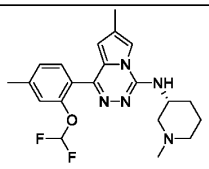
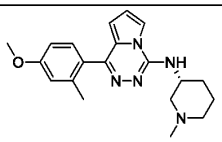
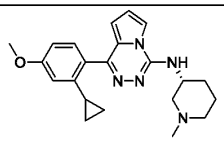
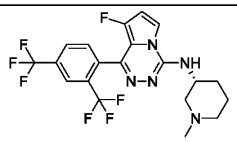
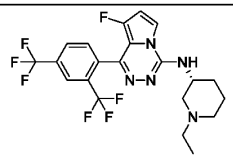
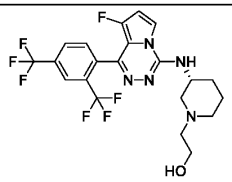
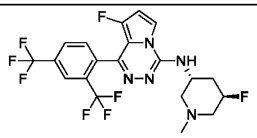
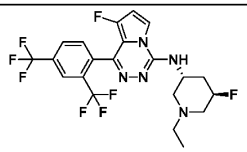
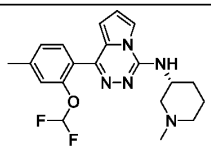
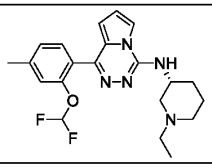
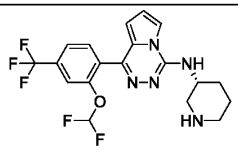
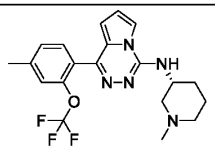
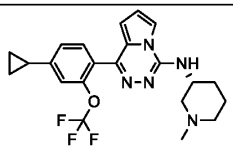
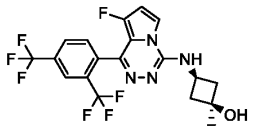
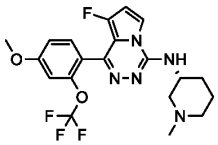
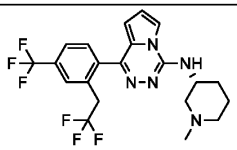
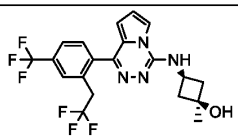
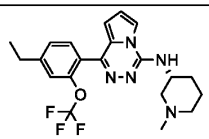
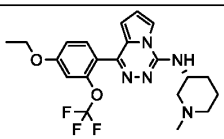
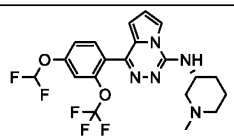
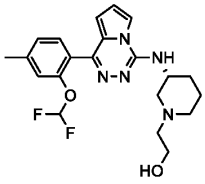
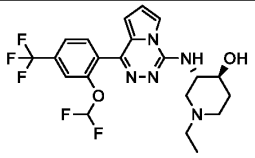
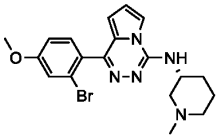
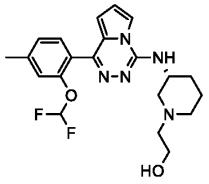
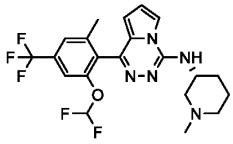
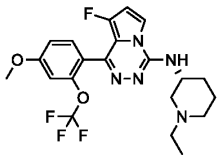
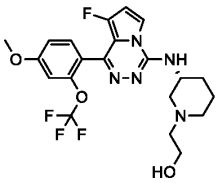
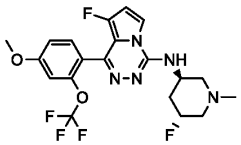
Another aspect of the invention relates to a compound of Formula I, or sub-Formula thereof, as disclosed herein, or a pharmaceutically acceptable salt thereof, for use as a medicament.

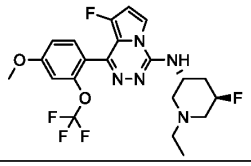
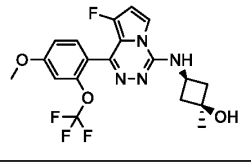
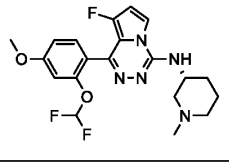
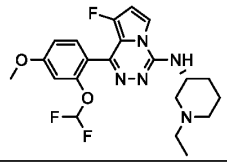
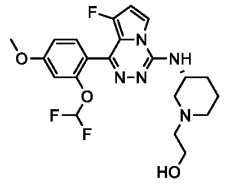
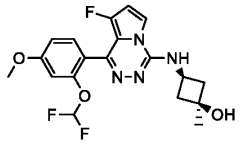
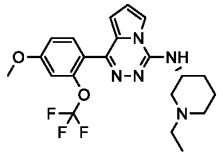
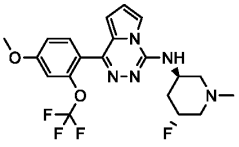
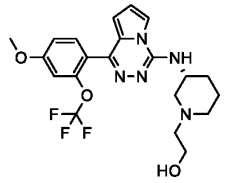
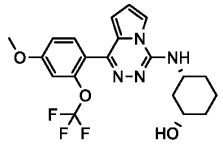
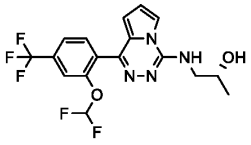
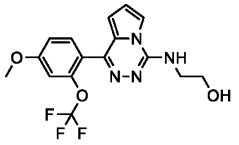
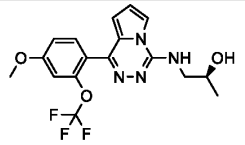
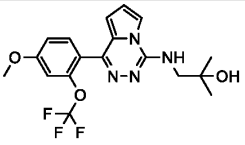
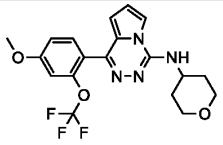
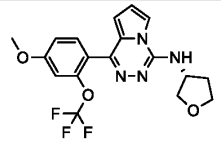
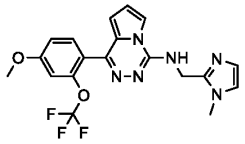
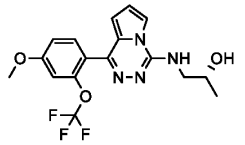
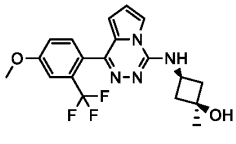
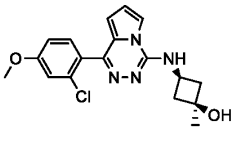
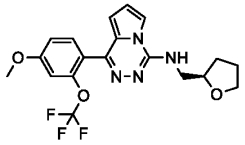
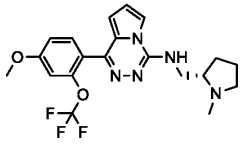
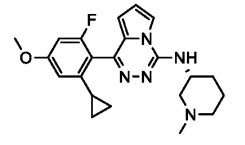
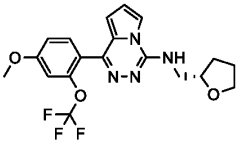
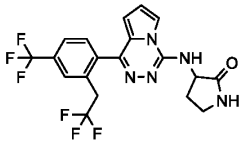
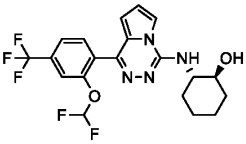
Another aspect of the invention also provides a compound of Formula I, or sub-Formula thereof, as disclosed herein, or a pharmaceutically acceptable salt thereof, for use in the treatment of a disease or disorder selected from inflammasome-related disease/disorders, immune diseases, inflammatory diseases, auto-immune diseases, and auto-inflammatory diseases.

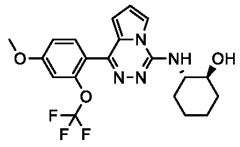
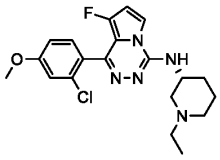
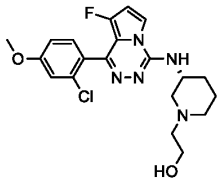
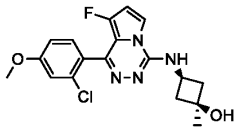
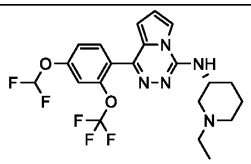
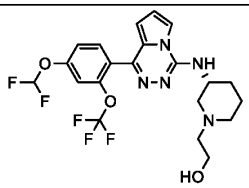
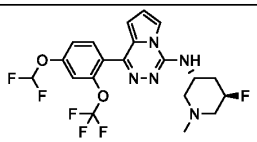
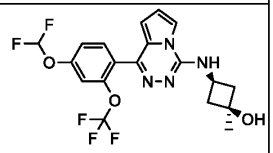
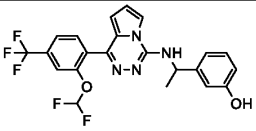
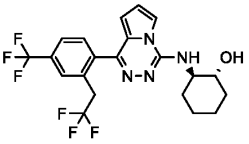
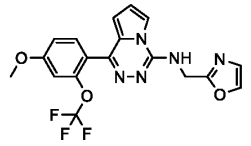
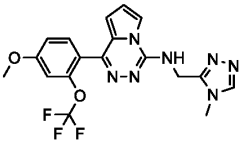
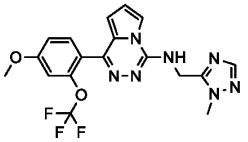
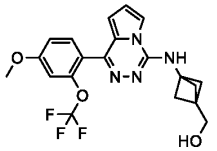
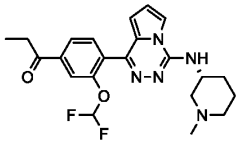
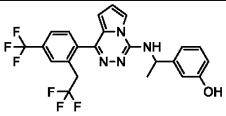
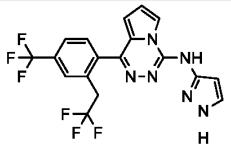
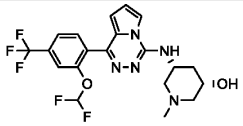
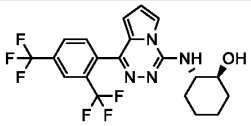
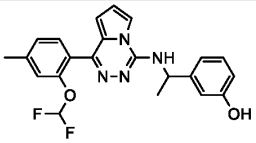
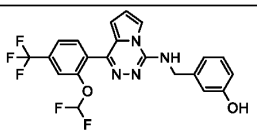
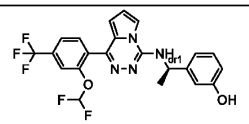
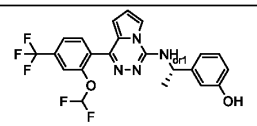
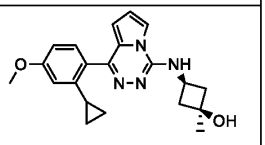
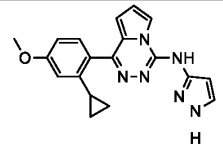
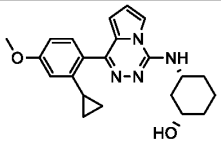
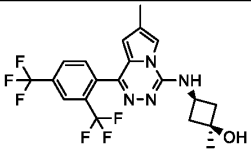
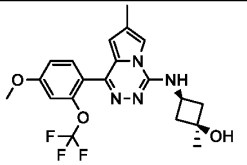
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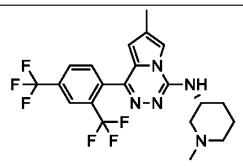
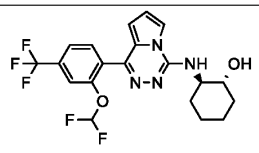
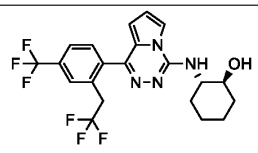
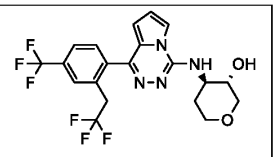
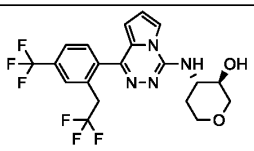
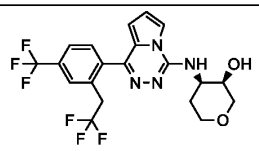
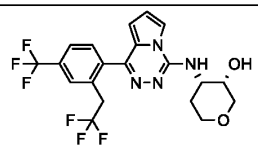
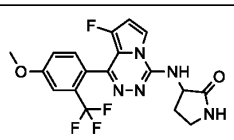
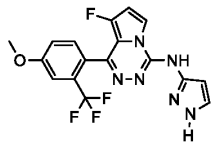
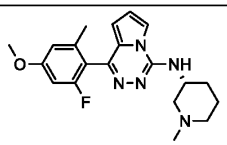
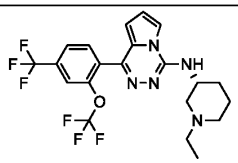
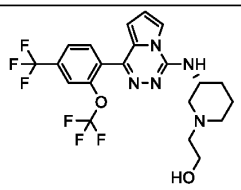
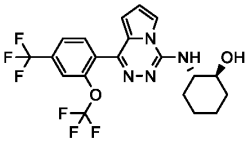
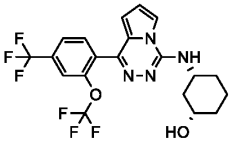
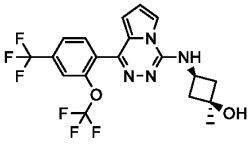
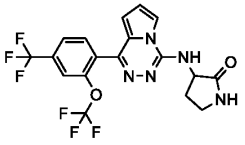
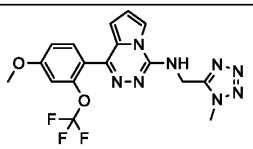
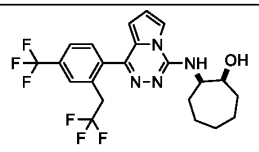
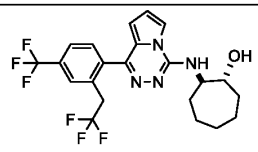
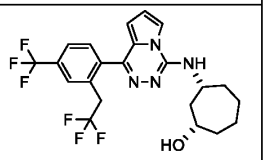
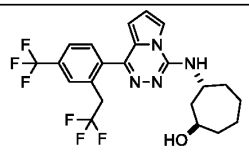
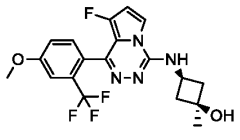
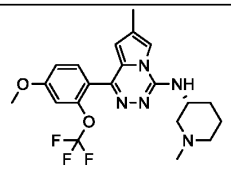
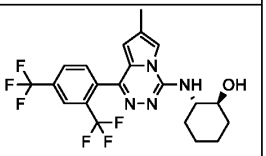
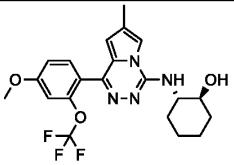
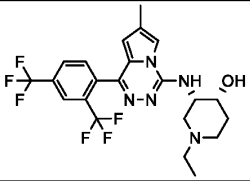
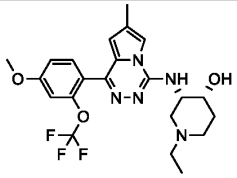
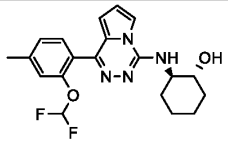
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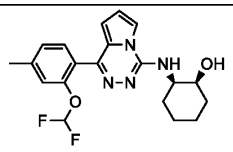
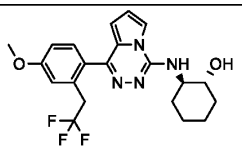
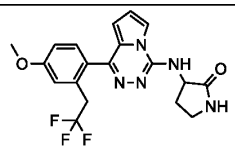
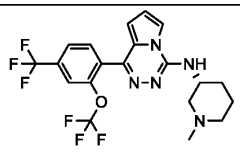
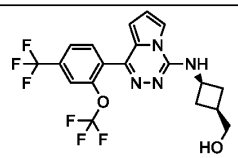
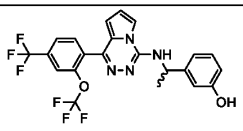
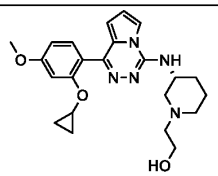
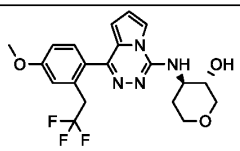
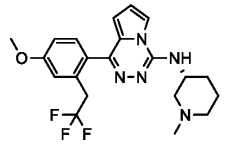
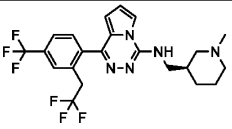
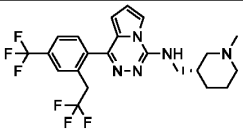
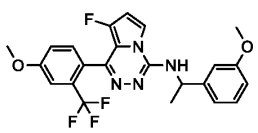
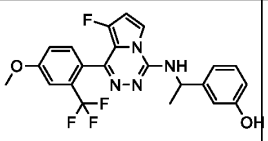
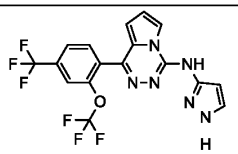
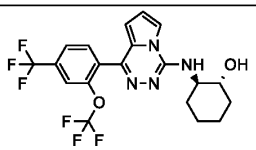
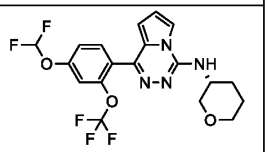
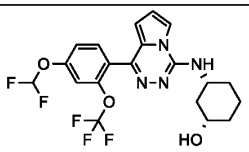
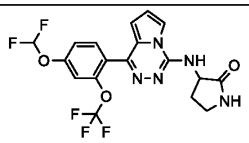
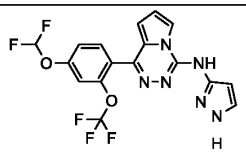
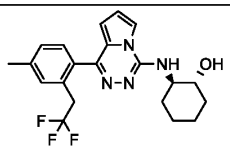
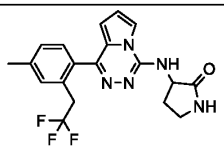
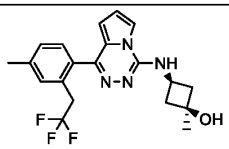
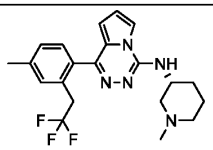
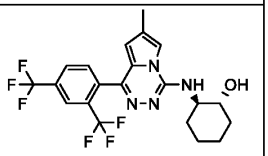
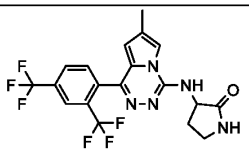
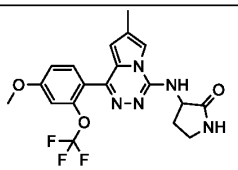
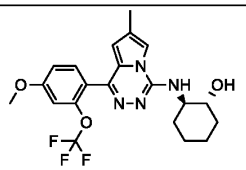
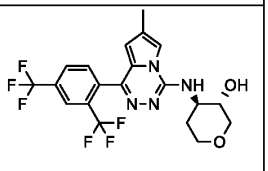
			
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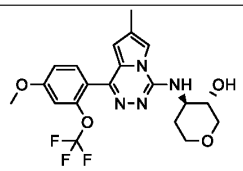
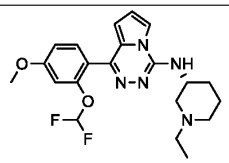
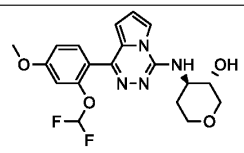
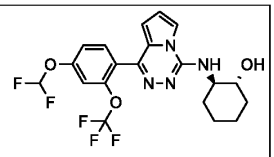
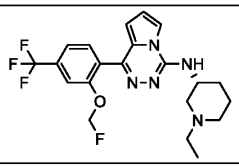
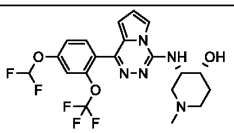
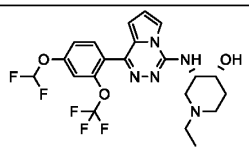
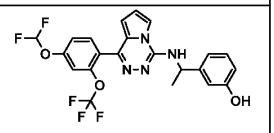
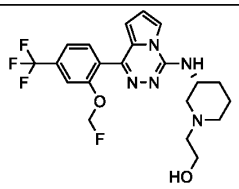
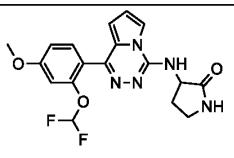
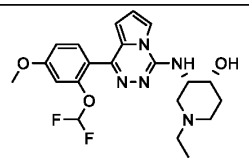
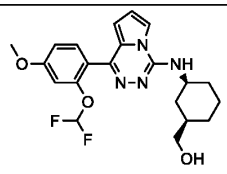
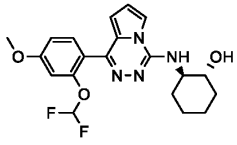
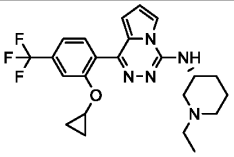
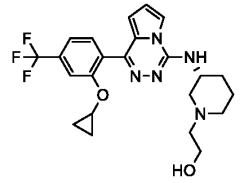
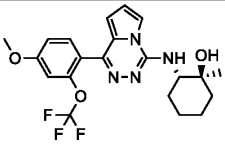
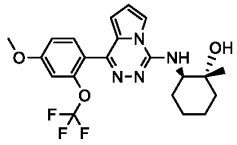
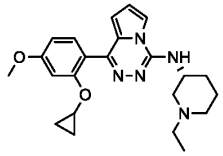
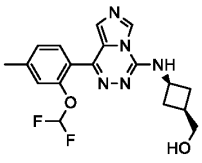
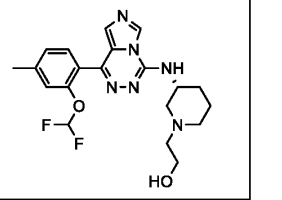
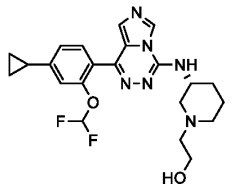
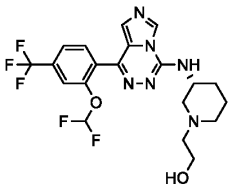
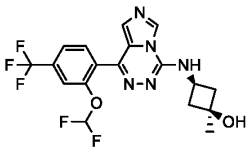
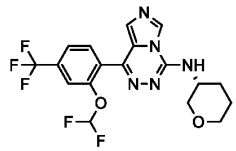
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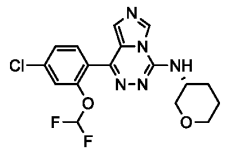
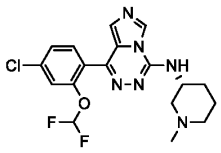
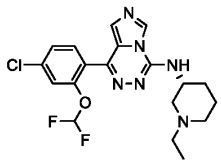
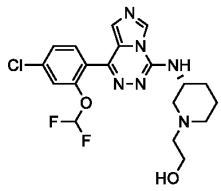
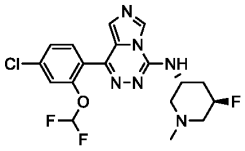
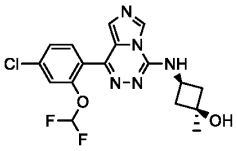
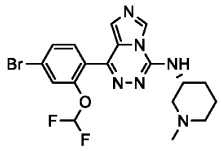
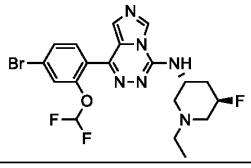
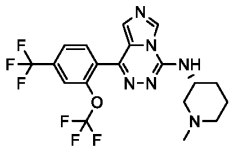
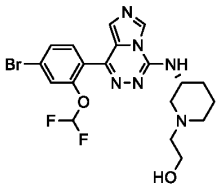
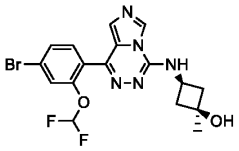
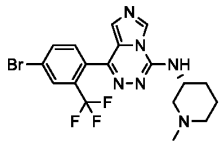
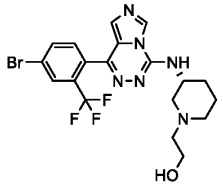
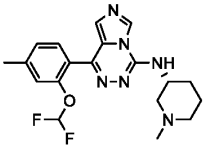
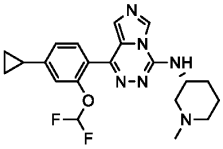
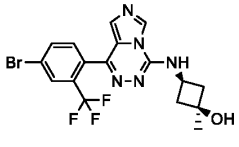
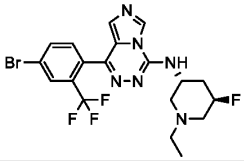
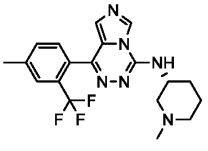
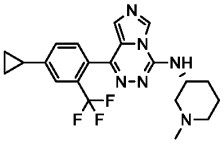
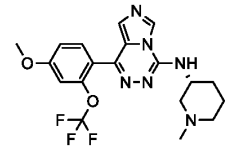
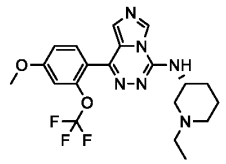
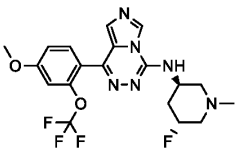
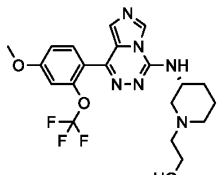
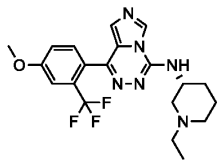
			
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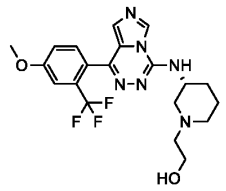
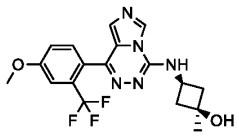
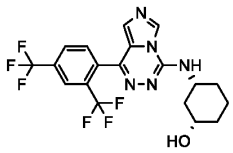
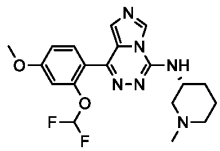
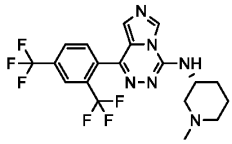
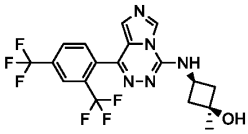
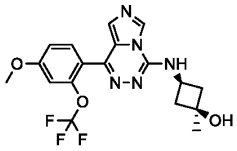
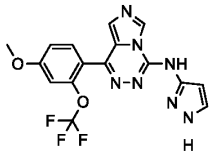
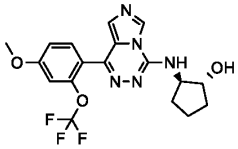
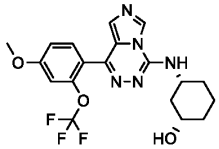
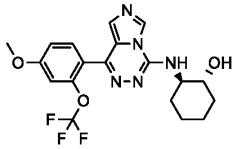
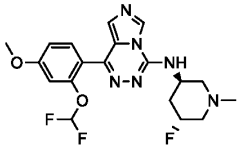
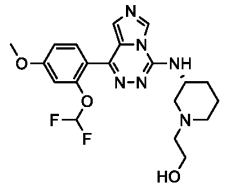
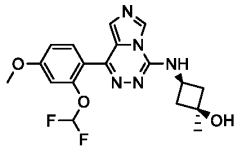
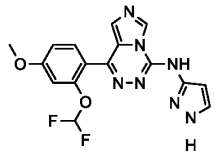
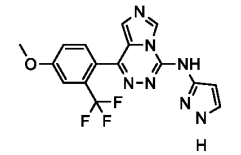
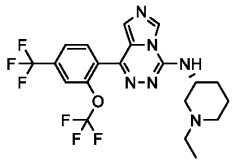
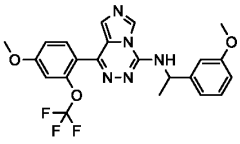
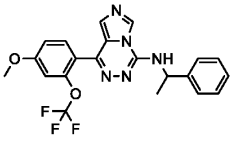
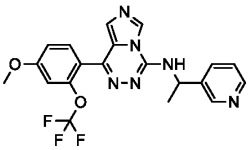
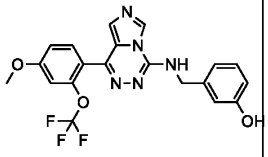
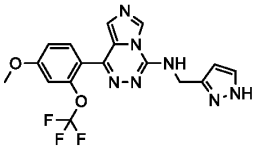
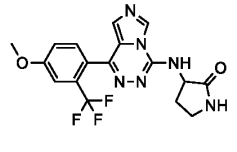
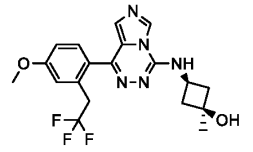
			
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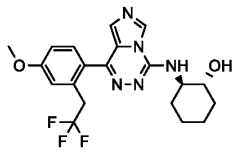
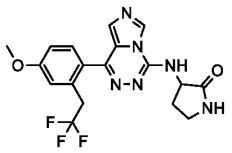
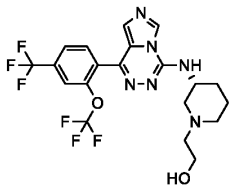
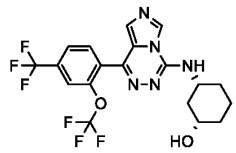
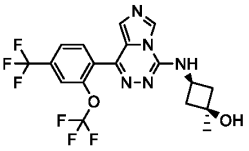
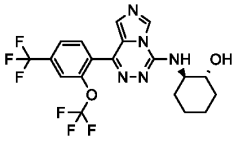
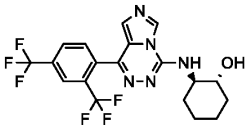
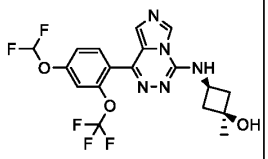
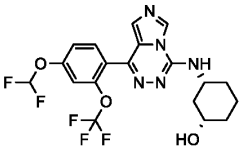
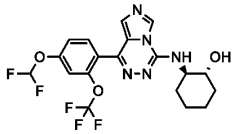
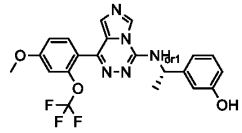
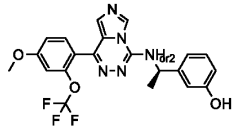
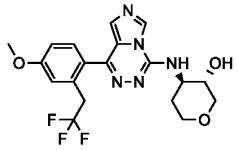
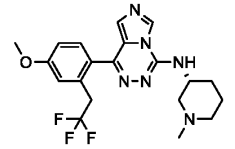
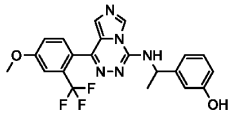
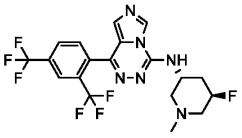
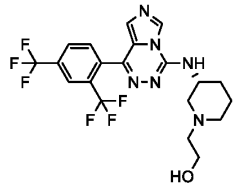
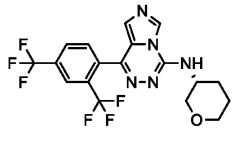
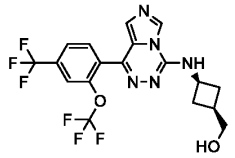
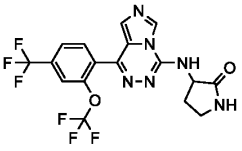
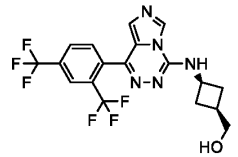
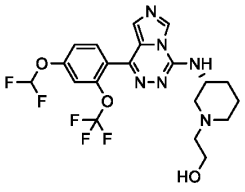
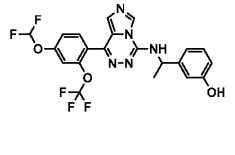
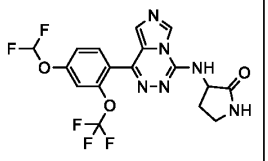
			
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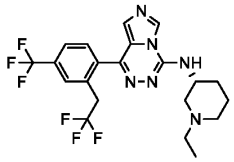
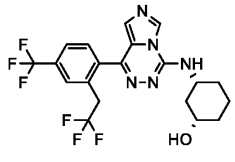
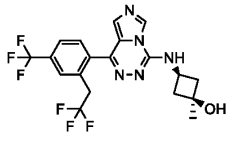
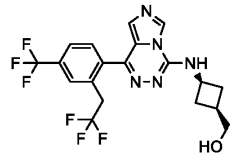
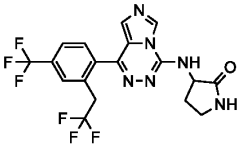
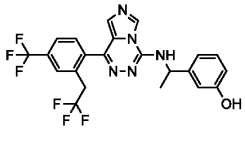
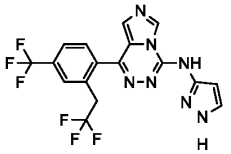
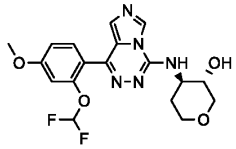
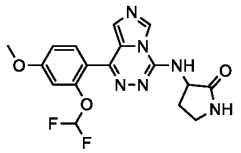
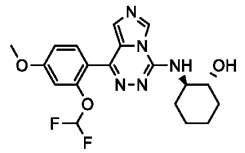
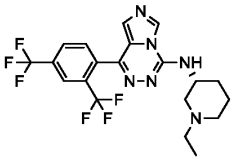
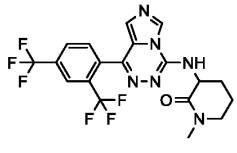
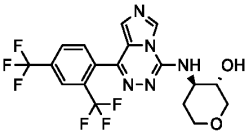
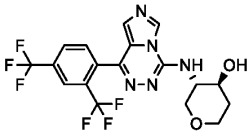
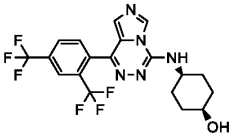
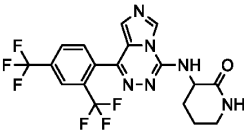
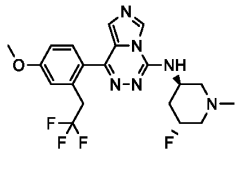
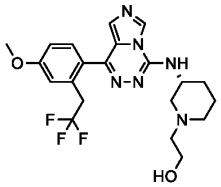
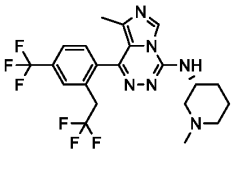
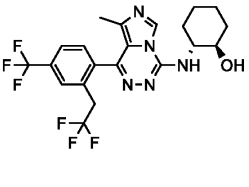
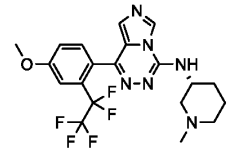
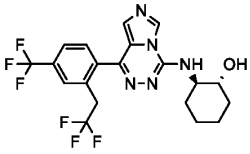
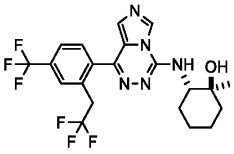
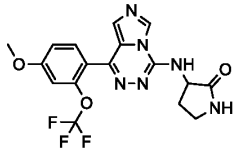
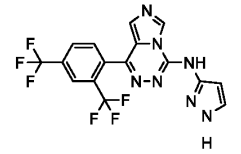
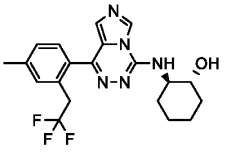
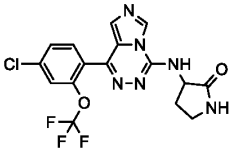
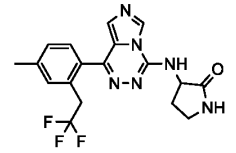
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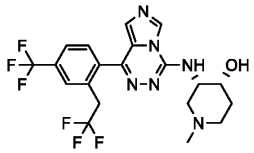
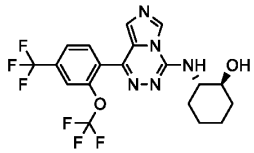
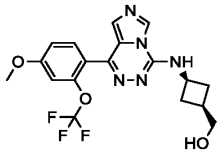
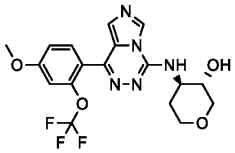
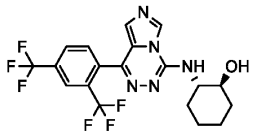
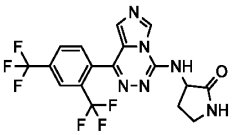
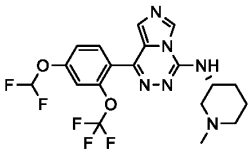
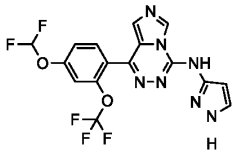
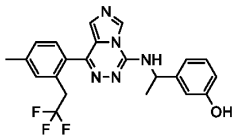
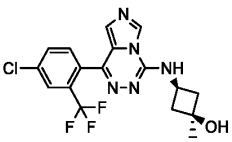
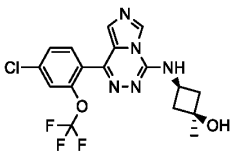
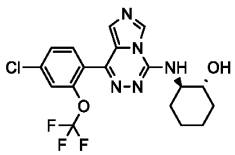
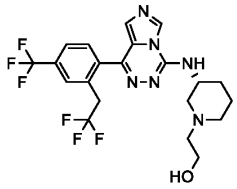
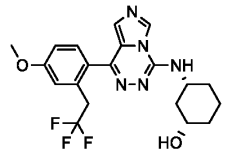
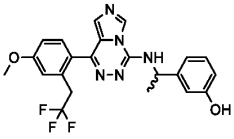
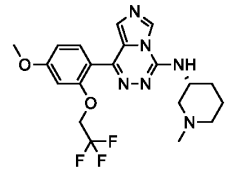
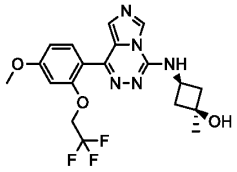
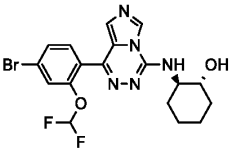
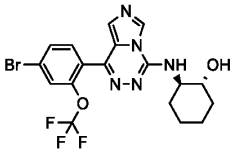
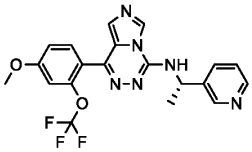
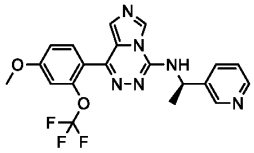
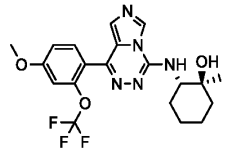
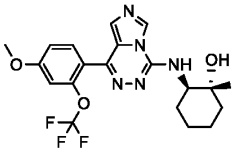
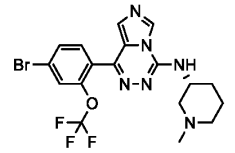
			
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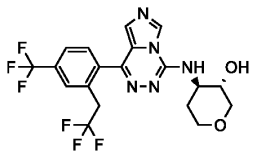
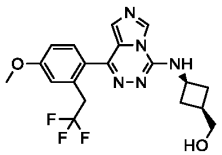
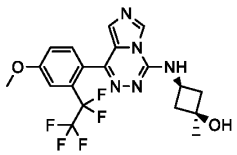
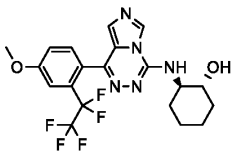
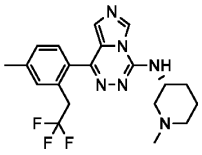
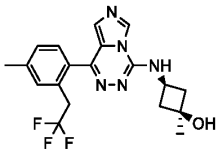
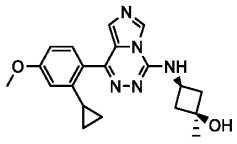
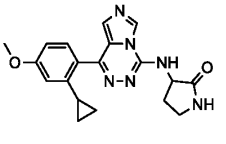
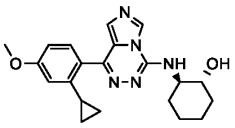
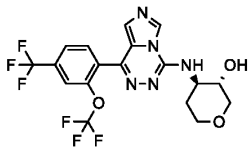
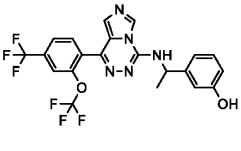
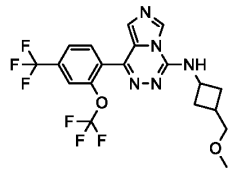
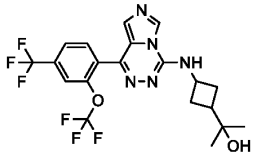
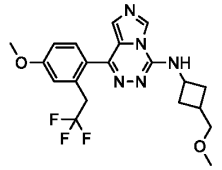
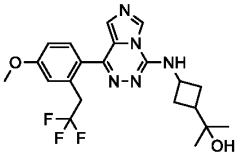
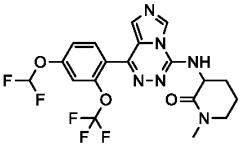
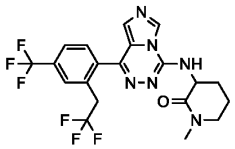
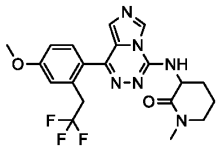
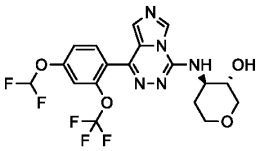
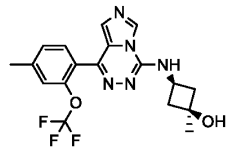
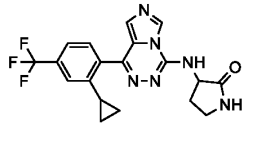
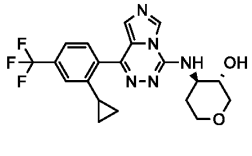
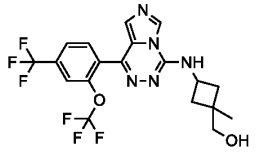
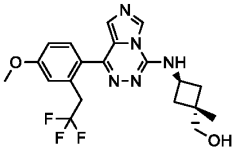
			
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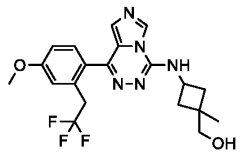
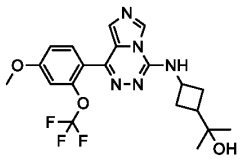
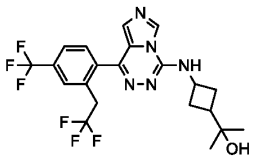
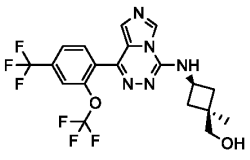
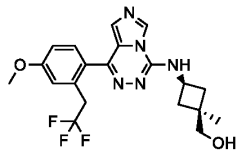
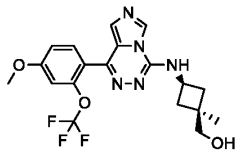
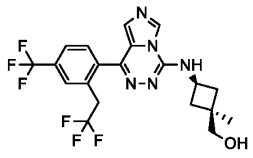
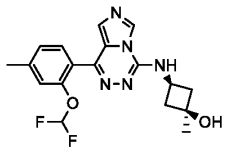
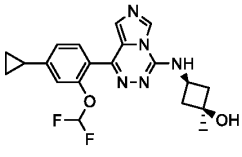
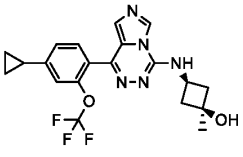
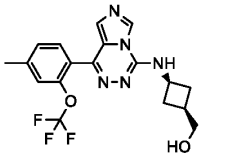
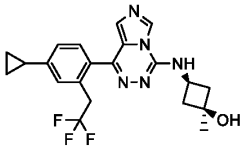
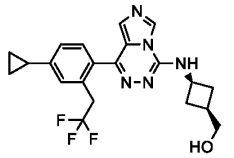
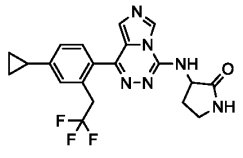
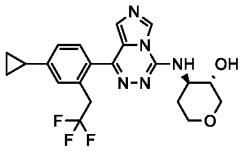
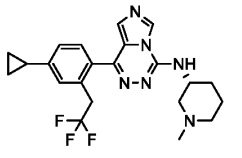
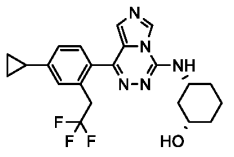
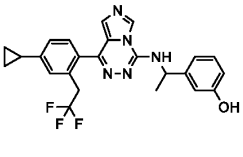
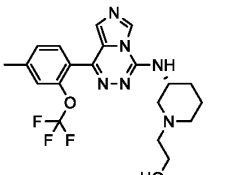
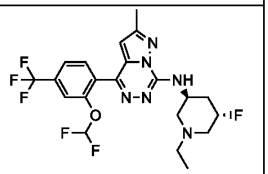
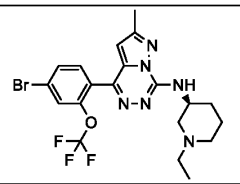
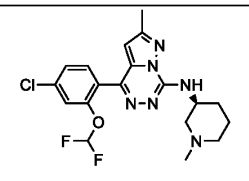
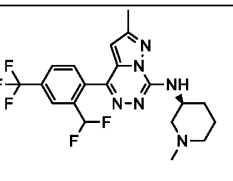
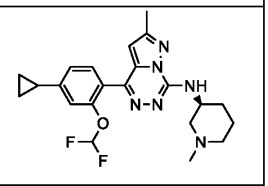
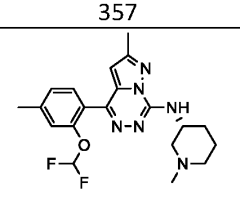
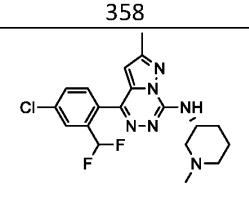
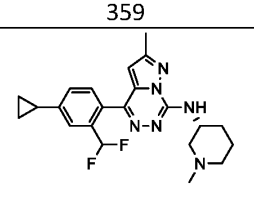
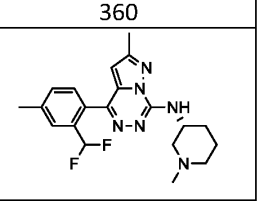
			
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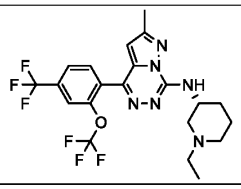
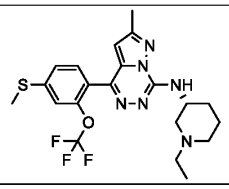
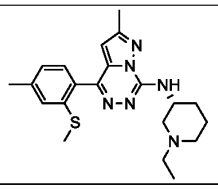
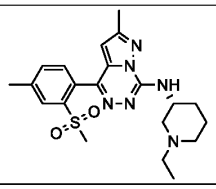
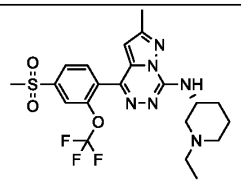
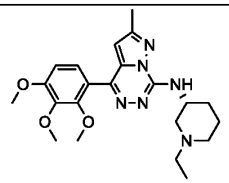
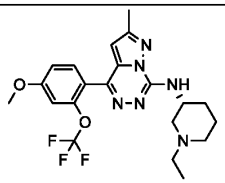
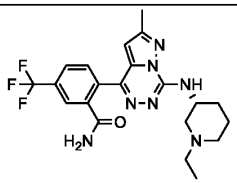
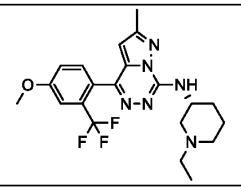
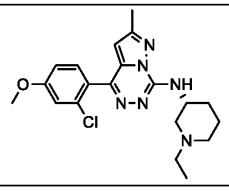
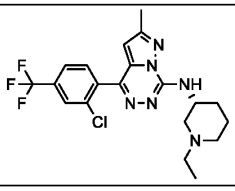
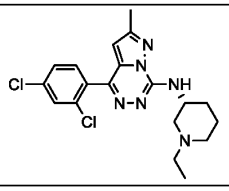
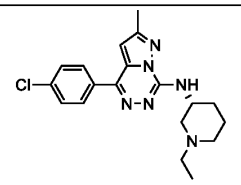
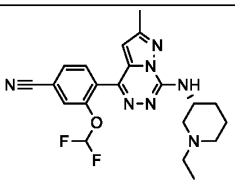
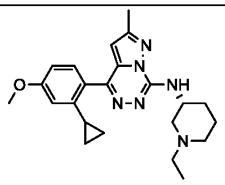
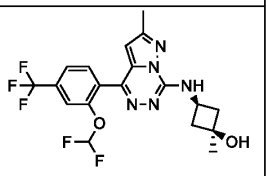
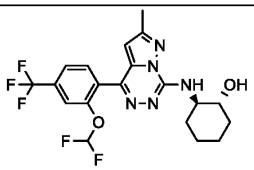
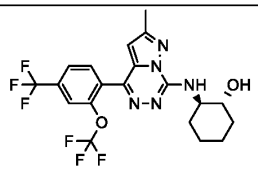
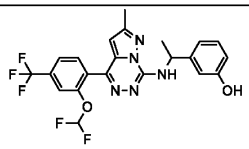
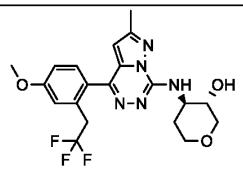
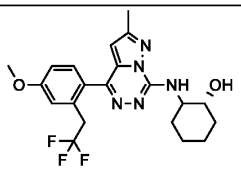
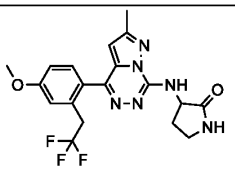
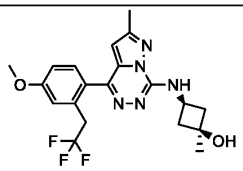
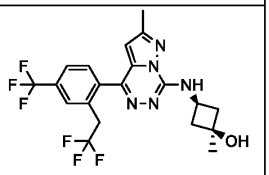
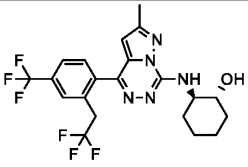
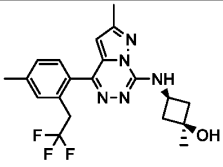
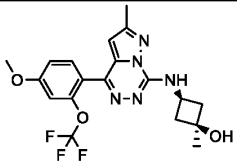
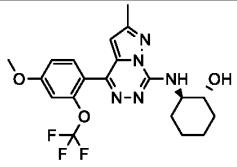
			
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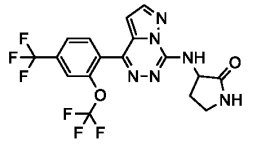
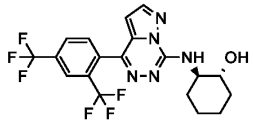
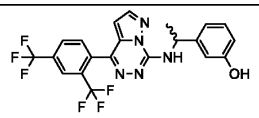
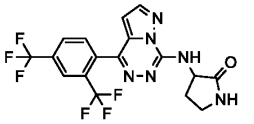
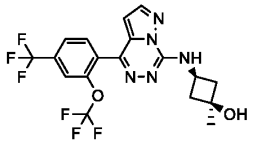
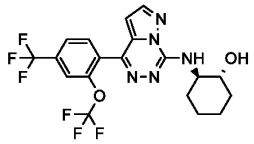
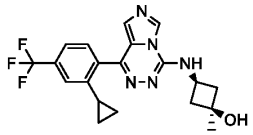
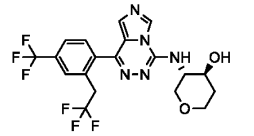
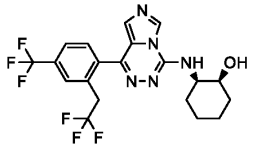
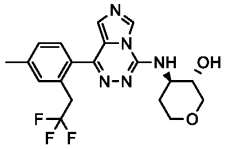
			
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 unassigned enantiomer	 unassigned enantiomer	 unassigned enantiomer	
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wherein a form of the compound is selected from the group consisting of a pharmaceutically acceptable salt, hydrate, solvate, racemate, enantiomer, diastereomer, stereoisomer, tautomer, and isotope enriched form thereof.

In embodiment 1, the invention provides compounds, or pharmaceutically acceptable salts thereof, as described above.

In embodiment 2, the invention provides compounds selected from:

Compound#	Name
1	(1s,3s)-3-({1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
2	N-[(3R)-1-methylpiperidin-3-yl]-1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine
3	(1s,3s)-1-methyl-3-({2-methyl-4-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]pyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)cyclobutan-1-ol
4	(1s,3s)-3-({4-[2,4-bis(trifluoromethyl)phenyl]pyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)-1-methylcyclobutan-1-ol
5	1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]-N-[(3R,5R)-1-ethyl-5-

	fluoropiperidin-3-yl]-8-fluoropyrrolo[1,2-d][1,2,4]triazin-4-amine
6	1-[2,4-bis(trifluoromethyl)phenyl]-N-[(3R)-1-(oxan-3-yl)piperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
7	1-{1-[2,4-bis(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}-N,N-dimethylpiperidin-3-amine
8	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
9	(1s,3s)-3-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
10	1-[2,4-bis(trifluoromethyl)phenyl]-N-[(3R)-1-(2-methylpropyl)piperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
11	1-[4-chloro-2-(difluoromethyl)phenyl]-7-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
12	1-[2-(difluoromethoxy)-4-methoxyphenyl]-7-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
13	1-[4-chloro-2-(difluoromethoxy)phenyl]-7-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
14	1-[4-cyclopropyl-2-(difluoromethyl)phenyl]-7-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
15	2-[(3R)-3-({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]-8-fluoropyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
16	(2S)-1-({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]-8-fluoropyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)propan-2-ol
17	N-[(3R)-1-ethylpiperidin-3-yl]-8-fluoro-1-[4-methoxy-2-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
18	2-[(3R)-3-({8-fluoro-1-[4-methoxy-2-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
19	1-[2-fluoro-4-(trifluoromethyl)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
20	N-[(3R)-1-ethylpiperidin-3-yl]-1-[2-fluoro-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
21	2-[(3R)-3-({1-[2-fluoro-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
22	2-[(3R)-3-({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]propan-1-ol
23	1-[2-(difluoromethyl)-4-methylphenyl]-7-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
24	1-[4-cyclopropyl-2-(difluoromethoxy)phenyl]-7-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
25	1-[2-(difluoromethoxy)-4-methylphenyl]-7-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
26	1-(4-methoxy-2-methylphenyl)-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
27	1-(2-cyclopropyl-4-methoxyphenyl)-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
28	1-[2,4-bis(trifluoromethyl)phenyl]-8-fluoro-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
29	1-[2,4-bis(trifluoromethyl)phenyl]-N-[(3R)-1-ethylpiperidin-3-yl]-8-fluoropyrrolo[1,2-d][1,2,4]triazin-4-amine

30	2-[(3R)-3-({1-[2,4-bis(trifluoromethyl)phenyl]-8-fluoropyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
31	1-[2,4-bis(trifluoromethyl)phenyl]-8-fluoro-N-[(3R,5R)-5-fluoro-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
32	1-[2,4-bis(trifluoromethyl)phenyl]-N-[(3R,5R)-1-ethyl-5-fluoropiperidin-3-yl]-8-fluoropyrrolo[1,2-d][1,2,4]triazin-4-amine
33	1-[2-(difluoromethoxy)-4-methylphenyl]-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
34	1-[2-(difluoromethoxy)-4-methylphenyl]-N-[(3R)-1-ethylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
35	1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]-N-[(3R)-piperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
36	N-[(3R)-1-methylpiperidin-3-yl]-1-[4-methyl-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
37	1-[4-cyclopropyl-2-(trifluoromethoxy)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
38	(1s,3s)-3-({1-[2,4-bis(trifluoromethyl)phenyl]-8-fluoropyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
39	8-fluoro-1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
40	N-[(3R)-1-methylpiperidin-3-yl]-1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
41	(1s,3s)-1-methyl-3-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclobutan-1-ol
42	1-[4-ethyl-2-(trifluoromethoxy)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
43	1-[4-ethoxy-2-(trifluoromethoxy)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
44	1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
45	2-[(3R)-3-({1-[2-(difluoromethoxy)-4-methylphenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
46	(3S,4S)-3-({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-ethylpiperidin-4-ol
47	1-(2-bromo-4-methoxyphenyl)-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
48	(3S,4R)-3-({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-ethylpiperidin-4-ol
49	1-[2-(difluoromethoxy)-6-methyl-4-(trifluoromethyl)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
50	N-[(3R)-1-ethylpiperidin-3-yl]-8-fluoro-1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
51	2-[(3R)-3-({8-fluoro-1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
52	8-fluoro-N-[(3R,5R)-5-fluoro-1-methylpiperidin-3-yl]-1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
53	N-[(3R,5R)-1-ethyl-5-fluoropiperidin-3-yl]-8-fluoro-1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
54	(1s,3s)-3-({8-fluoro-1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol

55	1-[2-(difluoromethoxy)-4-methoxyphenyl]-8-fluoro-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
56	1-[2-(difluoromethoxy)-4-methoxyphenyl]-N-[(3R)-1-ethylpiperidin-3-yl]-8-fluoropyrrolo[1,2-d][1,2,4]triazin-4-amine
57	2-[(3R)-3-({1-[2-(difluoromethoxy)-4-methoxyphenyl]-8-fluoropyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
58	(1s,3s)-3-({1-[2-(difluoromethoxy)-4-methoxyphenyl]-8-fluoropyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
59	N-[(3R)-1-ethylpiperidin-3-yl]-1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
60	N-[(3R,5R)-5-fluoro-1-methylpiperidin-3-yl]-1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
61	2-[(3R)-3-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
62	(1S,3R)-3-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
63	(2R)-1-({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)propan-2-ol
64	2-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)ethan-1-ol
65	(2S)-1-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)propan-2-ol
66	1-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-2-methylpropan-2-ol
67	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-(oxan-4-yl)pyrrolo[1,2-d][1,2,4]triazin-4-amine
68	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-[(3R)-oxolan-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
69	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-[(1-methyl-1H-imidazol-2-yl)methyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
70	(2R)-1-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)propan-2-ol
71	(1s,3s)-3-({1-[4-methoxy-2-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
72	(1s,3s)-3-{[1-(2-chloro-4-methoxyphenyl)pyrrolo[1,2-d][1,2,4]triazin-4-yl]amino}-1-methylcyclobutan-1-ol
73	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-{[(2R)-oxolan-2-yl]methyl}pyrrolo[1,2-d][1,2,4]triazin-4-amine
74	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-{[(2S)-1-methylpyrrolidin-2-yl]methyl}pyrrolo[1,2-d][1,2,4]triazin-4-amine
75	1-(2-cyclopropyl-6-fluoro-4-methoxyphenyl)-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
76	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-{[(2S)-oxolan-2-yl]methyl}pyrrolo[1,2-d][1,2,4]triazin-4-amine
77	3-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
78	(1S,2S)-2-({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
79	(1R,2S)-2-({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol

80	(1S,2S)-2-({1-[2-(difluoromethoxy)-4-methylphenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
81	(1S,2S)-2-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
82	1-(2-chloro-4-methoxyphenyl)-N-[(3R)-1-ethylpiperidin-3-yl]-8-fluoropyrrolo[1,2-d][1,2,4]triazin-4-amine
83	2-[(3R)-3-{[1-(2-chloro-4-methoxyphenyl)-8-fluoropyrrolo[1,2-d][1,2,4]triazin-4-yl]amino}piperidin-1-yl]ethan-1-ol
84	(1s,3s)-3-{[1-(2-chloro-4-methoxyphenyl)-8-fluoropyrrolo[1,2-d][1,2,4]triazin-4-yl]amino}-1-methylcyclobutan-1-ol
85	1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]-N-[(3R)-1-ethylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
86	2-[(3R)-3-({1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
87	1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]-N-[(3R,5R)-5-fluoro-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
88	(1s,3s)-3-({1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
89	3-[1-({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)ethyl]phenol
90	(1R,2R)-2-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
91	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-[(1,3-oxazol-2-yl)methyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
92	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-[(4-methyl-4H-1,2,4-triazol-3-yl)methyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
93	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-[(1-methyl-1H-1,2,4-triazol-5-yl)methyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
94	[3-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)bicyclo[1.1.1]pentan-1-yl]methanol
95	1-[3-(difluoromethoxy)-4-(4-{[(3R)-1-methylpiperidin-3-yl]amino}pyrrolo[1,2-d][1,2,4]triazin-1-yl)phenyl]propan-1-one
96	3-[1-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)ethyl]phenol
97	N-(1H-pyrazol-3-yl)-1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
98	(3S,5R)-5-({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-methylpiperidin-3-ol
99	(1S,2S)-2-({1-[2,4-bis(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
100	3-[1-({1-[2-(difluoromethoxy)-4-methylphenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)ethyl]phenol
101	3-[({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)methyl]phenol
102	3-[(1R)-1-({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)ethyl]phenol OR 3-[(1S)-1-({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)ethyl]phenol
103	3-[(1S)-1-({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)ethyl]phenol OR 3-[(1R)-1-({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)ethyl]phenol

104	(1s,3s)-3-{[1-(2-cyclopropyl-4-methoxyphenyl)pyrrolo[1,2-d][1,2,4]triazin-4-yl]amino}-1-methylcyclobutan-1-ol
105	1-(2-cyclopropyl-4-methoxyphenyl)-N-(1H-pyrazol-3-yl)pyrrolo[1,2-d][1,2,4]triazin-4-amine
106	(1S,3R)-3-{[1-(2-cyclopropyl-4-methoxyphenyl)pyrrolo[1,2-d][1,2,4]triazin-4-yl]amino}cyclohexan-1-ol
107	(1s,3s)-3-({1-[2,4-bis(trifluoromethyl)phenyl]-7-methylpyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
108	(1s,3s)-3-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]-7-methylpyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
109	1-[2,4-bis(trifluoromethyl)phenyl]-7-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
110	(1R,2R)-2-({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
111	(1S,2S)-2-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
112	(3S,4R)-4-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)oxan-3-ol
113	(3R,4S)-4-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)oxan-3-ol
114	(3R,4R)-4-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)oxan-3-ol
115	(3S,4S)-4-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)oxan-3-ol
116	3-({8-fluoro-1-[4-methoxy-2-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
117	8-fluoro-1-[4-methoxy-2-(trifluoromethyl)phenyl]-N-(1H-pyrazol-3-yl)pyrrolo[1,2-d][1,2,4]triazin-4-amine
118	1-(2-fluoro-4-methoxy-6-methylphenyl)-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
119	N-[(3R)-1-ethylpiperidin-3-yl]-1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
120	2-[(3R)-3-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
121	(1S,2S)-2-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
122	(1S,3R)-3-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
123	(1s,3s)-1-methyl-3-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclobutan-1-ol
124	3-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
125	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-[(1-methyl-1H-tetrazol-5-yl)methyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
126	(1S,2R)-2-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cycloheptan-1-ol AND (1R,2S)-2-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cycloheptan-1-ol
127	(1R,2R)-2-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cycloheptan-1-ol AND (1S,2S)-2-({1-[2-(2,2,2-

	trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cycloheptan-1-ol
128	(1S,3R)-3-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cycloheptan-1-ol AND (1R,3S)-3-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cycloheptan-1-ol
129	(1R,3R)-3-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cycloheptan-1-ol AND (1S,3S)-3-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cycloheptan-1-ol
130	(1s,3s)-3-({8-fluoro-1-[4-methoxy-2-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
131	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-7-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
132	(1S,2S)-2-({1-[2,4-bis(trifluoromethyl)phenyl]-7-methylpyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
133	(1S,2S)-2-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]-7-methylpyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
134	(3S,4R)-3-({1-[2,4-bis(trifluoromethyl)phenyl]-7-methylpyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-ethylpiperidin-4-ol
135	(3S,4R)-1-ethyl-3-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]-7-methylpyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)piperidin-4-ol
136	(1R,2R)-2-({1-[2-(difluoromethoxy)-4-methylphenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
137	(1S,2R)-2-({1-[2-(difluoromethoxy)-4-methylphenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
138	(1R,2R)-2-({1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
139	3-({1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
140	N-[(3R)-1-methylpiperidin-3-yl]-1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
141	[(1s,3s)-3-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclobutyl]methanol
142	3-[1-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)ethyl]phenol
143	2-[(3R)-3-({1-[2-(cyclopropyloxy)-4-methoxyphenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
144	(3S,4R)-4-({1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)oxan-3-ol
145	1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
146	N-{[(3S)-1-methylpiperidin-3-yl]methyl}-1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
147	N-{[(3R)-1-methylpiperidin-3-yl]methyl}-1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
148	8-fluoro-N-[1-(3-methoxyphenyl)ethyl]-1-[4-methoxy-2-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
149	3-[1-({8-fluoro-1-[4-methoxy-2-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)ethyl]phenol

150	N-(1H-pyrazol-3-yl)-1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
151	(1R,2R)-2-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
152	1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]-N-[(3R)-oxan-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
153	(1S,3R)-3-({1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
154	3-({1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
155	1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]-N-(1H-pyrazol-3-yl)pyrrolo[1,2-d][1,2,4]triazin-4-amine
156	(1R,2R)-2-({1-[4-methyl-2-(2,2,2-trifluoroethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
157	3-({1-[4-methyl-2-(2,2,2-trifluoroethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
158	(1s,3s)-1-methyl-3-({1-[4-methyl-2-(2,2,2-trifluoroethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclobutan-1-ol
159	N-[(3R)-1-methylpiperidin-3-yl]-1-[4-methyl-2-(2,2,2-trifluoroethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
160	(1R,2R)-2-({1-[2,4-bis(trifluoromethyl)phenyl]-7-methylpyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
161	3-({1-[2,4-bis(trifluoromethyl)phenyl]-7-methylpyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
162	3-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]-7-methylpyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
163	(1R,2R)-2-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]-7-methylpyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
164	(3S,4R)-4-({1-[2,4-bis(trifluoromethyl)phenyl]-7-methylpyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)oxan-3-ol
165	(3S,4R)-4-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]-7-methylpyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)oxan-3-ol
166	1-[2-(difluoromethoxy)-4-methoxyphenyl]-N-[(3R)-1-ethylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
167	(3S,4R)-4-({1-[2-(difluoromethoxy)-4-methoxyphenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)oxan-3-ol
168	(1R,2R)-2-({1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
169	N-[(3R)-1-ethylpiperidin-3-yl]-1-[2-(fluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
170	(3S,4R)-3-({1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-methylpiperidin-4-ol
171	(3S,4R)-3-({1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-ethylpiperidin-4-ol
172	3-[1-({1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)ethyl]phenol
173	2-[(3R)-3-({1-[2-(fluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
174	3-({1-[2-(difluoromethoxy)-4-methoxyphenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one

175	(3S,4R)-3-({1-[2-(difluoromethoxy)-4-methoxyphenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-ethylpiperidin-4-ol
176	[(1R,3S)-3-({1-[2-(difluoromethoxy)-4-methoxyphenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexyl]methanol
177	(1R,2R)-2-({1-[2-(difluoromethoxy)-4-methoxyphenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
178	1-[2-(cyclopropyloxy)-4-(trifluoromethyl)phenyl]-N-[(3R)-1-ethylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
179	2-[(3R)-3-({1-[2-(cyclopropyloxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
180	(1S,2S)-2-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-methylcyclohexan-1-ol OR (1R,2R)-2-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-methylcyclohexan-1-ol
181	(1R,2R)-2-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-methylcyclohexan-1-ol OR (1S,2S)-2-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-methylcyclohexan-1-ol
182	1-[2-(cyclopropyloxy)-4-methoxyphenyl]-N-[(3R)-1-ethylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
183	[(1s,3s)-3-({1-[2-(difluoromethoxy)-4-methylphenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutyl]methanol
184	2-[(3R)-3-({1-[2-(difluoromethoxy)-4-methylphenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
185	2-[(3R)-3-({1-[4-cyclopropyl-2-(difluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
186	2-[(3R)-3-({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
187	(1s,3s)-3-({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
188	1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]-N-[(3R)-oxan-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
189	1-[4-chloro-2-(difluoromethoxy)phenyl]-N-[(3R)-oxan-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
190	1-[4-chloro-2-(difluoromethoxy)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
191	1-[4-chloro-2-(difluoromethoxy)phenyl]-N-[(3R)-1-ethylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
192	2-[(3R)-3-({1-[4-chloro-2-(difluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
193	1-[4-chloro-2-(difluoromethoxy)phenyl]-N-[(3R,5R)-5-fluoro-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
194	(1s,3s)-3-({1-[4-chloro-2-(difluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
195	1-[4-bromo-2-(difluoromethoxy)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
196	1-[4-bromo-2-(difluoromethoxy)phenyl]-N-[(3R,5R)-1-ethyl-5-fluoropiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
197	N-[(3R)-1-methylpiperidin-3-yl]-1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine

198	2-[(3R)-3-({1-[4-bromo-2-(difluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
199	(1s,3s)-3-({1-[4-bromo-2-(difluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
200	1-[4-bromo-2-(trifluoromethyl)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
201	2-[(3R)-3-({1-[4-bromo-2-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
202	1-[2-(difluoromethoxy)-4-methylphenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
203	1-[4-cyclopropyl-2-(difluoromethoxy)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
204	(1s,3s)-3-({1-[4-bromo-2-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
205	1-[4-bromo-2-(trifluoromethyl)phenyl]-N-[(3R,5R)-1-ethyl-5-fluoropiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
206	N-[(3R)-1-methylpiperidin-3-yl]-1-[4-methyl-2-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine
207	1-[4-cyclopropyl-2-(trifluoromethyl)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
208	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
209	N-[(3R)-1-ethylpiperidin-3-yl]-1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine
210	N-[(3R,5R)-5-fluoro-1-methylpiperidin-3-yl]-1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine
211	2-[(3R)-3-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
212	N-[(3R)-1-ethylpiperidin-3-yl]-1-[4-methoxy-2-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine
213	2-[(3R)-3-({1-[4-methoxy-2-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
214	(1s,3s)-3-({1-[4-methoxy-2-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
215	(1S,3R)-3-({1-[2,4-bis(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
216	1-[2-(difluoromethoxy)-4-methoxyphenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
217	1-[2,4-bis(trifluoromethyl)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
218	(1s,3s)-3-({1-[2,4-bis(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
219	(1s,3s)-3-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
220	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-(1H-pyrazol-3-yl)imidazo[1,5-d][1,2,4]triazin-4-amine
221	(1R,2R)-2-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclopentan-1-ol
222	(1S,3R)-3-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol

223	(1R,2R)-2-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
224	1-[2-(difluoromethoxy)-4-methoxyphenyl]-N-[(3R,5R)-5-fluoro-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
225	2-[(3R)-3-({1-[2-(difluoromethoxy)-4-methoxyphenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
226	(1s,3s)-3-({1-[2-(difluoromethoxy)-4-methoxyphenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
227	1-[2-(difluoromethoxy)-4-methoxyphenyl]-N-(1H-pyrazol-3-yl)imidazo[1,5-d][1,2,4]triazin-4-amine
228	1-[4-methoxy-2-(trifluoromethyl)phenyl]-N-(1H-pyrazol-3-yl)imidazo[1,5-d][1,2,4]triazin-4-amine
229	N-[(3R)-1-ethylpiperidin-3-yl]-1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine
230	N-[1-(3-methoxyphenyl)ethyl]-1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine
231	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-(1-phenylethyl)imidazo[1,5-d][1,2,4]triazin-4-amine
232	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-[1-(pyridin-3-yl)ethyl]imidazo[1,5-d][1,2,4]triazin-4-amine
233	3-[({1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)methyl]phenol
234	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-[(1H-pyrazol-3-yl)methyl]imidazo[1,5-d][1,2,4]triazin-4-amine
235	3-({1-[4-methoxy-2-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
236	(1s,3s)-3-({1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
237	(1R,2R)-2-({1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
238	3-({1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
239	2-[(3R)-3-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
240	(1S,3R)-3-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
241	(1s,3s)-1-methyl-3-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutan-1-ol
242	(1R,2R)-2-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
243	(1R,2R)-2-({1-[2,4-bis(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
244	(1s,3s)-3-({1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
245	(1S,3R)-3-({1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
246	(1R,2R)-2-({1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
247	3-[(1S)-1-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)ethyl]phenol OR 3-[(1R)-1-({1-[4-methoxy-2-

	(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)ethyl]phenol
248	3-[(1R)-1-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)ethyl]phenol OR 3-[(1S)-1-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)ethyl]phenol
249	(3S,4R)-4-({1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)oxan-3-ol
250	1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
251	3-[1-({1-[4-methoxy-2-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)ethyl]phenol
252	1-[2,4-bis(trifluoromethyl)phenyl]-N-[(3R,5R)-5-fluoro-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
253	2-[(3R)-3-({1-[2,4-bis(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
254	1-[2,4-bis(trifluoromethyl)phenyl]-N-[(3R)-oxan-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
255	[(1s,3s)-3-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutyl]methanol
256	3-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
257	[(1s,3s)-3-({1-[2,4-bis(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutyl]methanol
258	2-[(3R)-3-({1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
259	3-[1-({1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)ethyl]phenol
260	3-({1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
261	N-[(3R)-1-ethylpiperidin-3-yl]-1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine
262	(1S,3R)-3-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
263	(1s,3s)-1-methyl-3-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutan-1-ol
264	[(1s,3s)-3-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutyl]methanol
265	3-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
266	3-[1-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)ethyl]phenol
267	N-(1H-pyrazol-3-yl)-1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine
268	(3S,4R)-4-({1-[2-(difluoromethoxy)-4-methoxyphenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)oxan-3-ol
269	3-({1-[2-(difluoromethoxy)-4-methoxyphenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
270	(1R,2R)-2-({1-[2-(difluoromethoxy)-4-methoxyphenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
271	1-[2,4-bis(trifluoromethyl)phenyl]-N-[(3R)-1-ethylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine

272	3-({1-[2,4-bis(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylpiperidin-2-one
273	(3S,4R)-4-({1-[2,4-bis(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)oxan-3-ol
274	(3S,4S)-3-({1-[2,4-bis(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)oxan-4-ol
275	(1s,4s)-4-({1-[2,4-bis(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
276	3-({1-[2,4-bis(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-2-one
277	N-[(3R,5R)-5-fluoro-1-methylpiperidin-3-yl]-1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine
278	2-[(3R)-3-({1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
279	8-methyl-N-[(3R)-1-methylpiperidin-3-yl]-1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine
280	(1R,2R)-2-({8-methyl-1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
281	1-[4-methoxy-2-(pentafluoroethyl)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
282	(1R,2R)-2-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
283	(1S,2S)-1-methyl-2-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol AND (1R,2R)-1-methyl-2-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
284	3-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
285	1-[2,4-bis(trifluoromethyl)phenyl]-N-(1H-pyrazol-3-yl)imidazo[1,5-d][1,2,4]triazin-4-amine
286	(1R,2R)-2-({1-[4-methyl-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
287	3-({1-[4-chloro-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
288	3-({1-[4-methyl-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
289	(3S,4R)-1-methyl-3-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-4-ol
290	(1S,2S)-2-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
291	[(1s,3s)-3-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutyl]methanol
292	(3S,4R)-4-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)oxan-3-ol
293	(1S,2S)-2-({1-[2,4-bis(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
294	3-({1-[2,4-bis(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
295	1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine

296	1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]-N-(1H-pyrazol-3-yl)imidazo[1,5-d][1,2,4]triazin-4-amine
297	3-[1-({1-[4-methyl-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)ethyl]phenol
298	(1s,3s)-3-({1-[4-chloro-2-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
299	(1s,3s)-3-({1-[4-chloro-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
300	(1R,2R)-2-({1-[4-chloro-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
301	2-[(3R)-3-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
302	(1S,3R)-3-({1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
303	3-[1-({1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)ethyl]phenol
304	1-[4-methoxy-2-(2,2,2-trifluoroethoxy)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
305	(1s,3s)-3-({1-[4-methoxy-2-(2,2,2-trifluoroethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
306	(1R,2R)-2-({1-[4-bromo-2-(difluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
307	(1R,2R)-2-({1-[4-bromo-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
308	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-[(1S)-1-(pyridin-3-yl)ethyl]imidazo[1,5-d][1,2,4]triazin-4-amine OR 1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-[(1R)-1-(pyridin-3-yl)ethyl]imidazo[1,5-d][1,2,4]triazin-4-amine
309	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-[(1R)-1-(pyridin-3-yl)ethyl]imidazo[1,5-d][1,2,4]triazin-4-amine OR 1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-[(1S)-1-(pyridin-3-yl)ethyl]imidazo[1,5-d][1,2,4]triazin-4-amine
310	(1S,2S)-2-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclohexan-1-ol OR (1R,2R)-2-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclohexan-1-ol
311	(1R,2R)-2-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclohexan-1-ol OR (1S,2S)-2-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclohexan-1-ol
312	1-[4-bromo-2-(trifluoromethoxy)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
313	(3S,4R)-4-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)oxan-3-ol
314	[(1s,3s)-3-({1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutyl]methanol
315	(1s,3s)-3-({1-[4-methoxy-2-(pentafluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
316	(1R,2R)-2-({1-[4-methoxy-2-(pentafluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol

317	N-[(3R)-1-methylpiperidin-3-yl]-1-[4-methyl-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine
318	(1s,3s)-1-methyl-3-({1-[4-methyl-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutan-1-ol
319	(1s,3s)-3-{[1-(2-cyclopropyl-4-methoxyphenyl)imidazo[1,5-d][1,2,4]triazin-4-yl]amino}-1-methylcyclobutan-1-ol
320	3-{[1-(2-cyclopropyl-4-methoxyphenyl)imidazo[1,5-d][1,2,4]triazin-4-yl]amino}pyrrolidin-2-one
321	(1R,2R)-2-{[1-(2-cyclopropyl-4-methoxyphenyl)imidazo[1,5-d][1,2,4]triazin-4-yl]amino}cyclohexan-1-ol
322	(3S,4R)-4-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)oxan-3-ol
323	3-[1-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)ethyl]phenol
324	N-[3-(methoxymethyl)cyclobutyl]-1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine
325	2-[3-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutyl]propan-2-ol
326	N-[3-(methoxymethyl)cyclobutyl]-1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine
327	2-[3-({1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutyl]propan-2-ol
328	3-({1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylpiperidin-2-one
329	1-methyl-3-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-2-one
330	3-({1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylpiperidin-2-one
331	(3S,4R)-4-({1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)oxan-3-ol
332	(1s,3s)-1-methyl-3-({1-[4-methyl-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutan-1-ol
333	3-({1-[2-cyclopropyl-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
334	(3S,4R)-4-({1-[2-cyclopropyl-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)oxan-3-ol
335	[1-methyl-3-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutyl]methanol
336	[(1r,3r)-3-({1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutyl]methanol
337	[3-({1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutyl]methanol
338	2-[3-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutyl]propan-2-ol
339	2-[3-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutyl]propan-2-ol
340	[(1s,3s)-1-methyl-3-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutyl]methanol
341	[(1s,3s)-3-({1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutyl]methanol

342	[(1s,3s)-3-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutyl]methanol
343	[(1s,3s)-1-methyl-3-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutyl]methanol
344	(1s,3s)-3-({1-[2-(difluoromethoxy)-4-methylphenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
345	(1s,3s)-3-({1-[4-cyclopropyl-2-(difluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
346	(1s,3s)-3-({1-[4-cyclopropyl-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
347	[(1s,3s)-3-({1-[4-methyl-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutyl]methanol
348	(1s,3s)-3-({1-[4-cyclopropyl-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
349	[(1s,3s)-3-({1-[4-cyclopropyl-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutyl]methanol
350	3-({1-[4-cyclopropyl-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
351	(3S,4R)-4-({1-[4-cyclopropyl-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)oxan-3-ol
352	1-[4-cyclopropyl-2-(2,2,2-trifluoroethyl)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
353	(1S,3R)-3-({1-[4-cyclopropyl-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
354	3-[1-({1-[4-cyclopropyl-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)ethyl]phenol
355	2-[(3R)-3-({1-[4-methyl-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
356	4-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]-N-[(3R,5R)-1-ethyl-5-fluoropiperidin-3-yl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-amine
357	4-[4-bromo-2-(trifluoromethoxy)phenyl]-N-[(3R)-1-ethylpiperidin-3-yl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-amine
358	4-[4-chloro-2-(difluoromethoxy)phenyl]-2-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrazolo[1,5-d][1,2,4]triazin-7-amine
359	4-[2-(difluoromethyl)-4-(trifluoromethyl)phenyl]-2-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrazolo[1,5-d][1,2,4]triazin-7-amine
360	4-[4-cyclopropyl-2-(difluoromethoxy)phenyl]-2-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrazolo[1,5-d][1,2,4]triazin-7-amine
361	4-[2-(difluoromethoxy)-4-methylphenyl]-2-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrazolo[1,5-d][1,2,4]triazin-7-amine
362	4-[4-chloro-2-(difluoromethyl)phenyl]-2-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrazolo[1,5-d][1,2,4]triazin-7-amine
363	4-[4-cyclopropyl-2-(difluoromethyl)phenyl]-2-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrazolo[1,5-d][1,2,4]triazin-7-amine
364	4-[2-(difluoromethyl)-4-methylphenyl]-2-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrazolo[1,5-d][1,2,4]triazin-7-amine
365	N-[(3R)-1-ethylpiperidin-3-yl]-2-methyl-4-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]pyrazolo[1,5-d][1,2,4]triazin-7-amine
366	N-[(3R)-1-ethylpiperidin-3-yl]-2-methyl-4-[4-(methylsulfanyl)-2-(trifluoromethoxy)phenyl]pyrazolo[1,5-d][1,2,4]triazin-7-amine

367	N-[(3R)-1-ethylpiperidin-3-yl]-2-methyl-4-[4-methyl-2-(methylsulfanyl)phenyl]pyrazolo[1,5-d][1,2,4]triazin-7-amine
368	N-[(3R)-1-ethylpiperidin-3-yl]-4-[2-(methanesulfonyl)-4-methylphenyl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-amine
369	N-[(3R)-1-ethylpiperidin-3-yl]-4-[4-(methanesulfonyl)-2-(trifluoromethoxy)phenyl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-amine
370	N-[(3R)-1-ethylpiperidin-3-yl]-2-methyl-4-(2,3,4-trimethoxyphenyl)pyrazolo[1,5-d][1,2,4]triazin-7-amine
371	N-[(3R)-1-ethylpiperidin-3-yl]-4-[4-methoxy-2-(trifluoromethoxy)phenyl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-amine
372	2-(7-{[(3R)-1-ethylpiperidin-3-yl]amino}-2-methylpyrazolo[1,5-d][1,2,4]triazin-4-yl)-5-(trifluoromethyl)benzamide
373	N-[(3R)-1-ethylpiperidin-3-yl]-4-[4-methoxy-2-(trifluoromethyl)phenyl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-amine
374	4-(2-chloro-4-methoxyphenyl)-N-[(3R)-1-ethylpiperidin-3-yl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-amine
375	4-[2-chloro-4-(trifluoromethyl)phenyl]-N-[(3R)-1-ethylpiperidin-3-yl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-amine
376	4-(2,4-dichlorophenyl)-N-[(3R)-1-ethylpiperidin-3-yl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-amine
377	4-(4-chlorophenyl)-N-[(3R)-1-ethylpiperidin-3-yl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-amine
378	3-(difluoromethoxy)-4-(7-{[(3R)-1-ethylpiperidin-3-yl]amino}-2-methylpyrazolo[1,5-d][1,2,4]triazin-4-yl)benzonitrile
379	4-(2-cyclopropyl-4-methoxyphenyl)-N-[(3R)-1-ethylpiperidin-3-yl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-amine
380	(1s,3s)-3-({4-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)-1-methylcyclobutan-1-ol
381	(1R,2R)-2-({4-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)cyclohexan-1-ol
382	(1R,2R)-2-({2-methyl-4-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]pyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)cyclohexan-1-ol
383	3-[1-({4-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)ethyl]phenol
384	(3S,4R)-4-({4-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)oxan-3-ol
385	(1R,2R)-2-({4-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)cyclohexan-1-ol
386	3-({4-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)pyrrolidin-2-one
387	(1s,3s)-3-({4-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)-1-methylcyclobutan-1-ol
388	(1s,3s)-1-methyl-3-({2-methyl-4-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)cyclobutan-1-ol
389	(1R,2R)-2-({2-methyl-4-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)cyclohexan-1-ol
390	(1s,3s)-1-methyl-3-({2-methyl-4-[4-methyl-2-(2,2,2-trifluoroethyl)phenyl]pyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)cyclobutan-1-ol
391	(1s,3s)-3-({4-[4-methoxy-2-(trifluoromethoxy)phenyl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)-1-methylcyclobutan-1-ol

392	(1R,2R)-2-({4-[4-methoxy-2-(trifluoromethoxy)phenyl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)cyclohexan-1-ol
393	3-({4-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]pyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)pyrrolidin-2-one
394	(1R,2R)-2-({4-[2,4-bis(trifluoromethyl)phenyl]pyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)cyclohexan-1-ol
395	3-[1-({4-[2,4-bis(trifluoromethyl)phenyl]pyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)ethyl]phenol
396	3-({4-[2,4-bis(trifluoromethyl)phenyl]pyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)pyrrolidin-2-one
397	(1s,3s)-1-methyl-3-({4-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]pyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)cyclobutan-1-ol
398	(1R,2R)-2-({4-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]pyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)cyclohexan-1-ol
399	(1s,3s)-3-({1-[2-cyclopropyl-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
400	(3S,4S)-3-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)oxan-4-ol
401	(1S,2R)-2-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
402	(3S,4R)-4-({1-[4-methyl-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)oxan-3-ol

wherein a form of the compound is selected from the group consisting of a pharmaceutically acceptable salt, hydrate, solvate, racemate, enantiomer, diastereomer, stereoisomer, tautomer, and isotope enriched form thereof.

In embodiment 3, the invention provides compounds selected from:

Compound #	Name
2	N-[(3R)-1-methylpiperidin-3-yl]-1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine formate
12	1-[2-(difluoromethoxy)-4-methoxyphenyl]-7-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine formate
13	1-[4-chloro-2-(difluoromethoxy)phenyl]-7-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine formate
14	1-[4-cyclopropyl-2-(difluoromethyl)phenyl]-7-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine formate
19	1-[2-fluoro-4-(trifluoromethyl)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine formate
23	1-[2-(difluoromethyl)-4-methylphenyl]-7-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine formate
24	1-[4-cyclopropyl-2-(difluoromethoxy)phenyl]-7-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine formate
25	1-[2-(difluoromethoxy)-4-methylphenyl]-7-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine formate

34	1-[2-(difluoromethoxy)-4-methylphenyl]-N-[(3R)-1-ethylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine formate
35	1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]-N-[(3R)-piperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine hydrochloride
37	1-[4-cyclopropyl-2-(trifluoromethoxy)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine formate
42	1-[4-ethyl-2-(trifluoromethoxy)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine formate
74	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-{[(2S)-1-methylpyrrolidin-2-yl]methyl}pyrrolo[1,2-d][1,2,4]triazin-4-amine trifluoroacetate
95	1-[3-(difluoromethoxy)-4-(4-{[(3R)-1-methylpiperidin-3-yl]amino}pyrrolo[1,2-d][1,2,4]triazin-1-yl)phenyl]propan-1-one formate
134	(3S,4R)-3-({1-[2,4-bis(trifluoromethyl)phenyl]-7-methylpyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-ethylpiperidin-4-ol formate
145	1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine formate
184	2-[(3R)-3-({1-[2-(difluoromethoxy)-4-methylphenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol formate
185	2-[(3R)-3-({1-[4-cyclopropyl-2-(difluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol formate
186	2-[(3R)-3-({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol formate
190	1-[4-chloro-2-(difluoromethoxy)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine formate
191	1-[4-chloro-2-(difluoromethoxy)phenyl]-N-[(3R)-1-ethylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine formate
192	2-[(3R)-3-({1-[4-chloro-2-(difluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol formate
193	1-[4-chloro-2-(difluoromethoxy)phenyl]-N-[(3R,5R)-5-fluoro-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine formate
216	1-[2-(difluoromethoxy)-4-methoxyphenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine formate
228	1-[4-methoxy-2-(trifluoromethyl)phenyl]-N-(1H-pyrazol-3-yl)imidazo[1,5-d][1,2,4]triazin-4-amine formate
250	1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine formate
261	N-[(3R)-1-ethylpiperidin-3-yl]-1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine formate
278	2-[(3R)-3-({1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol formate
279	8-methyl-N-[(3R)-1-methylpiperidin-3-yl]-1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine formate
281	1-[4-methoxy-2-(pentafluoroethyl)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine formate
317	N-[(3R)-1-methylpiperidin-3-yl]-1-[4-methyl-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine formate
357	4-[4-bromo-2-(trifluoromethoxy)phenyl]-N-[(3R)-1-ethylpiperidin-3-yl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-amine formate
358	4-[4-chloro-2-(difluoromethoxy)phenyl]-2-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrazolo[1,5-d][1,2,4]triazin-7-amine formate

359	4-[2-(difluoromethyl)-4-(trifluoromethyl)phenyl]-2-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrazolo[1,5-d][1,2,4]triazin-7-amine formate
360	4-[4-cyclopropyl-2-(difluoromethoxy)phenyl]-2-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrazolo[1,5-d][1,2,4]triazin-7-amine formate
361	4-[2-(difluoromethoxy)-4-methylphenyl]-2-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrazolo[1,5-d][1,2,4]triazin-7-amine formate
363	4-[4-cyclopropyl-2-(difluoromethyl)phenyl]-2-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrazolo[1,5-d][1,2,4]triazin-7-amine formate
364	4-[2-(difluoromethyl)-4-methylphenyl]-2-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrazolo[1,5-d][1,2,4]triazin-7-amine formate
368	N-[(3R)-1-ethylpiperidin-3-yl]-4-[2-(methanesulfonyl)-4-methylphenyl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-amine trifluoroacetate
369	N-[(3R)-1-ethylpiperidin-3-yl]-4-[4-(methanesulfonyl)-2-(trifluoromethoxy)phenyl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-amine trifluoroacetate
372	2-(7-{[(3R)-1-ethylpiperidin-3-yl]amino}-2-methylpyrazolo[1,5-d][1,2,4]triazin-4-yl)-5-(trifluoromethyl)benzamide formate

wherein a form of the compound is selected from the group consisting of a hydrate, solvate, racemate, enantiomer, diastereomer, stereoisomer, tautomer, free-base and isotope enriched form thereof.

In embodiment 4, the invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound according to any one of embodiments 1 to 3 or a pharmaceutically acceptable salt thereof and one or more pharmaceutically acceptable carriers.

In embodiment 5, the invention provides a method for treating or ameliorating a disease modulated by NLRP3 in a subject in need thereof comprising, administering to the subject an effective amount of the compound according to any one of embodiments 1to 3.

In embodiment 6, the invention provides a method of treating or ameliorating a disease modulated by NLRP3 according to embodiment 5 selected from Alzheimer disease, Frontotemporal dementia (FTD), Huntington's disease, Parkinson's disease**,** Perioperative neurocognitive disorders, Post–cardiac arrest cognitive impairment, Poststroke cognitive impairment, Sepsis, Sepsis associated encephalopathy, Subarachnoid hemorrhage, Macular Degeneration, Retinal neovascularization, Uveitis, Colitis, Endothelial dysfunction, Gout, Pseudogout, Graft-versus-host-disease (GvHD), Systemic lupus erythematosus–lupus nephritis, Cryopyrin-associated periodic syndromes (CAPS), Cystic fibrosis, Sickle-cell disease, VCP-

associated disease, Liver fibrosis, Nonalcoholic fatty liver disease (NASH), muscle atrophy, inherited and acquired myopathies, e.g. Duchenne Muscular Dystrophy (DMD), Hyperalgesia, Multiple sclerosis–associated neuropathic pain, Acute Kidney Injury, Chronic crystal nephropathy, Chronic Kidney Disease, asthma and allergic airway inflammation Diabetes-associated atherosclerosis, Diabetic encephalopathy, Diabetic kidney disease, Islet transplantation rejection, Obesity-associated renal disease, Oxalate-induced nephropathy, Renal fibrosis, Renal hypertension, Type I diabetes, Type II diabetes, Psoriasis, Hidradenitis suppurativa, Atherosclerosis and Cytokine Release Syndrome (CRS).

In embodiment 7, the invention provides the method of any one of embodiments 5 to 6, wherein the effective amount of the compound is in a range of from about 0.001 mg/kg/day to about 500 mg/kg/day.

In embodiment 8, the invention provides a compound according to any one of embodiments 1 to 3 or a pharmaceutically acceptable salt thereof, for use in treating or ameliorating a disease modulated by NLRP3 selected from Alzheimer disease, Frontotemporal dementia (FTD), Huntington's disease, Parkinson's disease, Perioperative neurocognitive disorders, Post–cardiac arrest cognitive impairment, Poststroke cognitive impairment, Sepsis, Sepsis associated encephalopathy, Subarachnoid hemorrhage, Macular Degeneration, Retinal neovascularization, Uveitis, Colitis, Endothelial dysfunction, Gout, Pseudogout, Graft-versus-host-disease (GvHD), Systemic lupus erythematosus–lupus nephritis, Cryopyrin-associated periodic syndromes (CAPS), Cystic fibrosis, Sickle-cell disease, VCP-associated disease, Liver fibrosis, Nonalcoholic fatty liver disease (NASH), muscle atrophy, inherited and acquired myopathies, Hyperalgesia, Multiple sclerosis–associated neuropathic pain, Acute Kidney Injury, Chronic crystal nephropathy, Chronic Kidney Disease, asthma and allergic airway inflammation Diabetes-associated atherosclerosis, Diabetic encephalopathy, Diabetic kidney disease, Islet transplantation rejection, Obesity-associated renal disease, Oxalate-induced nephropathy, Renal fibrosis, Renal hypertension, Type I diabetes, Type II diabetes, Psoriasis, Hidradenitis suppurativa, Atherosclerosis and Cytokine Release Syndrome (CRS).

In embodiment 9, the invention provides a compound's use according to embodiment 8, where the effective amount of the compound is in a range from about 0.001 mg/kg/day to about 500 mg/kg/day.

In embodiment 10, the invention provides a use of a compound according to any one of embodiments 1 to 3 in the preparation of a pharmaceutical composition for treating or ameliorating a disease modulated by NLRP3 in a subject in need thereof comprising, administering to the subject an effective amount of the compound or a form thereof in admixture with one or more of the pharmaceutically acceptable excipients.

METHOD OF USE OF THE INVENTION

There is evidence for a role of NLRP3-induced IL-1β and IL-18 in the inflammatory responses occurring in connection with, or as a result of, a multitude of different disorders (Menu et al, *Clinical and Experimental Immunology,* 2011, 166, 1-15; Strowig et al, *Nature,* 2012, 481, 278-286). NLRP3 mutations have been found to be responsible for a set of rare autoinflammatory diseases known as CAPS (Ozaki et al, *J. Inflammation Research,* 2015, 8, 15-27; Schroder et al, *Cell,* 2010, 140:821-832; Menu et al, *Clinical and Experimental Immunology,* 2011, 166, 1-15). CAPS are heritable diseases characterized by recurrent fever and inflammation and are comprised of three autoinflammatory disorders that form a clinical continuum. These diseases, in order of increasing severity, are familial cold autoinflammatory syndrome (FCAS), Muckle-Wells syndrome (MWS), and chronic infantile cutaneous neurological articular syndrome (CINCA; also called neonatal-onset multisystem inflammatory disease, NOMID), and all have been shown to result from gain-of-function mutations in the NLRP3 gene, which leads to increased secretion of IL-I beta. NLRP3 has also been implicated in a number of autoinflammatory diseases, including pyogenic arthritis, pyoderma gangrenosum and acne (PAPA), Sweet's syndrome, chronic nonbacterial osteomyelitis (CNO), and acne vulgaris (Cook et al, *Eur J. Immunol.,* 2010, 40, 595-653). A number of autoimmune diseases have been shown to involve NLRP3 including, in particular, multiple sclerosis, type-1 diabetes (TlD), psoriasis, rheumatoid arthritis (RA), Behcet's disease, Schnitzler syndrome, macrophage activation syndrome (Braddock et al. *Nat. Rev. Drug Disc.* 2004, 3, 1-10; Inoue et al, *Immunology,* 2013, 139, 11-18, Coll et al, *Nat. Med.* 2015, 21(3), 248-55; Scott et al, *Clin. Exp. Rheumatol.* 2016, 34(1), 88-93), systemic lupus erythematosus and its complications such as lupus nephritis (Lu et al, *J. Immunol.,* 2017, 198(3), 1119-29), and systemic sclerosis (Artlett et al, *Arthritis Rheum.*

2011, 63(11), 3563-74). NLRP3 has also been shown to play a role in a number of lung diseases including chronic obstructive pulmonary disorder (COPD), asthma (including steroid resistant asthma), asbestosis, and silicosis (De Nardo et al, *Am. J. Pathol.,* 2014, 184: 42-54; Kim et al. *Am. J. Respir Crit Care Med,* 2017, 196(3), 283-97). NLRP3 has also been suggested to have a role in a number of central nervous system conditions, including Multiple Sclerosis (MS), Parkinson's disease (PD), Alzheimer's disease (AD), dementia, Huntington's disease, cerebral malaria, brain injury from pneumococcal meningitis (Walsh et al, *Nature Reviews,* 2014, 15, 84-97; and Dempsey et al. *Brain. Behav. Immun.* 2017, 61, 306-16), intracranial aneurysms (Zhang et al. *J. Stroke and Cerebrovascular Dis.,* 2015, 24, 5, 972-9), and traumatic brain injury (Ismael et al. *J. Neurotrauma.,* 2018, 35(11), 1294-1303). NRLP3 activity has also been shown to be involved in various metabolic diseases including type 2 diabetes (T2D) and its organ-specific complications, atherosclerosis, obesity, gout, pseudo-gout, metabolic syndrome (Wen et al, *Nature Immunology,* 2012, 13, 352-357; Duewell et al, *Nature,* 2010, 464, 1357-1361; Strowig et al, *Nature,* 2014, 481, 278-286), and non-alcoholic steatohepatitis (Mridha et al. *J. Hepatol.* 2017, 66(5), 1037-46). NLRP3 is also suggested to play a key pathological role in the development and progression of several skeletal muscle diseases, e.g. muscle atrophy, inherited and acquired myopathies (Dubussion et al. *Cells* 2021, 10(11),3023). A role for NLRP3 via IL-I beta has also been suggested in atherosclerosis, myocardial infarction (van Hout et al. *Eur Heart J.* 2017, 38(11), 828-3-6), heart failure (Sano et al. *J. Am. Coll. Cardiol.* 2018, 71(8), 875-66), aortic aneurysm and dissection (Wu et al. *Arterioscler Thromb. Vase. Biol.,* 2017, 37(4), 694-706), and other cardiovascular events (Ridker et al, *N. Engl. J. Med,* 2017, 377(12), 1119-31). Other diseases in which NLRP3 has been shown to be involved include: ocular diseases such as both wet and dry age-related macular degeneration (Doyle et al. *Nature Medicine,* 2012, 18, 791-798; Tarallo et al. *Cell* 2012, 149(4), 847-59), diabetic retinopathy (Loukovaara et al. *Acta Ophthalmol.,* 2017, 95(8), 803-8), non-infectious uveitis and optic nerve damage (Puyang et al. *Sci. Rep.* 2016, 6, 20998); liver diseases including non-alcoholic steatohepatitis (NASH) and acute alcoholic hepatitis (Henao-Meija et al, *Nature,* 2012, 482, 179-185); inflammatory reactions in the lung and skin (Primiano et al. *J. Immunol.* 2016, 197(6), 2421-33) including contact hypersensitivity (such as bullous pemphigoid (Fang et al. *J Dermatol Sci.* 2016, 83(2),116-23)), atopic dermatitis (Niebuhr et al. *Allergy,* 2014, 69(8), 1058-67), Hidradenitis suppurativa (Alikhan et al. *J. Am. Acad. Dermatol.,* 2009, 60(4), 539-61), and sarcoidosis (Jager

et al. *Am. J. Respir Crit. Care Med.,* 2015, 191, A5816); inflammatory reactions in the joints (Braddock et al, *Nat. Rev. Drug Disc,* 2004, 3, 1-10); amyotrophic lateral sclerosis (Gugliandolo et al. *Int. J. Mol. Sci.,* 2018, 19(7), E1992); cystic fibrosis (larmitti et al. *Nat. Commun.,* 2016, 7, 10791); stroke (Walsh et al, *Nature Reviews,* 2014, 15, 84-97); chronic kidney disease (Granata et al. *PLoS One* 2015, 10(3), eoi22272); and inflammatory bowel diseases including ulcerative colitis and Crohn's disease (Braddock et al, *Nat. Rev. Drug Disc,* 2004, 3, 1-10; Neudecker et al. *J. Exp. Med.* 2017, 214(6), 1737-52; Lazaridis et al. *Dig. Dis. Sci.* 2017, 62(9), 2348-56). The NLRP3 inflammasome has been found to be activated in response to oxidative stress. NLRP3 has also been shown to be involved in inflammatory hyperalgesia (Dolunay et al, *Inflammation,* 2017, 40, 3-66-86). US application US202003-61898 in incorporated herein by reference.

DEFINITIONS

To assist in understanding the scope of the compounds of Formula I or a form thereof described herein, the following Specific Examples are included. The experiments relating to the compounds of Formula I or a form thereof described herein should not, of course, be construed as specifically limiting the scope of the compounds of Formula I or a form thereof described herein and such variations of the compounds of Formula I or a form thereof as described herein, now known or later developed, which would be within the purview of one skilled in the art are considered to fall within the scope as described herein and hereinafter claimed.

Other than in the working examples, unless indicated to the contrary, all numbers expressing quantities of ingredients, reaction conditions, experimental data, and so forth used in the specification and claims are to be understood as being modified by the term "about". Accordingly, all such numbers represent approximations that may vary depending upon the desired properties sought to be obtained by a reaction or as a result of variable experimental conditions. Therefore, within an expected range of experimental reproducibility, the term "about" in the context of the resulting data, refers to a range for data provided that may vary according to a standard deviation from the mean. As well, for experimental results provided, the resulting data may be rounded up or down to present data consistently, without loss of significant figures. At the very least, and not as an attempt to limit the application of the doctrine of

equivalents to the scope of the claims, each numerical parameter should be construed in light of the number of significant digits and ordinary rounding techniques.

While the numerical ranges and parameters setting forth the characterization of the compounds of Formula I or a form thereof described herein are approximations, the numerical values set forth in the working examples are reported as precisely as possible. Any numerical value, however, inherently contains certain errors necessarily resulting from the standard deviation found in their respective testing measurements.

The compounds of Formula I or a form thereof provided herein are described in more detail with reference to the following non-limiting examples, which are offered to more fully illustrate the scope of the compounds of Formula I or a form thereof described herein but are not to be construed as limiting the scope thereof. The examples illustrate the preparation of compounds of Formula I or a form thereof described herein, and the testing of these compounds of Formula I or a form thereof *in vitro* and/or *in vivo*. Those of skill in the art will understand that the synthesis techniques described in these examples represent techniques that fall within the practice of those having ordinary skill in the chemical arts, and as such constitute preferred modes for the practice thereof. However, it should be appreciated that those having skill in the art should, in light of the present disclosure, appreciate that many changes can be made in the specific methods that are disclosed herein while still obtaining a like or similar result without departing from the spirit and scope described herein.

In certain embodiments described herein, the compound of Formula I or a form thereof is isolated for use.

As used herein, the term "isolated" means the physical state of a compound of Formula I or a form thereof after being isolated and/or separated and/or purified from a synthetic process (*e.g.,* from a reaction mixture) or natural source or combination thereof according to an isolation, separation or purification process or processes described herein or which are well known to the skilled artisan (*e.g.,* chromatography, recrystallization and the like) in sufficient purity to be characterizable by standard analytical techniques described herein or well known to the skilled artisan.

As used herein, the term "protected" means that a functional group on a compound of Formula I or a form thereof is in a form modified to preclude undesired side reactions of the

functional group when the compound is subjected to a reaction. Suitable protecting groups will be recognized by those with ordinary skill in the art as well as by reference to standard textbooks such as, for example, T. W. Greene *et al*, *Protective Groups in Organic Synthesis* (2007), Wiley, New York.

Prodrugs and solvates of the compounds of Formula I or a form thereof described herein are also contemplated.

As used herein, the term "prodrug" means that a functional group on a compound of Formula I or a form thereof is in a form (*e.g.*, acting as an active or inactive drug precursor) that is transformed *in vivo* to yield an active or more active compound of Formula I or a form thereof. The transformation may occur by various mechanisms (*e.g.*, by metabolic and/or nonmetabolic chemical processes), such as, for example, by hydrolysis and/or metabolism in blood, liver and/or other organs and tissues. A discussion of the use of prodrugs is provided by V.J. Stella, et. al., "Biotechnology: Pharmaceutical Aspects, Prodrugs: Challenges and Rewards," American Association of Pharmaceutical Scientists and Springer Press, 2007.

In one example, when a compound of Formula I or a form thereof contains a carboxylic acid functional group, a prodrug can comprise an ester formed by the replacement of the hydrogen atom of the acid group with a functional group such as alkyl and the like. In another example, when a compound of Formula I or a form thereof contains an alcohol functional group, a prodrug can be formed by the replacement of the hydrogen atom of the alcohol group with a functional group such as alkyl or carbonyloxy and the like. In another example, when a compound of Formula I or a form thereof contains an amine functional group, a prodrug can be formed by the replacement of one or more amine hydrogen atoms with a functional group such as alkyl or substituted carbonyl.

Pharmaceutically acceptable prodrugs of compounds of Formula I or a form thereof include those compounds substituted with one or more of the following groups: carboxylic acid esters, sulfonate esters, amino acid esters, phosphonate esters (e.g., a phosphoramidic acid used to derive a phosphoramidic acid) and mono-, di- or triphosphate esters further substituted with alkyl, where appropriate. As described herein, it is understood by a person of ordinary skill in the art that one or more of such substituents may be used to provide a compound of Formula I or a form thereof as a prodrug.

The compounds of Formula I or a form thereof can form salts, which are intended to be included within the scope of this description. Reference to a compound of Formula I or a form thereof is understood to include reference to salts thereof, unless otherwise indicated. The term "salt(s)", as employed herein, denotes acidic salts formed with inorganic and/or organic acids, as well as basic salts formed with inorganic and/or organic bases. In addition, when a compound of Formula I or a form thereof contains both a basic moiety, such as, but not limited to a pyridine or imidazole, and an acidic moiety, such as, but not limited to a carboxylic acid, zwitterions ("inner salts") may be formed and are included within the term "salt(s)" as used herein.

The term "pharmaceutically acceptable salt(s)", as used herein, means those salts of compounds of Formula I or a form thereof described herein that are safe and effective (*i.e.*, non-toxic, physiologically acceptable) for use in mammals and that possess biological activity, although other salts are also useful. Salts of the compounds of the Formula I or a form thereof may be formed, for example, by reacting a compound of Formula I or a form thereof and compounds described herein with an amount of acid or base, such as an equivalent amount, in a medium such as one in which the salt precipitates or in an aqueous medium followed by lyophilization.

Additionally, acids which are considered suitable for the formation of pharmaceutically useful salts from basic pharmaceutical compounds are discussed, for example, by P. Stahl *et al*, Camille G. (eds.) *Handbook of Pharmaceutical Salts. Properties, Selection and Use.* (2002) Zurich: Wiley-VCH; S. Berge *et al*, *Journal of Pharmaceutical Sciences* (1977) 66(1) 1-19; P. Gould, *International J. of Pharmaceutics* (1986) 33, 201-217; Anderson *et al*, *The Practice of Medicinal Chemistry* (1996), Academic Press, New York; and in *The Orange Book* (Food & Drug Administration, Washington, D.C. on their website). These disclosures are incorporated herein by reference thereto.

Suitable basic salts include, but are not limited to, aluminum, ammonium, calcium, lithium, magnesium, potassium, sodium, zinc, and diethanolamine salts. Certain compounds of Formula I or a form thereof described herein can also form pharmaceutically acceptable salts with organic bases (for example, organic amines) such as, but not limited to, dicyclohexylamines, *tert*-butyl amines and the like, and with various amino acids such as, but not limited to, arginine, lysine and the like. Basic nitrogen-containing groups may be quarternized

with agents such as lower alkyl halides (*e.g.,* methyl, ethyl, and butyl chlorides, bromides and iodides), dialkyl sulfates (*e.g.,* dimethyl, diethyl, and dibutyl sulfates), long chain halides (*e.g.,* decyl, lauryl, and stearyl chlorides, bromides and iodides), aralkyl halides (*e.g.,* benzyl and phenethyl bromides), and others.

All such acid salts and base salts are intended to be included within the scope of pharmaceutically acceptable salts as described herein. In addition, all such acid and base salts are considered equivalent to the free forms of the corresponding compounds for purposes of this description.

Compounds of Formula I, and forms thereof, may further exist in a tautomeric form. All such tautomeric forms are contemplated and intended to be included within the scope of the compounds of Formula I or a form thereof as described herein.

The compounds of Formula I or a form thereof may contain asymmetric or chiral centers, and, therefore, may exist in different stereoisomeric forms. The present description is intended to include all stereoisomeric forms of the compounds of Formula I or a form thereof, as well as mixtures thereof, including racemic mixtures.

The compounds of Formula I or a form thereof described herein may include one or more chiral centers, and as such may exist as racemic mixtures (*R/S*) or as substantially pure enantiomers and diastereomers. The compounds may also exist as substantially pure (*R*) or (*S*) enantiomers (when one chiral center is present). In one embodiment, the compounds of Formula I or a form thereof described herein are (*S*) isomers and may exist as enantiomerically pure compositions substantially comprising only the (*S*) isomer. In another embodiment, the compounds of Formula I or a form thereof described herein are (*R*) isomers and may exist as enantiomerically pure compositions substantially comprising only the (*R*) isomer. As one of skill in the art will recognize, when more than one chiral center is present, the compounds of Formula I or a form thereof described herein may also exist as a (*R,R*), (*R,S*), (*S,R*) or (*S,S*) isomer, as defined by *IUPAC* Nomenclature Recommendations.

As used herein, the term "substantially pure" refers to compounds of Formula I or a form thereof consisting substantially of a single isomer in an amount greater than or equal to 90%, in an amount greater than or equal to 92%, in an amount greater than or equal to 95%, in an amount

greater than or equal to 98%, in an amount greater than or equal to 99%, or in an amount equal to 100% of the single isomer.

In one aspect of the description, a compound of Formula I or a form thereof is a substantially pure (*S*) enantiomer present in an amount greater than or equal to 90%, in an amount greater than or equal to 92%, in an amount greater than or equal to 95%, in an amount greater than or equal to 98%, in an amount greater than or equal to 99%, or in an amount equal to 100%.

In one aspect of the description, a compound of Formula I or a form thereof is a substantially pure (*R*) enantiomer present in an amount greater than or equal to 90%, in an amount greater than or equal to 92%, in an amount greater than or equal to 95%, in an amount greater than or equal to 98%, in an amount greater than or equal to 99%, or in an amount equal to 100%.

As used herein, the term "racemate" refers to any mixture of isometric forms that are not "enantiomerically pure", including mixtures such as, without limitation, in a ratio of about 50/50, about 60/40, about 70/30, or about 80/20, about 85/15 or about 90/10.

In addition, the compounds of Formula I or a form thereof described herein embrace all geometric and positional isomers. For example, if a compound of Formula I or a form thereof incorporates a double bond or a fused ring, both the cis- and trans-forms, as well as mixtures thereof, are embraced within the scope of the compounds of Formula I or a form thereof described herein.

Diastereomeric mixtures can be separated into their individual diastereomers on the basis of their physical chemical differences by methods well known to those skilled in the art, such as, for example, by chromatography and/or fractional crystallization. Enantiomers can be separated by use of a chiral HPLC column or other chromatographic methods known to those skilled in the art.

Enantiomers can also be separated by converting the enantiomeric mixture into a diastereomeric mixture by reaction with an appropriate optically active compound (*e.g.,* chiral auxiliary such as a chiral alcohol or Mosher's acid chloride), separating the diastereomers and

converting (*e.g.,* hydrolyzing) the individual diastereomers to the corresponding pure enantiomers.

All stereoisomers (for example, geometric isomers, optical isomers and the like) of the present compounds of Formula I or a form thereof (including salts, solvates, esters and prodrugs and transformed prodrugs thereof), which may exist due to asymmetric carbons on various substituents, including enantiomeric forms (which may exist even in the absence of asymmetric carbons), rotameric forms, atropisomers, diastereomeric and regioisomeric forms, are contemplated within the scope of the description herein. Individual stereoisomers of the compounds of Formula I or a form thereof described herein may, for example, be substantially free of other isomers, or may be present in a racemic mixture, as described *supra*.

The use of the terms "salt," "solvate," “ester,” "prodrug" and the like, is intended to apply equally to the salt, solvate, ester and prodrug of enantiomers, stereoisomers, rotamers, tautomers, positional isomers, racemates, isotope enriched or prodrugs of the instant compounds.

One or more compounds of Formula I or a form thereof described herein may exist in unsolvated as well as solvated forms with pharmaceutically acceptable solvents such as water, ethanol, and the like, and the description herein is intended to embrace both solvated and unsolvated forms.

As used herein, the term “solvate” means a physical association of a compound of Formula I or a form thereof described herein with one or more solvent molecules. This physical association involves varying degrees of ionic and covalent bonding, including hydrogen bonding. In certain instances the solvate will be capable of isolation, for example when one or more solvent molecules are incorporated in the crystal lattice of the crystalline solid. As used herein, “solvate” encompasses both solution-phase and isolatable solvates. Non-limiting examples of suitable solvates include ethanolates, methanolates, and the like.

One or more compounds of Formula I or a form thereof described herein may optionally be converted to a solvate. Preparation of solvates is generally known. A typical, non-limiting process involves dissolving a compound of Formula I or a form thereof in a desired amount of the desired solvent (organic or water or mixtures thereof) at a higher than ambient temperature and cooling the solution at a rate sufficient to form crystals which are then isolated by standard

methods. Analytical techniques such as, for example infrared spectroscopy, show the presence of the solvent (or water) in the crystals as a solvate (or hydrate).

As used herein, the term "hydrate" means a solvate wherein the solvent molecule is water.

Polymorphic crystalline and amorphous forms of the compounds of Formula I or a form thereof, and of the salts, solvates, esters and prodrugs of the compounds of Formula I or a form thereof, are further intended to be included in the scope of the compounds of Formula I or a form thereof described herein.

As used herein, the term "isotope enriched" means a compounds of Formula I or a form thereof which are identical to those recited herein, but for the fact that one or more atoms are replaced by an atom having an atomic mass or mass number different from the atomic mass or mass number usually found in nature. Examples of isotopes that can be incorporated into compounds of Formula I or a form thereof described herein include isotopes of hydrogen, carbon, nitrogen, oxygen, phosphorus, fluorine and chlorine, such as H^2, H^3, C^{13}, C^{14}, N^{15}, O^{18}, O^{17}, P^{31}, P^{32}, S^{35}, F^{18}, Cl^{35} and Cl^{36}, respectively, each of which is also within the scope of this description.

DOSAGE AND ADMINISTRATION

The compounds of the present invention may be formulated in a wide variety of oral administration dosage forms and carriers. Oral administration can be in the form of tablets, coated tablets, dragées, hard and soft gelatine capsules, solutions, emulsions, syrups, or suspensions. Compounds of the present invention are efficacious when administered by other routes of administration including continuous (intravenous drip) topical parenteral, intramuscular, intravenous, subcutaneous, transdermal (which may include a penetration enhancement agent), buccal, nasal, inhalation and suppository administration, among other routes of administration. The preferred manner of administration is generally oral using a convenient daily dosing regimen which can be adjusted according to the degree of affliction and the patient's response to the active ingredient.

A compound or compounds of the present invention, as well as their pharmaceutically useable salts, together with one or more conventional excipients, carriers, or diluents, may be placed into the form of pharmaceutical compositions and unit dosages. The pharmaceutical compositions and unit dosage forms may be comprised of conventional ingredients in conventional proportions, with or without additional active compounds or principles, and the unit dosage forms may contain any suitable effective amount of the active ingredient commensurate with the intended daily dosage range to be employed. The pharmaceutical compositions may be employed as solids, such as tablets or filled capsules, semisolids, powders, sustained release formulations, or liquids such as solutions, suspensions, emulsions, elixirs, or filled capsules for oral use; or in the form of suppositories for rectal or vaginal administration; or in the form of sterile injectable solutions for parenteral use. A typical preparation will contain from about 5% to about 95% active compound or compounds (w/w). The term "preparation" or "dosage form" is intended to include both solid and liquid formulations of the active compound and one skilled in the art will appreciate that an active ingredient can exist in different preparations depending on the target organ or tissue and on the desired dose and pharmacokinetic parameters.

The term “excipient” as used herein refers to a compound that is useful in preparing a pharmaceutical composition, generally safe, non-toxic and neither biologically nor otherwise undesirable, and includes excipients that are acceptable for veterinary use as well as human pharmaceutical use. The compounds of this invention can be administered alone but will generally be administered in admixture with one or more suitable pharmaceutical excipients, diluents or carriers selected with regard to the intended route of administration and standard pharmaceutical practice.

“Pharmaceutically acceptable” means that which is useful in preparing a pharmaceutical composition that is generally safe, non-toxic, and neither biologically nor otherwise undesirable and includes that which is acceptable for veterinary as well as human pharmaceutical use.

A "pharmaceutically acceptable salt" form of an active ingredient may also initially confer a desirable pharmacokinetic property on the active ingredient which were absent in the non-salt form, and may even positively affect the pharmacodynamics of the active ingredient with respect to its therapeutic activity in the body. The phrase “pharmaceutically acceptable salt” of a compound means a salt that is pharmaceutically acceptable and that possesses the

desired pharmacological activity of the parent compound. Such salts include: (1) acid addition salts, formed with inorganic acids such as hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid, and the like; or formed with organic acids such as acetic acid, propionic acid, hexanoic acid, cyclopentanepropionic acid, glycolic acid, pyruvic acid, lactic acid, malonic acid, succinic acid, malic acid, maleic acid, fumaric acid, tartaric acid, citric acid, benzoic acid, 3-(4-hydroxybenzoyl)benzoic acid, cinnamic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, 1,2-ethane-disulfonic acid, 2-hydroxyethanesulfonic acid, benzenesulfonic acid, 4-chlorobenzenesulfonic acid, 2-naphthalenesulfonic acid, 4-toluenesulfonic acid, camphorsulfonic acid, 4-methylbicyclo[2.2.2]-oct-2-ene-1-carboxylic acid, glucoheptonic acid, 3-phenylpropionic acid, trimethylacetic acid, tertiary butylacetic acid, lauryl sulfuric acid, gluconic acid, glutamic acid, hydroxynaphthoic acid, salicylic acid, stearic acid, muconic acid, and the like; or (2) salts formed when an acidic proton present in the parent compound either is replaced by a metal ion, *e.g.*, an alkali metal ion, an alkaline earth ion, or an aluminum ion; or coordinates with an organic base such as ethanolamine, diethanolamine, triethanolamine, tromethamine, N-methylglucamine, and the like.

Solid form preparations include powders, tablets, pills, capsules, cachets, suppositories, and dispersible granules. A solid carrier may be one or more substances which may also act as diluents, flavoring agents, solubilizers, lubricants, suspending agents, binders, preservatives, tablet disintegrating agents, or an encapsulating material. In powders, the carrier generally is a finely divided solid which is a mixture with the finely divided active component. In tablets, the active component generally is mixed with the carrier having the necessary binding capacity in suitable proportions and compacted in the shape and size desired. Suitable carriers include but are not limited to magnesium carbonate, magnesium stearate, talc, sugar, lactose, pectin, dextrin, starch, gelatin, tragacanth, methylcellulose, sodium carboxymethylcellulose, a low melting wax, cocoa butter, and the like. Solid form preparations may contain, in addition to the active component, colorants, flavors, stabilizers, buffers, artificial and natural sweeteners, dispersants, thickeners, solubilizing agents, and the like.

Liquid formulations also are suitable for oral administration include liquid formulation including emulsions, syrups, elixirs, aqueous solutions, aqueous suspensions. These include solid form preparations which are intended to be converted to liquid form preparations shortly before use. Emulsions may be prepared in solutions, for example, in aqueous propylene glycol

solutions or may contain emulsifying agents such as lecithin, sorbitan monooleate, or acacia. Aqueous solutions can be prepared by dissolving the active component in water and adding suitable colorants, flavors, stabilizing, and thickening agents. Aqueous suspensions can be prepared by dispersing the finely divided active component in water with viscous material, such as natural or synthetic gums, resins, methylcellulose, sodium carboxymethylcellulose, and other well known suspending agents.

The compounds of the present invention may be formulated for parenteral administration (*e.g.*, by injection, for example bolus injection or continuous infusion) and may be presented in unit dose form in ampoules, pre-filled syringes, small volume infusion or in multi-dose containers with an added preservative. The compositions may take such forms as suspensions, solutions, or emulsions in oily or aqueous vehicles, for example solutions in aqueous polyethylene glycol. Examples of oily or nonaqueous carriers, diluents, solvents or vehicles include propylene glycol, polyethylene glycol, vegetable oils (*e.g.*, olive oil), and injectable organic esters (*e.g.*, ethyl oleate), and may contain formulatory agents such as preserving, wetting, emulsifying or suspending, stabilizing and/or dispersing agents. Alternatively, the active ingredient may be in powder form, obtained by aseptic isolation of sterile solid or by lyophilisation from solution for constitution before use with a suitable vehicle, *e.g.*, sterile, pyrogen-free water.

The compounds of the present invention may be formulated for topical administration to the epidermis as ointments, creams or lotions, or as a transdermal patch. Ointments and creams may, for example, be formulated with an aqueous or oily base with the addition of suitable thickening and/or gelling agents. Lotions may be formulated with an aqueous or oily base and will in general also containing one or more emulsifying agents, stabilizing agents, dispersing agents, suspending agents, thickening agents, or coloring agents. Formulations suitable for topical administration in the mouth include lozenges comprising active agents in a flavored base, usually sucrose and acacia or tragacanth; pastilles comprising the active ingredient in an inert base such as gelatin and glycerin or sucrose and acacia; and mouthwashes comprising the active ingredient in a suitable liquid carrier.

The compounds of the present invention may be formulated for administration as suppositories. A low melting wax, such as a mixture of fatty acid glycerides or cocoa butter is

first melted and the active component is dispersed homogeneously, for example, by stirring. The molten homogeneous mixture is then poured into convenient sized molds, allowed to cool, and to solidify.

The compounds of the present invention may be formulated for vaginal administration. Pessaries, tampons, creams, gels, pastes, foams or sprays containing in addition to the active ingredient such carriers as are known in the art to be appropriate.

The compounds of the present invention may be formulated for nasal administration. The solutions or suspensions are applied directly to the nasal cavity by conventional means, for example, with a dropper, pipette or spray. The formulations may be provided in a single or multidose form. In the latter case of a dropper or pipette, this may be achieved by the patient administering an appropriate, predetermined volume of the solution or suspension. In the case of a spray, this may be achieved for example by means of a metering atomizing spray pump.

The compounds of the present invention may be formulated for aerosol administration, particularly to the respiratory tract and including intranasal administration. The compound will generally have a small particle size for example of the order of five (5) microns or less. Such a particle size may be obtained by means known in the art, for example by micronization. The active ingredient is provided in a pressurized pack with a suitable propellant such as a chlorofluorocarbon (CFC), for example, dichlorodifluoromethane, trichlorofluoromethane, or dichlorotetrafluoroethane, or carbon dioxide or other suitable gas. The aerosol may conveniently also contain a surfactant such as lecithin. The dose of drug may be controlled by a metered valve. Alternatively the active ingredients may be provided in a form of a dry powder, for example a powder mix of the compound in a suitable powder base such as lactose, starch, starch derivatives such as hydroxypropylmethyl cellulose and polyvinylpyrrolidine (PVP). The powder carrier will form a gel in the nasal cavity. The powder composition may be presented in unit dose form for example in capsules or cartridges of *e.g.*, gelatin or blister packs from which the powder may be administered by means of an inhaler.

When desired, formulations can be prepared with enteric coatings adapted for sustained or controlled release administration of the active ingredient. For example, the compounds of the present invention can be formulated in transdermal or subcutaneous drug delivery devices. These delivery systems are advantageous when sustained release of the compound is necessary

and when patient compliance with a treatment regimen is crucial. Compounds in transdermal delivery systems are frequently attached to an skin-adhesive solid support. The compound of interest can also be combined with a penetration enhancer, e.g., Azone (1-dodecylaza-cycloheptan-2-one). Sustained release delivery systems are inserted subcutaneously into to the subdermal layer by surgery or injection. The subdermal implants encapsulate the compound in a lipid soluble membrane, e.g., silicone rubber, or a biodegradable polymer, e.g., polyactic acid.

Suitable formulations along with pharmaceutical carriers, diluents and expcipients are described in *Remington: The Science and Practice of Pharmacy* 1995, edited by E. W. Martin, Mack Publishing Company, 19th edition, Easton, Pennsylvania. A skilled formulation scientist may modify the formulations within the teachings of the specification to provide numerous formulations for a particular route of administration without rendering the compositions of the present invention unstable or compromising their therapeutic activity.

The modification of the present compounds to render them more soluble in water or other vehicle, for example, may be easily accomplished by minor modifications (salt formulation, esterification, etc.), which are well within the ordinary skill in the art. It is also well within the ordinary skill of the art to modify the route of administration and dosage regimen of a particular compound in order to manage the pharmacokinetics of the present compounds for maximum beneficial effect in patients.

The term "therapeutically effective amount" as used herein means an amount required to reduce symptoms of the disease in an individual. The dose will be adjusted to the individual requirements in each particular case. That dosage can vary within wide limits depending upon numerous factors such as the severity of the disease to be treated, the age and general health condition of the patient, other medicaments with which the patient is being treated, the route and form of administration and the preferences and experience of the medical practitioner involved. For oral administration, a daily dosage of between about 0.01 and about 1000 mg/kg body weight per day should be appropriate in monotherapy and/or in combination therapy. A preferred daily dosage is between about 0.1 and about 500 mg/kg body weight, more preferred 0.1 and about 100 mg/kg body weight and most preferred 1.0 and about 10 mg/kg body weight per day. Thus, for administration to a 70 kg person, the dosage range would be about 7 mg to 0.7 g per day. The daily dosage can be administered as a single dosage or in divided dosages, typically

between 1 and 5 dosages per day. Generally, treatment is initiated with smaller dosages which are less than the optimum dose of the compound. Thereafter, the dosage is increased by small increments until the optimum effect for the individual patient is reached. One of ordinary skill in treating diseases described herein will be able, without undue experimentation and in reliance on personal knowledge, experience and the disclosures of this application, to ascertain a therapeutically effective amount of the compounds of the present invention for a given disease and patient.

The pharmaceutical preparations are preferably in unit dosage forms. In such form, the preparation is subdivided into unit doses containing appropriate quantities of the active component. The unit dosage form can be a packaged preparation, the package containing discrete quantities of preparation, such as packeted tablets, capsules, and powders in vials or ampoules. Also, the unit dosage form can be a capsule, tablet, cachet, or lozenge itself, or it can be the appropriate number of any of these in packaged form.

Examples of representative compounds encompassed by the present invention and within the scope of the invention are provided in the following Table. These examples and preparations which follow are provided to enable those skilled in the art to more clearly understand and to practice the present invention. They should not be considered as limiting the scope of the invention, but merely as being illustrative and representative thereof.

In general, the nomenclature used in this Application is based on AUTONOMTM v.4.0, a Beilstein Institute computerized system for the generation of IUPAC systematic nomenclature. If there is a discrepancy between a depicted structure and a name given that structure, the depicted structure is to be accorded more weight. In addition, if the stereochemistry of a structure or a portion of a structure is not indicated with, for example, bold or dashed lines, the structure or portion of the structure is to be interpreted as encompassing all stereoisomers of it.

The reagents and solvents were used as purchased (from a variety of vendors), except where noted. Where applicable, the term “Celite” is used as shown in the following examples to represent the tradename CELITE® (brand of diatomaceous earth). Where applicable, chromatographic separations were performed using techniques and equipment commonly available such as, for example, by using an ISCO CombiFlash® Rf system. Where applicable, NMR spectra were obtained using techniques and equipment commonly available such as, for

example, by using a Bruker Avance III^{500} spectrometer with deuterated solvents such as, for example, DMSO-d_6 or residual solvent as standard. Where applicable, melting points were determined using techniques and equipment commonly available such as, for example, by using a SRS OptiMelt® MPA100 (values as obtained without correction/calibration). Where applicable, TLC analysis was performed using techniques and equipment commonly available such as, for example, by using Aldrich 254 nm glass-backed plates (60 Å, 250 μm), visualized using UV and I_2 stains. Where applicable, ESI mass spectra were obtained using techniques and equipment commonly available such as, for example, by using an ACQUITY UPLC® System, with values shown as $[M+H]^+$ or $[M-H]^-$, unless otherwise indicated. Where applicable, the structure of the product was obtained via a 2D NOESY (Nuclear Overhauser SpectroscopY) experiment.

COMPOUNDS AND PREPARATION

Examples of representative compounds encompassed by the present invention and within the scope of the invention are provided herein. These examples and preparations which follow are provided to enable those skilled in the art to more clearly understand and to practice the present invention. They should not be considered as limiting the scope of the invention, but merely as being illustrative and representative thereof.

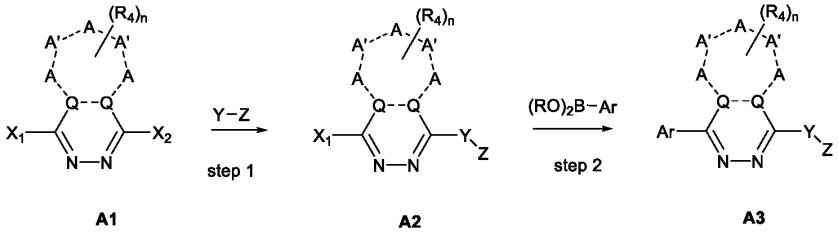
EXPERIMENTAL

As disclosed herein, general methods for preparing the compounds of Formula I or a form thereof as described herein can be prepared using the methods summarized in Schemes A-J by the suitable selection of reagents with appropriate substitution, solvents, temperatures, pressures, and other reaction conditions readily selected by one of ordinary skilled in the art. Many of the starting materials are commercially available or, when not available, can be prepared via standard, well-known synthetic methodology or using the routes described below using techniques known to those skilled in the art. The synthetic schemes provided herein comprise multiple reaction steps, each of which is intended to stand on its own and can be

carried out with or without any preceding or succeeding step(s). In other words, each of the individual reaction steps of the synthetic schemes provided herein in isolation is contemplated.

Depending on the nature of the groups depicted in the schemes below, the final compounds or their precursors may be further elaborated using the standard, well-known synthetic methods such as SN_2 displacement reaction, metal catalyzed coupling reactions like Suzuki coupling, Negishi coupling and Buchwald coupling, reductive amination, etc. to afford the compounds of the general Formula I-II.

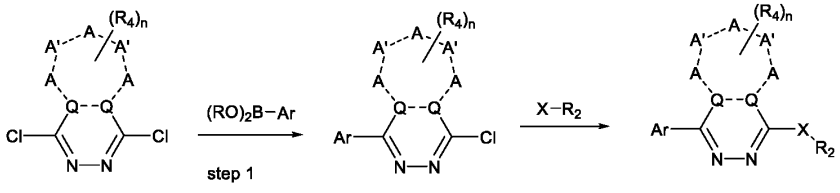
Scheme A:



A1 A2 A3

Compound **A1** (where X_1 and X_2 are independently bromine, chlorine and the like) is converted to Compound **A2** by a nucleophilic substitution with either an appropriate amine in the presence of a suitable base (such as DIEPA and the like) in a suitable solvent (such as NMP and the like) or with an appropriate alcohol in the presence of a suitable base (such as NaH and the like) in a suitable solvent (such as anhydrous THF and the like). Compound **A2** is converted to Compound **A3** by a Suzuki coupling with an aryl- or heteroaryl-boronic acid (or pinacol boronic ester) in the presence of a catalyst (such as $Pd(dppf)Cl_2$ and the like) and base (such as aqueous K_2CO_3 and the like) in a suitable solvent (such as 1,4-dioxane and the like).

Scheme B:

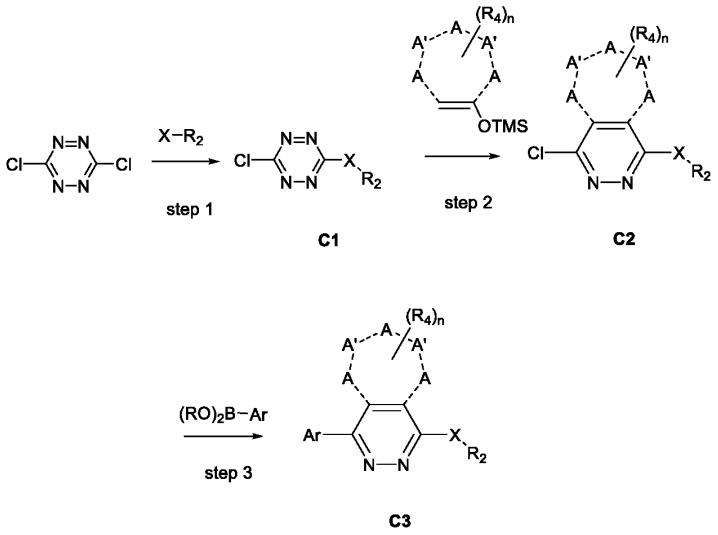


B1 B2 B3

Compound **B1** is converted to Compound **B2** by a Suzuki coupling with an aryl- or heteroaryl-boronic acid (or pinacol boronic ester) in the presence of a catalyst (such as $Pd(dppf)Cl_2$ and the

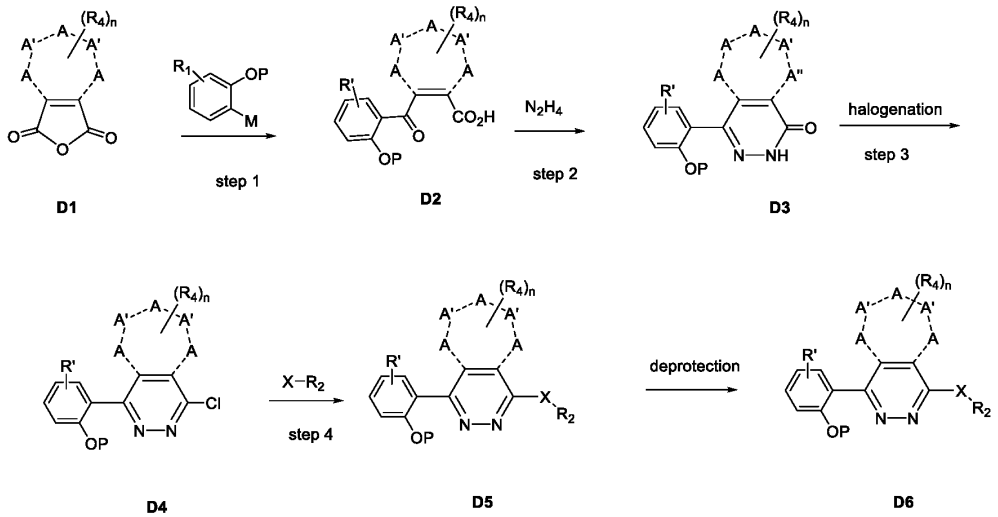
like) and base (such as aqueous K_2CO_3 and the like) in a suitable solvent (such as 1,4-dioxane and the like). Compound **B2** is converted to Compound **B3** by a Buchwald-Hartwig coupling with an appropriate amine in the present of a catalyst (such as $Pd_2(dba)_3$ and the like), a ligand (such as RuPhos and the like) and a base (such as NaO^tBu and the like) in a suitable solvent (such as PhMe and the like).

Scheme C:



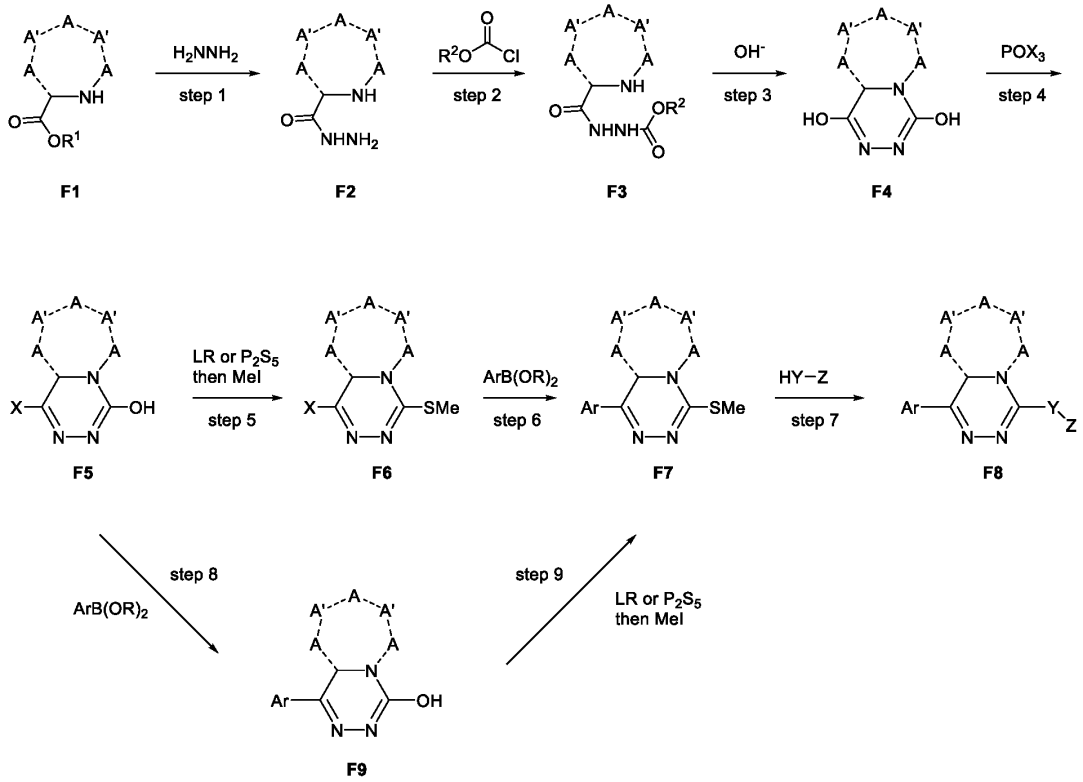
Compound **C1** is prepared from 1,2,4,5-tetrazines with an appropriate amine in the presence of a suitable base (such as DIEPA and the like) in a suitable solvent (such as DCM and the like). Compound **C1** is converted to Compound **C2** by inverse electron demand Diels-Alder reaction with an appropriate enol ethers or enamine in a suitable solvent (such as PhMe and the like). Following conditions described in Scheme A - step 2, compound **C2** was converted to compound **C3**.

Scheme D:



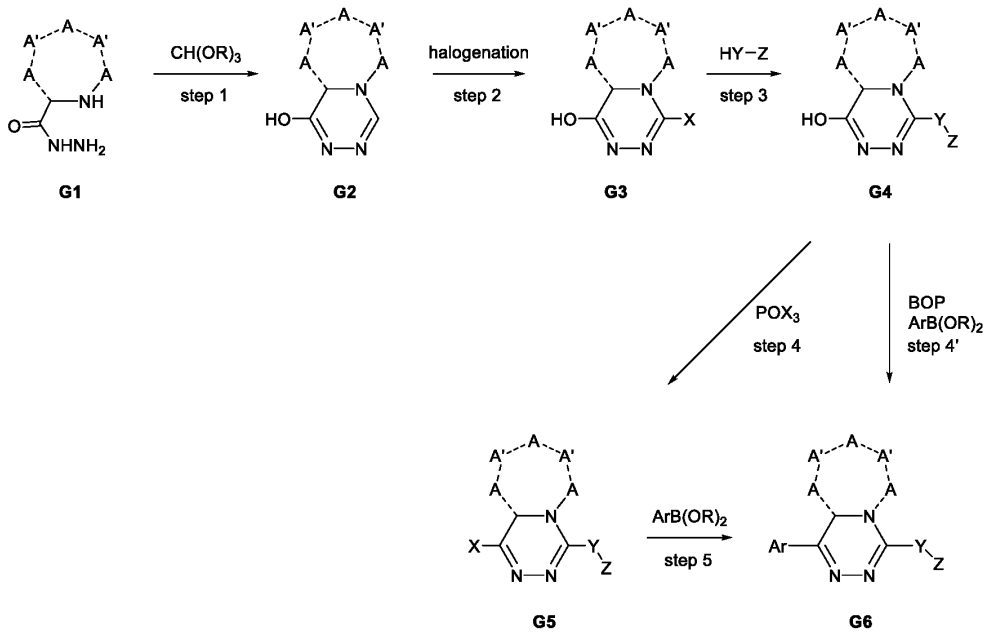
Compound **D1** is converted to Compound **D2** (where P is a protecting group such as Me and the like) by reacting with an appropriate organometallic compound (such as Grignard reagent and the like) in a suitable solvent (such as THF and the like). Compound **D2** is converted to Compound **D3** by condensation/cyclization sequence in the present of hydrazine in a suitable solvent (such as EtOH and the like). Compound **D3** is converted to Compound **D4** by treatment with a dehydrative halogenating agent (such as $POCl_3$ and the like). Compound **D4** is converted to Compound **D5** by a Buchwald-Hartwig coupling with an appropriate amine in the present of a catalyst (such as $Pd_2(dba)_3$ and the like), a ligand (such as RuPhos and the like) and a base (such as NaO^tBu and the like) in a suitable solvent (such as PhMe and the like). Compound **D5** is converted to Compound **D6** upon treatment with conditions appropriate to removal of the protection groups (such as BBr_3 in DCM for a Me protection group in suitable solvent (such as DCM and the like).

Scheme F:



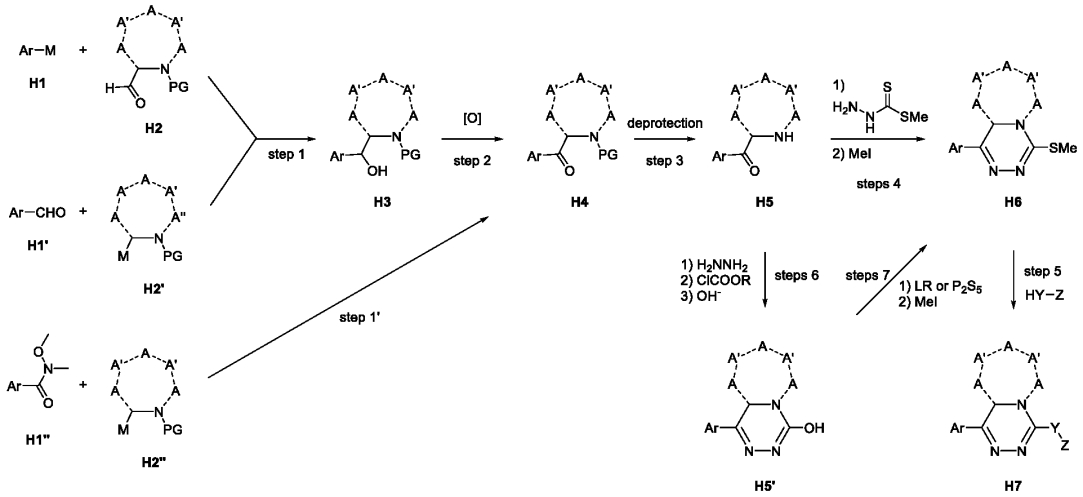
Compound **F1** is converted to compound **F2** by reacting with hydrazine in a suitable solvent (such as EtOH and the like). Reaction of **F2** with chloroformate in the presence of a base (such as DIPEA and the like) in a suitable solvent (such as DCM and the like) provides **F3**, which is cyclized to **F4** by treating with a base (such as KOH and the like) in a suitable solvent (such as EtOH and the like) at an elevated temperature (such as 80°C and the like). Compound **F4** is converted to compound **F5** by treating with POX_3 (X= Cl or Br) with or without a base (such as DIPEA and the like). Treatment of **F5** with a thionating reagent such as Lawesson's Reagent (LR) or P_2S_5 at an appropriate temperature such as 100°C, followed by alkylation with MeI provides **F6**. Compound **F6** is converted to **F7** by Suzuki coupling with an aryl or hetero boronic acid or borate in the presence of a suitable catalyst (such as $PdCl_2$dppf and the like) and a base (such as K_2CO_3 and the like) in a suitable solvent (such as dioxane and the like). Alternatively, compound **F5** is converted to compound **F7** by a Suzuki coupling first to give compound **F9**, followed by thionation with LR or P_2S_5 and subsequent alkylation with MeI. SNAr reaction of **F7** with a nucleophile in a suitable solvent (such as DMSO and the like) at an elevated temperature (such as 130°C and the like) provides **F8**.

Scheme G:



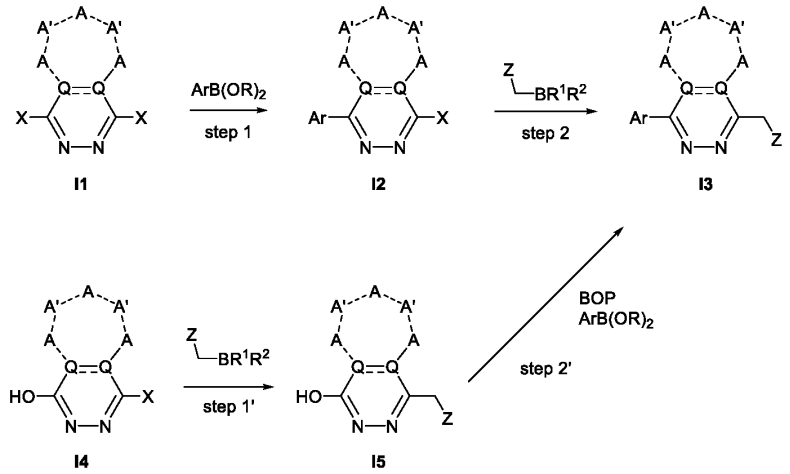
Compound **G1**, prepared according to step 1 in scheme F, is converted to compound **G2** by reacting with tri-alkoxy orthoformate in a suitable solvent (such as EtOH and the like) at an elevated temperature (such as 100°C and the like). Reaction of **G2** with a halogenation reagent (such as NBS and the like) in a suitable solvent (such as DMF and the like) provides **G3**, which is reacted with a nucleophile to give the compound **G4**. Compound **G4** is converted to compound **G5** by treating with POX_3 (X= Cl or Br) with or without a base (such as DIPEA and the like) at an elevated temperature (such as 100°C and the like). Suzuki coupling of compound **G5** with an aryl or heteroaryl boronic acid or borate in the presence of a suitable catalyst (such as $PdCl_2dppf$ and the like) and a base (such as K_2CO_3 and the like) in a suitable solvent (such as dioxane and the like) provides **G6**. Alternatively, compound **G4** can be converted to compound **G6** directly by a BOP-medicated Suzuki coupling.

Scheme H:



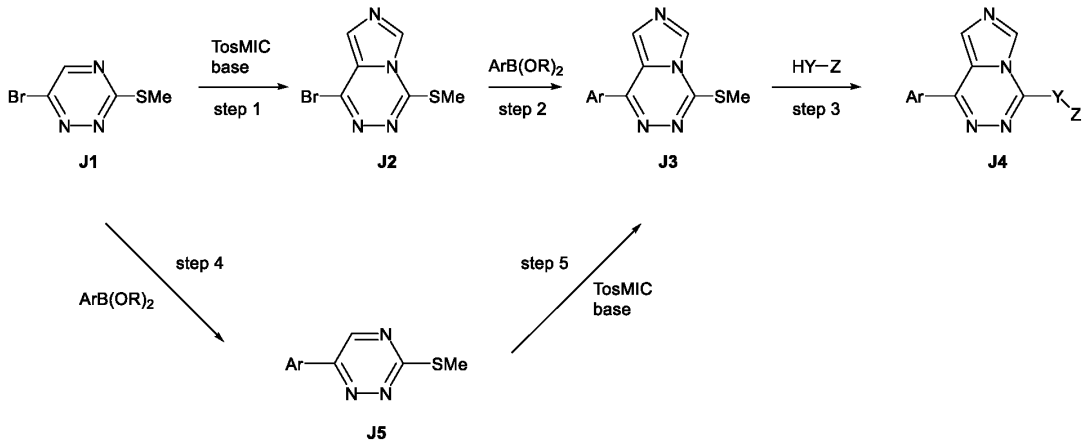
Reaction of an organometallic compound with an aldehyde, either **H1** with **H2**, or **H1'** with **H2'**, affords the alcohol **H3**. Compound **H3** is converted to **H4** by treating with an oxidant (such as MnO_2 and the like) in a suitable solvent (such as DCM and the like). Alternatively, reaction of compounds **H1"** with **H2"** yields **H4** directly. Deprotection of compound **H4** provides compound **H5**. Reaction of compound **H5** with methyl hydrazinecarbodithioate in a suitable solvent (such as EtOH and the like) at an elevated temperature (such as 80°C and the like) followed by alkylation with MeI in the presence of a base (such as K_2CO_3 and the like) provides compound **H6**. Alternatively, compound **H5** is converted to compound **H5'** by reacting with hydrazine in a suitable solvent (such as EtOH and the like), followed by reaction with chloroformate in the presence of a base (such as DIPEA and the like) in a suitable solvent (such as DCM and the like) and cyclization by treating with a base (such as KOH and the like) in a suitable solvent (such as EtOH and the like) at an elevated temperature (such as 80°C and the like). SNAr reaction of **H6** with a nucleophile in a suitable solvent (such as DMSO and the like) at an elevated temperature (such as 130°C and the like) provides **H7**.

Scheme I:



Compound **I1** is converted to compound **I3** by two coupling reactions with boronic acids or borates in the presence of a suitable catalyst (such as $PdCl_2$dppf and the like) and a base (such as K_2CO_3 and the like) in a suitable solvent (such as dioxane and the like). Alternatively, compound **I4** is converted to compound **I5** by coupling with a boronic acid or borate, which is further converted compound **I3** by a BOP-mediated Suzuki coupling with an aryl or heteroaryl boronic acid or borate.

Scheme J.



Compound **J1** is converted to compound **J2** by reacting with TosMIC in the presence of a suitable base (such as K_2CO_3, DBU and the like) in a suitable solvent (such as DCE and the like).

Suzuki coupling of compound **J2** with an aryl or heteroaryl boronic acid or borate in the presence of a suitable catalyst (such as $PdCl_2$dppf and the like) and a base (such as K_2CO_3 and the like) in a suitable solvent (such as dioxane and the like) provides **J3**. Alternatively, compound **J1** is converted to compound **J5** by coupling with a boronic acid or borate, which is further converted to compound **J3** by reacting with TosMIC in the presence of a suitable base (such as K_2CO_3, DBU and the like) in a suitable solvent (such as DCE and the like). SNAr reaction of **J3** with a nucleophile in a suitable solvent (such as DMSO and the like) at an elevated temperature (such as 130°C and the like) provides **J4**.

SYNTHETIC EXAMPLES

To describe in more detail and assist in understanding, the following non-limiting examples are offered to more fully illustrate the scope of compounds described herein and are not to be construed as specifically limiting the scope thereof. Such variations of the compounds described herein that may be now known or later developed, which would be within the purview of one skilled in the art to ascertain, are considered to fall within the scope of the compounds as described herein and hereinafter claimed. These examples illustrate the preparation of certain compounds. Those of skill in the art will understand that the techniques described in these examples represent techniques, as described by those of ordinary skill in the art, that function well in synthetic practice, and as such constitute preferred modes for the practice thereof. However, it should be appreciated that those of skill in the art should, in light of the present disclosure, appreciate that many changes can be made in the specific methods that are disclosed and still obtain a like or similar result without departing from the spirit and scope of the present description.

Other than in the following examples of the embodied compounds, unless indicated to the contrary, all numbers expressing quantities of ingredients, reaction conditions, experimental data, and so forth used in the specification and claims are to be understood as being modified by the term “about”. Accordingly, all such numbers represent approximations that may vary depending upon the desired properties sought to be obtained by a reaction or as a result of variable experimental conditions. Therefore, within an expected range of experimental reproducibility, the term “about” in the context of the resulting data, refers to a range for data provided that may vary according to a standard deviation from the mean. As well, for experimental results

provided, the resulting data may be rounded up or down to present data consistently, without loss of significant figures. At the very least, and not as an attempt to limit the application of the doctrine of equivalents to the scope of the claims, each numerical parameter should be construed in light of the number of significant digits and rounding techniques used by those of skill in the art.

While the numerical ranges and parameters setting forth the broad scope of the present description are approximations, the numerical values set forth in the examples set forth below are reported as precisely as possible. Any numerical value, however, inherently contains certain errors necessarily resulting from the standard deviation found in their respective testing measurements.

COMPOUND EXAMPLES

As used above, and throughout the present description, the following abbreviations, unless otherwise indicated, shall be understood to have the following meanings:

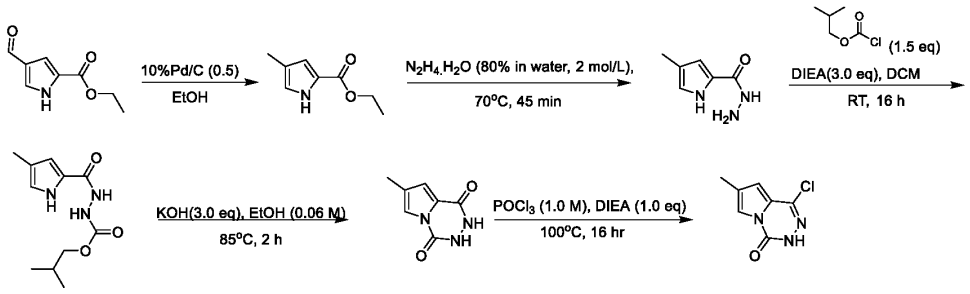
Abbreviation	**Meaning**
9-BBN	9-borabicyclo[3.3.1]nonane
AcOH or HOAc	acetic acid
ACN or MeCN	acetonitrile
Ar	argon gas
aq.	aqueous
BBr_3	boron tribromide
BippyPhos	5-(Di-tert-butylphosphino)-1′, 3′, 5′-triphenyl-1′H-[1,4′]bipyrazole
BOP	benzotriazol-1-yloxytris(dimethylamino)phosphonium hexafluorophosphate
Br_2	bromine
*n*BuLi	n-butyl lithium
$CaCO_3$	calcium carbonate
Cbz-Cl	benzyl chloroformate or benzyl chlorocarbonate or Z-chloride
$CDCl_3$	deuterated chloroform or chloroform-d
Celite	diatomaceous earth
CH_2Cl_2 or DCM	dichloromethane

Abbreviation	Meaning
m-CPBA	meta-chloroperoxybenzoic acid
Cs_2CO_3	cesium carbonate
CO	carbon monoxide
CuI	copper(I) iodide
DAST	diethylaminosulfur trifluoride
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCE	1,2-dichloroethane or ethylene dichloride
DIEA or DIPEA or *i*Pr_2NEt	N, N-diisopropylethylamine or Hünig's base
DMA	dimethylacetamide
DMF	dimethyl formamide
DMAP	4-dimethylaminopyridine
DMSO	dimethylsulfoxide
EtOAc or EA	ethyl acetate
EtOH	ethanol
EZ-Prep	CombiFlash® EZ Prep System by Teledyne ISCO
HATU	hexafluorophosphate azabenzotriazole tetramethyl uronium
HBr	hydrobromic acid
HBPin	pinacolborane
HCl	hydrochloric acid
(HCHO)n	formaldehyde
HPLC	high performance liquid chromatography
h, hr, min, s	hour (h or hr), minute (min), second (s)
iPrOH	isopropyl alcohol
K_2CO_3	potassium carbonate
KOAc	potassium acetate
KOH	potassium hydroxide
Lawesson's reagent	2,4-Bis-(4-methoxyphenyl)-1,3-dithia-2,4-diphosphetane 2,4-disulfide
LC/MS, LCMS or LC-MS	liquid chromatographic mass spectroscopy

Abbreviation	Meaning
LDA	lithium diisopropylamide
M	molarity
MeI	iododmethane
MeOH	methanol
MOM-Br	Bromomethyl methyl ether
MS	mass spectroscopy
MsCl	methanesulfonyl chloride
Mg_2SO_4	magnesium sulfate
N_2	nitrogen gas
$NaBH(OAc)_3$	sodium triacetoxyborohydride and sodium triacetoxyhydroborate
NaH	sodium hydride
$NaHCO_3$	sodium bicarbonate
$NaNO_2$	sodium nitrite
NaOH	sodium hydroxide
Na_2SO_4	sodium sulfate
NH_3	ammonia
NH_4HCO_3	ammonium bicarbonate
NH_4OH	ammonium hydroxide
$N_2H_4H_2O$	hydrazine hydrate
NMP	N-methylpyrrolidone
NMR	nuclear magnetic resonance
$Pd(OAc)_2$	palladium(II) acetate
Pd/C^o	palladium on carbon
$Pd_2(dba)_3$ or Pd_2dba_3	tris(dibenzylideneacetone)dipalladium(0)
$Pd(dppf)Cl_2$	[1,1′-bis(diphenylphosphino)ferrocene] dichloropalladium(II)
PE	petroleum ether
PhMe	toluene
$POBr_3$	phosphoryl bromide or phosphorus oxybromide
prep-HPLC	preparative high performance liquid chromatography

Abbreviation	Meaning
RT or R.T. or rt	room temperature
RuPhos	2-Dicyclohexylphosphino-2′,6′-diisopropoxybiphenyl
sat.	saturated
SFC	supercritical fluid chromatography
SGC	solvating gas chromatography
SiO_2	silicon dioxide or silica gel
TBAF	tetra-n-butylammonium fluoride
t-Bu	tert-butyl
TEA, NEt_3, Et_3N	triethylamine
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TLC	thin layer chromatography
TosMIC, TsMIC	Toluenesulfonylmethyl isocyanide
UPLC	Ultra Performance Liquid Chromatography
Pd XPhos G3	(2-dicyclohexylphosphino-2′,4′,6′-triisopropyl-1,1′-biphenyl)[2-(2′-amino-1,1′-biphenyl)]palladium(II) methanesulfonate
Pd XPhos G4	methanesulfonato(2-dicyclohexylphosphino-2',4',6'-tri-i-propyl-1,1'-biphenyl)(2'-methylamino-1,1'-biphenyl-2-yl)palladium(II)

Intermediate 1a: 1-Chloro-7-methylpyrrolo[1,2-d][1,2,4]triazin-4(3H)-one



Step 1. Ethyl 4-methyl-1H-pyrrole-2-carboxylate

A mixture of ethyl 4-formyl-1H-pyrrole-2-carboxylate (10.3 g, 61.6 mmol, 1.0 eq.) and Pd/C (10%, 2.0 g) in EtOH (150 mL) was stirred at rt overnight under hydrogen (balloon). The

mixture was filtered. The filtrate was concentrated under reduced pressure. The crude colorless oil (8.50 g, 90% yield) was used in the next step without further purification. MS *m/z* 154.2 $[M+H]^+$.

Step 2. 4-Methyl-1H-pyrrole-2-carbohydrazide

A solution of ethyl 4-methyl-1H-pyrrole-2-carboxylate (8.50 g, 55.5 mmol) in $N_2H_4 H_2O$ (80%, 28 mL) was heated at 70°C for 45 min. After cooling to rt, the mixture was filtered. The filter cake was washed with EtOH and dried in vacuo to give 4-methyl-1H-pyrrole-2-carbohydrazide as a white solid (7.5 g, 97% yield). MS *m/z* 140.2 $[M+H]^+$; ^1H NMR (400 MHz, DMSO-d_6) δ 11.07 (s, 1H), 9.14 (s, 1H), 6.62 (s, 1H), 6.55 (s, 1H), 4.27 (s, 2H), 2.00 (s, 3H).

Step 3. Isobutyl 2-(4-methyl-1H-pyrrole-2-carbonyl) hydrazine-1-carboxylate

To a suspension of 4-methyl-1H-pyrrole-2-carbohydrazide (7.5 g, 53.9 mmol, 1.0 eq.) and DIEA (20.9 g, 161 mmol, 3.0 eq.) in DCM (540 mL) was added isobutyl carbonochloridate (11.1 g, 80.9 mmol, 1.5 eq.) dropwise with ice-water cooling bath. The mixture was stirred at rt overnight. Upon completion, the reaction mixture was diluted with DCM, washed with water and brine. The organic phase was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified by silica gel column chromatography eluting with 0-30% EtOAc in hexanes to afford isobutyl 2-(4-methyl-1H-pyrrole-2-carbonyl) hydrazine-1-carboxylate (12.0 g, 93%) as a white solid. MS *m/z* 240.2 $[M+H]^+$.

Step 4. 7-Methyl-2,3-dihydropyrrolo[1,2-d][1,2,4]triazine-1,4-dione

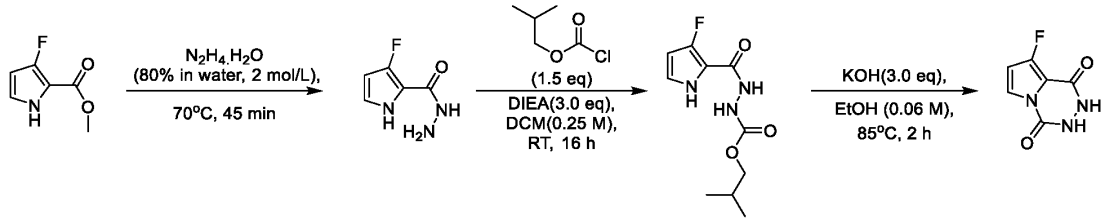
To a solution of isobutyl 2-(4-methyl-1H-pyrrole-2-carbonyl) hydrazine-1-carboxylate (12.0 g, 50.2 mmol, 1.0 eq.) in EtOH (840 mL) was added KOH (8.40 g, 151 mmol, 3.0 eq.). The mixture was stirred at 85°C for 2 h. The reaction mixture was cooled to room temperature and filtered. The filter cake was washed with EtOH. The solid was dissolved with water, and adjusted to pH = 4 with 1M HCl. The precipitate was filtered. The filter cake was washed with water and dried in vacuo to afford 7-methyl-2,3-dihydropyrrolo[1,2-d][1,2,4]triazine-1,4-dione (4.0 g, 48% yield) as a white solid. MS *m/z* 166.2 $[M+H]^+$.

Step 5. 1-Chloro-7-methylpyrrolo[1,2-d][1,2,4]triazin-4(3H)-one

To a solution of 7-methyl-2,3-dihydropyrrolo[1,2-d][1,2,4]triazine-1,4-dione (4.0 g, 24.2 mmol, 1.0 eq.) in $POCl_3$ (1.0 M, 25 mL) was added DIEA (3.12 g, 24.2 mmol, 1.0 eq.) dropwise with ice cooling bath. The mixture was stirred at 100°C for 16h, then cooled to room temperature and concentrated. The residue was carefully poured into ice water, adjusted pH=8 with sat

$NaHCO_3$ aq. The mixture was extracted with DCM: MeOH (10:1, 100 mLx3), dried over Na_2SO_4, concentrated, purified by silica gel column chromatography eluting with 0-50% EtOAc in hexanes to afford 1-chloro-7-methylpyrrolo[1,2-d][1,2,4]triazin-4(3H)-one (2.0 g, 45% yield) as a white solid. MS *m/z* 184.3 $[M+H]^+$; ^1H NMR (400 MHz, DMSO-d_6) δ 12.43 (s, 1H), 7.66 (s, 1H), 6.75 (s, 1H), 2.23 (s, 3H).

Intermediate 1b: 8-Fluoro-2,3-dihydropyrrolo[1,2-d][1,2,4]triazine-1,4-dione



Step 1. 3-Fluoro-1H-pyrrole-2-carbohydrazide

A mixture of $N_2H_4 \cdot H_2O$ (80% in water, 18 mL) and methyl 3-fluoro-1H-pyrrole-2-carboxylate (3.14 g, 20.0 mmol) was stirred at 70 °C for 45 minutes. After cooling to rt, the precipitate was filtered, the filter cake was washed with water and dried under vacuum to obtain 3-fluoro-1H-pyrrole-2-carbohydrazide (2.30 g, 73%) as a white solid. MS *m/z* 144.1 $[M+H]^+$, ^1H NMR (400 MHz, DMSO-d_6) δ 11.31 (s, 1H), 8.55 (s, 1H), 6.74 (dd, *J* = 4.6, 3.0 Hz, 1H), 5.97 (d, *J* = 3.0 Hz, 1H), 4.39 (s, 2H).

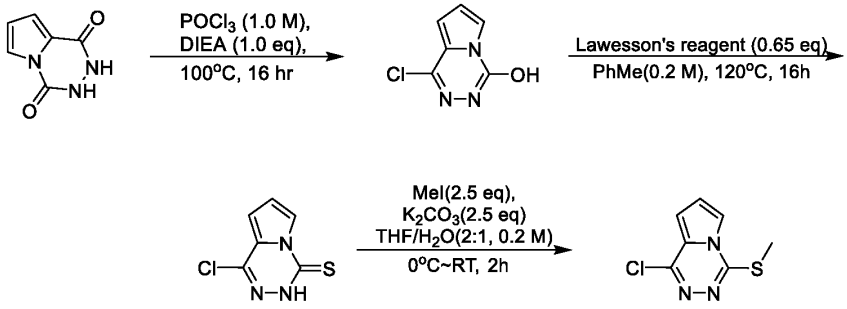
Step 2. Isobutyl 2-(3-fluoro-1H-pyrrole-2-carbonyl)hydrazine-1-carboxylate

To a solution of 3-fluoro-1H-pyrrole-2-carbohydrazide (2.15 g, 15.0 mmol, 1.0 eq.) in DCM (60 mL) was added DIPEA (5.80 g, 45.0 mmol, 3.0 eq.). Isobutyl carbonochloridate (3.00 g, 22.5 mmol, 1.5 eq.) was added to the mixture slowly. The mixture was stirred at rt for 16 h. After concentration, the mixture was diluted with EtOAc (200 mL). The organic layer was washed with water and brine, then dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude was purified by silica gel column chromatography eluting with 0-50% EtOAc in hexanes to afford isobutyl 2-(3-fluoro-1H-pyrrole-2-carbonyl)hydrazine-1-carboxylate (2.44 g, 66.7% yield) as yellow solid. MS *m/z* 244.1 $[M+H]^+$; ^1H NMR (400 MHz, DMSO-d_6) δ 11.46 (s, 1H), 9.18 (s, 1H), 9.09 (s, 1H),6.82 (d, *J* = 4.4 Hz, 1H), 6.01 (d, *J* = 2.5 Hz, 1H), 3.82 (d, *J* = 6.6 Hz, 2H), 2.02 – 1.67 (m, 1H), 0.92 (d, *J* = 6.7 Hz, 6H).

Step 3. 8-Fluoro-2,3-dihydropyrrolo[1,2-d][1,2,4]triazine-1,4-dione

To a solution of isobutyl 2-(3-fluoro-1H-pyrrole-2-carbonyl)hydrazine-1-carboxylate(2.44 g, 10.0 mmol, 1.0 eq.) in EtOH (60 mL) was added KOH (1.68 g, 30 mmol, 3 eq.). The mixture was stirred at 85 °C for 2 h. After cooling to rt, the mixture was concentrated. The residue was diluted with water (50 mL) and adjusted to pH to 6-7 with 1M HCl. The precipitates were filtered, the filter cake was washed with water and dried under vacuum to obtain 8-fluoro-2,3-dihydropyrrolo[1,2-d][1,2,4]triazine-1,4-dione (1.16 g, 68.7% yield) as brown solid. MS *m/z* 168.0 $[M-H]^-$; ^1H NMR (400 MHz, DMSO-d_6) δ 11.52 (s, 2H), 7.57 (t, J = 4.1 Hz, 1H), 6.68 (d, J = 3.4 Hz, 1H).

Intermediate 1c: 1-chloro-4-(methylthio)pyrrolo[1,2-d][1,2,4]triazine



Step 1. 1-Chloropyrrolo[1,2-d][1,2,4]triazin-4-ol

To a stirred solution of 2,3-dihydropyrrolo[1,2-d][1,2,4]triazine-1,4-dione (prepared as the procedure of Intermediate 1b, 2 g, 13.2 mmol) in $POCl_3$ (60 mL) was added DIEA (1.84 g, 14.2 mmol). The reaction mixture was heated at 100 °C for 16 h. After cooling to rt, the mixture was concentrated under reduced pressure to give a residue. The residue was diluted with cold saturated sodium bicarbonate solution and extracted with dichloromethane (3 x 50 mL). The combined organic extracts were dried over sodium sulfate and evaporated under reduced pressure. The crude was further triturated with DCM to give the title compound 1-chloropyrrolo[1,2-d][1,2,4]triazin-4-ol (0.867 g, 38.6% yield) as an off-white solid, which was used to next step without further purification. MS *m/z* 169.6 $[M+H]^+$; ^1H NMR (400 MHz, DMSO-d_6) δ 12.54 (s, 1H), 7.88 - 7.87 (m, 1H), 6.92 - 6.89 (m, 2H).

Step 2. 1-Chloropyrrolo[1,2-d][1,2,4]triazine-4(3H)-thione

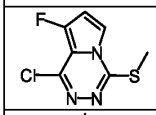
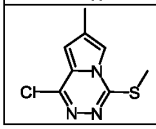
To a solution of 1-chloropyrrolo[1,2-d][1,2,4]triazin-4-ol (30.0 g, 177 mmol) in toluene (1200 mL) was added Lawesson's Reagent (46.2 g, 114 mmol). The reaction was stirred at 120

°C for 16 h. The mixture was diluted with H_2O (1.5 L), acidified with aqueous HCl (1 M) till pH = 3 and extracted with EA. The EA layer was wash with sat. $NaHCO_3$ aqueous solution (1 L) and brine (1 L), then dried over anhydrous Na_2SO_4 and concentrated to give crude 1-chloro-3H-pyrrolo[1,2-d][1,2,4]triazine-4-thione (crude 35.0 g, overweight), which was used in the next step without further purification. MS *m/z* 184.1 $[M-H]^-$.

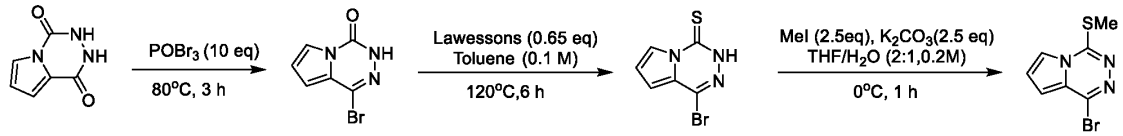
Step 3. 1-Chloro-4-(methylthio)pyrrolo[1,2-d][1,2,4]triazine

To a solution of 1-chloro-3H-pyrrolo[1,2-d][1,2,4]triazine-4-thione (crude 35.0 g, 189 mmol) in THF (600 mL) and water (300 mL) was added K_2CO_3 (65.2 g, 472 mmol), followed by iodomethane (68.6 g, 483 mmol) at 0 °C. The reaction mixture was stirred for 2 h at room temperature, then diluted with water and extracted with EA (3 x 100 mL). The combined organic layers were washed with water, brine, dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by column chromatography (SiO_2, Petroleum ether/Ethyl acetate = 50/1 to 20/1) to afford title product 1-chloro-4-methylsulfanyl-pyrrolo[1,2-d][1,2,4]triazine (21.8 g, 57.9% yield over two steps) as a white solid. MS *m/z* 200.0 $[M+H]^+$, 1H NMR (400 MHz, DMSO-d_6) δ: 7.83 (dd, J = 2.8 Hz, 1.2 Hz, 1H), 7.16 (dd, J = 4.0 Hz, 2.8 Hz, 1H), 7.11 (dd, J = 4.0 Hz, 1.2 Hz, 1H), 2.81 (s, 3H).

The intermediates below were prepared according to the procedure of Intermediate 1c by substituting the appropriate starting materials, reagents and reaction conditions.

Structure	Spectral Data
	From Intermediate 1b; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.65 (s, 1H), 6.94 (s, 1H), 2.79 (s, 1H), 2.33 (s, 1H).
	From Intermediate 1a; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.73 – 7.71 (m, 1H), 7.14 (d, J = 3.2 Hz, 1H), 2.79 (s, 3H).

Intermediate 1d: 1-Bromo-4-(methylthio)pyrrolo[1,2-d][1,2,4]triazine



Step 1. 1-Bromopyrrolo[1,2-d][1,2,4]triazin-4(3H)-one

A mixture of 2,3-dihydropyrrolo[1,2-d][1,2,4]triazine-1,4-dione (30.0 g, 0.199 mol, 1.0

eq.) and $POBr_3$ (570 g, 1.99 mol, 10 eq.) was heated at 80°C for 3 hours. The hot reaction mixture was slowly poured into a stirring mixture of ice and aqueous sat. $NaHCO_3$. The mixture was neutralized with solid $NaHCO_3$ to pH ~ 7 and extracted with a mixture of MeOH/DCM (1 L x 2, 1:10). The combined organic phase was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was triturated with DCM, filtered and washed with DCM. The solid was dried under vacuum to afford 1-bromopyrrolo[1,2-d][1,2,4]triazin-4(3H)-one (21.9 g, 51.8% yield) as a pink solid. MS *m/z* 214.0, 215.9 $[M+H]^+$.

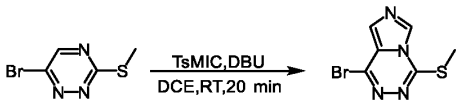
Step 2. 1-Bromopyrrolo[1,2-d][1,2,4]triazine-4(3H)-thione

To a solution of 1-bromopyrrolo[1,2-d][1,2,4]triazin-4(3H)-one (10.0 g, 46.7 mmol, 1.0 eq.) in DMSO (472 mL) was added Lawesson's Reagent (12.4 g, 30.7 mmol, 0.65 eq.). The reaction mixture was heated at 120°C for 6 hours. The reaction mixture was cooled to room temperature, diluted with aqueous saturated $NaHCO_3$ and extracted with EtOAc (300 mL x 3). The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude was purified by silica gel column chromatography eluting with 0-30% EtOAc in hexanes to afford 1-bromopyrrolo[1,2-d][1,2,4]triazine-4(3H)-thione as a white solid (1.56 g, 14.5% yield). MS *m/z* 228.0, 230.0 $[M-H]^-$; ^1H NMR (400Hz, DMSO-d_6) δ 14.15 (s, 1H), 8.23 (dd, J = 2.9, 1.4 Hz, 1H), 7.10 (dd, J = 3.7, 3.1 Hz, 1H), 7.06 (dd, J = 3.9, 1.4 Hz, 1H).

Step 3. 1-Bromo-4-(methylthio)pyrrolo[1,2-d][1,2,4]triazine

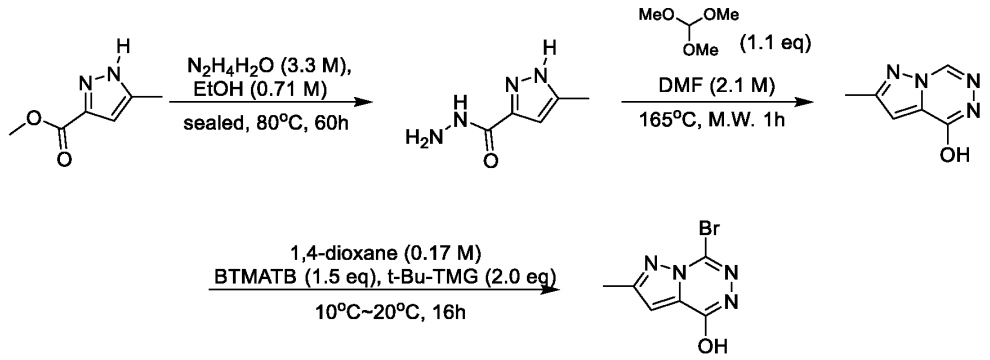
To a mixture of 1-bromopyrrolo[1,2-d][1,2,4]triazine-4(3H)-thione (2.00 g, 8.69 mmol, 1.0 eq.) and K_2CO_3 (3.00 g, 21.7 mmol, 2.5 eq.) in THF (43 mL) and water (21 mL) was added iodomethane (1.35 mL, 2.28 g/mL, 21.7 mmol, 2.5 eq.) dropwise at 0°C. The reaction was stirred at 0°C for 1 hour. The reaction mixture was diluted with water (50 mL) and extracted with EtOAc (50 mL x 3). The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography eluting with 0-30% EtOAc in hexanes to afford 1-bromo-4-(methylthio)pyrrolo[1,2-d][1,2,4]triazine (1.40 g, 66.1% yield) as a white solid. MS *m/z* 243.9, 246.0 $[M+H]^+$; ^1H NMR (400Hz, DMSO-d_6) δ 7.83 (dd, *J* = 2.8, 1.0 Hz, 1H), 7.15 (dd, *J* = 4.0, 2.8 Hz, 1H), 7.03 (dd, *J* = 4.0, 1.0 Hz, 1H), 2.79 (s, 3H).

Intermediate 1e: 1-Bromo-4-(methylthio)imidazo[1,5-d][1,2,4]triazine



To a solution of TsMIC (5.21 g, 26.69 mmol, 1.1 eq.) and DBU (4.43 mg, 29.12 mmol, 1.2 eq.) in DCE (50 mL) was added 6-Bromo-3-(methylthio)-1,2,4-triazine (5 g, 24.26 mmol, 1.0 eq.) at rt. The reaction mixture was stirred for 20 min, then diluted with water (50 mL) and extracted with EtOAc (50 mL x 3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel (PE: EA = 15:1) to afford 1-bromo-4-(methylthio)imidazo[1,5-d][1,2,4]triazine (3.71 g, 62.38% yield) as yellow solid. MS *m/z* 244.9, 246.9 $[M+1]^+$; 1H NMR (400 MHz, DMSO-d_6) δ 8.84 (s, 1H), 7.93 (s, 1H), 2.80 (s, 3H).

Intermediate 1f: 7-Bromo-2-methylpyrazolo[1,5-d][1,2,4]triazin-4-ol



Step 1. 5-Methyl-1H-pyrazole-3-carbohydrazide

Hydrazine hydrate (54 mL, 1.032 g/mL, 1.11 mol, 6.2 eq.) was added to a solution of methyl 5-methyl-1H-pyrazole-3-carboxylate (25.0 g, 0.178 mol, 1.0 eq.) in EtOH (250 mL). The mixture was sealed and heated at 80 °C for 60 h, then cooled to room temperature. The solvent was evaporated in vacuo. The crude product was treated with a 1/1 mixture of water/MeOH, filtered and the filter cake was washed with water. The solid was dried under vacuum to afford 5-methyl-1H-pyrazole-3-carbohydrazide (21.7 g, 87.0% yield) as a white solid. MS *m/z* 141.1 $[M+H]^+$.

Step 2. 2-Methylpyrazolo[1,5-d][1,2,4]triazin-4-ol

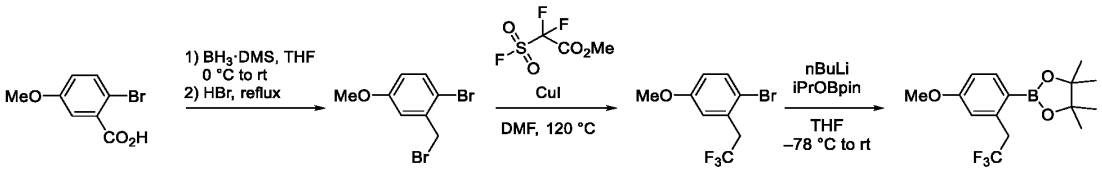
A mixture of 5-methyl-1H-pyrazole-3-carbohydrazide (3.00 g, 21.4 mmol, 1.0 eq.) and trimethoxymethane (2.57 mL, 0.970 g/mL, 23.5 mmol, 1.1 eq.) in DMF (10 mL) was sealed in a

tube. The reaction mixture was stirred at 165°C for 1 hour under microwave then cooled to room temperature. The precipitate was collected by filtration, washed with EtOH and dried under vacuum to afford 2-methylpyrazolo[1,5-d][1,2,4]triazin-4-ol (1.70 g, 52.9% yield) as a white solid. MS *m/z* 149.2 $[M-H]^-$.

Step 3. 7-Bromo-2-methylpyrazolo[1,5-d][1,2,4]triazin-4-ol

Benzyltrimethylammonium tribromide (26.5 g, 68.0 mmol, 1.5 eq.) was added in portions to a stirred solution of 2-methylpyrazolo[1,5-d][1,2,4]triazin-4-ol (6.80 g, 45.3 mmol, 1.0 eq.) and 2-(tert-butyl)-1,1,3,3-tetramethylguanidine (18.3 mL, 0.85 g/mL, 90.6 mmol, 2.0 eq.) in 1,4-dioxane (290 mL) under N_2 at 10 °C. Once the addition was completed the mixture was warmed to 20 °C and stirred at this temperature for 16 hours. Then the mixture was quenched with a mixture of aqueous sat. $Na_2S_2O_3$ and aqueous sat. $NaHCO_3$ and then extracted with EtOAc (150 mL x 3). The combined organic layers were dried over Na_2SO_4, filtered and concentrated. The crude product was triturated with EtOAc, filtered and washed with EtOAc. The solid was dried under vacuum to afford 7-bromo-2-methylpyrazolo[1,5-d][1,2,4]triazin-4-ol (7.60 g, 73.6% yield) as an off-white solid. MS *m/z* 229.0, 230.9 $[M+H]^+$; ^1H NMR (400Hz, DMSO-d_6) δ 12.60 (s, 1H), 7.15 (s, 1H), 2.42 (s, 3H).

Intermediate 2a: 2-(4-methoxy-2-(2,2,2-trifluoroethyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



Step 1: (2-bromo-5-methoxy-phenyl)methanol

To an ice-cooled solution of 2-bromo-5-methoxy-benzoic acid (9.95 g, 43.1 mmol) in THF (86 mL) was added borane-dimethylsulfide complex (6.01 mL, 64.6 mmol). The resulting mixture was warmed to rt and stirred for 16 hours. The reaction mixture was quenched with methanol and stirred for 5 min. The reaction was concentrated, and the resulting yellow oil was dissolved in EtOAc (150 mL) and washed with 10% Na_2CO_3 (30 mL). The aqueous phase was extracted with EtOAc. The combined organic extracts were washed with brine (50 mL), dried ($MgSO_4$) and concentrated to give a colorless oil, which was applied to the next step without

further purification.

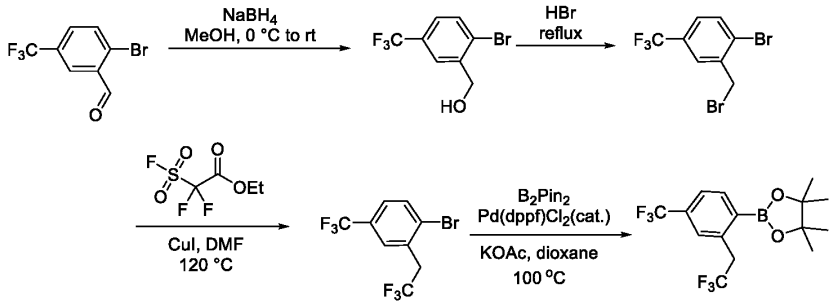
Step 2: 1-bromo-2-(bromomethyl)-4-methoxy-benzene

The crude [2-bromo-5-(trifluoromethyl)phenyl]methanol in conc. HBr (30 mL) was heated to reflux for 2 hours. The reaction was cooled to rt and extracted with DCM. The combined organic extracts were washed with sat. $NaHCO_3$, brine, dried (Na_2SO_4), filtered, and concentrated to give a white solid. Purification by chromatography on SiO_2 (EtOAc:hexanes, 10 to 30%) gave a white solid (10.99 g, 91% 2 steps). ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 8.9 Hz, 1 H), 7.00 (d, J = 3.0 Hz, 1 H), 6.75 (dd, J = 8.9 Hz, 3.0 Hz, 1H), 4.57 (s, 2 H), 3.81 (s, 3 H).

Step 3: 1-bromo-4-methoxy-2-(2,2,2-trifluoroethyl)benzene

To a solution of 1-bromo-2-(bromomethyl)-4-methoxy-benzene (5.62 g, 20.1 mmol) in DMF (45 ml) was added CuI (9.56 g, 50.2 mmol) and the solution was sparged with Ar. To this solution was added difluoro-fluorosulfonyl-acetic acid methyl ester (6.4 mL, 50.2 mmol), and the resulting reaction mixture was heated at 120 °C for 4 h. The reaction mixture was cooled to 0 °C, diluted with EtOAc (200 ml) and stirred for 10 min. Conc. ammonium hydroxide (30 mL) was added dropwise, and the mixture was stirred at 0°C for 15 min before warming to rt. EtOAc (200ml) and water (100mL) were added and the layers were separated. The aqueous layer was extracted with EtOAc (2 x 100 mL). The combined organic layers were washed with water (100 mL) and brine (100ml), dried ($MgSO_4$), filtered, and concentrated. Purification by chromatography on SiO_2 (EtOAc:hexanes, 0 to 10%) gave a light yellow oil (4.13 g, 77%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, J = 8.9 Hz, 1 H), 6.93 (d, J = 2.8 Hz, 1 H), 6.78 (dd, J = 8.8 Hz, 3.1 Hz, 1H), 3.81 (s, 3 H), 3.60 (q, J = 10.5 Hz, 2H).

Intermediate 2b: 4,4,5,5-Tetramethyl-2-(2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl)-1,3,2-dioxaborolane



Step 1. (2-Bromo-5-(trifluoromethyl)phenyl)methanol

To a solution of 2-bromo-5-(trifluoromethyl)benzaldehyde (30.0 g, 118.6 mmol, 1.0 eq.) in MeOH (300 mL) was added $NaBH_4$ (13.5 g, 3 eq.) slowly at 0 °C . The mixture was stirred for 16 h at room temperature. The reaction mixture was diluted with water (100 mL) and extracted with EtOAc (250 mL x 3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated. The filtrate was concentrated in vacuo to afford (2-bromo-5-(trifluoromethyl)phenyl)methanol (27 g, 78.4 % Yield) as white solid. The crude product used directly without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (s, 1H), 7.67 (d, J = 8.3 Hz, 1H), 7.44 – 7.39 (m, 1H), 4.81 (s, 2H).

Step 2. 1-Bromo-2-(bromomethyl)-4-(trifluoromethyl)benzene

2-Bromo-5-(trifluoromethyl)phenyl)methanol (26.0 g, 102.0 mmol, 1.0 eq.) was added to HBr aqueous solution (156 mL). The reaction mixture was stirred for 2 h at 120 °C under N_2 atmosphere. The reaction mixture was diluted with $NaHCO_3$ (100 mL) and extracted with DCM (250 mL x 3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel (PE: EA = 0% ~ 10%) to afford 1-bromo-2-(bromomethyl)-4-(trifluoromethyl)benzene (25 g, 76.9% yield) as colorless oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.08 (d, J = 2.0 Hz, 1H), 7.92 (d, J = 8.4 Hz, 1H), 7.65 (dd, J = 8.4, 2.1 Hz, 1H), 4.83 (s, 2H).

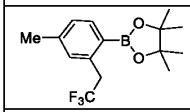
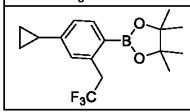
Step 3. 1-Bromo-2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)benzene

To a solution of 1-bromo-2-(bromomethyl)-4-(trifluoromethyl)benzene (40.5 g, 127.4 mmol, 1.0 eq.) in DMF (280 mL) was added CuI (60.7 g, 2.5 eq.) and ethyl 2,2-difluoro-2-(fluorosulfonyl)acetate (65.7 g, 2.5 eq.) under N_2 at rt. The reaction mixture was stirred overnight at 120°C under N_2 atmosphere. The reaction mixture was cooled to 0 °C, diluted with EtOAc (1200 mL) and stirred for 10 minutes at 0°C. A solution of ammonium hydroxide (240 mL) was added dropwise. The mixture was stirred as it warmed from 0°C to room temperature over 20 minutes. The reaction mixture was diluted with water (500 mL) and extracted with EtOAc (550 mL x 3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel (PE: EA = 0% ~ 10%) to afford 1-bromo-2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)benzene (16.8 g, 17.9% Yield) as yellow oil. ^{1}HNMR (400 MHz, DMSO-d_6) δ 7.95 (dd, J = 15.1, 8.2 Hz, 2H), 7.70 (dd, J = 8.4, 2.1 Hz, 1H), 3.97 (q, J= 11.0 Hz, 2H).

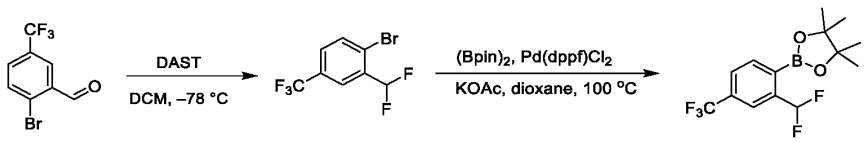
Step 4. 4,4,5,5-Tetramethyl-2-(2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl)-1,3,2-dioxaborolane

To a solution of 1-bromo-2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)benzene (16.8 g, 54.7 mmol, 1.0 eq.) in 1,4-dioxane (160 mL) was added 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (27.8 g, 2 eq.), $Pd(dppf)Cl_2$ (4.0 g, 0.1 eq.) and KOAc (16.1 g, 3 eq.) under N_2 atmosphere at rt. The reaction mixture was stirred for 12 h at 100 °C under N_2. The reaction mixture was diluted with water (90 mL) and extracted with EtOAc (150 mL x 3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel (PE: EA = 0% ~ 10%) to afford 4,4,5,5-tetramethyl-2-(2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl)-1,3,2-dioxaborolane (10.5 g, 45.8% Yield) as yellow oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.95 (d, J = 7.8 Hz, 1H), 7.79 – 7.73 (m, 2H), 4.08 (q, J = 11.2 Hz, 2H), 1.32 (s, 12H).

The intermediates below were prepared according to the procedure of Intermediate 2a and 2b by substituting the appropriate starting materials, reagents and reaction conditions.

Structure	Spectral Data
	^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 7.5 Hz, 1H), 7.15 (d, J = 7.8 Hz, 1H), 7.12 (s, 1H), 3.81 (q, J = 11.0 Hz, 2H), 2.37 (s, 3H), 1.34 (s, 12H).
	^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, J = 8.2 Hz, 1H), 7.02 – 6.98 (m, 2H), 3.81 (q, J = 10.9 Hz, 2H), 1.94 – 1.84 (m, 1H), 1.33 (s, 12H), 1.02 – 0.95 (m, 2H), 0.76 – 0.71 (m, 2H).

Intermediate 2c: 2-[2-(Difluoromethyl)-4-(trifluoromethyl)phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



Step 1. 1-Bromo-2-(difluoromethyl)-4-(trifluoromethyl)benzene

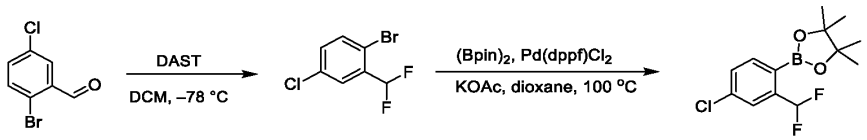
DAST (10 eq., 39.5 mmol) was added dropwise to a -78°C solution of 2-bromo-5-(trifluoromethyl)benzaldehyde (1 g, 3.9mmol) in DCM (5 mL, 78.0 mmol). The reaction was stirred for 15 min and then allowed to warm to room temperature. After 4 hours, TLC showed incomplete conversion, so the mixture was cooled again to -78°C and additional DAST (1 eq., 3.9 mmol) was added. The mixture was allowed to warm to rt and stirred overnight, then poured in ice and dilute NH_4OH and extracted 2x with DCM. The combined organic extracts were washed with brine and dried over sodium sulfate. Solvent was evaporated in vacuum to give a

residue which was purified with a short plug of silica to give the crude product 1-bromo-2-(difluoromethyl)-4-(trifluoromethyl)benzene (350 mg, 1.2mmol, 32.2% Yield) as colorless oil.

Step 2. 2-[2-(Difluoromethyl)-4-(trifluoromethyl)phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

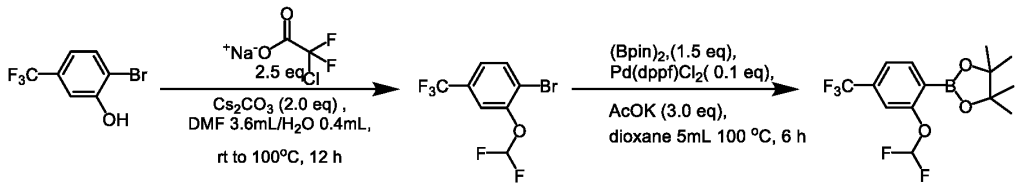
To a solution of 1-bromo-2-(difluoromethyl)-4-(trifluoromethyl)benzene (100 mg, 0.36 mmol) in 1,4-dioxane (2 mL) was added bis(pinacolato)diboron (1.5 eq., 0.5 mmol), potassium acetate (2 eq., 0.72 mmol) and [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(ii) (0.15 eq., 0.05 mmol). The mixture was stirred for 16 h at 100 °C for 16 hours under N_2 atmosphere, monitored by TLC and LCMS. After the reaction, the solvent was removed under vacuum and the residue was purified by column chromatography (10-15% EA in PE) to afford 2-[2-(difluoromethyl)-4-(trifluoromethyl)phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (30 mg, 0.09 mmol, 25.6% Yield) as colorless oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.00 (d, J= 7.6 Hz, 1H),7.94 (d, J= 8.4 Hz, 1H),7.92 (s, 1H), 7.38 (t, J= 55.6 Hz, 1H),1.34 (s, 12H).

Intermediate 2d: 2-(4-Chloro-2-(difluoromethyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



The title compound was prepared in analogous manner according to the procedure of Intermediate 2c, using 2-bromo-5-chlorobenzaldehyde in place of 2-bromo-5-(trifluoromethyl)benzaldehyde in step 1. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.79 (d, J= 2.0 Hz, 1H), 7.68 –7.63 (m, 2H), 7.32(t, J= 55.6Hz, 1H), 1.32 (s, 12H).

Intermediate 2e: 2-(2-(Difluoromethoxy)-4-(trifluoromethyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



Step 1. 1-Bromo-2-(difluoromethoxy)-4(trifluoromethyl)benzene

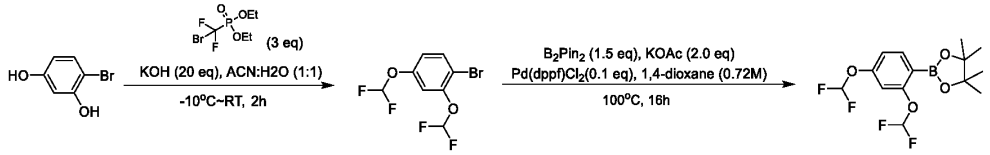
A mixture of 2-bromo-5-(trifluoromethyl)phenol (5.00 g, 20.7 mmol, 1.0 eq.), sodium 2-

chloro-2,2-difluoroacetae (7.07 g, 51.9 mmol, 2.50 eq.) and cesium carbonate (11.5 g, 41.5 mmol, 2.0 eq.) in water (20 mL) and N,N-dimethylformamide (80 mL) was heated at 100 °C for 12 hours. Upon completion, the reaction mixture was cooled to room temperature and diluted with EtOAc. The reaction mixture was washed with water and brine. The organic phase was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified by silica gel column chromatography eluting with 0-50% EtOAc in hexanes to afford 1-bromo-2-difluoromethoxy)-4(trifluoromethyl)benzene (2.8 g, 47% yield) as a yellow solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.01 (d, J = 8.4 Hz, 1H), 7.69 (s, 1H), 7.46 (t, J = 72.8 Hz, 1H), 7.5 (d, J = 8.4 Hz, 1H).

Step 2. 2-(2-(Difluoromethoxy)-4-(trifluoromethyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

To a solution of 1-bromo-2-difluoromethoxy)-4(trifluoromethyl)benzene (2.80 g , 9.62 mmol) in 1,4-dioxane (30 mL) was added bis(pinacolato)diboron (36.6 g, 14.4 mmol, 1.50 eq.), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalldium(II) (704 mg, 0.96 mmol, 0.1eq.), potassium acetate (2.82 g, 28.9 mmol, 3.0 eq.). The reaction mixture was heated at 100 °C for 16 hours under nitrogen. The reaction mixture was cooled to room temperature and filtered. The filtrate was diluted EA, washed with water and brine. The organic phase was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude was purified by silica gel column chromatography eluting with hexane to afford 2-(2-(difluoromethoxy)-(trifluoromethyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane as a white solid (1.70 g, 52% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.87 (d, J = 7.6 Hz, 1H), 7.66 (d, J = 7.6 Hz, 1H), 7.50 (s, 1H), 7.24 (t, J = 74.0 Hz, 1H), 1.31 (s, 12H).

Intermediate 2f: 2-(2,4-Bis(difluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



Step 1. 1-Bromo-2,4-bis(difluoromethoxy)benzene

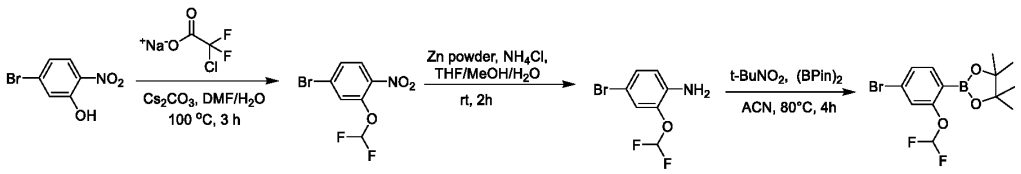
To a solution of 4-bromobenzene-1,3-diol (10.0 g, 53.4 mmol, 1.0 eq.) in ACN/H_2O (1:1, 100 mL) was slowly added KOH (60.0 g, 1.07 mol, 20 eq.) at 0 °C. The mixture was stirred for

10 min and cooled to -10 °C. Diethyl (bromodifluoromethyl) phosphonate (42.70 g, 160.2 mmol, 3.0 eq.) was slowly added and the mixture was stirred for 10 min and warmed to room temperature and stirred for 2 h. The reaction mixture was diluted with water (100 mL) and extracted with EtOAc (100 mL x 3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel (PE:EA = 0% ~ 5%) to give 1-bromo-2,4-bis(difluoromethoxy)benzene (3.30 g, 21.3% Yield) as yellow oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.84 (d, J = 8.8 Hz, 1H), 7.38 (t, J = 72.0 Hz, 1H), 7.35 (t, J = 76.0 Hz, 1H), 7.26 (d, J = 2.8 Hz, 1H), 7.11 (dd, J = 8.8, 2.8 Hz, 1H).

Step 2. 2-(2,4-Bis(difluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

To a solution of 1-bromo-2,4-bis(difluoromethoxy)benzene (3.30 g, 11.4 mmol, 1.0 eq.) in 1,4-dioxane was added KOAc (2.23 g, 22.8 mmol, 2.0 eq.), Pd(dppf)Cl_2 (0.830 g, 1.10 mmol, 0.1 eq.) and bis(pinacolato)diboron (4.34 g, 17.1 mmol, 1.5 eq.). The reaction mixture was stirred for 16 h at 100°C under N_2. The mixture was filtered and concentrated. The residue was purified by flash chromatography on silica gel (PE: EA = 0% ~ 10%) to obtain 2-(2,4-bis(difluoromethoxy) phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.0 g, 52% yield) as yellow oil. ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.72 (d, J = 8.0 Hz, 1H), 7.36 (t, J = 73.2 Hz, 1H), 7.12 (t, J = 74.4 Hz, 1H), 7.12 – 7.08 (m, 1H), 7.02 – 6.97 (m, 1H), 1.29 (s, 12H).

Intermediate 2g. 2-(4-bromo-2-(difluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



Step 1. 4-Bromo-2-(difluoromethoxy)-1-nitrobenzene

To a solution of 5-bromo-2-nitrophenol (5.7 g, 26.15 mmol) in DMF (135 mL) / H_2O (15 mL) was added Cs_2CO_3 (17.0 g, 52.29 mmol) and sodium 2-chloro-2,2-difluoroacetate (10.0 g, 65.37 mmol). The mixture was stirred for 15 minutes at room temperature and then heated to 100 °C for 16 hours. The reaction mixture was cooled to room temperature and partitioned between water (500 mL) and EA (200 mL). The aqueous phase was extracted with EA (2 x 200 mL). The combined organic extracts were washed with brine (300 mL), dried over Na_2SO_4, filtered, and

concentrated. The residue was purified by silica gel column (0-20% EA in PE) to obtain 4-bromo-2-(difluoromethoxy)-1-nitrobenzene as a yellow oil (4.0 g, 57% yield). 1H NMR (400 MHz, DMSO-d_6) δ 8.05 (d, J = 8.8 Hz, 1H), 7.83 (d, J = 1.6 Hz, 1H), 7.74 (dd, J = 8.8, J = 1.6 Hz, 1H), 7.43 (t, J = 72.4 Hz, 1H).

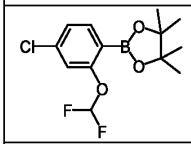
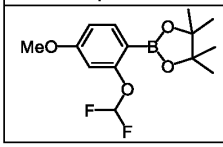
Step 2. 4-Bromo-2-(difluoromethoxy) aniline

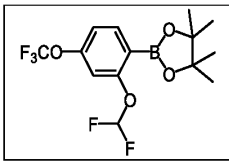
To a solution of 4-bromo-2-(difluoromethoxy)-1-nitrobenzene (1.0 g, 3.73 mmol) in THF (10 mL) / H_2O (5 mL) was added the solution of NH_4Cl (1.6 g, 29.85 mmol) in H_2O (10 mL), Zn (1.95 g, 29.85 mmol). The mixture was stirred at rt for 2 h, then filtered through a pad of celite and rinsed with EA. The filtrate was extracted with EA (30 mL x 2). The organic extracts were dried over Na_2SO_4, decanted, concentrated, and purified by silica gel column (0-10% EA in PE) to afford 4-bromo-2-(difluoromethoxy) aniline as a yellow oil (750 mg, 84% yield). MS m/z 236.0 $[M-1]^-$; 1H NMR (400 MHz, DMSO-d_6) δ 7.15 (s, 1H), 7.11 (dd, J = 8.8, 2.0 Hz, 1H), 7.09 (t, J = 74.0 Hz, 1H), 6.73 (d, J = 8.8 Hz, 1H), 5.28 (s, 2H).

Step 3. 2-(4-Bromo-2-(difluoromethoxy) phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

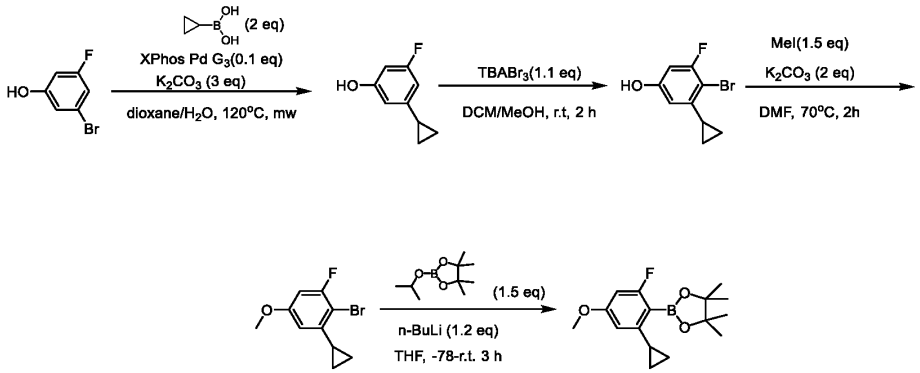
To a solution of 4-bromo-2-(difluoromethoxy) aniline (13.0 g, 54.61 mmol) in MeCN (300 mL) was added t-$BuNO_2$ (8.45 g, 81.92 mmol), $(BPin)_2$ (15.26 g, 60.08 mmol) at 0°C. The mixture was stirred at 80°C for 4 h, then concentrated and purified by silica gel column (0-5% EA in PE) to afford 2-(4-bromo-2-(difluoromethoxy) phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane as a yellow oil (5.4 g, 28% yield). 1H NMR (400 MHz, DMSO-d_6) δ 7.60 (d, J = 8.0 Hz, 1H), 7.51 (dd, J = 8.0, J = 1.6 Hz, 1H), 7.42 (s, 1H), 7.15 (t, J = 74.2 Hz, 1H), 1.29 (s, 12H).

The intermediates below were prepared according to the procedure of Intermediate 2e-2g by substituting the appropriate starting materials, reagents and reaction conditions.

Structure	Spectral Data
	MS *m/z* 304.5 $[M+H]^+$; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.68 (d, J= 8.4 Hz, 1H), 7.38 (d, J= 7.6 Hz, 1H), 7.30 (s, 1H), 7.16 (t, J= 74.4Hz, 1H), 1.30 (s, 12H).
	^{1}H NMR (400 MHz, DMSO-d_6) δ 7.60 (d, J = 8.4 Hz, 1H), 7.05 (t, J = 70.4 Hz, 1H), 6.86 (dd, J = 8.6, 2.0 Hz, 1H), 6.70 (d, J = 2.0 Hz, 1H), 3.80 (s, 3H), 1.27 (s, 12H).

	^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J = 8.3 Hz, 1H), 7.11 (d, J = 8.2 Hz, 1H), 7.02 (s, 1H), 6.53 (t, J = 74.7 Hz, 1H), 1.26 (s, 12H).

Intermediate 2h: 2-(2-cyclopropyl-6-fluoro-4-methoxyphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



Step 1. 3-cyclopropyl-5-fluorophenol

To a solution of 3-bromo-5-fluorophenol (5.0 g, 26.3 mmol, 1.0 eq.) in dioxane (40 mL) and water (10 mL) was added cyclopropylboronic acid (4.5 g, 52.6 mmol, 2.0 eq.), $Pd(dppf)Cl_2$ (377 mg, 0.52 mmol, 0.2 eq.) and cesium carbonate (25.7 g, 78.9 mmol, 3.0 eq.). The resulting mixture was stirred at 100oC for 16 hours under nitrogen atmosphere, then diluted with ethyl acetate (200 mL), washed with water (200 mL). The aqueous phase was adjusted to pH~4 by addition of 6M HCl, then extracted with ethyl acetate (3 x 100 mL). The organic phase was dried with sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (10% ethyl acetate in petroleum ether) to afford 4-bromo-3-cyclopropyl-5-fluorophenol (3.1 g, 77.5% yield) as a yellow oil. 1H NMR (400 MHz, Methanol-d_4) δ 6.31 (t, J = 1.8 Hz, 1H), 6.28 – 6.25 (m, 1H), 6.25 – 6.22 (m, 1H), 1.85 -1.76 (m, 1H), 0.97 – 0.88 (m, 2H), 0.66 – 0.58 (m, 2H).

Step 2. 4-bromo-3-cyclopropyl-5-fluorophenol

To a solution of 4-bromo-3-cyclopropyl-5-fluorophenol (3 g, 19.7 mmol, 1.0 eq.) in dichloromethane (15 mL) and methanol (15 mL) was added tetrabutylammonium tribromide (10.4 g, 21.7 mmol, 1.1 eq.). The resulting mixture was stirred at room temperature for 2 h.

Water (100 mL) was then added. The mixture was extracted with dichloromethane (3 x 50 mL). The organic phase was washed with brine (50 mL), dried with sodium sulfate, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (10% ethyl acetate in petroleum ether) to afford 4-bromo-3-cyclopropyl-5-fluorophenol (3.9 g, 85.7% yield) as a yellow oil. 1H NMR (400 MHz, Methanol-d_4) δ 6.50 – 6.42 (m, 1H), 6.27 – 6.20 (m, 1H), 2.23 – 2.09 (m, 1H), 1.03 – 0.97 (m, 2H), 0.66 – 0.59 (m, 2H).

Step 3. 2-bromo-1-cyclopropyl-3-fluoro-5-methoxybenzene

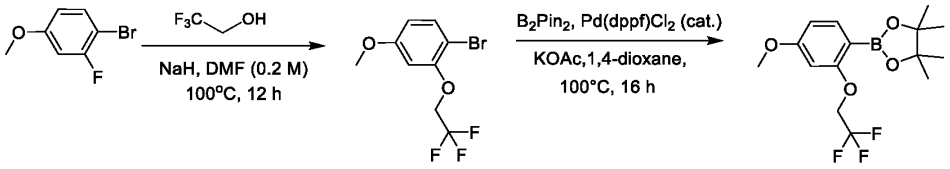
To a solution of 4-bromo-3-cyclopropyl-5-fluorophenol (3.9 g, 16.9 mmol, 1.0 eq.) in N,N-dimethylformamide (40 mL) was added methyl iodide (1.58 mL, 25.4 mmol, 1.5 eq.) and potassium carbonate (4.67 g, 33.8 mmol, 2.0 eq.). The resulting mixture was stirred at 70 °C for 2h. The reaction mixture was diluted with ethyl acetate (150 mL) and washed with water (3 x 100 mL) and brine (100 mL). The organic phase was dried with sodium sulfate, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (3% ethyl acetate in petroleum ether) to afford 2-bromo-1-cyclopropyl-3-fluoro-5-methoxybenzene (3.1 g, 74.8% yield) as a pink oil. 1H NMR (400 MHz, Methanol-d_4) δ 6.69 – 6.55 (m, 1H), 6.48 – 6.28 (m, 1H), 3.87 – 3.72 (m, 3H), 2.26 – 2.08 (m, 1H), 1.03 – 0.93 (m, 2H), 0.77 – 0.59 (m, 2H).

Step 4. 2-(2-cyclopropyl-6-fluoro-4-methoxyphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

To a solution of 2-bromo-1-cyclopropyl-3-fluoro-5-methoxybenzene (3.0 g, 12.2 mmol, 1.0 eq.) in tetrahydrofuran (30 mL) was added n-butyllithium (6.3 mL, 15.9 mmol, 1.3 eq., 2.5M in hexane) at -78°C. The resulting mixture was stirred at -78°C for 30 min, then 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane was added dropwise (2.97 mL, 14.6 mmol, 1.2 eq.). The resulting mixture was allowed to warm to room temperature and stirred for another 2 h.
The reaction was quenched by water (100 mL), and the mixture was extracted with ethyl acetate (4 x 50 mL). The organic phase was dried with sodium sulfate, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (3% ethyl acetate in petroleum ether) to afford 2-(2-cyclopropyl-6-fluoro-4-methoxyphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1.9 g, 53.3% yield) as a light yellow oil. MS *m/z* 293.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 6.52 – 6.37 (m, 1H), 6.31 – 6.17 (m, 1H), 3.79 – 3.69 (m, 3H), 2.34 –

2.19 (m, 0.8H), 2.00 – 1.90 (m, 0.16H), 1.39 – 1.33 (m, 12H), 0.95 – 0.84 (m, 2H), 0.69 – 0.60 (m, 2H).

Intermediate 2i. 2-(4-Methoxy-2-(2,2,2-trifluoroethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



Step1. 1-bromo-4-methoxy-2-(2,2,2-trifluoroethoxy)benzene

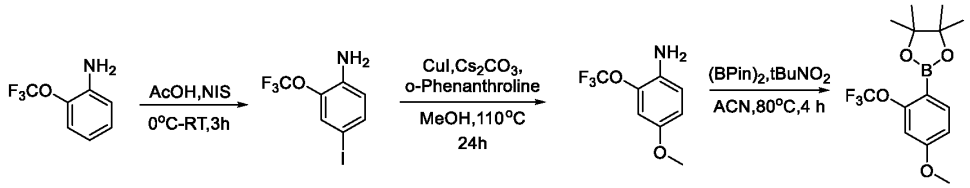
To a solution of NaH (2.2 g, 53.6 mmol, 60% in oil, 2.2 eq.) in DMF (20 mL) and 2,2,2-trifluoroethan-1-ol (4.9 g, 48.8 mmol, 2.0 eq.) was added dropwise at 0°C under N_2. The mixture was stirred at 0°C for 0.5 hours under N_2 and 1-bromo-2-fluoro-4-methoxybenzene (5.0 g, 24.4 mmol, 1.0 eq.) was added. The mixture was allowed to warm to 100°C and stirred for 16 hours under N_2, then poured into water (100 mL) and extracted with dichloromethane (3 x 50 mL). The combined organic extracts were washed with brine (50 mL), dried with sodium sulfate, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (0-7% ethyl acetate in petroleum ether) to afford 1-bromo-4-methoxy-2-(2,2,2-trifluoroethoxy)benzene (3.5 g, 12.3 mmol, 50.4% yield) a colorless oil. 1H NMR (400 MHz, DMSO-d_6) δ 7.49 (d, J = 8.8 Hz, 1H), 6.85 (d, J = 2.8 Hz, 1H), 6.61 (dd, J = 8.8, 2.8 Hz, 1H), 4.86 (q, J = 8.8 Hz, 2H), 3.78 (s, 3H).

Step 2. 2-(4-Methoxy-2-(2,2,2-trifluoroethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

To a solution of 1-bromo-4-methoxy-2-(2,2,2-trifluoroethoxy)benzene (3.50 g, 12.3 mmol, 1.0 eq.) in dioxane (40 mL) was added 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (3.7 g, 14.7 mmol, 1.2 eq.), Pd(dppf)Cl_2 (898.4 mg, 1.2 mmol, 0.1 eq.) and KOAc (3.6 g, 36.8 mmol, 3.0 eq.). The resulting mixture was stirred at 100°C for 16 hours under nitrogen atmosphere Then cooled, diluted with ethyl acetate (200 mL), washed with water (200 mL), and extracted with ethyl acetate (3 x 100 mL). The organic phase was dried with sodium sulfate, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (0-10% ethyl acetate in petroleum ether) to afford 2-(4-methoxy-2-

(2,2,2-trifluoroethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1.5 g, 4.5 mmol, 36.8% yield) as a white solid. MS *m/z* 333.1[M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.56 (d, J = 8.4 Hz, 1H), 6.63 (dd, J = 8.0, 2.0 Hz, 1H), 6.54 (d, J = 2.0Hz, 1H), 4.47 (q, J = 8.4 Hz, 2H), 3.81 (s, 3H), 1.32 (s, 12H).

Intermediate 2j. 2-(4-methoxy-2-(trifluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



Step 1. 4-Iodo-2-(trifluoromethoxy)aniline

To a solution of 2-(trifluoromethoxy)aniline (29 g, 163.73 mmol, 1.0 eq.) in acetic acid (80 mL) was added NIS (40.52 g, 180.10 mmol, 1.1 eq.) slowly at 0 °C . The mixture was stirred for 3 h at room temperature. The reaction solution was concentrated in vacuo to remove acetic acid and then the reaction mixture was diluted with water (200 mL) and extracted with ethyl acetate (200 mL x 3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel (EA in PE = 0%-20) to afford 4-iodo-2-(trifluoromethoxy)aniline (40.6 g, 81.8 % yield) as a red solid. MS *m/z* 303.9 $[M+1]^+$; ^1H NMR (400 MHz, DMSO-d_6) δ 7.35 – 7.32 (m, 2H), 6.66 (d, *J* = 8.4 Hz, 1H), 5.59 (s, 2H).

Step 2. 4-Methoxy-2-(trifluoromethoxy)aniline

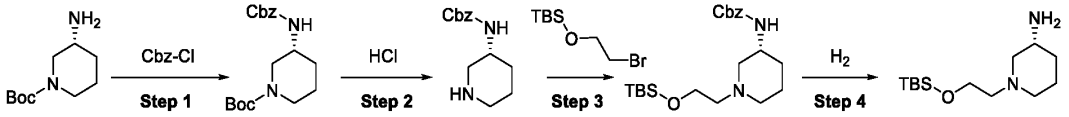
To a solution of 4-iodo-2-(trifluoromethoxy)aniline (23.8 g, 78.54 mmol, 1.0 eq.) in MeOH (200 mL) was added 1,10-phenanthroline (1.42 g, 7.85 mmol, 0.1 eq.),Cs_2CO_3 (51.18 g, 157.08 mmol, 2.0 eq.) and CuI (0.748 g, 3.93 mmol, 0.05 eq.) under N_2 at rt. The reaction mixture was stirred for 16 h at 110 °C in an autoclave reactor. The reaction solution was concentrated in vacuo to remove MeOH and then the reaction mixture was diluted with water (200 mL) and extracted with ethyl acetate (250 mLx3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel (EA in PE = 0% ~ 10%) to afford 4-methoxy-2-

(trifluoromethoxy)aniline (11 g, 67.61% yield) as yellow oil. MS *m/z* 208.2 $[M+1]^+$; ^1H NMR (400 MHz, Methanol-d_4) δ 6.91 – 6.67 (m, 3H), 3.71 (s, 3H).

Step 3. 2-(4-Methoxy-2-(trifluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

To a solution of 4-methoxy-2-(trifluoromethoxy)aniline (11 g, 53.10 mmol, 1.0 eq.) in ACN (25 mL) was added $tBuNO_2$ (8.21 g, 79.65 mmol, 1.5 eq.) and $(BPin)_2$ (16.18 g, 63.72 mmol, 1.2 eq.) at 0 °C. The reaction mixture was stirred for 4 h at 80 °C under N_2 atmosphere, then cooled, and concentrated in vacuo before diluted with water (200 mL) and extracted with ethyl acetate (150 mLx3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel (EA in PE = 0% ~ 2%) to afford 2-(4-methoxy-2-(trifluoromethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5.6 g, 33.15% yield) as yellow oil. MS *m/z* 319.0 $[M+1]^+$; ^1H NMR (400 MHz, DMSO-d_6) δ 7.71 (d, *J* = 8.4 Hz, 1H), 7.08 – 7.03 (m, 1H), 6.92 (s, 1H), 3.87 (s, 3H), 1.32 (s, 12H).

Intermediate 3a: (3R)-1-[2-[tert-Butyl(dimethyl)silyl]oxyethyl]piperidin-3-amine



Step 1. tert-Butyl (3R)-3-(benzyloxycarbonylamino)piperidine-1-carboxylate

To a solution of tert-butyl (R)-3-aminopiperidine-1-carboxylate (30 g, 0.15 mol) in THF (330 mL) and water (83 mL) was added Na_2CO_3(43 g, 0.31 mol). Then Cbz-Cl (34, 0.199 mol) was added dropwise to the mixture with ice bath, monitored by TLC. After 5 hours, the reaction mixture was extracted with EA, dried over Na_2SO_4 and evaporated in vacuo. The crude product was purified via flash chromatography (PE: EA = 4:1) to give tert-butyl (3R)-3-(benzyloxycarbonylamino) piperidine-1-carboxylate (35 g, 84% Yield). MS *m/z* 235.1 $[M-Boc+H]^+$

Step 2. Benzyl N-[(3R)-3-piperidyl]carbamate

To a solution of tert-butyl (3R)-3-(benzyloxycarbonylamino)piperidine-1-carboxylate (35g, 0.104 mol) in 450 mL DCM was added HCl (350 mL, 4M in 1,4-dioxane), monitored by TLC. After 2 h, the solvent was removed in vacuo to give crude benzyl N-[(3R)-3-piperidyl]carbamate (25 g, 100% yield) which was used for next step without purification. MS

m/z 234.1 $[M+H]^+$.

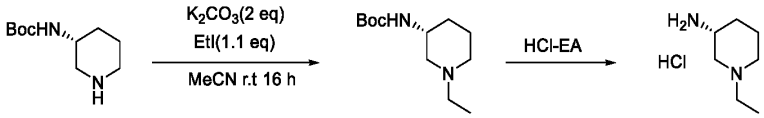
Step 3. Benzyl N-[(3R)-1-[2-[tert-butyl(dimethyl)silyl]oxyethyl]-3-piperidyl]carbamate

To a solution of benzyl N-[(3R)-3-piperidyl]carbamate (25 g, 0.106 mol) in CH_3CN (680 mL) was added Cs_2CO_3 (175 g, 0.537 mol) and (2-bromoethoxy)(tert-butyl)dimethylsilane (40 g, 0.167 mol). The reaction mixture was stirred at 90 °C for 16 h, then filtered and the solvent was removed in vacuo. The crude product was purified via flash chromatography to give the product benzyl N-[(3R)-1-[2-[tert-butyl(dimethyl)silyl]oxyethyl]-3-piperidyl]carbamate (22.5 g, 53% yield). MS *m/z* 393.2 $[M+H]^+$.

Step 4. (3R)-1-[2-[tert-Butyl(dimethyl)silyl]oxyethyl]piperidin-3-amine

To a solution of benzyl N-[(3R)-1-[2-[tert-butyl(dimethyl)silyl]oxyethyl]-3-piperidyl]carbamate (22.5 g, 0.057 mol) in MeOH (60 mL) was added Pd/C (4.5 g, 20%). The system was evacuated and refilled with hydrogen. Then the mixture stirred at R.T overnight. After reaction, the mixture was filtered, the solvent was removed in vacuo and the crude product was purified via flash chromatography to give the product (3R)-1-[2-[tert-butyl(dimethyl)silyl]oxyethyl]piperidin-3-amine (12 g, 81% yield). MS *m/z* 259.2 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 3.68 (t, J = 6.6 Hz, 2H), 2.85 – 2.74 (m, 2H), 2.67 – 2.58 (m, 1H), 2.46 (t, J = 6.4 Hz, 2H), 2.11 – 2.01 (m, 1H), 1.94 – 1.83 (m, 1H), 1.83 – 1.71 (m, 4H), 1.68 – 1.58 (m, 1H), 1.56 – 1.43 (m, 1H), 1.09 – 0.96 (m, 1H), 0.88 – 0.79 (m, 9H), 0.04 – (-)0.04 (m, 6H).

Intermediate 3b: (R)-1-Ethylpiperidin-3-amine hydrochloride



Step 1. tert-Butyl (R)-(1-ethylpiperidin-3-yl)carbamate

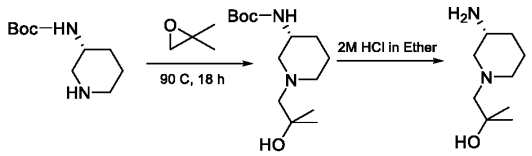
To a solution of tert-butyl (R)-piperidin-3-ylcarbamate (4 g, 20 mmol) in MeCN (40 mL) was added K_2CO_3 (2.76 g, 20 mmol) and MeI (3.12 g, 20 mmol) at 20°C under N_2. The mixture was stirred at 20°C for 16 hours. TLC showed the reaction was completed. The reaction mixture was poured into water (100 mL) and extracted with EA (100 mL x 2). The combined organic layers were washed with brine (100 mL x 2). dried over Na_2SO_4, filtered and concentrated. Purified by column (DCM:MeOH=0-10%) to give tert-butyl (R)-(1-ethylpiperidin-3-

yl)carbamate (3.6 g, 15.8 mmol, 78.9% yield) as yellow oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.65 (d, J = 7.8 Hz, 1H), 3.32 (s, 1H), 2.70 (dd, J = 41.0, 9.7 Hz, 2H), 2.29 (q, J = 7.1 Hz, 2H), 1.83 – 1.53 (m, 4H), 1.48 – 1.40 (m, 1H), 1.37 (s, 9H), 1.11 (qd, J = 11.8, 3.7 Hz, 1H), 0.96 (t, J = 7.2 Hz, 3H).

Step 2. **(R)-1-Ethylpiperidin-3-amine hydrochloride**

To a solution of tert-butyl (R)-(1-ethylpiperidin-3-yl)carbamate (3.6 g, 15.8 mmol) in MeOH (10 mL) was added HCl (30 mL, 3 M in EA) at RT. The mixture was stirred at 20°C for 16 hours. TLC showed the reaction was completed. The reaction mixture was concentrated to give(R)-1-ethylpiperidin-3-amine hydrochloride (3.03 g, 15.0 mmol, 95.0% yield) as yellow oil. MS m/z 129.2 $[M+H]^+$; ^{1}H NMR (400 MHz, Methanol-d_4) δ 3.83 – 3.59 (m, 3H), 3.36 – 3.30 (m, 2H), 3.18 – 2.96 (m, 2H), 2.25 (d, J = 12.7 Hz, 1H), 2.15 (d, J = 14.9 Hz, 1H), 2.07 – 1.92 (m, 1H), 1.76-1.72 (m, 1H), 1.43 (t, J = 7.3 Hz, 3H).

Intermediate 9c: (*R*)-1-(3-Aminopiperidin-1-yl)-2-methylpropan-2-ol



Step-1: *tert*-Butyl (R)-(1-(2-hydroxy-2-methylpropyl)piperidin-3-yl)carbamate

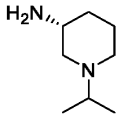
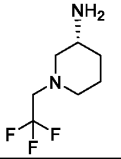
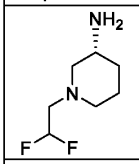
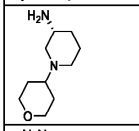
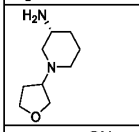
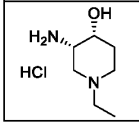
A mixture of *tert*-butyl (R)-piperidin-3-ylcarbamate (700 mg, 3.5 mmol, 1.0 eq.), and 2,2-dimethyloxirane (800 mg, 11.1 mmol, 3.2 eq.) was stirred at 90°C for 18 h. The crude reaction mixture was allowed to cool to room temperature and diluted with DCM (20 mL). The organic phase was washed with saturated aqueous $NaHCO_3$ solution (4 mLx2) followed by water and brine. The organic phase was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude material was used then for the following step. MS m/z 273.3 $[M+H]^+$.

Step-2: (*R*)-1-(3-Aminopiperidin-1-yl)-2-methylpropan-2-ol

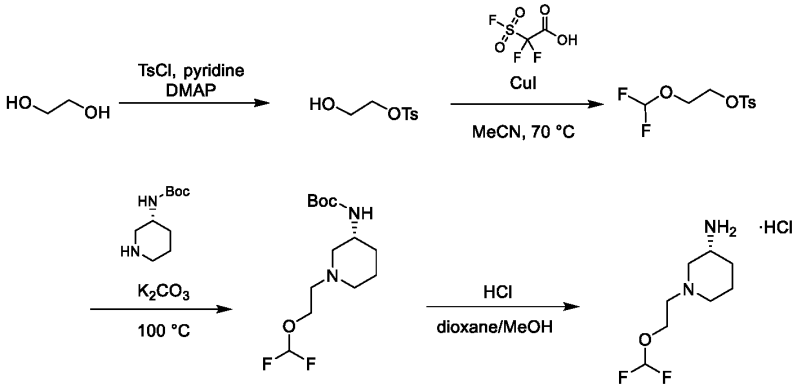
The crude compound from previous step was dissolved in DCM (5 mL) and then 2M HCl solution in ether (10 mL) was added slowly at rt while the mixture was vigorously stirred. The reaction mixture was stirred at rt for overnight and concentrated *in vacuo* to afford a light brown solid (520 mg) of HCl salt. The amine was used without further purification. MS m/z 173.2 $[M+H]^+$.

The intermediates below were prepared according to the procedure of Intermediate 3b-c

or c by substituting the appropriate starting materials, reagents and reaction conditions.

Structure	Spectral Data
	MS *m/z* 243.2 $[M+H]^+$; ^1H NMR (400 MHz, Methanol-d_4) δ 3.83–3.72 (m, 1H), 3.71–3.61 (m, 2H), 3.56–3.48 (m, 1H), 3.15 –3.03 (m, 2H), 2.30–2.19 (m, 1H), 2.18–2.10 (m, 1H), 2.09–1.97 (m, 1H), 1.81–1.66 (m, 1H), 1.43 (d, *J* = 6.7 Hz, 6H).
	MS *m/z* 183.2 $[M+H]^+$; ^1H NMR(400 MHz, Methanol-d_4) δ 4.00 (q, J = 9.3 Hz, 2H), 3.65 (ddd, J = 22.7, 13.2, 8.3 Hz, 2H), 3.39 (d, J = 12.2 Hz, 1H), 3.26 – 3.06 (m, 2H), 2.09 (dtd, J = 23.9, 8.6, 4.2 Hz, 2H), 2.01 – 1.85 (m, 1H), 1.72 (dtd, J = 13.8, 10.1, 3.7 Hz, 1H).
	^1H NMR(400 MHz, Methanol-d_4) δ 6.48 (tt, J = 53.5, 3.7 Hz, 1H), 3.84 – 3.64 (m, 4H), 3.59 (d, J = 11.9 Hz, 1H), 3.22 (dt, J = 12.2, 7.1 Hz, 2H), 2.15 (dtd, J = 15.1, 7.9, 3.8 Hz, 2H), 2.07 – 1.93 (m, 1H), 1.71 (ddd, J = 15.2, 11.9, 3.8 Hz, 1H).
	MS *m/z* 185.2$[M+H]^+$
	MS *m/z* 171.2$[M+H]^+$
	MS *m/z* 145.2$[M+H]^+$

Intermediate 3d: (*R*)-1-(2-(Difluoromethoxy)ethyl)piperidin-3-amine hydrochloride



Step 1: 2-Hydroxyethyl 4-methylbenzenesulfonate

A mixture of ethylene glycol (2.5 g, 40 mmol), TsCl (1.90 g, 10 mmol), pyridine (1.1 g,

12 mmol) and DMAP (12 mg, 0.1 mmol) was stirred at rt for 18 h. The reaction mixture was partitioned between DCM (20 mL) and 0.5 M hydrochloric acid. The organic layer was dried (Na_2SO_4), filtered, and concentrated. Purification by chromatography on SiO_2 (EtOAc:hexanes, 0 to 60%) gave a colorless oil (1.32 g, 78%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.25 Hz, 2 H), 7.37 (d, *J* = 8.13 Hz, 2 H), 4.15 (t, *J* = 4.50 Hz, 2 H), 3.83 (t, *J* = 4.63 Hz, 2 H), 2.46 (s, 3 H), 2.00 (br s, 1 H).

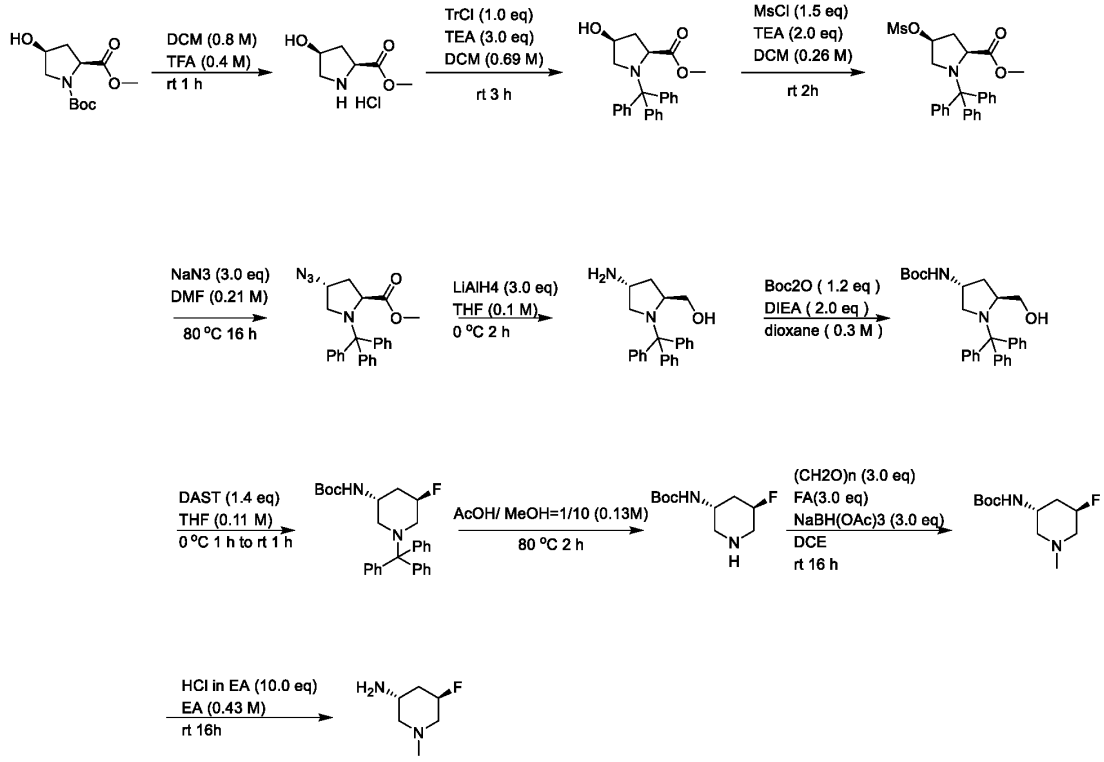
Step 2. 2-(Difluoromethoxy)ethyl 4-methylbenzenesulfonate

To a stirred solution of 2-hydroxyethyl 4-methylbenzenesulfonate (1.70 g, 7.86 mmol) in MeCN (13 mL) was added copper (I) iodide (0.300 g, 1.57 mmol). The resulting mixture was stirred at 70 °C and treated with 2,2-difluoro-2-fluorosulfonyl-acetic acid (2.80 g, 15.7 mmol) as a solution in MeCN (10 mL) dropwise over a period of 25 min. The resulting mixture was treated with anhydrous Na_2SO_4 (small scoop) and stirring continued for 1.5 h. The mixture was then cooled to rt, diluted with Et_2O and washed with brine, a 1:1 mixture of brine: water (2x), and brine. The organic phase was dried (Na_2SO_4), filtered and concentrated. Purification by chromatography on SiO_2 (EtOAc:hexanes, 0-25%) gave a pale yellow oil (0.759 g, 36%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.25 Hz, 2 H), 7.49 (d, *J* = 8.13 Hz, 2 H), 6.65 (t, *J* = 75.04 Hz, 1 H), 4.22 – 4.16 (m, 2 H), 4.04 – 3.98 (m, 2 H), 2.43 (s, 3 H)

Step 3 and 4: **(*R*)-1-(2-(Difluoromethoxy)ethyl)piperidin-3-amine hydrochloride**

t-Butyl *N*-[(3*R*)-3-piperidyl]carbamate (0.500 g, 2.50 mmol) in DMF (10 mL) was added 2-(difluoromethoxy)ethyl 4-methylbenzenesulfonate (0.764 g, 2.87 mmol) and K_2CO_3 (0.690 g, 4.99 mmol). The mixture was stirred at 100 °C for 2 h, then diluted with DCM/iPrOH (9:1) and washed with water, brine, dried over Na_2SO_4, filtered and concentrated. Purification by chromatography on SiO_2 (EtOAc:hexanes, 5 to 60%) gave a pale yellow oil (0.709 g). The oil was dissolved in MeOH (2.0 mL), treated with HCl/dioxane (4.0 M, 3 mL) and stirred for 4 h. The mixture was concentrated, resuspended in ether and filtered to give a white solid (0.371 g, 67%). ^{1}H NMR (400 MHz, D_2O) δ 6.45 (t, *J* = 73.6 Hz, 1 H), 4.26 (t, *J* = 5.2 Hz, 2 H), 3.81 (d, *J* = 11.2 Hz, 1 H), 3.67 -3.58 (m, 2 H), 3.55 (t, *J* = 4.8 Hz, 2 H), 3.15 - 3.02 (m, 2 H), 2.21 (d, *J* = 12.4 Hz, 1 H), 2.11 (d, *J* = 15.2 Hz, 1 H), 1.90 – 1.79 (m, 1 H), 1.70 -1.60 (m, 1 H).

Intermediate 3f: (3R,5R)-5-Fluoro-1-methylpiperidin-3-amine hydrochloride



Step 1. Methyl (2S,4S)-4-hydroxypyrrolidine-2-carboxylate

1-(tert-Butyl) 2-methyl (2S,4S)-4-hydroxypyrrolidine-1,2-dicarboxylate (10.0 g, 40.8 mmol) was dissolved in DCM (50 mL) and cooled to 0 °C. TFA (10 mL, 132.3 mmol) was slowly added and the mixture was warmed to room temperature and stirred for 1 h. The mixture was concentrated in vacuo to give crude methyl (2S,4S)-4-hydroxypyrrolidine-2-carboxylate as yellow oil, which was used to next step without further purification. MS *m/z* 146.1 $[M+H]^+$.

Step 2. Methyl (2S,4S)-4-hydroxy-1-tritylpyrrolidine-2-carboxylate

To a solution of crude methyl (2S,4S)-4-hydroxypyrrolidine-2-carboxylate from above step in DCM (50 mL) was added TEA (12.4 g, 123 mmol) and Ph_3CCl (11.4 g, 40.9 mmol,). The reaction mixture was stirred for 2 h at rt. The mixture was poured into water and extracted with DCM (30 mL x 2). The organic layer was washed with brine, dried over anhydrous Na_2SO_4, and evaporated in vacuo. The residue was purified by flash chromatography on silica gel (PE: EA =10:1 to 5:1) to obtain methyl (2S,4S)-4-hydroxy-1-trityl-pyrrolidine-2-carboxylate (7.60 g, 48% yield for two steps) as a white solid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.50 (m, 6H), 7.32 –

7.23 (m, 6H), 7.21 – 7.13 (m, 3H), 3.92 – 3.80 (m, 3H), 3.65 (s, 3H), 3.46 (d, J = 11.5 Hz, 1H), 2.80 (dd, J = 11.5, 3.8 Hz, 1H), 1.62 (d, J = 13.8 Hz, 1H), 1.38 – 1.11 (m, 1H).

Step 3. Methyl (2S,4S)-4-((methylsulfonyl)oxy)-1-tritylpyrrolidine-2-carboxylate

To a solution of methyl (2S,4S)-4-hydroxy-1-trityl-pyrrolidine-2-carboxylate (10.0 g, 25.8 mmol) in DCM (100 mL) was added TEA (7.90 g, 78.0 mmol) and MsCl (4.50 g, 39.0 mmol). The reaction mixture was stirred for 2 h at rt. The mixture was diluted with water and extracted with DCM (80 mL x 2). The organic layer was washed with brine, dried over anhydrous Na_2SO_4, and evaporated in vacuo to give crude methyl (2S,4S)-4-methylsulfonyloxy-1-trityl-pyrrolidine-2-carboxylateas yellow oil, which was used in the next step directly.

Step 4. Methyl (2S,4R)-4-azido-1-tritylpyrrolidine-2-carboxylate

To a solution of methyl (2S,4S)-4-methylsulfonyloxy-1-trityl-pyrrolidine-2-carboxylate from above step in DMF (140 mL) was added sodium azide (7.80 g, 120 mmol). The reaction mixture was stirred for 16 h at 80 °C, then diluted with water and extracted with EA (3 x 100 mL). The combined organic layers were washed with water, brine, dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel (PE: EA = 0% ~ 10%) to give methyl (2S,4R)-4-azido-1-trityl-pyrrolidine-2-carboxylate (8.00 g, 64.5% yield for two steps) as yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 – 7.51 (m, 6H), 7.33 – 7.24 (m, 6H), 7.18 (t, J = 7.3 Hz, 3H), 4.20 – 4.06 (m, 1H), 3.91 (d, J = 8.9 Hz, 1H), 3.72 (dd, J = 10.3, 7.6 Hz, 1H), 3.63 (s, 3H), 2.63 (dd, J = 10.3, 7.8 Hz, 1H), 1.90 – 1.79 (m, 1H), 0.94 – 0.88 (m, 1H).

Step 5. ((2S,4R)-4-Amino-1-tritylpyrrolidin-2-yl)methanol

To a stirred suspension of $LiAlH_4$ (2.20 g, 58.0 mmol) in THF (80 mL) at 0 °C was added a solution of a solution of methyl (2S,4R)-4-azido-1-trityl-pyrrolidine-2-carboxylate (8.00 g, 19.4 mmol) in THF (10 mL). After the addition was completed, the reaction mixture was stirred at 0 °C for 1 h. The reaction was quenched with water (2.5 mL), 15% NaOH solution (2.5 mL) and water (6 mL). After stirring for 0.5 h, the mixture was dried over Na_2SO_4, filtered and concentrated to give crude product [(2S,4R)-4-amino-1-trityl-pyrrolidin-2-yl]methanol as yellow oil (7.00 g), which was applied to the next step without purification.

Step 6. tert-Butyl ((3R,5S)-5-(hydroxymethyl)-1-tritylpyrrolidin-3-yl)carbamate

To a solution of [(2S,4R)-4-amino-1-trityl-pyrrolidin-2-yl]methanol (7.00 g, 19.5 mmol) in 1,4-dioxane (70 mL) was added TEA (3.90 g, 39.0 mmol) and $(Boc)_2O$ (5.10 g, 23.0 mmol).

The mixture was stirred for 2 h at rt, then diluted with water and extracted with EA (3 x 100 mL). The combined organic layers were washed with water, brine, dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by silica gel column chromatography (PE: EA = 20:1) to give tert-butyl N-[(3R,5S)-5-(hydroxymethyl)-1-trityl-pyrrolidin-3-yl]carbamate (8.00 g, 89.3% yield) as colorless oil. MS *m/z* 459.3 $[M+H]^+$, ^1H NMR (400 MHz, $CDCl_3$) δ 7.67 – 7.50 (m, 6H), 7.33 – 7.23 (m, 7H), 7.18 (t, *J* = 7.3 Hz, 3H), 4.27 – 4.18 (m, 1H), 3.77 – 3.64 (m, 2H), 3.58 – 3.51 (m, 1H), 3.50 – 3.32 (m, 2H), 2.60 – 2.48 (m, 1H), 2.03 – 1.94 (m, 1H), 1.90 – 1.81 (m, 1H), 1.36 (s, 9H).

Step 7. tert-Butyl ((3R,5R)-5-fluoro-1-tritylpiperidin-3-yl)carbamate

DAST (2.80 mL, 21.0 mmol) was added dropwise to a stirred solution of tert-butyl N-[(3R,5S)-5-(hydroxymethyl)-1-trityl-pyrrolidin-3-yl]carbamate (6.80 g, 15.0 mmol) in THF (70 mL) at 0 °C. The mixture was stirred for 1 h at 0 °C and 1 h at RT, then cooled to 0°C again. A saturated aqueous solution of Na_2CO_3 was added to adjust pH to 12. The phases were separated and the aqueous phase was extracted with EtOAc (2 x 40 mL). The organic extracts were combined, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude material was purified by flash chromatography (silica gel, PE/EtOAc= 20/1) to afford tert-butyl N-[(3R,5R)-5-fluoro-1-trityl-3-piperidyl]carbamate (3.90 g, 57% yield) as a white solid. MS *m/z* 483.3 $[M+Na]^+$.

Step 8. tert-Butyl ((3R,5R)-5-fluoropiperidin-3-yl)carbamate

To a solution of tert-butyl N-[(3R,5R)-5-fluoro-1-trityl-3-piperidyl]carbamate (3.90 g, 8.50 mmol) in MeOH (80 mL) was added AcOH (8 mL, 139.6 mmol). The mixture was stirred for 2 h at 80 °C, then concentrated under reduced pressure. The residue was diluted with EA (20 mL) and H_2O (20 mL). The mixture was acidified with aqueous HCl till pH = 2-3 and extracted with EA (10 mL x 2). The aqueous layers were basified with aqueous K_2CO_3 till pH = 9-10 and extracted with DCM (50 mL x 3). The DCM layers were combined and dried over Na_2SO_4, filtered and concentrated under reduced pressure to provide tert-butyl N-[(3R,5R)-5-fluoro-3-piperidyl]carbamate (1.60 g, 87% yield) as a white solid. MS *m/z* 219.1 $[M+H]^+$, ^1H NMR (400 MHz, DMSO-d_6) δ 6.61 (s, 1H), 4.77 (d, *J* = 48.5 Hz, 1H), 3.60 (br s, 1H), 2.96 – 2.82 (m, 2H), 2.77 – 2.62 (m, 1H), 2.43 – 2.33 (m, 1H), 2.09 – 1.97 (m, 1H), 1.78 – 1.55 (m, 1H), 1.39 (s, 9H)

Step 9. tert-Butyl ((3R,5R)-5-fluoro-1-methylpiperidin-3-yl)carbamate

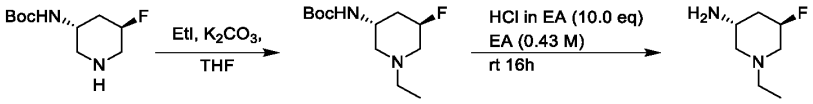
To a solution of tert-butyl N-[(3R,5R)-5-fluoro-3-piperidyl]carbamate (1.60 g, 7.30

mmol) in DCE (20 mL) was added formic acid (1.20 g, 26.0 mmol,) and (HCHO)n (0.75 g, 25 mmol) and stirred for 1 h at rt. To the mixture was added $NaBH(OAc)_3$ (5.4 g, 25.0 mmol) and stirred for 16 h at rt. The reaction mixture was quenched with water, basified with aqueous K_2CO_3 solution and extracted with DCM. The organic phase was combined and washed with brine. The organic phase was dried over Na_2SO_4 and concentrated in vacuum. The residue was purified by silica gel chromatography (PE/EA = 3/1) to afford tert-butyl N-[(3R,5R)-5-fluoro-1-methyl-3-piperidyl]carbamate (1.00 g, 59.0% yield) as a white solid. MS *m/z* 233.1 $[M+H]^+$,

Step 10. (3R,5R)-5-Fluoro-1-methylpiperidin-3-amine hydrogen chloride

To a solution of tert-butyl N-[(3R,5R)-5-fluoro-1-methyl-3-piperidyl]carbamate (1.00 g, 4.30 mmol) in EA (10 mL) was added HCl in 1,4-dioxane (14 mL, 56 mmol, 4 mol/L). The resulting mixture was stirred at room temperature for 2 h, then filtered and the solid was wash with EA (2 mL) and dried under vacuum to give (3R,5R)-5-fluoro-1-methyl-piperidin-3-amine hydrogen chloride (750 mg, 75% yield) as a white solid. MS *m/z* 133.1 $[M+H]^+$, ^1H NMR (400 MHz, DMSO-d_6) δ 11.18 (d, J = 3.6 Hz, 1H), 8.94 (s, 3H), 5.25 (d, J = 44.4 Hz, 1H), 3.72 – 3.66 (m, 2H), 3.56 – 3.50 (m, 1H), 3.41 – 3.27 (m, 1H), 3.13 (t, J = 11.2 Hz, 1H), 2.85 (s, 3H), 2.47 – 2.41 (m, 1H), 2.01 – 1.83 (m, 1H).

Intermediate 3g: (3R,5R)-5-Fluoro-1-ethylpiperidin-3-amine hydrochloride



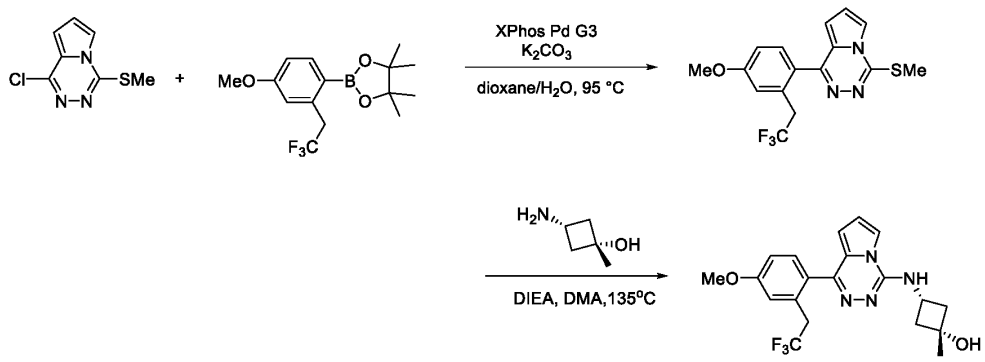
The starting material, tert-butyl ((3R,5R)-5-fluoropiperidin-3-yl) carbamate, was prepared as the procedure of Intermediate 3f step 1 to 8.

The title compound was prepared in analogous manner according to the procedure of Intermediate 3b, using tert-butyl ((3R,5R)-5-fluoropiperidin-3-yl)carbamate in place of tert-butyl (R)-piperidin-3-ylcarbamate in step 1. MS *m/z* 147.2 $[M+H]^+$; ^1H NMR (400 MHz, DMSO-d_6) δ 11.02 (s, 1H), 8.94 (s, 3H), 5.27 (d, J = 44.8 Hz, 1H), 3.74 - 3.62 (m, 3H), 3.32 - 3.22 (m, 3H), 3.09 - 3.05 (m, 1H), 2.48-2.43 (m, 1H), 2.06-1.89 (m, 1H), 1.28 – 1.25 (t, J = 14.0 Hz, 3H).

Example 1

Preparation of Compound 1

(1s,3s)-3-((1-(4-Methoxy-2-(2,2,2-trifluoroethyl)phenyl)pyrrolo[1,2-d][1,2,4]triazin-4-yl)amino)-1-methylcyclobutan-1-ol



Step 1: 1-[4-Methoxy-2-(2,2,2-trifluoroethyl)phenyl]-4-methylsulfanyl-pyrrolo[1,2-d][1,2,4]triazine

1-Chloro-4-methylsulfanyl-pyrrolo[1,2-d][1,2,4]triazine (Intermediate 1c, 0.380 g, 1.90 mmol), 2-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxa-borolane (Intermediate 2a, 0.842 g, 2.66 mmol) and XPhos Pd G3 (0.164 g, 0.190 mmol) were added to a vial and evacuated and refilled with Ar, to which was added dioxane (9.5 mL) and K_2CO_3 (2 M, 2.9 mL, 5.71 mmol). The mixture was sparged with Ar for 5 min, then heated to 95 °C for 3 h. After cooled to rt, the mixture was diluted with EtOAc and filtered through Celite. The filtrate was washed with brine, dried ($MgSO_4$), filtered, and concentrated. Purification by chromatography on SiO_2 (EtOAc:hexanes, 0 to 30%) gave a pink solid (0.329 g, 49%). MS *m/z* 354.4 $[M+H]^+$.

Step 2: (1s,3s)-3-((1-(4-Methoxy-2-(2,2,2-trifluoroethyl)phenyl)pyrrolo[1,2-d][1,2,4]triazin-4-yl)amino)-1-methylcyclobutan-1-ol

1-[4-Methoxy-2-(2,2,2-trifluoroethyl)phenyl]-4-methylsulfanyl-pyrrolo[1,2-d][1,2,4]triazine (0.070 g, 0.18 mmol) and 3-amino-1-methyl-cyclobutanol hydrochloride (0.030 g, 0.22 mmol) in DMA (0.10 mL) and *i*Pr_2NEt (0.10 mL, 0.57 mmol) was heated to 135 °C for 4 h. The reaction was cooled to rt and diluted with DCM/iPrOH (9:1). The solution was washed with brine, dried (Na_2SO_4), filtered, and concentrated. Purification by chromatography on SiO_2 (MeOH:DCM, 0 to 10%) followed by reverse phase chromatography (0.1% formic acid in

MeCN:0.1% formic acid in H_2O, 5 to 100%) gave a white solid (0.010 g, 28%). MS *m/z* 407.3 [M+H]+; 1H NMR (500 MHz, Methanol-d_4) δ 7.83 (d, *J* = 1.8 Hz, 1H), 7.47 (d, *J* = 8.5 Hz, 1H), 7.10 (s, 1H), 7.09 – 7.04 (m, 1H), 6.96 (t, *J* = 3.4 Hz, 1H), 6.53 (d, *J* = 3.8 Hz, 1H), 4.31 – 4.21 (m, 1H), 3.89 (s, 3H), 3.69 (q, *J* = 11.14 Hz, 2H), 2.69 – 2.62 (m, 2H), 2.31 – 2.22 (m, 2H), 1.44 (s, 3H). 2H not observed (NH and OH).

The compounds below were prepared according to the procedure of Example 1 by substituting the appropriate starting materials, reagents and reaction conditions.

Compound#	Spectral Data
5	MS *m/z* 492.3 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.81 – 7.74 (m, 1H), 7.73 – 7.66 (m, 2H), 7.62 – 7.54 (m, 1H), 7.15 – 6.73 (m, 2H), 5.14 – 4.96 (m, 1H), 4.84 – 4.71 (m, 1H), 3.51 – 3.39 (m, 1H), 3.26 – 3.17 (m, 1H), 2.78 – 2.65 (m, 2H), 2.64 – 2.27 (m, 3H), 2.06 – 1.83 (m, 1H), 1.25 – 1.10 (m, 3H). 1H not observed (NH).
6	MS *m/z* 514.3 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 8.29 - 8.09 (m, 2H), 7.99 - 7.77 (m, 2H), 7.02 (s, 1H), 6.49 (s, 1H), 4.73 - 4.52 (m, 1H), 4.19 - 4.00 (m, 2H), 3.97 - 3.81 (m, 1H), 3.60 - 3.38 (m, 4H), 3.14 - 2.91 (m, 2H), 2.43 - 1.67 (m, 8H). 1H not observed (NH).
7	MS *m/z* 458.9 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 8.30 - 8.05 (m, 2H), 7.96 - 7.71 (m, 2H), 7.10 (s, 1H), 6.62 (s, 1H), 4.32 - 4.16 (m, 1H), 3.97 - 3.84 (m, 1H), 3.81-3.68 (m, 1H), 3.54 - 3.39 (m, 1H), 3.27 - 3.11 (m, 1H), 2.98 (s, 6H), 2.46 - 2.26 (m, 1H), 2.17 - 1.82 (m, 3H). NH not observed.
8	MS *m/z* 422.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.83 (dd, J = 3.0, 1.2 Hz, 1H), 7.55 (d, J = 8.6 Hz, 1H), 7.09 (dd, J = 8.6, 2.5 Hz, 1H), 7.01 (dq, J = 2.8, 1.4 Hz, 1H), 6.95 (dd, J = 4.0, 2.9 Hz, 1H), 6.54 (dd, J = 3.9, 1.2 Hz, 1H), 4.48 (tt, J = 8.9, 4.0 Hz, 1H), 3.90 (s, 3H), 3.27 – 3.13 (m, 1H), 2.87 – 2.68 (m, 1H), 2.50 – 2.27 (m, 5H), 2.10 (d, J = 9.8 Hz, 1H), 1.90 (dp, J = 13.2, 4.8 Hz, 1H), 1.78 (dtt, J = 13.7, 6.3, 3.2 Hz, 1H), 1.68 (dd, J = 24.3, 13.5 Hz, 1H). NH not observed.
9	MS *m/z* 409.3 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.80 (dd, J = 2.9, 1.2 Hz, 1H), 7.55 (d, J = 8.6 Hz, 1H), 7.09 (dd, J = 8.6, 2.5 Hz, 1H), 7.01 (dq, J = 2.9, 1.5 Hz, 1H), 6.94 (dd, J = 3.9, 2.9 Hz, 1H), 6.53 (dd, J = 4.0, 1.2 Hz, 1H), 4.35 – 4.18 (m, 1H), 3.90 (s, 3H), 2.65 – 2.58 (m, 2H), 2.34 – 2.18 (m, 2H), 1.44 (s, 3H). NH and OH not observed.
10	MS *m/z* 484.4 [M-H]-; 1H NMR (400 MHz, Methanol-d_4) δ = 8.14 (s, 1H), 8.08 - 8.06 (m, 1H), 7.84 (s, 1H), 7.79 (d, J = 8.0 Hz, 1H), 6.98 - 6.92 (m, 1H), 6.45 - 6.39 (m, 1H), 4.64 - 4.53 (m, 1H), 3.79 (d, J = 10.0 Hz, 1H), 3.42 (d, J = 10.9 Hz, 1H), 3.04 - 2.87 (m, 4H), 2.28 - 2.05 (m, 3H), 2.04 - 1.77 (m, 2H), 1.03-0.98 (m, 6H); NH not observed.
11	MS *m/z* 406.3, 408.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.82 (s, 1H), 7.72 – 7.58 (m, 3H), 6.93 (m, 1H), 6.44 (s, 1H), 4.47 (m, 1H), 3.47 (m, 1H), 3.06 (m, 1H), 2.75 – 2.56 (m, 5H), 2.33 (s, 3H), 2.16 (m, 1H), 2.03 (m, 1H), 1.83 (m, 1H), 1.71 (m, 1H).

12	MS *m/z* 418.3 [M+H]+;1H NMR (400 MHz, DMSO-d_6)δ 8.20 (s, 1H, formate CH), 7.78 – 7.69 (m, 1H), 7.45 (d, J = 8.5 Hz, 1H), 7.20 (s, 1H), 7.03 – 7.00 (m, 1H), 6.96 (m, 1H), 6.91 – 6.84 (m, 1H), 6.23 (s, 1H), 4.36 – 4.20 (m, 1H), 3.85 (s, 3H), 3.05 (m, 1H), 2.71 (m, 1H), 2.23 (m, 6H), 2.05 – 1.86 (m, 3H), 1.75 (m, 1H), 1.70 – 1.51 (m, 1H), 1.51 – 1.23 (m, 1H).
13	MS *m/z* 422.3, 424.3 [M+H]+; 1H NMR (400 MHz, DMSO-d_6) δ 8.17 (s, 1H, formate CH), 7.80 – 7.72 (m, 1H), 7.62 – 7.54 (m, 1H), 7.51 – 7.44 (m, 2H), 7.16 – 7.07 (m, 1H), 6.27 (s, 1H), 4.27 (br, s, 1H), 3.45 (br, 1H), 3.07 (d, J = 10.0 Hz, 1H), 2.72 (d, J = 10.8 Hz, 1H), 2.24 (m, 6H), 2.04 – 1.89 (m, 3H), 1.84 – 1.71 (m, 1H), 1.59 (m, 1H), 1.51 – 1.36 (m, 1H).
14	MS *m/z* 412.4 [M+H]+; 1H NMR (400 MHz, DMSO-d_6) δ 8.14 (s, 1H, formate CH), 7.83 – 7.74 (m, 1H), 7.61 – 7.49 (m, 2H), 7.33 (d, J = 8.3 Hz, 1H), 7.16 – 7.05 (m, 2H), 6.35 (s, 1H), 4.30 – 4.28 (m, 1H), 3.10 – 3.08 (m, 1H), 2.77 – 2.74 (m, 1H), 2.26 (s, 6H), 2.11 (m, 1H), 1.99 (m, 3H), 1.79 – 1.76 (m, 1H), 1.62 (m, 1H), 1.51 – 1.44 (m, 1H), 1.07 – 1.04 (m, 2H), 0.79 (m, 2H).
15	MS m/z 490.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.80 – 7.74 (m, 2H), 7.73 – 7.68 (m, 1H), 7.61 – 7.57 (m, 1H), 7.13 – 6.72 (m, 2H), 4.54 – 4.40 (m, 1H), 3.81 – 3.65 (m, 2H), 3.22 – 3.09 (m, 1H), 2.81 – 2.70 (m, 1H), 2.69 – 2.55 (m, 2H), 2.51 – 2.35 (m, 2H), 2.10 – 1.97 (m, 1H), 1.93 – 1.82 (m, 1H), 1.81 – 1.62 (m, 2H). 2H not observed (NH and OH).
16	MS *m/z* 421.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.80 – 7.74 (m, 1H), 7.74 – 7.69 (m, 1H), 7.69 – 7.65 (m, 1H), 7.60 – 7.57 (m, 1H), 7.13 – 6.72 (m, 2H), 4.25 – 4.13 (m, 1H), 3.72 (dd, 1H), 3.53 (dd, 1H), 1.27 (d, 3H). 2H not observed (NH and OH).
17	MS *m/z* 438.3 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.68 (t, J = 3.6 Hz, 1H), 7.46 (d, J = 8.5 Hz, 1H), 7.34 (d, J = 2.5 Hz, 1H), 7.28 (dd, J = 8.4, 2.5 Hz, 1H), 6.75 (d, J = 3.1 Hz, 1H), 4.54 – 4.37 (m, 1H), 3.93 (s, 3H), 3.31 – 3.18 (m, 1H), 2.96 – 2.80 (m, 1H), 2.71 – 2.54 (m, 2H), 2.44 – 2.27 (m, 2H), 2.21 – 2.05 (m, 1H), 2.00 – 1.84 (m, 1H), 1.83 – 1.71 (m, 1H), 1.70 – 1.55 (m, 1H), 1.18 (t, J = 7.2 Hz, 3H). 1H not observed (NH).
18	MS *m/z* 454.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.70 (t, J = 3.7 Hz, 1H), 7.46 (d, J = 8.5 Hz, 1H), 7.35 (d, J = 2.5 Hz, 1H), 7.29 (dd, J = 8.5, 2.6 Hz, 1H), 6.76 (d, J = 3.3 Hz, 1H), 4.58 – 4.41 (m, 1H), 3.93 (s, 3H), 3.84 – 3.74 (m, 2H), 3.54 – 3.39 (m, 1H), 3.16 – 3.00 (m, 1H), 2.97 – 2.82 (m, 2H), 2.78 – 2.58 (m, 2H), 2.19 – 2.06 (m, 1H), 2.04 – 1.92 (m, 1H), 1.92 – 1.66 (m, 2H). 2H not observed (NH and OH).
19	MS *m/z* [M+H]+ 394.1; 1H NMR (400 MHz, Methanol-d_4) δ 8.52 (br s, 1H, formic acid), 7.89 – 7.81 (m, 2H), 7.72 – 7.763 (m, 2H), 7.03 – 6.99 (m, 1H), 6.68 (s, 1H), 4.58 – 4.45 (m, 1H), 3.43 – 3.33 (m, 1H), 2.99 – 2.85 (m, 1H), 2.59 – 2.42 (m, 5H), 2.21 – 2.06 (m, 1H), 2.06 – 1.90 (m, 1H), 1.90 – 1.75 (m, 1H), 1.75 – 1.64 (m, 1H). 1H not observed (NH).
20	MS *m/z* [M+H]+ 408.3; 1H NMR (400 MHz, Methanol-d_4) δ 7.89 – 7.83 (m, 2H), 7.72 – 7.66 (m, 2H), 7.02 (t, J = 3.3 Hz, 1H), 6.69 (s, 1H), 4.58 – 4.58 (m, 1H), 3.66 – 3.53 (m, 1H), 3.25 – 3.13 (m, 1H), 2.96 – 2.86 (m, 2H), 2.77 – 2.57 (m, 2H), 2.26 – 2.14 (m, 1H), 2.11 – 1.99 (m, 1H), 1.95 – 1.71

	(m, 2H), 1.28 (t, J = 7.3 Hz, 3H). 1H not observed (NH).
21	MS *m/z* [M+H]+ 424.2; 1H NMR (400 MHz, Methanol-d_4) δ 7.90 – 7.83 (m, 2H), 7.73 – 7.66 (m, 2H), 7.03 (t, J = 3.4 Hz, 1H), 6.70 (s, 1H), 4.63 – 4.54 (m, 1H), 3.84 (t, J = 5.4 Hz, 2H), 3.75 – 3.63 (m, 1H), 3.28 – 3.23 (m, 1H), 3.05 (q, J = 5.1 Hz, 2H), 2.91 – 2.76 (m, 2H), 2.23 – 2.14 (m, 1H), 2.13 – 2.01 (m, 1H), 2.00 – 1.75 (m, 2H). 2H not observed (NH and OH).
22	MS *m/z* 486.3 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.84 - 7.93 (m, 1 H) 7.73 - 7.84 (m, 2 H) 7.69 (s, 1 H) 6.72 - 7.15 (m, 2 H) 6.62 (d, J=3.63 Hz, 1 H) 4.53 - 4.75 (m, 1 H) 3.67 - 4.00 (m, 3 H) 3.43 - 3.58 (m, 2 H) 2.99 - 3.26 (m, 2 H) 2.11 - 2.36 (m, 2 H) 1.76 - 2.10 (m, 2 H) 1.37 (dd, J=6.44, 3.69 Hz, 3 H); 2H not observed (NH and OH).
23	MS *m/z* 386.4 [M+H]+;1H NMR(400 MHz, Methanol-d_4) δ 8.67 – 8.44 (s, formate CH), 7.63 (d, J = 9.6 Hz, 2H), 7.48 (m, 2H), 7.06 – 6.62 (m, 1H), 6.38 (s, 1H), 4.56 – 4.37 (m, 1H), 3.00 – 2.83 (m, 1H), 2.60 – 2.43 (m, 8H), 2.32 (s, 4H), 2.21 – 2.06 (m, 1H), 2.04 – 1.89 (m, 1H), 1.87 – 1.77 (m, 1H), 1.69 (m, 1H). NH peak was not observed.
24	MS *m/z* 428.5 [M+H]+;1H NMR (400 MHz, Methanol-d_4) δ 8.63 – 8.39 (s, 1H, formate CH), 7.57 (s, 1H), 7.40 (d, J = 7.9 Hz, 1H), 7.09 (d, J = 7.9 Hz, 1H), 7.04 (s, 1H), 6.94 – 6.53 (m, 1H), 6.36 (s, 1H), 4.55 – 4.38 (m, 1H), 3.39 (m, 1H), 3.06 – 2.90 (m, 1H), 2.57 (br, s, 5H), 2.32 (s, 3H), 2.20 – 2.07 (m, 1H), 2.07 – 1.92 (m, 2H), 1.89 – 1.76 (m, 1H), 1.74 – 1.63 (m, 1H), 1.14 – 1.01 (m, 2H), 0.85 – 0.72 (m, 2H). NH peak not observed.
25	MS *m/z* 402.4 [M+H]+;1H NMR (400 MHz, Methanol-d_4) δ 8.53 (s, 1H, formate CH), 7.67 – 7.53 (m, 1H), 7.45 – 7.36 (m, 1H), 7.27 – 7.10 (m, 2H), 6.73 (m, 1H), 6.36 (s, 1H), 4.54 – 4.40 (m, 1H), 3.51 – 3.38 (m, 1H), 3.09 – 2.93 (m, 1H), 2.66 – 2.54 (m, 5H), 2.46 (s, 3H), 2.32 (s, 3H), 2.13 (m, 1H), 2.05 – 1.94 (m, 1H), 1.85 (m, 1H), 1.72 (m, 1H). NH peak was not observed.
26	MS *m/z* 352.5 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.85 (s, 1H), 7.29 (d, J = 8.4 Hz, 1H), 6.96 (t, J = 3.2 Hz, 1H), 6.93 (d, J = 7.2 Hz, 1H), 6.88 (dd, J= 2.4 Hz, 8.4 Hz, 1H), 6.49 (d, J = 3.2 Hz, 1H), 4.54 (s, 1H), 3.85(s, 3H), 3.66 (s, 1H), 3.30– 3.29 (m, 1H), 2.92 (s, 1H), 2.79 (s, 3H), 2.21 (s, 3H), 2.13 (s, 1H), 2.10 – 2.11 (m, 2H), 1.84–1.93 (m, 2H). NH peak not observed.
27	MS *m/z* 378.3 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.84 (d, J = 1.6 Hz, 1H), 7.26 (d, J = 8.8 Hz, 1H), 6.95 (t, J = 4.0 Hz, 1H), 6.86 (dd, J = 2.4 Hz, 8.4 Hz, 1H), 6.57 (d, J = 2.8 Hz, 1H), 6.53 (d, J = 4.0 Hz, 1H), 4.54 (s, 1H), 3.82 (s, 3H), 3.57 (s, 1H), 3.12 – 3.16 (m, 1H), 2.79 – 2.85 (m, 2H), 2.73 (s, 3H), 2.18 (dd, J = 3.2 Hz, 9.2 Hz, 1H), 2.07 (dd, J = 4.4 Hz, 9.6 Hz, 1H), 1.82– 1.93 (m, 1H), 1.74– 1.81 (m, 2H), 0.70– 0.76 (m, 2H), 0.62– 0.68 (m, 2H). NH not observed
28	MS *m/z* 462.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 8.15 (s, 1H), 8.10 (d, J = 8.0 Hz, 1H), 7.81 (d, J = 7.9 Hz, 1H), 7.74 (t, J = 3.7 Hz, 1H), 6.80 (d, J = 3.0 Hz, 1H), 4.55 – 4.37 (m, 1H), 3.22 – 3.07 (m, 1H), 2.82 – 2.66 (m, 1H), 2.45 – 2.19 (m, 5H), 2.15 – 2.00 (m, 1H), 1.97 – 1.82 (m, 1H), 1.82 – 1.69 (m, 1H), 1.68 – 1.52 (m, 1H). 1H not observed (NH).

29	MS *m/z* 476.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 8.15 (s, 1H), 8.10 (d, J = 8.0 Hz, 1H), 7.81 (d, J = 8.0 Hz, 1H), 7.74 (t, J = 3.7 Hz, 1H), 6.80 (d, J = 3.2 Hz, 1H), 4.55 – 4.39 (m, 1H), 3.28 – 3.13 (m, 1H), 2.93 – 2.73 (m, 1H), 2.68 – 2.47 (m, 2H), 2.42 – 2.22 (m, 2H), 2.18 – 2.04 (m, 1H), 1.97 – 1.84 (m, 1H), 1.82 – 1.70 (m, 1H), 1.69 – 1.53 (m, 1H), 1.16 (t, J = 7.2 Hz, 3H). 1H not observed (NH).
30	MS m/z 492.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 8.16 (s, 1H), 8.11 (d, J = 8.3 Hz, 1H), 7.82 (d, J = 8.0 Hz, 1H), 7.77 (t, J = 3.7 Hz, 1H), 6.81 (d, J = 3.3 Hz, 1H), 4.60 – 4.43 (m, 1H), 3.90 – 3.72 (m, 2H), 3.58 – 3.41 (m, 1H), 3.18 – 3.03 (m, 1H), 3.00 – 2.82 (m, 2H), 2.80 – 2.55 (m, 2H), 2.22 – 2.07 (m, 1H), 2.06 – 1.94 (m, 1H), 1.92 – 1.69 (m, 2H). 2H not observed (NH and OH).
31	MS *m/z* 480.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 8.15 (s, 1H), 8.10 (d, J = 7.9 Hz, 1H), 7.81 (d, J = 7.9 Hz, 1H), 7.71 (t, J = 3.6 Hz, 1H), 6.80 (d, J = 3.1 Hz, 1H), 5.10 – 4.91 (m, 1H), 4.83 – 4.69 (m, 1H), 3.29 – 3.23 (m, 1H), 3.11 – 2.97 (m, 1H), 2.53 – 2.33 (m, 5H), 2.31 – 2.22 (m, 1H), 2.00 – 1.78 (m, 1H). NH not observed.
32	MS *m/z* 494.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 8.15 (s, 1H), 8.10 (d, J = 8.3 Hz, 1H), 7.82 (d, J = 7.9 Hz, 1H), 7.71 (t, J = 3.6 Hz, 1H), 6.80 (d, J = 3.1 Hz, 1H), 5.10 – 4.92 (m, 1H), 4.82 – 4.71 (m, 1H), 3.40 – 3.32 (m, 1H), 3.19 – 3.05 (m, 1H), 2.69 – 2.57 (m, 2H), 2.53 – 2.37 (m, 2H), 2.35 – 2.23 (m, 1H), 2.03 – 1.81 (m, 1H), 1.16 (t, J = 7.2 Hz, 3H). NH not observed.
33	MS *m/z* 388.3 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.85 (s, 1H), 7.45 (d, J = 5.9 Hz, 1H), 7.33 - 6.73 (m, 4H), 6.58 (s, 1H), 4.52 (s, 1H), 3.90 - 3.66 (m, 1H), 3.47 - 3.35 (m, 1H), 3.18 - 2.97 (m, 2H), 2.88 (s, 3H), 2.48 (s, 3H), 2.33 - 2.09 (m, 2H), 2.05 - 1.76 (m, 2H); NH not observed.
34	MS *m/z* 402.3 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 8.49 (br, 1H), 7.85 (s, 1H), 7.45 (d, J = 7.8 Hz, 1H), 7.31 - 6.75 (m, 4H), 6.58 (d, J = 4.1 Hz, 1H), 4.69 - 4.52 (m, 1H), 3.99 - 3.79 (m, 1H), 3.56 - 3.41 (m, 1H), 3.29 - 3.17 (m, 2H), 3.17 - 2.91 (m, 2H), 2.48 (s, 3H), 2.37 - 2.11 (m, 2H), 2.06 - 1.85 (m, 2H), 1.38 (t, J = 7.2 Hz, 3H). NH not observed.
35	MS *m/z* 428.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 8.60 (d, J = 1.2 Hz, 1H), 7.90 (dd, J = 55.6, 7.6 Hz, 2H), 7.83 (s, 1H), 7.41 - 7.38 (m, 2H), 7.10 (t, J = 72.4 Hz, 1H), 4.64 – 4.57 (m, 1H), 3.77 – 3.73 (m, 1H), 3.46 – 3.84 (m, 1H), 3.28 – 3.22 (m, 1H), 3.17 – 3.11 (m, 1H). 2.33 – 2.30 (m, 1H), 2.21 – 2.16 (m, 1H), 2.08 – 1.94 (m, 1H). NH not observed
36	MS *m/z* 406.3 [M+H]+; ^{1}HNMR (400 MHz, Methanol-d_4) δ 7.82 (d,J = 2.1 Hz, 1H), 7.50 (d, J = 7.8 Hz, 1H), 7.35 –7.29 (m, 2H), 6.97 – 6.92 (m, 1H), 6.51 (d, J = 3.8 Hz, 1H), 4.47 (s, 1H), 3.18 – 3.07 (m,1H), 2.74 – 2.65 (m, 1H), 2.48 (s, 3H), 2.34 (s, 3H), 2.32 – 2.19 (m, 2H), 2.12 – 2.04 (m,1H), 1.90 – 1.83 (m, 1H), 1.79 – 1.71 (m, 1H), 1.61 (dt, J = 11.2, 6.7 Hz, 1H). NH not observed.
37	MS *m/z* 432.2 [M+H]+; ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.53 (s, 1H), 7.82 (s, 1H), 7.49 (d, J = 7.9 Hz, 1H), 7.25 –7.16 (m, 2H), 6.99 – 6.91 (m, 1H), 6.55 (d, J = 3.5 Hz, 1H), 4.56 – 4.45 (m, 1H), 3.51 – 3.39(m, 1H), 3.07

	– 2.95 (m, 1H), 2.72 – 2.60 (m, 2H), 2.58 (s, 3H), 2.23 – 2.12 (m, 1H), 2.09 –1.96 (m, 2H), 1.88 – 1.69 (m, 2H), 1.14 – 1.07 (m, 2H), 0.84 – 0.76 (m, 2H). NH not observed.
38	MS *m/z* 449.2 [M+H]+; ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.15 (s, 1H), 8.10 (d, J = 8.0 Hz, 1H), 7.81 (d, J = 8.0 Hz, 1H), 7.73 (t, J = 3.7 Hz, 1H), 6.79 (d, J = 3.4 Hz, 1H), 4.29 – 4.19 (m, 1H), 2.70 – 2.61 (m, 2H), 2.30 – 2.21 (m, 2H), 1.43 (s, 3H). 2H not observed (NH and OH)
39	MS *m/z* 440.3 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.72 (t, J = 3.7 Hz, 1H), 7.53 (d, J = 8.6 Hz, 1H), 7.10 (dd, J = 8.6, 2.4 Hz, 1H), 7.03 – 6.96 (m, 1H), 6.82 (d, J = 3.3 Hz, 1H), 4.58 – 4.43 (m, 1H), 3.93 (s, 3H), 3.71 – 3.53 (m, 1H), 3.26 – 3.16 (m, 1H), 2.95 – 2.78 (m, 2H), 2.76 (s, 3H), 2.25 – 2.04 (m, 2H), 1.97 – 1.70 (m, 2H). NH not observed.
40	MS *m/z* 458.3 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.94 – 7.87 (m, 2H), 7.84 (d, J = 8.25 Hz, 1H), 7.76 (d, 9.26 Hz, 1H), 7.01 (dd, J = 3.8, 3.0 Hz, 1H), 6.57 (dd, J = 3.9, 0.9 Hz, 1H), 4.58 – 4.49 (m, 1H), 3.83 (q, J = 10.9 Hz, 2H), 3.62 – 3.52 (m, 1H), 3.21 – 3.11 (m, 1H), 2.87 – 2.73 (m, 2H), 2.70 (s, 3H), 2.26 – 2.14 (m, 1H), 2.12 – 2.01 (m, 1H), 1.97 – 1.68 (m, 2H). 1H not observed (NH).
41	MS m/z 445.2 [M+H]+;1H NMR (400 MHz, Methanol-d_4) δ 7.92 – 7.86 (m, 2H), 7.83 (d, J = 7.88 Hz, 1H), 7.77 (d, J = 8.13 Hz, 1H), 6.99 (t, J = 3.4 Hz, 1H), 6.55 (d, J = 3.9 Hz, 1H), 4.33 – 4.23 (m, 1H), 3.85 (q, J = 11.0 Hz, 2H), 2.71 – 2.62 (m, 2H), 2.34 – 2.23 (m, 2H), 1.45 (s, 3H). 2H not observed (NH and OH)
42	MS *m/z* 420.2 [M+H]+; 1HNMR(400 MHz, Methanol-d_4) δ 8.50 – 8.44 (m, 1H), 7.84 (d, J = 1.8 Hz, 1H), 7.54 (d, J = 7.8 Hz, 1H), 7.39 (d, J = 7.8 Hz, 1H), 7.34 (s, 1H), 7.01 – 6.95 (m, 1H), 6.57 (d, J = 3.7 Hz, 1H), 4.57 – 4.49 (m, 1H), 3.67 (tdd, J = 10.2, 6.6, 3.1 Hz, 1H), 3.29 – 3.24 (m, 1H), 3.00 – 2.85 (m, 2H), 2.82 (d, J = 7.6 Hz, 1H), 2.78 (d, J = 4.8 Hz, 4H), 2.21 (dt, J = 18.3, 6.6 Hz, 1H), 2.14 – 2.07 (m, 1H), 1.95 – 1.79 (m, 2H), 1.32 (t, J = 7.6 Hz, 3H). NH not observed.
43	MS *m/z* 436.3 [M+H]+; 1H NMR (500 MHz, Methanol-d_4) δ 7.84 (d, J = 2.8 Hz, 1H), 7.55 (d, J = 8.5 Hz, 1H), 7.10 (dd, J = 8.6, 2.4 Hz, 1H), 7.00 (dd, J = 7.4, 3.7 Hz, 2H), 6.60 (d, J = 3.9 Hz, 1H), 4.56 (tt, J = 9.7, 4.1 Hz, 1H), 4.16 (q, J = 7.0 Hz, 2H), 3.80 (s, 1H), 3.48 – 3.36 (m, 1H), 3.05 (d, J = 12.7 Hz, 2H), 2.90 (s, 3H), 2.28 – 2.12 (m, 2H), 2.03 – 1.84 (m, 2H), 1.46 (t, J = 6.9 Hz, 3H). NH not observed.
44	MS *m/z* 458.3 [M+H]+; 1H NMR (500 MHz, Methanol-d_4) δ 7.87 (d, J = 2.9 Hz, 1H), 7.69 (d, J = 8.5 Hz, 1H), 7.36 (dd, J = 8.4, 2.4 Hz, 1H), 7.32 (t, J = 1.9 Hz, 1H), 7.04 (t, J = 75 Hz, 1H), 7.02 – 6.98 (m, 1H), 6.61 (dd, J = 4.0, 1.1 Hz, 1H), 4.57 (tt, J = 9.2, 3.7 Hz, 1H), 3.86 – 3.73 (m, 1H), 3.50 – 3.36 (m, 1H), 3.18 – 2.99 (m, 2H), 2.91 (s, 3H), 2.30 – 2.12 (m, 2H), 2.01 – 1.81 (m, 2H).NH not observed.
45	MS *m/z* 418.3 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.80 - 7.95 (m, 1 H) 7.38 - 7.53 (m, 1 H) 7.13 - 7.30 (m, 2 H) 6.46 - 7.03 (m, 3 H) 4.39 - 4.57 (m, 1 H) 3.74 (d, J=5.75 Hz, 2 H) 3.08 - 3.26 (m, 1 H) 2.70 - 2.81 (m, 1 H) 2.54 - 2.70 (m, 2 H) 2.52-2.33 (m, 5 H) 1.97 - 2.14 (m, 1 H) 1.61 - 1.95

	(m, 3 H); 2H not observed (NH and OH).
46	MS *m/z* 472.3 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.97 (s, 1H), 7.86 - 7.74 (m, 2H), 7.73 - 7.67 (m, 1H), 7.20 - 6.76 (m, 2H), 6.76 - 6.66 (m, 1H), 4.65 - 4.39 (m, 1H), 4.26 - 3.91 (m, 2H), 3.81 - 3.57 (m, 1H), 3.32 - 3.24 (m, 2H), 3.23 - 2.96 (m, 1H), 2.52 - 2.29 (m, 1H), 2.13 - 1.84 (m, 1H), 1.50 - 1.30 (m, 3H); 2H not observed (NH and OH). CH obscured by the signal of Methanol-d_4.
47	MS *m/z* 416.2, 418.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 8.38 (s, 1H), 7.62 (d, J = 8.8 Hz, 1H), 7.48 (d, J = 2.4 Hz, 1H), 7.37 (s, 1H), 7.29 (d, J = 4.4 Hz, 1H), 7.22 (dd, J = 2.0 Hz, J = 8.4 Hz, 1H), 4.67 – 4.54 (m, 1H), 4.00 – 3.94 (m, 1H), 3.94 (s, 3H), 3.60 – 3.58 (m, 1H), 3.06 – 2.92 (m, 2H), 2.97 (s, 3H), 2.35 – 2.33 (m, 1H), 2.19 – 2.16 (m, 1H), 2.03 – 1.84 (m, 2H). NH not observed.
48	MS *m/z* 472.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.99 - 7.87 (m, 1H), 7.80 (d, J = 8.0 Hz, 1H), 7.77 - 7.71 (m, 1H), 7.67 (s, 1H), 7.13 - 6.69 (m, 2H), 6.58 (d, J = 3.8 Hz, 1H), 4.71 - 4.58 (m, 1H), 4.34 - 4.20 (m, 1H), 3.04 - 2.47 (m, 6H), 2.06 - 1.85 (m, 2H), 1.18 (t, J = 7.2 Hz, 3H); 2H not observed (NH and OH).
49	MS *m/z* 456.1 [M+H]+; 1HNMR (400 MHz, Methanol-d_4) δ 7.85 (d ,J = 2.0 Hz, 1H), 7.59 (s, 1H), 7.45 (s, 1H), 6.97 – 6.94 (m, 1H), 6.98 – 6.60 (m, 1H), 6.39 (d, J = 3.6 Hz, 1H), 4.54 –4.42 (m, 1H), 3.27 – 3.20 (m, 1H), 2.86 – 2.75 (m, 1H), 2.42 (s, 3H), 2.41 – 2.30 (m, 2H), 2.20 (s, 3H), 2.16 – 2.06 (m, 1H), 1.96 – 1.86 (m, 1H), 1.85 – 1.72 (m, 1H), 1.72 – 1.58 (m, 1H). NH not observed.
50	MS *m/z* 454.3 [M+H]+; 1H NMR (400 MHz, DMSO-d_6) δ 7.89 – 7.79 (m, 1H), 7.54 (d, J = 8.6 Hz, 1H), 7.31 (s, 1H), 7.11 (dd, J = 8.6, 2.4 Hz, 1H), 7.05 – 6.99 (m, 1H), 6.91 (d, J = 3.3 Hz, 1H), 4.39 – 4.16 (m, 1H), 3.87 (s, 3H), 3.26 – 3.06 (m, 1H), 2.94 – 2.73 (m, 1H), 2.46 – 2.29 (m, 2H), 2.11 – 1.70 (m, 4H), 1.67 – 1.36 (m, 2H), 1.12 – 0.92 (m, 3H).
51	MS *m/z* 470.2 [M+H]+; 1H NMR (400 MHz, DMSO-d_6) δ 7.83 (t, J = 3.7 Hz, 1H), 7.54 (d, J = 8.6 Hz, 1H), 7.32 – 7.22 (m, 1H), 7.11 (dd, J = 8.6, 2.4 Hz, 1H), 7.05 – 6.99 (m, 1H), 6.91 (d, J = 3.3 Hz, 1H), 4.55 – 4.34 (m, 1H), 4.33 – 4.19 (m, 1H), 3.87 (s, 3H), 3.58 – 3.45 (m, 2H), 3.25 – 3.07 (m, 1H), 2.94 – 2.72 (m, 1H), 2.48 – 2.37 (m, 2H), 2.15 – 1.92 (m, 3H), 1.81 – 1.68 (m, 1H), 1.66 – 1.50 (m, 1H), 1.44 (t, J = 10.2 Hz, 1H).
52	MS *m/z* 458.2 [M+H]+; 1H NMR (400 MHz, Methanol-d4) δ 7.65 (t, J = 3.7 Hz, 1H), 7.52 (d, J = 8.5 Hz, 1H), 7.08 (dd, J = 8.5, 2.3 Hz, 1H), 7.00 – 6.94 (m, 1H), 6.79 (d, J = 3.3 Hz, 1H), 5.10 – 4.92 (m, 1H), 4.82 – 4.69 (m, 1H), 3.90 (s, 3H), 3.30 – 3.27 (m, 1H), 3.12 – 3.02 (m, 1H), 2.54 – 2.36 (m, 5H), 2.34 – 2.22 (m, 1H), 2.01 – 1.76 (m, 1H). NH not observed.
53	MS m/z 472.2 [M+H]+; 1H NMR (400 MHz, Methanol-d4) δ 7.65 (t, J = 3.6 Hz, 1H), 7.53 (d, J = 7.9 Hz, 1H), 7.12 – 7.05 (m, 1H), 6.99 – 6.94 (m, 1H), 6.79 (d, J = 3.3 Hz, 1H), 5.14 – 4.92 (m, 1H), 4.81 – 4.70 (m, 1H), 3.90 (s, 3H), 3.41 – 3.33 (m, 1H), 3.22 – 3.07 (m, 1H), 2.63 (q, 2H), 2.56 – 2.40 (m, 2H), 2.36 – 2.23 (m, 1H), 2.02 – 1.77 (m, 1H), 1.16 (t, J = 7.2 Hz, 3H). NH not observed.

54	MS *m/z* 427.2 [M+H]+. 1H NMR (400 MHz, Methanol-d4) δ 7.68 (t, J = 3.7 Hz, 1H), 7.52 (d, J = 8.6 Hz, 1H), 7.07 (dd, J = 8.6, 2.4 Hz, 1H), 7.00 – 6.93 (m, 1H), 6.78 (d, J = 3.4 Hz, 1H), 4.23 (quint, J = 8.0 Hz, 1H), 3.90 (s, 3H), 2.69 – 2.59 (m, 2H), 2.30 – 2.19 (m, 2H), 1.43 (s, 3H). 2H not observed (NH and OH).
55	MS *m/z* 422.3 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.67 (t, J = 3.7 Hz, 1H), 7.45 (d, J = 8.5 Hz, 1H), 6.94 (dd, J = 8.5, 2.3 Hz, 1H), 6.83 (d, J = 2.3 Hz, 1H), 6.80 (t, J = 73.7 Hz, 1H) 6.78 (d, J = 3.3 Hz, 1H), 4.56 – 4.39 (m, 1H), 3.89 (s, 3H), 3.70 – 3.52 (m, 1H), 3.25 – 3.14 (m, 1H), 2.98 – 2.68 (m, 5H), 2.28 – 2.02 (m, 2H), 1.97 – 1.66 (m, 2H). NH not observed.
56	MS *m/z* 436.3 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.67 (t, J = 3.7 Hz, 1H), 7.45 (d, J = 8.6 Hz, 1H), 6.94 (dd, J = 8.5, 2.3 Hz, 1H), 6.83 (d, J = 2.1 Hz, 1H), 6.80 (t, J = 74.1 Hz, 1H), 6.78 (d, J = 3.3 Hz, 1H), 4.55 – 4.40 (m, 1H), 3.89 (s, 3H), 3.68 – 3.53 (m, 1H), 3.26 – 3.14 (m, 1H), 3.01 – 2.86 (m, 2H), 2.79 – 2.58 (m, 2H), 2.27 – 2.13 (m, 1H), 2.10 – 1.98 (m, 1H), 1.95 – 1.69 (m, 2H), 1.28 (t, J = 7.3 Hz, 3H). NH not observed.
57	MS *m/z* 452.3 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.67 (t, J = 3.7 Hz, 1H), 7.45 (d, J = 8.5 Hz, 1H), 6.95 (dd, J = 8.5, 2.3 Hz, 1H), 6.83 (d, J = 2.3 Hz, 1H), 6.80 (t, J = 73.7 Hz, 1H), 6.79 (d, J = 3.4 Hz, 1H),4.60 – 4.50 (m, 1H), 3.92 – 3.84 (m, 5H), 3.83 – 3.72 (m, 1H), 3.45 – 3.35 (m, 1H), 3.21 – 3.09 (m, 2H), 3.03 – 2.82 (m, 2H), 2.27 – 2.06 (m, 2H), 2.02 – 1.75 (m, 2H). 2H not observed (NH and OH).
58	MS *m/z* 409.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.67 (t, J = 3.7 Hz, 1H), 7.45 (d, J = 8.5 Hz, 1H), 6.94 (dd, J = 8.6, 2.4 Hz, 1H), 6.82 (d, J = 2.3 Hz, 1H), 6.78 (t, J = 73.7 Hz, 1H), 6.76 (d, J = 3.4 Hz, 1H), 4.22 (quint., J = 8.1 Hz, 1H), 3.89 (s, 3H), 2.72 – 2.57 (m, 2H), 2.24 (t, J = 10.3 Hz, 2H), 1.43 (s, 3H).
59	MS *m/z* 436.3 [M+H]+; 1H NMR (500 MHz, Methanol-d_4) δ 7.21 (dd, J = 3.0, 1.2 Hz, 1H), 6.95 (d, J = 8.6 Hz, 1H), 6.50 (dd, J = 8.6, 2.5 Hz, 1H), 6.41 (dq, J = 2.9, 1.4 Hz, 1H), 6.36 (dd, J = 3.9, 2.9 Hz, 1H), 5.94 (dd, J = 4.0, 1.2 Hz, 1H), 3.88 (tt, J = 8.7, 3.8 Hz, 1H), 2.74 (s, 3H), 2.62 (s, 1H), 2.26 – 2.12 (m, 1H), 1.99 – 1.86 (m, 2H), 1.76 – 1.60 (m, 2H), 1.60 – 1.46 (m, 1H), 1.26 (dq, J = 13.1, 4.5 Hz, 1H), 1.16 (dtt, J = 13.9, 10.2, 3.8 Hz, 1H), 1.04 (d, J = 11.1 Hz, 1H), 0.55 (t, J = 7.2 Hz, 3H). NH not observed.
60	MS *m/z* 440.3 [M+H]+; 1H NMR (500 MHz, Methanol-d_4) δ 7.78 (dd, J = 2.9, 1.2 Hz, 1H), 7.55 (d, J = 8.7 Hz, 1H), 7.10 (dd, J = 8.6, 2.5 Hz, 1H), 7.01 (dq, J = 2.8, 1.5 Hz, 1H), 6.96 (t, J = 3.4 Hz, 1H), 6.55 (dd, J = 4.0, 1.2 Hz, 1H), 5.09 – 4.89 (m, 1H), 4.79 (dp, J = 14.6, 4.2 Hz, 1H), 3.91 (s, 3H), 3.29 – 3.17 (m, 1H), 3.08 – 2.92 (m, 1H), 2.48 – 2.38 (m, 1H), 2.36 (s, 3H), 2.24 (t, J = 10.2 Hz, 1H), 1.92 (t, J = 11.8 Hz, 1H), 1.84 (t, J = 13.0 Hz, 1H). NH not observed.
61	MS *m/z* 452.3 [M+H]+; 1H NMR (500 MHz, Methanol-d_4) δ 7.75 (dd, J = 2.9, 1.2 Hz, 1H), 7.46 (d, J = 8.5 Hz, 1H), 7.00 (dd, J = 8.6, 2.5 Hz, 1H), 6.91 (dq, J = 3.0, 1.5 Hz, 1H), 6.88 – 6.74 (m, 1H), 6.44 (dd, J = 4.0, 1.2 Hz, 1H), 4.45 – 4.28 (m, 1H), 3.81 (s, 3H), 3.71 – 3.54 (m, 2H), 3.07 (m, 1H), 2.72 – 2.60 (m, 1H), 2.51 (dtd, J = 24.3, 12.6, 5.8 Hz, 2H), 2.33 (s, 2H),

	2.01 – 1.87 (m, 1H), 1.77 (t, J = 6.9 Hz, 1H), 1.71 – 1.52 (m, 2H). NH and OH not observed
62	MS *m/z* 423.3 [M+H]+; 1H NMR (500 MHz, Methanol-d_4) δ 7.79 (dd, J = 2.9, 1.2 Hz, 1H), 7.56 (d, J = 8.6 Hz, 1H), 7.09 (dd, J = 8.5, 2.5 Hz, 1H), 7.05 – 6.97 (m, 1H), 6.95 (t, J = 3.5 Hz, 1H), 6.53 (dd, J = 3.9, 1.2 Hz, 1H), 4.24 (tt, J = 11.3, 3.9 Hz, 1H), 3.91 (s, 3H), 3.74 (tt, J = 10.7, 4.1 Hz, 1H), 2.43 (d, J = 12.0 Hz, 1H), 2.18 – 2.07 (m, 1H), 1.98 (d, J = 12.4 Hz, 1H), 1.88 (dt, J = 13.1, 3.6 Hz, 1H), 1.55 – 1.39 (m, 2H), 1.27 (dt, J = 16.4, 10.4 Hz, 2H). NH and OH peak not observed.
63	MS *m/z* 403.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.80 (s, 2H), 7.76 – 7.70 (m, 1H), 7.66 (s, 1H), 7.01 – 6.97 (m, 1H), 6.90 (t, J = 73.17 Hz, 1H), 6.57 (dd, J = 3.9, 1.0 Hz, 1H), 4.25 – 4.15 (m, 1H), 3.74 (dd, J = 13.8, 4.1 Hz, 1H), 3.56 (dd, J = 13.6, 7.6 Hz, 1H), 1.28 (d, J = 6.3 Hz, 3H), 2H not observed (NH and OH).
64	MS *m/z* 369.0 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.75 (dd, J = 2.8 Hz, 0.8 Hz, 1H), 7.56 (d, J = 8.8 Hz, 1H), 7.10 (dd, J = 8.4, 3.6 Hz, 1H), 7.01 (br s, 1H), 6.96 (t, J = 4.0 Hz, 1H), 6.54 (dd, J = 4.0, 0.8 Hz, 1H), 3.91 (s, 3H), 3.89 (t, J = 5.6 Hz, 2H), 3.79 (t, J = 5.6 Hz, 2H). NH and OH not observed.
65	MS *m/z* 383.1 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.77 (dd, J = 2.8, 0.8 Hz, 1H), 7.55 (d, J = 8.8 Hz, 1H), 7.10 (dd, J = 8.4, 2.4 Hz, 1H), 7.04 - 7.00 (m, 1H), 6.97 (dd, J = 4.0, 2.8 Hz, 1H), 6.55 (dd, J = 4.0, 1.2 Hz, 1H), 4.24 – 4.14 (m, 1H), 3.91 (s, 3H), 3.73 (dd, J = 14.0, 4.0 Hz, 1H), 3.54 (dd, J = 13.6, 7.6 Hz, 1H), 1.27 (d, J = 6.4 Hz, 3H). NH and OH not observed.
66	MS *m/z* 397.1 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.80 (dd, J = 2.8, 1.2 Hz, 1H), 7.55 (d, J = 8.8 Hz, 1H), 7.09 (dd, J = 8.4, 2.4 Hz, 1H), 7.01 (br s, 1H), 6.98 (t, J = 7.2 Hz, 1H), 6.56 (d, J = 3.2 Hz, 1H), 3.90 (s, 3H), 3.71 (s, 2H), 1.31 (s, 6H). NH and OH not observed.
67	MS *m/z* 409.1 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.82 (dd, J = 1.2 Hz, 3.2 Hz, 1H), 7.55 (d, J = 8.4 Hz, 1H), 7.07 – 7.10 (m, 1H), 7.01 (s,1H), 6.94 (t, J = 1.2 Hz, 1H),6.53 (dd, J = 1.2 Hz, 4.0 Hz, 1H), 4.42 – 4.37(m, 1H), 4.02 – 4.05 (m, 2H), 3.90 (s,3H),3.62 – 3.56 (m, 2H),2.13 – 2.16 (m, 2H),1.72 – 1.82 (m, 2H). NH not observed.
68	MS *m/z* 395.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.85 (dd, J = 2.8, 1.2 Hz, 1H), 7.56 (d, J = 8.4 Hz, 1H), 7.09 (dd, J = 8.4, 2.4 Hz, 1H), 7.04 - 6.99 (m, 1H), 6.95 (t, J = 3.6 Hz, 1H), 6.55 (dd, J = 4.0, 0.8 Hz, 1H), 4.85 - 4.77 (m, 1H), 4.14 – 4.02 (m, 2H), 3.95 – 3.85 (m, 5H), 2.50 – 2.36 (m, 1H), 2.22 – 2.10 (m, 1H). NH not observed.
69	MS *m/z* 419.1 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.78 (dd, J = 2.8, 1.2 Hz, 1H), 7.55 (d, J = 8.4 Hz, 1H), 7.10 (dd, J = 8.4, 2.4 Hz, 1H), 7.07 (d, J = 1.2 Hz, 1H), 7.04 - 7.00 (m, 1H), 6.96 (t, J = 3.2 Hz, 1H), 6.91 (d, J = 1.2 Hz, 1H), 6.56 (dd, J = 4.0, 0.8 Hz, 1H), 4.91 (s, 2H), 3.91 (s, 3H), 3.84 (s, 3H). NH not observed.
70	MS *m/z* 383.1 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.77 (dd, J = 2.8, 0.8 Hz, 1H), 7.56 (d, J = 8.4 Hz, 1H), 7.10 (dd, J = 8.4, 2.4 Hz, 1H),

	7.01 (br s, 1H), 6.96 (t, J = 3.6 Hz, 1H), 6.55 (dd, J = 4.0, 0.8 Hz, 1H), 4.24 – 4.14 (m, 1H), 3.91 (s, 3H), 3.73 (dd, J = 14.0, 4.0 Hz, 1H), 3.54 (dd, J = 13.6, 7.6 Hz, 1H), 1.27 (d, J = 6.0 Hz, 3H). NH and OH not observed.
71	MS *m/z* 393.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.82 (d, J = 1.9 Hz, 1H), 7.48 (d, J = 8.5 Hz, 1H), 7.36 (d, J = 2.4 Hz, 1H), 7.30 (dd, J = 8.6, 2.4 Hz, 1H), 6.93 (t, J = 3.4 Hz, 1H), 6.38 (d, J = 3.8 Hz, 1H), 4.31 – 4.21 (m, 1H), 3.94 (s, 3H), 2.69 – 2.62 (m, 2H), 2.30 – 2.22 (m, 2H), 1.44 (s, 3H). 2 H not observed (NH and OH)
72	MS *m/z* 359.2, 361.1 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.84 (d, J = 2.0 Hz, 1H), 7.43 (d, J = 8.5 Hz, 1H), 7.15 (d, J = 2.5 Hz, 1H), 7.04 (dd, J = 8.5, 2.4 Hz, 1H), 6.96 (t, J = 3.4 Hz, 1H), 6.50 (d, J = 3.9 Hz, 1H), 4.31 – 4.21 (m, 1H), 3.89 (s, 3H), 2.69 – 2.69 (m, 2H), 2.31 – 2.23 (m, 2H), 1.44 (s, 3H). 2 H not observed (NH and OH)
73	MS *m/z* 409.1 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.67 (dd, J = 2.8, 1.2 Hz, 1H), 7.56 (d, J = 8.8 Hz, 1H), 7.10 (dd, J = 8.4, 2.4 Hz, 1H), 7.04 - 6.99 (m, 1H), 6.95 (t, J = 3.2 Hz, 1H), 6.54 (dd, J = 4.0, 0.8 Hz, 1H), 4.39 – 4.31 (m, 1H), 3.97 – 3.92 (m, 1H), 3.91 (s, 3H), 3.85 – 3.76 (m, 2H), 3.64 (dd, J = 14.0, 8.0 Hz, 1H), 2.16 – 2.07 (m, 1H), 2.06 – 1.90 (m, 2H), 1.78 – 1.68 (m, 1H). NH not observed.
74	MS *m/z* 422.1 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 8.22 (br s, 1H), 7.76 (d, J = 8.4 Hz, 1H), 7.39 – 7.34 (m, 1H), 7.34 - 7.29 (m, 1H), 7.25 (dd, J = 8.8, 2.4 Hz, 1H), 7.19 (br s, 1H), 4.18 (dd, J = 15.2, 4.4 Hz, 1H), 4.03 (dd, J = 15.2, 4.4 Hz, 1H), 3.96 (s, 3H), 3.86 – 3.72 (m, 2H), 3.28 – 3.19 (m, 1H), 3.12 (s, 3H), 2.48 – 2.36 (m, 1H), 2.25 – 2.01 (m, 3H). NH not observed.
75	MS *m/z* 396.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.81 (d, J = 2.4 Hz, 1H), 6.93 (t, J = 3.2 Hz, 1H), 6.65 (dd, J = 11.6, 2.4 Hz, 1H), 6.43 (d, J = 4.0 Hz, 1H), 6.41 (d, J = 2.0 Hz, 1H), 4.54 - 4.42 (m, 1H), 3.83 (s, 3H), 3.20 - 3.06 (m, 1H), 2.76 - 2.64 (m, 1H), 2.34 (s, 3H), 2.31 - 2.19 (m, 2H), 2.15 - 2.00 (m, 1H), 1.91 - 1.82 (m, 1H), 1.82 - 1.72 (m, 1H), 1.72 - 1.55 (m, 2H), 0.85 – 0.69 (m, 2H), 0.69 – 0.60 (m, 1H), 0.59 - 0.50 (m, 1H). NH not observed.
76	MS *m/z* 409.0 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.76 (dd, J = 3.2, 1.2 Hz, 1H), 7.55 (d, J = 8.8 Hz, 1H), 7.09 (dd, J = 8.8, 2.4 Hz, 1H), 7.01 (d, J = 1.2 Hz, 1H), 6.95 (t, J = 3.2 Hz, 1H), 6.53 (dd, J = 4.0, 1.2 Hz, 1H), 4.39 – 4.31 (m, 1H), 3.98 – 3.92 (m, 1H), 3.90 (s, 3H), 3.85 – 3.77 (m, 2H), 3.63 (dd, J = 14.0, 8.0 Hz, 1H), 2.16 – 2.06 (m, 1H), 2.05 – 1.88 (m, 2H), 1.78 – 1.68 (m, 1H). NH not observed.
77	MS *m/z* 444.3 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.90 (s, 1H), 7.86 – 7.81 (m, 2H), 7.80 – 7.73 (m, 1H), 7.01 (t, J = 3.4 Hz, 1H), 6.56 (d, J = 3.8 Hz, 1H), 5.06 (t, J = 9.5 Hz, 1H), 3.83 (q, J = 10.9 Hz, 2H), 3.56 – 3.43 (m, 2H), 2.80 – 2.70 (m, 1H), 2.35 (dd, J = 12.3, 9.9 Hz, 1H). 2H not observed (2NH)
78	MS *m/z* 443.3 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.91 - 7.87 (m, 1H), 7.80 (d, J = 8.0 Hz, 1H), 7.77 - 7.71 (m, 1H), 7.66 (s, 1H), 7.11 - 6.71 (m, 2H), 6.56 (d, J = 3.9 Hz, 1H), 4.24 - 4.11 (m, 1H), 3.68 (dt, J = 4.3, 10.0

	Hz, 1H), 2.34 - 2.21 (m, 1H), 2.19 - 2.07 (m, 1H), 1.91 - 1.74 (m, 2H), 1.56 - 1.35 (m, 4H); 2H not observed (NH and OH).
79	MS *m/z* 443.3 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.97 - 7.93 (m, 1H), 7.80 (d, J = 8.0 Hz, 1H), 7.77 - 7.72 (m, 1H), 7.67 (s, 1H), 7.13 - 6.71 (m, 2H), 6.56 (d, J = 3.9 Hz, 1H), 4.35 - 4.25 (m, 2H), 2.04 - 1.90 (m, 2H), 1.90 - 1.81 (m, 2H), 1.80 - 1.64 (m, 2H), 1.60 - 1.44 (m, 2H); 2H not observed (NH and OH).
80	MS *m/z* 389.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.85 (d, J = 1.9 Hz, 1H), 7.44 (d, J = 7.8 Hz, 1H), 7.26 - 7.16 (m, 2H), 6.97 - 6.55 (m, 2H), 6.55 - 6.48 (m, 1H), 4.21 - 4.08 (m, 1H), 3.66 (dt, J = 4.3, 10.0 Hz, 1H), 2.47 (s, 3H), 2.30 - 2.21 (m, 1H), 2.21 - 2.04 (m, 1H), 1.89 - 1.74 (m, 2H), 1.57 - 1.35 (m, 4H); 2H not observed (NH and OH).
81	MS *m/z* 423.3 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.86 (d, J = 2.0 Hz, 1H), 7.57 (d, J = 8.5 Hz, 1H), 7.11 (dd, J = 2.4, 8.6 Hz, 1H), 7.03 (s, 1H), 7.00 - 6.92 (m, 1H), 6.54 (d, J = 3.8 Hz, 1H), 4.89 (s, 3H), 4.23 - 4.08 (m, 1H), 3.66 (dt, J = 4.3, 10.0 Hz, 1H), 2.34 - 2.04 (m, 2H), 1.89 - 1.72 (m, 2H), 1.59 - 1.36 (m, 4H); 2H not observed (NH and OH).
82	MS *m/z* 404.3, 406.2 [M+H]+; 1H NMR (400 MHz, Methanol-d4) δ 7.68 (t, J = 3.7 Hz, 1H), 7.40 (d, J = 8.5 Hz, 1H), 7.12 (d, J = 2.4 Hz, 1H), 7.02 (dd, J = 8.4, 2.4 Hz, 1H), 6.78 (d, J = 3.2 Hz, 1H), 4.55 – 4.40 (m, 1H), 3.88 (s, 3H), 3.60 – 3.42 (m, 1H), 3.20 – 3.03 (m, 1H), 2.92 – 2.75 (m, 2H), 2.68 – 2.43 (m, 2H), 2.26 – 2.10 (m, 1H), 2.05 – 1.93 (m, 1H), 1.89 – 1.64 (m, 2H), 1.24 (t, J = 7.2 Hz, 3H). NH not observed.
83	MS *m/z* 420.2, 422.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.70 (t, J = 3.7 Hz, 1H), 7.40 (d, J = 8.5 Hz, 1H), 7.12 (d, J = 2.4 Hz, 1H), 7.02 (dd, J = 8.5, 2.4 Hz, 1H), 6.78 (d, J = 3.3 Hz, 1H), 4.57 – 4.46 (m, 1H), 3.88 (s, 3H), 3.81 (t, J = 5.2 Hz, 2H), 3.62 – 3.50 (m, 1H), 3.22 – 3.08 (m, 1H), 3.03 – 2.88 (m, 2H), 2.82 – 2.63 (m, 2H), 2.22 – 2.08 (m, 1H), 2.06 – 1.95 (m, 1H), 1.93 – 1.71 (m, 2H). 2H not observed (NH and OH).
84	MS *m/z* 377.2, 379.1 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.67 (t, J = 3.7 Hz, 1H), 7.39 (d, J = 8.5 Hz, 1H), 7.11 (d, J = 2.4 Hz, 1H), 7.01 (dd, J = 8.5, 2.4 Hz, 1H), 6.76 (d, J = 3.2 Hz, 1H), 4.34 – 4.14 (m, 1H), 3.88 (s, 3H), 2.69 – 2.56 (m, 2H), 2.30 – 2.17 (m, 2H), 1.43 (s, 3H). 2H not observed (NH and OH).
85	MS *m/z* 472.3 [M+H]+; 1H NMR (500 MHz, Methanol-d_4) δ 7.89 – 7.79 (m, 1H), 7.69 (d, J = 8.5 Hz, 1H), 7.33 (dd, J = 8.6, 2.3 Hz, 1H), 7.29 (s, 1H), 7.02 (t, J = 75 Hz, 1H), 6.97 (t, J = 3.5 Hz, 1H), 6.55 (d, J = 4.0 Hz, 1H), 4.56 – 4.44 (m, 1H), 3.36 (tp, J = 4.0, 1.9 Hz, 2H), 2.84 – 2.74 (m, 1H), 2.53 (s, 1H), 2.33 – 2.22 (m, 1H), 2.17 – 2.04 (m, 1H), 1.94 – 1.80 (m, 1H), 1.83 – 1.71 (m, 1H), 1.69 – 1.57 (m, 1H), 1.36 – 1.24 (m, 1H), 1.15 (t, J = 7.3 Hz, 3H). NH peak not observed.
86	MS *m/z* 488.3 [M+H]+; 1H NMR (500 MHz, Methanol-d_4) δ 7.87 (dd, J = 2.9, 1.2 Hz, 1H), 7.69 (d, J = 8.5 Hz, 1H), 7.33 (dd, J = 8.5, 2.4 Hz, 1H), 7.29 (s, 1H), 7.02 (t, J = 75 Hz, 1H), 6.97 (t, J = 3.4 Hz, 1H), 6.55 (dd, J = 3.9, 1.2 Hz, 1H), 4.47 (dd, J = 8.8, 4.5 Hz, 1H), 3.78 – 3.65 (m, 2H), 3.19 – 3.09 (m, 1H), 2.78 – 2.69 (m, 1H), 2.63 (dt, J = 12.3, 6.0 Hz, 1H), 2.56 (dt, J

	= 12.5, 5.7 Hz, 1H), 2.48 – 2.32 (m, 2H), 2.10 – 1.98 (m, 1H), 1.86 (dd, J = 14.1, 5.2 Hz, 1H), 1.80 – 1.62 (m, 2H). NH and OH peak not observed.
87	MS *m/z* 476.2 [M+H]+; 1H NMR (500 MHz, Methanol-d_4) δ 7.81 (dd, J = 2.9, 1.2 Hz, 1H), 7.69 (d, J = 8.5 Hz, 1H), 7.33 (dd, J = 8.5, 2.4 Hz, 1H), 7.29 (s, 1H), 7.02 (t, J = 75 Hz, 1H), 6.98 (t, J = 3.5 Hz, 1H), 6.56 (d, J = 3.9 Hz, 1H), 5.08 – 4.90 (m, 1H), 4.80 (ddd, J = 12.7, 10.4, 4.1 Hz, 1H), 3.28 – 3.19 (m, 1H), 3.01 (t, J = 11.8 Hz, 1H), 2.41 (dd, J = 12.3, 6.3 Hz, 1H), 2.36 (s, 3H), 2.24 (t, J = 10.3 Hz, 1H), 1.92 (t, J = 12.4 Hz, 1H), 1.84 (t, J = 12.2 Hz, 1H). NH peak not observed.
88	MS *m/z* 445.2 [M+H]+..1H NMR (500 MHz, Methanol-d_4) δ 7.84 (dd, J = 3.0, 1.4 Hz, 1H), 7.69 (d, J = 8.5 Hz, 1H), 7.34 (d, J = 8.6 Hz, 1H), 7.30 (s, 1H), 7.03 (t, J = 75 Hz, 1H) 6.97 (m, 1H), 6.55 (d, J = 3.8 Hz, 1H), 4.28 (p, J = 7.9 Hz, 1H), 2.74 – 2.52 (m, 2H), 2.37 – 2.17 (m, 2H), 1.44 (s, 3H). NH and OH peak not observed.
89	MS *m/z* 465.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.99 (dd, J = 0.9, 2.8 Hz, 1H), 7.78 (d, J = 8.0 Hz, 1H), 7.74 - 7.69 (m, 1H), 7.65 (s, 1H), 7.21 - 7.11 (m, 1H), 7.09 - 6.65 (m, 5H), 6.57 (d, J = 3.9 Hz, 1H), 5.52 (q, J = 7.0 Hz, 1H), 1.71 (d, J = 7.0 Hz, 3H); NH and OH peak not observed.
90	MS *m/z* 459.2 [M+H]+; 1H NMR (500 MHz, Methanol-d_4) δ 7.92 – 7.88 (m, 2H), 7.83 (d, J = 8.2 Hz, 1H), 7.80 – 7.74 (m, 1H), 6.99 (t, J = 3.4 Hz, 1H), 6.53 (d, J = 3.5 Hz, 1H), 4.21 – 4.11 (m, 1H), 3.92 – 3.77 (m, 2H), 3.66 (td, J = 10.1, 4.3 Hz, 1H), 2.30 – 2.20 (m, 1H), 2.20 – 2.03 (m, 1H), 1.87 – 1.73 (m, 2H), 1.52 – 1.36 (m, 4H). 2H not observed (NH and OH).
91	MS *m/z* 406.0 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.90 (s, 1H), 7.78 (dd, J = 2.8, 1.2 Hz, 1H), 7.55 (d, J = 8.8 Hz, 1H), 7.14 (s, 1H), 7.10 (dd, J = 8.4, 2.4 Hz, 1H), 7.04 - 6.97 (m, 2H), 6.59 (dd, J = 4.0, 0.8 Hz, 1H), 4.99 (s, 2H), 3.91 (s, 3H). NH not observed.
92	MS *m/z* 420.0 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 8.45 (s, 1H), 7.78 (dd, J = 2.8, 1.2 Hz, 1H), 7.55 (d, J = 8.4 Hz, 1H), 7.10 (dd, J = 8.4, 2.4 Hz, 1H), 7.04 - 6.97 (m, 2H), 6.58 (d, J = 4.0 Hz, 1H), 5.01 (s, 2H), 3.91 (s, 3H), 3.91 (s, 3H). NH not observed.
93	MS *m/z* 420.0 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.85 (s, 1H), 7.77 (dd, J = 2.8, 0.8 Hz, 1H), 7.54 (d, J = 8.8 Hz, 1H), 7.09 (dd, J = 8.4, 2.4 Hz, 1H), 7.03 - 6.97 (m, 2H), 6.58 (dd, J = 4.4, 0.4 Hz, 1H), 4.96 (s, 2H), 4.09 (s, 3H), 3.91 (s, 3H). NH not observed.
94	MS *m/z* 421.1 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.73 (dd, J = 2.8, 1.2 Hz, 1H), 7.56 (d, J = 8.4 Hz, 1H), 7.10 (dd, J = 8.8, 2.4 Hz, 1H), 7.01 (s, 1H), 6.94 (t, J = 3.6 Hz, 1H), 6.53 (dd, J = 4.0, 0.8 Hz, 1H), 3.91 (s, 3H), 3.70 (s, 2H), 2.23 (s, 6H). NH and OH not observed.
95	MS *m/z* 430.1 [M+H]+; 1HNMR (400 MHz, Methanol-d_4) δ 8.46 (br s, 1.2H), 8.02 (d, J = 8.0 Hz, 1H), 7.92 (s, 1H), 7.87 (d, J = 2.0 Hz, 1H), 7.71 (d, J = 8.0 Hz, 1H), 6.99 (t, J = 3.2 Hz, 1H), 6.88 (t, J = 73.6 Hz, 1H), 6.58 (d, J = 3.6 Hz, 1H), 4.64 – 4.53 (m, 1H), 3.79 – 3.64 (d, J = 9.2 Hz, 1H), 3.38 – 3.32 (m, 1H), 3.13 (q J = 7.2 Hz, 2H), 3.09 – 2.95 (m, 2H), 2.84 (s, 3H), 2.26 – 2.12 (m, 2H), 2.00 - 1.82 (m, 2H), 1.23 (t, J = 7.2 Hz, 3H). NH not observed.

96	MS *m/z* 481.2 [M+H]+; 1H NMR (500 MHz, Methanol-d_4) δ 8.01 (d, J = 2.0 Hz, 1H), 7.88 (s, 1H), 7.80 (d, J = 7.9 Hz, 1H), 7.75 (d, J = 8.54 Hz, 1H), 7.15 (t, J = 7.9 Hz, 1H), 7.00 (t, J = 3.3 Hz, 1H), 6.96 (d, J = 7.8 Hz, 1H), 6.93 (s, 1H), 6.66 (d, J = 7.9 Hz, 1H), 6.54 (d, J = 3.7 Hz, 1H), 5.50 (q, J = 7.3 Hz, 1H), 3.94 – 3.70 (m, 2H), 1.70 (d, J = 7.2 Hz, 3H). 2H not observed (NH and OH).
97	MS *m/z* 427.2 [M+H]; 1H NMR (500 MHz, Methanol-d_4) δ 8.07 – 8.02 (m, 1H), 7.89 (s, 1H), 7.87 – 7.78 (m, 2H), 7.61 (s, 1H), 6.84 (s, 1H), 6.53 (d, J = 3.1 Hz, 1H), 6.21 (br s, 1H), 3.89 (q, J = 10.8 Hz, 2H). 2H not observed (2 NH).
98	MS *m/z* 458.2 [M+H]+;1H NMR (500 MHz, Methanol-d_4) δ 7.81 – 7.68 (m, 3H), 7.66 (s, 1H), 7.01 (t, J = 3.4 Hz, 1H), 6.92 (t, J = 72.78 Hz, 1H), 6.60 (d, J = 3.5 Hz, 1H), 4.68 – 4.61 (m, 1H), 4.17 – 4.07 (m, 1H), 3.43 – 3.33 (m, 1H), 3.16 (d, J = 11.1 Hz, 1H), 3.06 – 2.84 (m, 1H), 2.71 – 2.62 (m, 4H), 2.38 – 2.28 (m, 1H), 1.94 - 1.81 (m, 1H). 2H not observed (NH and OH).
99	MS *m/z* 445.3 [M+H]+;1H NMR (400 MHz, Methanol-d_4) δ 8.19 (s, 1H), 8.17 - 8.08 (m, 1H), 7.92 (d, J = 2.9 Hz, 1H), 7.89 - 7.81 (m, 1H), 6.98 (t, J = 3.4 Hz, 1H), 6.43 (d, J = 3.9 Hz, 1H), 4.23 - 4.10 (m, 1H), 3.68 (dt, J = 4.3, 10.0 Hz, 1H), 2.35 (br s, 1H), 2.09 (br s, 1H), 1.90 (br s, 2H), 1.56 - 1.36 (m, 4H); 2H not observed (NH and OH).
100	MS *m/z* 411.3 [M+H]+;1H NMR (400 MHz, Methanol-d_4) δ 7.95 (d, J = 2.1 Hz, 1H), 7.42 (d, J = 7.8 Hz, 1H), 7.23 - 7.12 (m, 3H), 6.99 - 6.92 (m, 3H), 6.54 - 6.53 (m, 1H), 6.92 - 6.48 (m, 2H), 5.50 (q, J = 6.8 Hz, 1H), 2.46 (s, 3H), 1.70 (d, J = 7.0 Hz, 3H); 2H not observed (NH and OH).
101	MS *m/z* 451.3 [M+H]+;1H NMR (400 MHz, Methanol-d_4) δ 7.86 - 7.78 (m, 2H), 7.77 - 7.71 (m, 1H), 7.67 (s, 1H), 7.21 - 7.14 (m, 1H), 7.12 - 6.88 (m, 4H), 6.76 - 6.67 (m, 1H), 6.59 (d, J = 3.9 Hz, 1H), 4.83 (s, 2H); 2H not observed (NH and OH).
102	MS *m/z* 465.2 [M+H]+;1H NMR (400 MHz, Methanol-d_4) δ 7.99 (dd, J = 0.9, 2.8 Hz, 1H), 7.78 (d, J = 8.0 Hz, 1H), 7.74 - 7.69 (m, 1H), 7.65 (s, 1H), 7.21 - 7.11 (m, 1H), 7.09 - 6.65 (m, 5H), 6.57 (d, J = 3.9 Hz, 1H), 5.52 (q, J = 7.0 Hz, 1H), 1.71 (d, J = 7.0 Hz, 3H); 2H not observed (NH and OH).
103	MS *m/z* 465.2 [M+H]+;1H NMR (400 MHz, Methanol-d_4) δ 7.99 (dd, J = 0.9, 2.8 Hz, 1H), 7.78 (d, J = 8.0 Hz, 1H), 7.74 - 7.69 (m, 1H), 7.65 (s, 1H), 7.21 - 7.11 (m, 1H), 7.09 - 6.65 (m, 5H), 6.57 (d, J = 3.9 Hz, 1H), 5.52 (q, J = 7.0 Hz, 1H), 1.71 (d, J = 7.0 Hz, 3H); 2H not observed (NH and OH).
104	MS *m/z* 365.3 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.91 – 7.90 (m, 1H), 7.30 (d, J = 8.3 Hz, 1H), 6.99 (t, J = 3.3 Hz, 1H), 6.90 – 6.89 (m, 1H), 6.65 – 6.57 (m, 2H), 4.25 (quint, J = 7.9 Hz, 1H), 3.84 (s, 3H), 2.65 (ddd, J = 9.4, 7.2, 2.6 Hz, 2H), 2.31 – 2.23 (m, 2H), 1.87 – 1.77 (m, 1H), 1.44 (s, 3H), 0.80 – 0.70 (m, 2H), 0.70 – 0.62 (m, 2H). 2H not observed (NH and OH).
105	MS *m/z* 347.2 [M+H]+;1H NMR (400 MHz, Methanol-d_4) δ 8.02 – 7.98 (m, 1H), 7.59 (d, J = 2.1 Hz, 1H), 7.31 (d, J = 8.5 Hz, 1H), 6.85 (dd, J = 8.4, 2.5 Hz, 1H), 6.81 (t, J = 3.2 Hz, 1H), 6.59 (d, J = 2.3 Hz, 1H), 6.48 (d, J = 3.1

	Hz, 1H), 6.20 – 6.17 (m, 1H), 3.83 (s, 3H), 1.98 – 1.89 (m, 1H), 0.86 – 0.78 (m, 2H), 0.69 – 0.62 (m, 2H). 2H not observed (2 NH).
106	MS *m/z* 379.3 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.89 – 7.82 (m, 1H), 7.31 (d, J = 8.3 Hz, 1H), 7.01 – 6.95 (m, 1H), 6.95 – 6.82 (m, 1H), 6.63 – 6.56 (m, 2H), 4.27 – 4.18 (m, 1H), 3.84 (s, 3H), 3.82 – 3.69 (m, 1H), 2.44 (d, J = 11.9 Hz, 1H), 2.14 (d, J = 11.4 Hz, 1H), 1.99 (d, J = 11.9 Hz, 1H), 1.93 – 1.79 (m, 2H), 1.53 – 1.34 (m, 3H), 1.34 – 1.23 (m, 1H), 0.82 – 0.72 (m, 2H), 0.70 – 0.62 (m, 2H). 2H not observed (NH and OH).
107	MS *m/z* 445.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 8.16 (s, 1H), 8.10 (d, J = 8.1 Hz, 1H), 7.81 (d, J = 8.0 Hz, 1H), 7.64 (s, 1H), 6.25 (s, 1H), 4.25 (t, J = 7.9 Hz, 1H), 2.72 – 2.57 (m, 2H), 2.36 – 2.17 (m, 5H), 1.44 (s, 3H). NH and OH peaks not observed.
108	MS *m/z* 423.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.58 (s, 1H), 7.54 (d, J = 8.5 Hz, 1H), 7.09 (dd, J = 8.6, 2.3 Hz, 1H), 7.01 (s, 1H), 6.37 (m, 1H), 4.28-4.20 (m, 1H), 3.91 (s, 3H), 2.67 – 2.62 (m, 2H), 2.33 (s, 3H), 2.27 – 2.22 (m, 2H), 1.43 (s, 3H). NH and OH peak not observed.
109	MS *m/z* 458.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 8.17 (s, 1H), 8.10 (d, J = 7.9 Hz, 1H), 7.81 (d, J = 8.0 Hz, 1H), 7.65 (s, 1H), 6.26 (s, 1H), 4.47-4,49 (m, 1H), 2.91 – 2.88 (m, 1H), 2.55-2.42 (m, 5H), 2.32 (s, 3H), 2.15-2.10 (m, 1H), 2.01 – 1.89 (m, 1H), 1.87 – 1.73 (m, 1H), 1.73 – 1.57 (m, 1H), 1.39 – 1.29 (m, 1H). NH peak not observed.
110	MS *m/z* 443.5 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.89 (d, J = 2.0 Hz, 1H), 7.80 (br d, J = 8.0 Hz, 1H), 7.77 - 7.71 (m, 1H), 7.66 (s, 1H), 7.18 - 6.68 (m, 2H), 6.56 (d, J = 3.6 Hz, 1H), 4.28 - 4.08 (m, 1H), 3.77 - 3.60 (m, 1H), 2.36 - 2.01 (m, 2H), 1.92 - 1.70 (m, 2H), 1.59 - 1.32 (m, 4H); 2H not observed (NH and OH).
111	MS *m/z* 459.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.92 – 7.88 (m, 2H), 7.85 – 7.75 (m, 2H), 6.99 (t, J = 3.4 Hz, 1H), 6.54 (d, J = 3.9 Hz, 1H), 4.20 – 4.11 (m, 1H), 3.85 (br dd, J = 10.8, 5.6 Hz, 2H), 3.71 – 3.62 (m, 1H), 2.31 – 2.22 (m, 1H), 2.17 – 2.08 (m, 1H), 1.87 – 1.75 (m, 2H), 1.54 – 1.36 (m, 4H). 2H not observed (NH and OH).
112	MS *m/z* 461.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.94 – 7.88 (m, 2H), 7.86 – 7.75 (m, 2H), 7.01 (t, J = 3.4 Hz, 1H), 6.56 (d, J = 3.8 Hz, 1H), 4.34 (td, J = 10.51, 3.5 Hz, 1H), 4.04 (dd, J = 11.2, 4.9 Hz, 1H), 3.98 (br dd, J = 11.3, 4.3 Hz, 1H), 3.90 – 3.74 (m, 3H), 3.56 (td, J = 11.1, 1.75 Hz, 1H), 3.26 (t, J = 10.5 Hz, 1H), 2.31 – 2.24 (m, 1H), 1.79 (qd, J = 12.38, 5.13 Hz, 1H). 2H not observed (NH and OH).
113	MS *m/z* 461.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.94 – 7.88 (m, 2H), 7.86 – 7.75 (m, 2H), 7.01 (t, J = 3.4 Hz, 1H), 6.56 (d, J = 3.8 Hz, 1H), 4.34 (td, J = 10.51, 3.5 Hz, 1H), 4.04 (dd, J = 11.2, 4.9 Hz, 1H), 3.98 (br dd, J = 11.3, 4.3 Hz, 1H), 3.90 – 3.74 (m, 3H), 3.56 (td, J = 11.1, 1.75 Hz, 1H), 3.26 (t, J = 10.5 Hz, 1H), 2.31 – 2.24 (m, 1H), 1.79 (qd, J = 12.38, 5.13 Hz, 1H). 2H not observed (NH and OH).
114	MS *m/z* 461.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 8.00 (d, J = 2.4 Hz, 1H), 7.90 (s, 1H), 7.86 – 7.74 (m, 2H), 7.00 (t, J = 3.4 Hz, 1H), 6.55 (d, J = 3.8 Hz, 1H), 4.47 (td, J = 11.88, 3.13 Hz, 1H), 4.19 – 4.14 (m, 1H),

	4.04 (dd, J = 11.6, 4.1 Hz, 1H), 3.98 (d, J = 12.5 Hz, 1H), 3.85 (q, J = 11.0 Hz, 2H), 3.70 (d, J = 12.1 Hz, 1H), 3.62 (t, J = 11.0 Hz, 1H), 2.30 (qd, J = 12.6, 4.7 Hz, 1H), 1.88 – 1.81 (m, 1H). 2H not observed (NH and OH).
115	MS *m/z* 461.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 8.00 (d, J = 2.4 Hz, 1H), 7.90 (s, 1H), 7.86 – 7.74 (m, 2H), 7.00 (t, J = 3.4 Hz, 1H), 6.55 (d, J = 3.8 Hz, 1H), 4.47 (td, J = 11.88, 3.13 Hz, 1H), 4.19 – 4.14 (m, 1H), 4.04 (dd, J = 11.6, 4.1 Hz, 1H), 3.98 (d, J = 12.5 Hz, 1H), 3.85 (q, J = 11.0 Hz, 2H), 3.70 (d, J = 12.1 Hz, 1H), 3.62 (t, J = 11.0 Hz, 1H), 2.30 (qd, J = 12.6, 4.7 Hz, 1H), 1.88 – 1.81 (m, 1H). 2H not observed (NH and OH).
116	MS *m/z* 410.2 [M+H]+; 1H NMR (400 MHz, Methanol-d4) δ 7.63 (t, J = 3.7 Hz, 1H), 7.46 (d, J = 8.4 Hz, 1H), 7.34 (d, J = 2.3 Hz, 1H), 7.29 (dd, J = 8.3, 2.6 Hz, 1H), 6.76 (d, J = 3.1 Hz, 1H), 5.09 – 4.94 (m, 1H), 3.93 (s, 3H), 3.57 – 3.39 (m, 2H), 2.81 – 2.67 (m, 1H), 2.39 – 2.21 (m, 1H).
117	MS *m/z* 393.1 [M+H]+. 1H NMR (400 MHz, Methanol-d4) δ 7.86 (t, J = 4.1 Hz, 1H), 7.59 (d, J = 2.1 Hz, 1H), 7.54 (d, J = 8.4 Hz, 1H), 7.34 (d, J = 2.4 Hz, 1H), 7.29 (dd, J = 8.5, 2.3 Hz, 1H), 6.61 (d, J = 3.3 Hz, 1H), 6.18 (d, J = 2.1 Hz, 1H), 3.93 (s, 3H). NH not observed.
118	MS *m/z* 370.1 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.81 (d, J = 2.8 Hz, 1H), 6.94 (dd, J = 3.6, 2.8 Hz, 1H), 6.77 (s, 1H), 6.67 (dd, J = 10.8, 2.0 Hz, 1H), 6.42 (d, J = 4.0 Hz, 1H), 4.56 - 4.43 (m, 1H), 3.85 (s, 3H), 2.90 - 2.77 (m, 1H), 2.53 - 2.34 (m, 5H), 2.18 – 2.04 (m, 4H), 1.97 - 1.86 (m, 2H), 1.85 – 1.73 (m, 1H), 1.73 - 1.59 (m, 1H). NH not observed.
119	MS *m/z* 474.1 [M+H]+; 1H NMR (400 MHz, DMSO-d_6) δ 8.00 (d, J = 2.1 Hz, 1H), 7.96 (d, J = 2.6 Hz, 2H), 7.93 (s, 1H), 7.39 (d, J = 7.7 Hz, 1H), 7.01 – 6.94 (m, 1H), 6.51 (d, J = 3.3 Hz, 1H), 4.33 (s, 1H), 3.17 (d, J = 7.6 Hz, 1H), 2.84 (d, J = 10.4 Hz, 1H), 2.39 (q, J = 7.1 Hz, 2H), 2.03 (s, 1H), 1.99 – 1.86 (m, 2H), 1.77 (d, J = 12.9 Hz, 1H), 1.59 (d, J = 12.4 Hz, 1H), 1.45 (dd, J = 17.3, 6.1 Hz, 1H), 1.02 (t, J = 7.1 Hz, 3H).
120	MS *m/z* 490.1 [M+H]+; 1H NMR (400 MHz, DMSO-d_6) δ 8.01 (s, 1H), 7.96 (d, J = 2.3 Hz, 2H), 7.93 (s, 1H), 7.36 (d, J = 7.9 Hz, 1H), 7.01 – 6.95 (m, 1H), 6.51 (d, J = 3.9 Hz, 1H), 4.42 (t, J = 5.4 Hz, 1H), 4.35 (s, 1H), 3.52 (d, J = 5.5 Hz, 2H), 3.17 (s, 1H), 2.81 (s, 1H), 2.45 (d, J = 6.2 Hz, 2H), 2.06 (dd, J = 21.3, 11.1 Hz, 3H), 1.73 (s, 1H), 1.46 (s, 1H), 1.23 (s, 1H).
121	MS *m/z* 461.0 [M+H]+; 1H NMR (400 MHz, DMSO-d_6) δ 8.01 (d, J = 1.9 Hz, 1H), 7.97 – 7.91 (m, 3H), 7.41 (d, J = 7.9 Hz, 1H), 7.00 – 6.94 (m, 1H), 6.49 (d, J = 4.0 Hz, 1H), 4.82 (d, J = 5.1 Hz, 1H), 4.09 (s, 1H), 3.57 (s, 1H), 2.09 (s, 1H), 1.98 (s, 1H), 1.71 (s, 2H), 1.32 (s, 4H).
122	MS *m/z* 461.0 [M+H]+; 1H NMR (400 MHz, DMSO-d_6) δ 7.98 (d, J = 2.0 Hz, 1H), 7.97 – 7.91 (m, 3H), 7.48 (d, J = 7.7 Hz, 1H), 7.02 – 6.92 (m, 1H), 6.50 (d, J = 3.2 Hz, 1H), 4.75 (d, J = 4.5 Hz, 1H), 4.18 (s, 1H), 3.55 (d, J = 4.2 Hz, 1H), 2.29 (d, J = 11.6 Hz, 1H), 2.03 (d, J = 10.6 Hz, 1H), 1.87 (d, J = 13.1 Hz, 1H), 1.77 (d, J = 13.3 Hz, 1H), 1.39 – 1.30 (m, 2H), 1.25 (d, J = 12.8 Hz, 1H), 1.18 – 1.08 (m, 1H).
123	MS *m/z* 447.0 [M+H]+; 1H NMR (400 MHz, DMSO-d_6) δ 8.00 (d, J = 1.8 Hz, 1H), 7.98 – 7.91 (m, 3H), 7.85 (d, J = 6.1 Hz, 1H), 7.00 – 6.96 (m, 1H), 6.50 (d, J = 3.0 Hz, 1H), 5.09 (s, 1H), 4.25 (dd, J = 14.3, 7.1 Hz, 1H), 2.47

	(d, J = 2.7 Hz, 2H), 2.21 (dd, J = 11.3, 8.8 Hz, 2H), 1.34 (s, 3H).
124	MS *m/z* 446.1 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.89 (s, 2H), 7.84 – 7.81 (m, 1H), 7.80 (s, 1H), 7.06 – 6.98 (m, 1H), 6.60 (d, J = 3.9 Hz, 1H), 5.07 (t, J = 9.5 Hz, 1H), 3.55 – 3.45 (m, 2H), 2.79 – 2.69 (m, 1H), 2.40 – 2.28 (m, 1H). NH not observed.
125	MS *m/z* 421.0 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.76 (dd, J = 2.8, 1.0 Hz, 1H), 7.53 (d, J = 8.6 Hz, 1H), 7.09 (dd, J = 8.6, 2.5 Hz, 1H), 7.03 – 6.98 (m, 2H), 6.59 (d, J = 3.6 Hz, 1H), 5.08 (s, 2H), 4.30 (s, 3H), 3.90 (s, 3H). NH not observed.
126	MS *m/z* 473.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.76 (s, 1H), 7.69 (d, J = 8.5 Hz, 1H), 7.58 (d, J = 8.1 Hz, 1H), 7.03 – 6.98 (m, 1H), 6.11 – 6.06 (m, 1H), 5.77 (d, J = 2.5 Hz, 1H), 4.96 (td, J = 9.0, 4.2 Hz, 1H), 4.13 – 4.05 (m, 1H), 3.75 – 3.61 (m, 2H), 2.13 – 1.90 (m, 2H), 1.89 – 1.60 (m, 4H), 1.57 – 1.30 (m, 4H). 2H not observed (NH and OH).
127	MS *m/z* 473.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.75 (s, 1H), 7.69 (d, J = 8.3 Hz, 1H), 7.58 (d, J = 8.1 Hz, 1H), 7.03 – 6.98 (m, 1H), 6.11 – 6.07 (m, 1H), 5.78 (d, J = 2.5 Hz, 1H), 4.47 – 4.37 (m, 1H), 3.77 – 3.56 (m, 3H), 2.41 – 2.29 (m, 1H), 2.20 – 2.09 (m, 1H), 1.85 – 1.66 (m, 4H), 1.67 – 1.43 (m, 4H). 2H not observed (NH and OH).
128	MS *m/z* 473.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.91 – 7.75 (m, 4H), 6.98 (t, J = 3.4 Hz, 1H), 6.53 (d, J = 3.8 Hz, 1H), 4.44 – 4.34 (m, 1H), 4.10 – 3.95 (m, 1H), 3.86 (q, J = 11.0 Hz, 2H), 2.37 (d, J = 13.0 Hz, 1H), 2.21 – 2.10 (m, 1H), 2.07 – 1.57 (m, 8H). 2H not observed (NH and OH).
129	MS *m/z* 473.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.92 – 7.88 (m, 2H), 7.85 – 7.81 (m, 1H), 7.79 – 7.75 (m, 1H), 6.98 (t, J = 3.4 Hz, 1H), 6.53 (d, J = 3.8 Hz, 1H), 4.65 – 4.55 (m, 1H), 4.12 – 4.04 (m, 1H), 3.86 (q, J = 11.0 Hz, 2H), 2.29 – 2.20 (m, 3H), 2.05 – 1.94 (m, 1H), 1.92 – 1.78 (m, 2H), 1.77 – 1.60 (m, 3H), 1.54 – 1.41 (m, 1H). 2H not observed (NH and OH).
130	MS *m/z* 411.2 [M+H]+. 1H NMR (400 MHz, Methanol-d4) δ 7.68 (t, J = 3.7 Hz, 1H), 7.45 (d, J = 8.5 Hz, 1H), 7.33 (d, J = 2.3 Hz, 1H), 7.28 (dd, J = 8.5, 2.4 Hz, 1H), 6.74 (d, J = 3.4 Hz, 1H), 4.23 (quint., J = 8.1 Hz, 1H), 3.93 (s, 3H), 2.73 – 2.55 (m, 2H), 2.32 – 2.18 (m, 2H), 1.43 (s, 3H). 2H not observed (NH and OH).
131	MS *m/z* 436.3 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.59 (s, 1H), 7.55 – 7.52 (m, 1H), 7.09 (dd, J = 8.6, 2.1 Hz, 1H), 7.01 (s, 1H), 6.38 (m, 1H), 4.50-4.44 (m, 1H), 3.91 (s, 3H), 3.01 – 2.87 (m, 1H), 2.60 – 2.41 (m, 5H), 2.33 (s, 3H), 2.17 – 2.06 (m, 1H), 2.02 – 1.89 (m, 1H), 1.88 – 1.75 (m, 1H), 1.74 – 1.57 (m, 1H), 1.28 (m, 1H). NH peak not observed.
132	MS *m/z* 459.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 8.54 – 8.44 (br s, 1H, formate CH), 8.16 (s, 1H), 8.10 (d, J = 7.9 Hz, 1H), 7.81 (d, J = 8.1 Hz, 1H), 7.67 (s, 1H), 6.24 (m, 1H), 4.19 – 4.06 (m, 1H), 3.70 – 3.57 (m, 1H), 2.31 (s, 3H), 2.29 – 2.19 (m, 1H), 2.17 – 2.07 (m, 1H), 1.88 – 1.70 (m, 2H), 1.54 – 1.32 (m, 2H), 1.32 – 1.22 (m, 2H). NH and OH peak not observed.

133	MS *m/z* 437.3 [M+H]+;1H NMR (400 MHz, Methanol-d_4) δ 7.62 (s, 1H), 7.54 (d, J = 8.5 Hz, 1H), 7.09 (dd, J = 8.6, 2.3 Hz, 1H), 7.04 – 6.96 (m, 1H), 6.42 – 6.31 (m, 1H), 4.15 – 4.05 (m, 1H), 3.91 (s, 3H), 3.68 – 3.58 (m, 1H), 2.33 (s, 3H), 2.23 (m, 1H), 2.14 – 2.07 (m, 1H), 1.85 – 1.74 (m, 2H), 1.52 – 1.36 (m, 4H). NH and OH peak not observed.
134	MS *m/z* 488.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 8.60 – 8.49 (br, 1H, formate CH), 8.17 (s, 1H), 8.14 – 8.05 (m, 1H), 7.85 – 7.78 (m, 1H), 7.71 (s, 1H), 6.27 (s, 1H), 4.66 – 4.57 (m, 1H), 4.28 – 4.18 (m, 1H), 2.91 – 2.81 (m, 1H), 2.78 – 2.60 (m, 4H), 2.32 (s, 3H), 2.05 – 1.87 (m, 3H), 1.21-1.15 (m, 3H). NH and OH peak not observed.
135	MS *m/z* 466.2 [M+H]+ ;1H NMR (400 MHz, Methanol-d_4) δ 7.66-7.62 (m, 1H), 7.58 – 7.47 (m, 1H), 7.16 – 7.06 (m, 1H), 7.05 – 6.96 (m, 1H), 6.39-6.36 (m, 1H), 4.66 – 4.55 (m, 1H), 4.29 – 4.18 (m, 1H), 3.91 (s, 3H), 2.97 – 2.86 (m, 2H), 2.86 – 2.72 (m, 4H), 2.34 (s, 3H), 2.00-1.93 (m, 2H), 1.21 (t, J = 7.2 Hz, 3H). NH and OH peak not observed.
136	MS *m/z* 389.3 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ = 7.85 (s, 1H), 7.44 (dd, J = 2.3, 7.7 Hz, 1H), 7.29 - 7.13 (m, 2H), 6.98 - 6.47 (m, 3H), 4.21 - 4.08 (m, 1H), 3.73 - 3.60 (m, 1H), 2.47 (s, 3H), 2.33 - 2.20 (m, 1H), 2.18 - 2.06 (m, 1H), 1.90 - 1.73 (m, 2H), 1.57 - 1.34 (m, 4H); 2H not observed (NH and OH).
137	MS *m/z* 389.3 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.93 - 7.87 (m, 1H), 7.44 (d, J = 7.8 Hz, 1H), 7.27 - 7.16 (m, 2H), 6.98 - 6.56 (m, 2H), 6.55 - 6.48 (m, 1H), 4.36 - 4.22 (m, 2H), 2.48 (s, 3H), 2.07 - 1.80 (m, 4H), 1.79 - 1.63 (m, 2H), 1.58 - 1.44 (m, 2H); 2H not observed (NH and OH).
138	MS *m/z* 421.2 [M+H]+; 1H NMR (500 MHz, Methanol-d_4) δ 7.91 – 7.88 (m, 1H), 7.48 (d, J = 8.4 Hz, 1H), 7.11 (s, 1H), 7.08 (d, J = 8.4 Hz, 1H), 6.98 (t, J = 3.3 Hz, 1H), 6.56 (d, J = 3.8 Hz, 1H), 4.16 – 4.08 (m, 1H), 3.89 (s, 3H), 3.75 – 3.61 (m, 3H), 2.27 – 2.21 (m, 1H), 2.15 – 2.07 (m, 1H), 1.85 – 1.74 (m, 2H), 1.54 – 1.34 (m, 4H). 2H not observed (NH and OH).
139	MS *m/z* 406.2 [M+H]+; 1H NMR (500 MHz, Methanol-d_4) δ 7.81 – 7.78 (m, 1H), 7.47 (d, J = 8.5 Hz, 1H), 7.11 (s, 1H), 7.07 (dd, J = 8.5, 2.2 Hz, 1H), 6.98 (t, J = 3.3 Hz, 1H), 6.55 (d, J = 3.8 Hz, 1H), 5.03 (t, J = 9.5 Hz, 1H), 3.89 (s, 3H), 3.67 (q, J = 11.0 Hz, 2H), 3.53 – 3.44 (m, 2H), 2.77 – 2.71 (m, 1H), 2.37 – 2.29 (m, 1H). 2H not observed (2 NH).
140	MS *m/z* 460.1 [M+H]+; 1H NMR (400 MHz, DMSO-d_6) δ 8.01 (d, J = 2.0 Hz, 1H), 7.98 – 7.93 (m, 2H), 7.92 (s, 1H), 7.37 (d, J = 7.8 Hz, 1H), 6.99 – 6.96 (m, 1H), 6.51 (d, J = 3.3 Hz, 1H), 4.32 (s, 1H), 3.07 (d, J = 7.1 Hz, 1H), 2.75 – 2.67 (m, 1H), 2.22 (s, 3H), 2.02 (d, J = 9.5 Hz, 1H), 1.92 (dd, J = 23.8, 10.7 Hz, 2H), 1.76 (d, J = 12.9 Hz, 1H), 1.60 (d, J = 12.6 Hz, 1H), 1.43 (dd, J = 11.5, 4.1 Hz, 1H).
141	MS *m/z* 447.1 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.91 – 7.86 (m, 2H), 7.86 (dd, J = 2.9, 1.1 Hz, 1H), 7.78 (s, 1H), 7.00 – 6.96 (m, 1H), 6.58 – 6.54 (m, 1H), 4.60 (t, J = 8.1 Hz, 1H), 3.59 (d, J = 6.1 Hz, 2H), 2.63 (ddd, J = 16.6, 7.6, 2.8 Hz, 2H), 2.36 – 2.27 (m, 1H), 1.95 (dt, J = 11.8, 9.3 Hz, 2H). NH and OH not observed.
142	MS *m/z* 483.0 [M+H]+; 1H NMR (400 MHz, DMSO-d_6) δ 9.33 (s, 1H),

	8.15 (dd, J = 2.9, 1.1 Hz, 1H), 7.99 – 7.90 (m, 4H), 7.13 (t, J = 7.8 Hz, 1H), 7.01 (dd, J = 3.9, 2.9 Hz, 1H), 6.89 (dd, J = 9.7, 4.9 Hz, 2H), 6.63 (dd, J = 8.0, 1.6 Hz, 1H), 6.52 (dd, J = 3.9, 1.0 Hz, 1H), 5.49 (p, J = 7.0 Hz, 1H), 1.61 (d, J = 7.0 Hz, 3H).
143	MS *m/z* 424.4 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.76 (s, 1H), 7.29 (d, J = 8.4 Hz, 1H), 7.01 (d, J = 2 Hz, 1H), 6.88 (t, J = 3.2 Hz, 1H), 6.66 (dd, J = 2.4 Hz, J = 8.4 Hz, 1H), 7.04 (d, J = 2.8 Hz, 1H),4.43(s, 1H), 3.87(s, 3H), 3.78 – 3.67 (m, 3H), 3.13 – 3.12 (m, 1H), 2.69(S, 1H), 2.63 – 2.53 (m, 2H), 2.39(S, 2H), 2.02 – 2.00 (m, 1H), 1.85 – 1.83 (m, 1H), 1.74 – 1.67 (m, 2H), 0.74 – 0.69 (m, 2H), 0.59 – 0.55 (m, 2H).
144	MS *m/z* 423.3 [M+H]+; 1H NMR (500 MHz, Methanol-d_4) δ 7.90 (d, J = 1.7 Hz, 1H), 7.47 (d, J = 8.4 Hz, 1H), 7.11 (s, 1H), 7.08 (dd, J = 8.5, 2.4 Hz, 1H), 6.99 (t, J = 3.4 Hz, 1H), 6.57 (d, J = 3.8 Hz, 1H), 4.30 (td, J = 10.7, 3.2 Hz, 1H), 4.03 (dd, J = 11.1, 4.9 Hz, 1H), 3.97 (dd, J = 11.7, 4.1 Hz, 1H), 3.89 (s, 3H), 3.77 (td, J = 9.7, 4.9 Hz, 1H), 3.73 – 3.63 (m, 2H), 3.55 (t, J = 11.1 Hz, 1H), 3.26 (t, J = 11.1 Hz, 1H), 2.26 (dd, J = 13.1, 4.1 Hz, 1H), 1.79 (qd, J = 12.2, 4.6 Hz, 1H). 2H not observed (NH and OH).
145	MS *m/z* 420.4 [M+H]+; 1H NMR (500 MHz, Methanol-d_4) δ 8.76 (brs, 1 H, formic acid), 7.85 (s, 1H), 7.46 (d, J = 8.5 Hz, 1H), 7.12 (s, 1H), 7.08 (dd, J = 8.5, 2.3 Hz, 1H), 6.99 (t, J = 3.2 Hz, 1H), 6.56 (d, J = 3.8 Hz, 1H), 4.58 – 4.51 (m, 1H), 3.89 (s, 3 H), 3.81 – 3.73 (m, 1H), 3.67 (q, J = 11.0 Hz, 2H), 3.44 – 3.34 (m, 1H), 3.11 – 2.95 (m, 2H), 2.87 (s, 3H), 2.30 – 2.11 (m, 2H), 2.01 – 1.80 (m, 2H). 1H not observed (NH).
146	MS *m/z* 472.3 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.92 (s, 1H), 7.85 (d, J = 8.6 Hz, 1H), 7.82 – 7.74 (m, 2H), 7.03 (t, J = 3.3 Hz, 1H), 6.58 (d, J = 3.9 Hz, 1H), 3.91 – 3.74 (m, 2H), 3.72 – 3.63 (m, 2H), 3.61 – 3.51 (m, 1H), 3.46 – 3.34 (m, 1H), 3.08 – 2.89 (m, 2H), 2.84 (s, 3H), 2.53 – 2.37 (m, 1H), 2.11 – 1.97 (m, 2H), 1.91 – 1.73 (m, 1H), 1.51 – 1.33 (m, 1H). 1H not observed (NH).
147	MS *m/z* 472.3 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.92 (s, 1H), 7.85 (d, J = 8.6 Hz, 1H), 7.82 – 7.74 (m, 2H), 7.03 (t, J = 3.3 Hz, 1H), 6.58 (d, J = 3.9 Hz, 1H), 3.91 – 3.74 (m, 2H), 3.72 – 3.63 (m, 2H), 3.61 – 3.51 (m, 1H), 3.46 – 3.34 (m, 1H), 3.08 – 2.89 (m, 2H), 2.84 (s, 3H), 2.53 – 2.37 (m, 1H), 2.11 – 1.97 (m, 2H), 1.91 – 1.73 (m, 1H), 1.51 – 1.33 (m, 1H). 1H not observed (NH).
148	MS *m/z* 461.2 [M+H]+; 1H NMR (400 MHz, Methanol-d4) δ 7.80 (t, J = 3.6 Hz, 1H), 7.44 (d, J = 8.7 Hz, 1H), 7.32 (s, 1H), 7.28 – 7.20 (m, 2H), 7.09 – 7.01 (m, 2H), 6.80 (d, J = 9.0 Hz, 1H), 6.76 (d, J = 3.3 Hz, 1H), 5.48 (d, J = 7.1 Hz, 1H), 3.92 (s, 3H), 3.78 (s, 3H), 1.68 (d, J = 7.0 Hz, 3H). 1H not observed (NH).
149	MS *m/z* 447.2 [M+H]+; 1H NMR (400 MHz, Methanol-d4) δ 7.81 (t, J = 3.6 Hz, 1H), 7.44 (d, J = 8.3 Hz, 1H), 7.32 (s, 1H), 7.26 (d, J = 8.3 Hz, 1H), 7.14 (t, J = 7.8 Hz, 1H), 6.97 – 6.89 (m, 2H), 6.76 (d, J = 3.3 Hz, 1H), 6.66 (d, J = 8.2 Hz, 1H), 5.45 (q, J = 6.7 Hz, 1H), 3.92 (s, 3H), 1.67 (d, J = 7.0 Hz, 3H). NH and OH not observed.
150	MS *m/z* 429.0 [M+H]+; 1H NMR (400 MHz, DMSO-d_6) δ 8.04 – 8.03 (m,

	1H), 7.94 (d, J = 8.0 Hz, 1H), 7.88 (d, J = 8.0 Hz, 1H), 7.80 (s, 1H), 7.61 (d, J = 2.4 Hz, 1H), 6.86 – 6.84 (m, 1H), 6.57 (dd, J = 1.2 3.6 Hz, 1H), 6.21 (s, 1H). NH not observed.
151	MS *m/z* 461.1 [M+H]+; 1H NMR (400 MHz, DMSO-d_6) δ 8.02 – 7.99 (m, 1H), 7.98 – 7.93 (m, 2H), 7.92 (s, 1H), 7.41 (d, J = 7.8 Hz, 1H), 6.97 (dd, J = 3.8, 2.9 Hz, 1H), 6.49 (dd, J = 3.9, 1.0 Hz, 1H), 4.81 (d, J = 5.2 Hz, 1H), 4.19 – 3.98 (m, 1H), 3.65 – 3.48 (m, 1H), 2.17 – 2.05 (m, 1H), 2.03 – 1.94 (m, 1H), 1.80 – 1.64 (m, 2H), 1.42 – 1.23 (m, 4H).
152	MS *m/z* 445.1 [M+H]+; 1H NMR (400 MHz, DMSO-d_6) δ 7.85 (dd, J =2.8, 0.8 Hz, 1H), 7.69 (d, J = 8.4 Hz, 1H), 7.33 (dd, J =8.4, 2.4 Hz, 1H), 7.29 (s, 1H), 7.03 (t, J=73.2 Hz, 1H), 6.98 (t, J=3.6 Hz, 1H), 6.56 (d, J = 3.2 Hz, 1H), 4.39-4.37 (m, 1H), 4.19-4.15 (m, 1H), 3.89-3.86 (m, 1H), 3.52-3.42 (m, 2H), 2.22 (s, 1H),1.86-1.79 (m, 3H). NH not observed.
153	MS *m/z* 459.0 [M+H]+; 1H NMR (400 MHz, DMSO-d_6) δ 7.83 (d, J =2.4 Hz, 1H), 7.70 (d, J = 8.0 Hz, 1H), 7.33 (dd, J =8.4, 3.0 Hz, 1H), 7.29 (s, 1H), 7.03 (t, J=73.2 Hz, 1H), 6.97 (dd, J=4.0, 3.2 Hz, 1H), 6.55 (d, J = 4.0 Hz, 1H), 4.27-4.21 (m, 1H), 3.76-3.71 (m, 1H), 2.43 (d, J =11.6 Hz, 1H), 2.13 (d, J =11.6 Hz, 1H), 1.99 (d, J =12.4 Hz, 1H), 1.91-1.86 (m, 1H), 1.50-1.37 (m, 3H), 1.31-1.259 (m, 1H). NH and OH not observed.
154	MS *m/z* 444.0 [M+H]+; 1H NMR (400 MHz, DMSO-d_6) δ 7.79 (s, 1H), 7.69 (d, J =8.4 Hz, 1H), 7.34-7.29 (m, 2H), 7.04 (t, J=73.2 Hz, 1H), 6.98 (s, 1H), 6.57 (s, 1H), 5.07-5.03 (m, 1H), 3.51-3.46 (m, 2H), 2.73-2.72 (m, 1H), 2.36-2.31 (m, 1H). NH not observed.
155	MS *m/z* 427.0 [M+H]+; 1H NMR (400 MHz, DMSO-d_6) δ 8.01 (s, 1H), 7.73 (d, J = 8.4 Hz, 1H), 7.60 (s, 1H), 7.33 (d, J = 8.8 Hz, 1H), 7.30 (s, 1H), 7.04 (t, J = 73.2 Hz, 1H), 6.83 (m, 1H), 6.54 (d, J = 2.8 Hz, 1H), 6.20 (s, 1H). NH not observed.
156	MS *m/z* 405.3 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.89 (d, J = 2.4 Hz, 1H), 7.44 – 7.37 (m, 2H), 7.33 (d, J = 7.9 Hz, 1H), 6.97 (t, J = 3.3 Hz, 1H), 6.53 (d, J = 3.8 Hz, 1H), 4.18 – 4.07 (m, 1H), 3.74 – 3.58 (m, 3H), 2.45 (s, 3H), 2.30 – 2.20 (m, 1H), 2.17 – 2.06 (m, 1H), 1.86 – 1.74 (m, 2H), 1.53 – 1.34 (m, 4H). 2H not observed (NH and OH).
157	MS *m/z* 390.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.80 (d, J = 2.6 Hz, 1H), 7.44 – 7.37 (m, 2H), 7.33 (d, J = 7.9 Hz, 1H), 6.98 (t, J = 3.1 Hz, 1H), 6.53 (d, J = 3.9 Hz, 1H), 5.04 (t, J = 9.5 Hz, 1H), 3.65 (q, J = 11.1 Hz, 2H), 3.55 – 3.44 (m, 2H), 2.79 – 2.71 (m, 1H), 2.45 (s, 3H), 2.40 – 2.28 (m, 1H). 2 H not observed (2 NH).
158	MS m/z 391.1 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.86 (d, J = 2.5 Hz, 1H), 7.44 – 7.37 (m, 2H), 7.33 (d, J = 7.9 Hz, 1H), 6.97 (t, J = 3.3 Hz, 1H), 6.54 (d, J = 3.8 Hz, 1H), 4.26 (quint, J = 8.0 Hz, 1H), 3.67 (q, J = 11.1 Hz, 2H), 2.70 – 2.62 (m, 2H), 2.45 (s, 3H), 2.32 – 2.23 (m, 2H), 1.44 (s, 3H). 2H not observed (NH and OH).
159	MS *m/z* 404.3 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 8.03 – 7.95 (m, 1H), 7.47 – 7.41 (m, 2H), 7.39 (d, J = 7.9 Hz, 1H), 7.13 – 7.07 (m, 1H), 6.78 – 6.73 (m, 1H), 4.61 – 4.49 (m, 1H), 4.04 – 3.94 (m, 1H), 3.69 – 3.53 (m, 3H), 3.10 – 2.83 (m, 5H), 2.47 (s, 3H), 2.39 – 2.09 (m, 2H), 2.09 – 1.89

	(m, 1H), 1.89 – 1.75 (m, 1H). 1H not observed (NH).
160	MS *m/z* 459.2 [M+H]+;1H NMR (400 MHz, Methanol-d_4) δ 8.20 – 8.13 (m, 1H), 8.13 – 8.06 (m, 1H), 7.87 – 7.78 (m, 1H), 7.72 – 7.62 (m, 1H), 6.24 (s, 1H), 4.18 – 4.06 (m, 1H), 3.72 – 3.58 (m, 1H), 2.31 (s, 3H), 2.29 – 2.18 (m, 1H), 2.15 – 2.06 (m, 1H), 1.86 – 1.71 (m, 3H), 1.54 – 1.32 (m, 3H). NH and OH peak not observed.
161	MS *m/z* 444.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 8.22 – 8.14 (m, 1H), 8.13 – 8.07 (m, 1H), 7.82 (d, J = 8.0 Hz, 1H), 7.59 (s, 1H), 6.27 (m, 1H), 5.13 – 4.97 (m, 1H), 3.57 – 3.43 (m, 1H), 2.85 – 2.67 (m, 2H), 2.40 – 2.21 (m, 4H). NH peaks were not observed.
162	MS *m/z* 422.3 [M+H]+;1H NMR (400 MHz, Methanol-d_4) δ 7.61 – 7.48 (m, 2H), 7.16 – 7.05 (m, 1H), 7.04 – 6.92 (m, 1H), 6.43 – 6.30 (m, 1H), 5.07 – 4.95 (m, 1H), 3.91 (s, 3H), 3.56 – 3.40 (m, 2H), 2.81 – 2.68 (m, 1H), 2.33 (s, 4H), NH peak not observed.
163	MS *m/z* 437.3 [M+H]+; 1H NMR (500 MHz, Methanol-d_4) δ 7.62 (s, 1H), 7.53 (d, J = 8.5 Hz, 1H), 7.08 (d, J = 8.6, 1H), 7.00 (s, 1H), 6.36 (s, 1H), 4.17 – 4.06 (m, 1H), 3.90 (s, 3H), 3.70 – 3.57 (m, 1H), 2.32 (s, 3H), 2.27 – 2.20 (m, 1H), 2.15 – 2.05 (m, 1H), 1.86 – 1.72 (m, 2H), 1.49-1.37 (m, 4H), NH and OH peak not observed.
164	MS *m/z* 461.2 [M+H]+; 1H NMR (500 MHz, Methanol-d_4) δ 8.24 (s, 1H), 8.18 (d, J = 7.9 Hz, 1H), 8.02 (s, 1H), 7.92 (d, J = 8.1 Hz, 1H), 6.66 (m, 1H), 4.22 – 4.12 (m, 1H), 4.07 – 3.97 (m, 2H), 3.80 – 3.72 (m, 1H), 3.59 – 3.50 (m, 1H), 3.29 – 3.22 (m, 1H), 2.36 (s, 3H), 2.22 – 2.11 (m, 1H), 1.97 – 1.83 (m, 1H). NH and OH peak not observed.
165	MS *m/z* 439.2 [M+H]+; 1H NMR (500 MHz, Methanol-d_4) δ 8.00 (s, 1H), 7.68 (d, J = 8.7 Hz, 1H), 7.23 – 7.16 (m, 1H), 7.12 (s, 1H), 6.94 – 6.85 (m, 1H), 4.27 – 4.16 (m, 1H), 4.09 – 4.02 (m, 1H), 3.95 (s, 3H), 3.81 – 3.72 (m, 1H), 3.57 – 3.48 (m, 1H), 3.27 – 3.19 (m, 2H), 2.40 (s, 3H), 2.22 – 2.16 (m, 1H), 1.90 – 1.77 (m, 1H). NH and OH Peak not observed.
166	MS *m/z* 418.3 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.81 (d, J = 2.3 Hz, 1H), 7.48 (d, J = 8.5 Hz, 1H), 7.01 - 6.57 (m, 4H), 6.57 - 6.51 (m, 1H), 4.57 - 4.40 (m, 1H), 3.90 (s, 3H), 3.29 - 3.17 (m, 1H), 2.86 - 2.73 (m, 1H), 2.61 - 2.47 (m, 2H), 2.35 - 2.20 (m, 2H), 2.18 - 2.07 (m, 1H), 1.94 - 1.57 (m, 3H), 1.16 (t, J = 7.2 Hz, 3H). NH not observed
167	MS *m/z* 407.3 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.90 - 7.81 (m, 1H), 7.49 (d, J = 8.5 Hz, 1H), 7.03 - 6.58 (m, 4H), 6.58 - 6.53 (m, 1H), 4.41 - 4.25 (m, 1H), 4.09 - 3.95 (m, 2H), 3.91 (s, 3H), 3.86 - 3.69 (m, 1H), 3.57 (t, J = 11.8 Hz, 1H), 3.31 - 3.22 (m, 1H), 2.33 - 2.22 (m, 1H), 1.88 - 1.71 (m, 1H); 2H (OH and NH) not observed
168	MS *m/z* 459.1 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.87 (dd, J= 2. 8, 0.8 Hz, 1H), 7.69 (d, J= 8.4 Hz, 1H), 7.33 (dd, J= 8.4, 2.0 Hz, 1H), 7.29 (s, 1H), 7.03 (t, J= 73.2, 1H), 6.98 – 6.96 (m, 1H), 6.54 (d, J= 3.2 Hz, 1H), 4.17 – 4.13 (m, 1H), 3.67 – 3.62 (m, 1H), 2.27 – 2.21(m, 1H), 2.14 – 2.01 (m, 1H), 1.83 – 1.77 (m, 2H), 1.48 – 1.40 (m, 4H). 2H not observed (NH and OH).
169	MS *m/z* 438.1 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.82 (d, J =

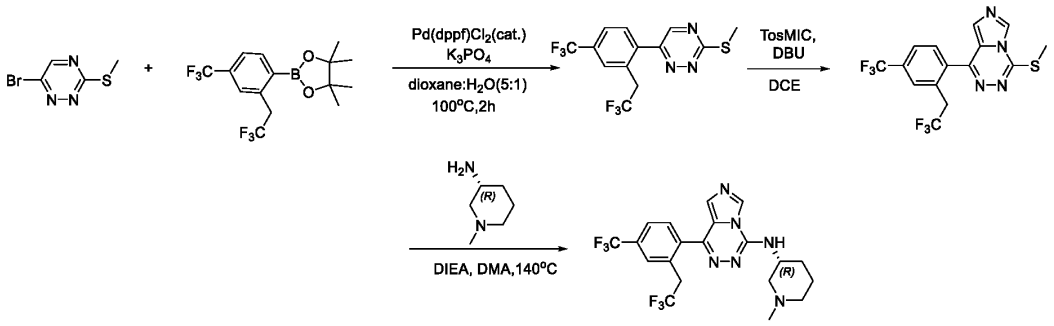
	2.8 Hz, 1H), 7.69 (d, J = 8.0 Hz, 1H), 7.62 – 7.56 (m, 2H), 6.95 (t, J = 3.2 Hz, 1H), 6.52 (d, J = 4.0 Hz, 1H), 5.80 (s, 1H), 5.67 (s, 1H), 4.53 – 4.43 (m, 1H), 3.26 – 3.18 (m, 1H), 2.84 – 2.75 (m, 1H), 2.60 – 2.45 (m, 2H), 2.33 – 2.19 (m, 2H), 2.16 – 2.06 (m, 1H), 1.91 - 1.82 (m, 1H), 1.81 – 1.70 (m, 1H), 1.69 – 1.59 (m, 1H), 1.15 (t, J = 7.2 Hz, 3H). 1H not observed (NH).
170	MS *m/z* 474.1 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.91 (dd, J = 3.2, 1.2 Hz, 1H), 7.68 (d, J = 8.4 Hz, 1H), 7.33 (dd, J = 8.8, 2.4 Hz, 1H), 7.29 (s, 1H), 7.03 (t, J = 73.2, 1H), 6.99 – 6.98 (m, 1H), 6.56 (dd, J = 4.0, 0.8 Hz, 1H), 4.65 - 4.56 (m, 1H), 4.27-4.17 (m, 1H), 2.91 - 2.71 (m, 2H), 2.67 - 2.50 (m, 2H), 2.38 (s, 3H), 1.93 – 1.90 (m, 2H). 2H not observed (NH and OH).
171	MS *m/z* 488.1 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.91 (dd, J = 3.2, 1.2 Hz, 1H), 7.69 (d, J = 8.4 Hz, 1H), 7.34 (dd, J = 8.4, 2.4 Hz, 1H), 7.30 (s, 1H), 7.03 (t, J = 73.2, 1H), 7.00 (t, J = 3.2, 1H), 6.58 (dd, J = 4.0 1.2 Hz, 1H), 4.66 - 4.63 (m, 1H), 4.28 - 4.26 (m, 1H), 3.13 - 3.05 (m, 1H), 2.95 - 2.88 (m, 1H), 2.81 - 2.74 (m, 4H), 2.00 - 1.97 (m, 2H), 1.23 (t, J = 7.2, 3H). 2H not observed (NH and OH).
172	MS *m/z* 481.1 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.97 (dd, J = 3.2, 1.2 Hz, 1H), 7.66 (d, J = 7.6 Hz, 1H), 7.31 (dd, J = 8.8, 2.4 Hz, 1H), 7.27 (s, 1H), 7.14 (t, J = 8.0 Hz, 1H), 7.02 (t, J = 73.2 Hz, 1H), 6.99 – 6.98 (m, 1H), 6.95 (d, J = 7.6 Hz, 1H), 6.92-6.91 (m, 1H), 6.65 (dd, J = 7.2, 1.6 Hz, 1H), 6.55 (dd, J = 4.0, 1.2 Hz, 1H), 5.51 - 5.46 (m, 1H), 1.68 (d, J = 6.8 Hz, 3H). 2H not observed (NH and OH).
173	MS *m/z* 454.1 [M+H]+; 1H NMR (400 MHz, DMSO-d_6) δ 7.95 (s, 1H), 7.71 (d, J = 8.0 Hz, 1H), 7.64 - 7.62 (m, 2H), 7.25 (d, J = 8.0 Hz, 1H), 6.95 – 6.91 (m, 1H), 6.41 (d, J = 4.0 Hz, 1H), 5.98 (s, 1H), 5.84 (s, 1H), 4.41 - 4.30 (m, 2H), 3.55 - 3.49 (m, 2H), 3.17 - 3.15 (m, 1H), 2.84 - 3.81 (m, 1H), 2.47 – 2.44 (m, 2H), 2.10 – 2.00 (m, 3H), 1.78 -1.69 (m, 1H), 1.60 - 1.57 (m, 1H), 1.47 - 1.44 (m, 1H).
174	MS *m/z* 390.3 [M+H]+; 1H NMR (500 MHz, Methanol-d_4) δ 7.77 (s, 1H), 7.49 (d, J = 8.5 Hz, 1H), 7.01 - 6.94 (m, 2H), 6.94 - 6.61 (m, 2H), 6.61 - 6.52 (m, 1H), 5.12 - 5.00 (m, 1H), 3.91 (s, 3H), 3.56 - 3.44 (m, 2H), 2.81 - 2.69 (m, 1H), 2.40 - 2.28 (m, 1H) ; 2H (NH) not observed
175	MS *m/z* 434.4 [M+H]+; 1H NMR (500 MHz, Methanol-d_4) δ 7.87 (s, 1H), 7.48 (d, J = 8.4 Hz, 1H), 7.03 - 6.60 (m, 4H), 6.58 - 6.53 (m, 1H), 4.72 - 4.52 (m, 1H), 4.33 - 4.15 (m, 1H), 3.91 (s, 3H), 3.00 - 2.42 (m, 6H), 2.05 - 1.82 (m, 2H), 1.17 (t, J = 7.2 Hz, 3H); 2H (NH and OH) not observed.
176	MS *m/z* 419.4 [M+H]+; 1H NMR (500 MHz, Methanol-d_4) δ 7.83 - 7.78 (m, 1H), 7.49 (d, J = 8.4 Hz, 1H), 7.00 - 6.61 (m, 4H), 6.52 (d, J = 3.7 Hz, 1H), 4.28 - 4.17 (m, 1H), 3.91 (s, 3H), 3.50 - 3.43 (m, 2H), 2.34 - 2.18 (m, 2H), 1.98 - 1.80 (m, 2H), 1.79 - 1.67 (m, 1H), 1.62 - 1.35 (m, 2H), 1.23 - 1.10 (m, 1H), 1.07 - 0.94 (m, 1H); 2H (NH and OH) not observed.
177	MS *m/z* 405.4 [M+H]+; 1H NMR (500 MHz, Methanol-d_4) δ 7.87 - 7.82 (m, 1H), 7.48 (d, J = 8.5 Hz, 1H), 7.00 - 6.93 (m, 2H), 6.93 - 6.61 (m, 2H), 6.57 - 6.50 (m, 1H), 4.20 - 4.09 (m, 1H), 3.91 (s, 3H), 3.72 - 3.60 (m, 1H), 2.36 - 2.19 (m, 1H), 2.18 - 2.06 (m, 1H), 1.90 - 1.71 (m, 2H), 1.53 - 1.38 (m, 4H);

	2H (NH and OH) not observed.
178	MS *m/z* 446.2 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.80 – 7.77 (m, 1H), 7.72 (s, 1H), 7.57 (d, J= 8.0 Hz, 1H), 7.41 (d, J= 8.4 Hz, 1H), 6.95 – 6.90 (m, 1H), 6.43 (d, J= 3.6 Hz, 1H), 4.48 (s, 1H), 3.93 –3.84 (m, 1H), 3.28 – 3.17 (m, 1H), 2.78 – 2.81(m, 1H),2.53 – 2.55 (m, 2H), 2.26–2.28 (m, 2H), 2.08 –2.10 (m, 1H), 1.84–1.86 (m, 1H), 1.76–1.78 (m, 1H), 1.59–1.61 (m, 1H), 1.16 (t, J= 7. 2Hz, 3H), 0.76–0.83 (m, 2H), 0.61–0.63 (m, 2H). 1H not observed (NH).
179	MS *m/z* 462.1 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.82 (dd, J= 2.8, 1.2 Hz, 1H), 7.72 (s, 1H), 7.57 (d, J= 8.0 Hz, 1H), 7.41 (d, J= 8.0 Hz, 1H), 6.95 –6.90 (m, 1H), 6.43 (dd, J= 4.0, 1.2Hz, 1H), 4.47 (s, 1H), 3.93 – 3.84 (m, 1H), 3.70 –3.74(m, 2H), 3.19 –3.21(m, 1H), 2.73 –2.75 (m, 1H), 2.61 –2.65(m, 2H), 2.42 –2.44 (m, 2H), 2.03 –2.05 (m, 1H), 1.86 –1.91(m, 1H), 1.72 –1.77(m, 2H), 0.76 –0.81(m, 2H),0.61 –0.64(m, 2H). 2H not observed (NH and OH).
180	MS *m/z* 437.1 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.95 (dd, J = 1.2, 2.8 Hz, 1H), 7.54 (d, J = 8.4 Hz, 1H), 7.09 (dd, J = 2.4, 8.8 Hz, 1H), 6.97 – 7.01 (m, 2H), 6.56 (d, J = 3.2, 1H), 4.37 (dd, J = 4.0, 16.0 Hz,1H), 3.91 (s, 3H), 2.00 – 2.03 (m, 1H), 1.82 – 1.88 (m,2H), 1.62 – 1.74 (m, 3H), 1.44 – 1.50 (m, 2H), 1.28 (s, 3H). 2H not observed (NH and OH).
181	MS *m/z* 437.1 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 7.95 (d, J = 1.6 Hz, 1H), 7.55 (d, J= 8.4 Hz, 1H), 7.09 (dd, J = 2.4, 8.8 Hz, 1H), 6.97 – 7.01 (m, 2H), 6.56 (d, J = 3.6, 1H), 4.37 (dd, J = 4.0, 11.6 Hz, 1H), 3.91 (s, 3H),2.00 – 2.03 (m, 1H), 1.81 – 1.88 (m, 2H), 1.62 – 1.71 (m, 3H),1.40 – 1.55 (m, 2H), 1.28 (s, 3H). 2H not observed (NH and OH).
182	MS *m/z* 408.2 [M+H]+; 1H NMR (400 MHz, DMSO-d_6) δ 7.85 (s, 1H), 7.27 (dd, J = 3.6 Hz, J = 8.4 Hz, 1H), 7.07 (d, J = 5.2 Hz, 1H), 6.98 (s, 1H), 6.86 (d, J = 2.8 Hz, 1H), 6.87 (t, J = 2.4 Hz, 1H), 6.27 (s, 1H), 3.94(s, 1H), 3.81(dd, J = 2.4 Hz, J = 24.4 Hz, 1H), 3.18 – 3.15 (m, 1H), 2.83-2.71 (s, 1H), 2.50(m, 1H), 2.39 – 2.37 (m, 2H), 2.04 – 1.99 (m, 1H), 1.92 –1.86 (m, 2H), 1.77 – 1.74 (m, 1H), 1.91 – 1.53 (m, 1H), 1.47 – 1.38 (m, 1H), 1.07 – 1.00 (m, 3H), 0.73(m, 1H), 0.52(m, 1H). 1H not observed (NH).

Example 2

Preparation of Compound 2

(R)-N-(1-methylpiperidin-3-yl)-1-(2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl)imidazo[1,5-d][1,2,4]triazin-4-amine



Step 1. 3-(Methylthio)-6-(2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl)-1,2,4-triazine

To a solution of 4,4,5,5-tetramethyl-2-(2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl)-1,3,2-dioxaborolane (Intermediate 2b, 2 g, 5.7 mmol, 1.0 eq.) in 1,4-dioxane/H_2O (5:1, 24 mL) was added 6-bromo-3-(methylthio)-1,2,4-triazine (1.1 g, 5.1 mmol, 1 eq.), $Pd(dppf)Cl_2$ (372.6 mg, 0.1 eq.) and K_3PO_4 (2.16 g, 2 eq.) under N_2 atmosphere at rt. The reaction mixture was stirred for 2 h at 90 °C under N_2, then diluted with water (20 mL) and extracted with EtOAc (50 mL x 3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel (PE: EA = 0% ~ 10%) to afford 3-(methylthio)-6-(2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl)-1,2,4-triazine (1.6 g, 81.1% yield) as yellow oil. ^1H NMR (400 MHz, DMSO-d_6) δ 8.95 (s, 1H), 8.03 – 7.97 (m, 2H), 7.89 (d, J = 8.0 Hz, 1H), 4.10 (q, J = 11.2 Hz, 2H), 2.70 (s, 3H).

Step 2. 4-(Methylthio)-1-(2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl)imidazo[1,5-d][1,2,4]triazine

To a solution of TosMIC (1.1 g, 5.4 mmol, 1.2 eq.) and DBU (827.4 mg, 5.4 mmol, 1.2 eq.) in DCE (20 mL) was added 3-(methylthio)-6-(2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl)-1,2,4-triazine (1.6 g, 4.5 mmol, 1.0 eq.) under N_2 at rt. The reaction mixture was stirred for 2 h at rt, then diluted with water (50 mL) and extracted with EtOAc (50 mL x 3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel (PE: EA = 0% ~ 25%) to afford title product (1.29 g, 44.9% yield) as yellow oil. MS *m/z* 392.9 $[M+1]^+$; ^1H NMR (400 MHz, DMSO-d_6) δ 8.84 (s, 1H), 8.04 (s, 1H), 7.95 (dd, J = 19.0, 8.2 Hz, 2H), 7.71 (s, 1H), 4.13 – 4.04 (m, 2H), 2.89 (s, 3H).

Step 3. (R)-N-(1-methylpiperidin-3-yl)-1-(2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl) phenyl)imidazo[1,5-d][1,2,4]triazin-4-amine

To a solution of 4-(methylthio)-1-(2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl)-imidazo[1,5-d][1,2,4]triazine (100 mg, 0.25 mmol, 1.0 eq.) in DMA (1 mL) was slowly added (R)-1-methylpiperidin-3-amine dihydrochloride (119 mg, 0.64 mmol, 2.5 eq.) and DIEA (329.4 mg, 10.0 eq.) under N_2 at rt. The reaction mixture was stirred for 12 h at 140 °C under N_2, then filtered and concentrated under reduced pressure. The crude product was purified by reverse phase chromatography (0.1% formic acid in MeCN:0.1% formic acid in H_2O, 5 to 100%) to give title product (16.4 mg, 13.8% yield) as a pale-yellow solid as a formic acid salt. MS *m/z* 459.0 $[M+1]^+$; ^1H NMR (400 MHz, Methanol-d_4) δ 8.77 (s, 1H), 8.49 (s, 1H), 7.92 (s, 1H), 7.85 (dd, J = 19.2, 8.2 Hz, 2H), 7.50 (s, 1H), 4.63 – 4.36 (m, 1H), 3.92 (q, J = 10.9 Hz, 2H), 3.64 – 3.47 (m, 1H), 3.29 – 3.08 (m, 2H), 3.02 – 2.79 (m, 2H), 2.72 – 2.57 (m, 1H), 2.31 – 1.70 (m, 4H), 1.28 (t, J = 6.8 Hz, 3H).

The compounds below were prepared according to the procedure of Example 2 by substituting the appropriate starting materials, reagents and reaction conditions.

Compound#	Spectral Data
183	MS *m/z* 376.3 $[M+1]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.53-8.79 (m, 1H), 7.32-7.47 (m, 2H), 7.07-7.19 (m, 2H), 6.46-6.92 (m, 1H), 4.47 (quin, J=8.2 Hz, 1H), 3.41-3.52 (m, 2H), 2.46-2.64 (m, 2H), 2.37 (s, 3H), 2.15-2.28 (m, 1H), 1.77-1.99 (m, 2H). NH and OH not observed.
184	MS *m/z* 419.3 $[M+1]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.64 (s, 1H), 8.33 (s, 1H), 7.33-7.43 (m, 2H), 7.07-7.21 (m, 2H), 6.37-6.97 (m, 1H), 4.40-4.55 (m, 1H), 3.69-3.77 (m, 2H), 3.39-3.60 (m, 1H), 3.07-3.17 (m, 1H), 2.85-2.97 (m, 2H), 2.66-2.87 (m, 2H), 2.37 (s, 3H), 1.89-2.26 (m, 2H), 1.60-1.86 (m, 2H). NH and OH not observed.
185	MS *m/z* 445.4 $[M+1]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.64 (s, 1H), 8.37 (s, 1H), 7.28-7.49 (m, 2H), 6.93-7.13 (m, 2H), 6.51-6.92 (m, 1H), 4.21-4.52 (m, 1H), 3.60-3.79 (m, 2H), 3.29-3.44 (m, 1H), 2.90-3.09 (m, 1H), 2.73-2.89 (m, 2H), 2.47-2.69 (m, 2H), 1.83-2.13 (m, 3H), 1.58-1.82 (m, 2H), 0.93-1.13 (m, 2H), 0.60-0.83 (m, 2H). NH and OH not observed.
186	MS *m/z* 473.2 $[M+1]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.77 (s, 1H), 8.38 (s, 1H), 7.85 (d, J = 8.0 Hz, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.68 (s, 1H), 7.54 (s, 1H), 6.88 (d, J = 73.0 Hz, 1H), 4.64 – 4.49 (m, 1H), 3.94 – 3.80 (m, 2H), 3.69 – 3.58 (m, 1H), 3.27 – 3.21 (m, 1H), 3.08 (dd, J = 25.6, 13.8 Hz, 2H), 2.93 – 2.78 (m, 2H), 2.20 – 2.05 (m, 2H), 1.88 (ddd, J = 28.1, 14.1, 8.1 Hz, 2H). NH and OH not observed.
187	MS *m/z* 430.2 $[M+1]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.82 (s, 1H), 7.86 (d, J = 8.1 Hz, 1H), 7.75 (d, J = 8.3 Hz, 1H), 7.69 (s, 1H), 7.60 (s, 1H), 6.98 (t, J = 72.9 Hz, 1H), 4.36 – 4.18 (m, 1H), 2.67 (td, J = 9.6, 6.0 Hz, 2H), 2.36 –

	2.27 (m, 2H), 1.44 (s, 3H). NH and OH not observed
188	MS *m/z* 430.5 $[M+1]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.83 (s, 1H), 7.86 (d, J = 8.0 Hz, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.68 (s, 1H), 7.58 (s, 1H), 6.97 (t, J = 72.9 Hz, 1H), 4.34 (s, 1H), 4.16 (d, J = 10.6 Hz, 1H), 3.90 – 3.85 (m, 1H), 3.57 – 3.46 (m, 2H), 2.24 (s, 1H), 1.84 (dt, J = 21.1, 9.3 Hz, 3H). NH not observed
189	MS *m/z* 396.1, 398.1 $[M+1]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.91 (s, 1H), 7.72 – 7.64 (m, 2H), 7.48 (d, J = 12.3 Hz, 2H), 6.94 (t, J = 72.9 Hz, 1H), 4.34 – 4.26 (m, 1H), 4.18 – 4.12 (m, 1H), 3.91 – 3.84 (m, 1H), 3.58 – 3.48 (m, 2H), 2.33 – 2.18 (m, 1H), 1.94 – 1.83 (m, 2H), 1.83 – 1.75 (m, 1H). NH not observed
190	MS m/z 409.1, 411.1 $[M+1]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.75 (s, 1H), 8.45 (br s, 1H), 7.62 (d, J = 8.8 Hz, 1H), 7.51 (br s, 1H), 7.48 - 7.43 (m, 2H), 6.91 (t, J = 72.8 Hz, 1H), 4.61 – 4.36 (m, 1H), 3.59 – 3.44 (m, 1H), 3.28 – 3.06 (m, 2H), 2.94 – 2.78 (m, 1H), 2.72 (s, 3H), 2.26 – 2.00 (m, 2H), 1.94 – 1.69 (m, 2H). NH not observed
191	MS *m/z* 423.1, 425.1 $[M+1]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.75 (s, 1H), 8.45 (s, 1H), 7.62 (d, J = 8.7 Hz, 1H), 7.51 (s, 1H), 7.45 (s, 2H), 7.00 (d, J = 73.2 Hz, 1H), 4.55 – 4.44 (m, 1H), 3.80 – 3.64 (m, 1H), 3.42 – 3.33 (m, 1H), 3.12 (dd, J = 14.1, 7.1 Hz, 2H), 3.02 – 2.81 (m, 2H), 2.23 – 2.10 (m, 2H), 1.96 – 1.83 (m, 2H), 1.34 (t, J = 7.3 Hz, 3H). NH not observed
192	MS *m/z* 439.1, 441.1 $[M+1]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.77 (s, 1H), 8.43 (s, 1H), 7.62 (d, J = 8.8 Hz, 1H), 7.51 (s, 1H), 7.48 - 7.42 (m, 2H), 6.91 (t, J = 73.2 Hz, 1H), 4.62 – 4.47 (m, 1H), 3.85 (t, J = 5.2 Hz, 2H), 3.66 – 3.58 (m, 1H), 3.28 – 3.21 (m, 1H), 3.10 – 3.04 (m, 2H), 2.99 - 2.80 (m, 2H), 2.19 – 2.07 (m, 2H), 1.98 – 1.77 (m, 2H). NH and OH not observed
193	MS m/z 427.2, 429.2 $[M+1]^+$. 1H NMR (400 MHz, Methanol-d_4) δ 8.71 (s, 1H), 8.23 (s, 0.79H), 7.62 (d, J = 8.8 Hz, 1H), 7.52 (s, 1H), 7.48 - 7.40 (m, 2H), 6.90 (t, J = 73.2 Hz, 1H), 5.11 (d, J = 46.5 Hz, 1H), 4.80 – 4.73 (m, 1H), 3.50 (d, J = 11.6 Hz, 1H), 3.29 – 3.19 (m, 1H), 2.83 – 2.71 (m, 1H), 2.60 (s, 3H), 2.57 – 2.47 (m, 2H), 2.05 – 1.90 (m, 1H). NH not observed.
194	MS *m/z* 396.0; 398.0 $[M+1]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.72 (s, 1H), 7.67 – 7.59 (m, 1H), 7.47 (d, J = 21.8 Hz, 3H), 6.88 (t, J = 73.3 Hz, 1H), 4.32 – 4.19 (m, 1H), 2.69 – 2.63 (m, 2H), 2.32 – 2.23 (m, 2H), 1.44 (s, 3H). NH and OH not observed
195	MS *m/z* 453.1, 455.1 $[M+1]^+$. ^{1}HNMR (400 MHz, DMSO-d_6) δ 8.85 (s, 1H), 7.77 (d, J = 8.4 Hz, 1H), 7.67 – 7.60 (m, 2H), 7.59 – 7.54 (m, 1H), 7.47 (s, 1H), 7.32 (t, J = 73.6, 1H), 4.42 – 4.20 (m, 1H), 3.18 – 2.99 (m, 1H), 2.82 – 2.67 (m, 1H), 2.25 (s, 3H), 2.10 – 1.93 (m, 3H), 1.82 – 1.75 (m, 1H), 1.66 – 1.55 (m, 1H), 1.49 – 1.39 (m, 1H).
196	MS *m/z* 485.1, 487.1 [M+H]+; 1H NMR (400 MHz, DMSO-d_6) δ 8.80 (s, 1H), 7.80 (d, J = 7.4 Hz, 1H), 7.65 – 7.55 (m, 3H), 7.48 (s, 1H), 7.32 (t, J = 73.6 Hz, 1H), 5.02 (d, J = 47.1 Hz, 1H), 4.59 (s, 1H), 3.18 (d, J = 12.0 Hz, 1H), 3.02 (t, J = 12.0 Hz, 1H), 2.48 – 2.42 (m, 2H), 2.36 – 2.16 (m, 2H), 2.13 – 2.00 (m, 1H), 1.90 – 1.68 (m, 1H), 1.02 (t, J = 7.1 Hz, 3H).
197	MS *m/z* 461.1 $[M+1]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.79 (s, 1H), 7.96

	(d, J = 8.1 Hz, 1H), 7.90 (d, J = 8.1 Hz, 1H), 7.83 (s, 1H), 7.55 (s, 1H), 4.46 (s, 1H), 3.21 – 3.04 (m, 1H), 2.82 – 2.66 (m, 1H), 2.35 (s, 3H), 2.33 – 2.17 (m, 2H), 2.16 – 2.06 (m, 1H), 1.95 – 1.83 (m, 1H), 1.82 – 1.71 (m, 1H), 1.68 – 1.56 (m, 1H). NH not observed.
198	MS *m/z* 483.2, 485.2 $[M+1]^+$. ^{1}HNMR (400 MHz, DMSO-d_6) δ 8.83 (s, 1H), 7.71 (d, J = 7.5 Hz, 1H), 7.64 – 7.55 (m, 3H), 7.47 (s, 1H), 7.32 (t, J = 73.6 Hz, 1H), 4.40 (t, J = 5.2 Hz, 1H), 4.28 (s, 1H), 3.52 (q, J = 5.9 Hz, 2H), 3.16 (d, J = 6.7 Hz, 1H), 2.82 (d, J = 10.3 Hz, 1H), 2.45 (t, J = 6.2 Hz, 2H), 2.10 – 1.99 (m, 3H), 1.80 – 1.71 (m, 1H), 1.63 – 1.53 (m, 1H), 1.51 – 1.36 (m, 1H).
199	MS *m/z* 440.1, 442.1 $[M+1]^+$. ^{1}HNMR (400 MHz, DMSO-d_6) δ 8.80 (s, 1H), 8.19 (d, J = 6.0 Hz, 1H), 7.70 – 7.53 (m, 3H), 7.46 (s, 1H), 7.31 (t, J = 73.6 Hz, 1H), 5.11 (s, 1H), 4.34 – 4.12 (m, 1H), 2.49 – 2.45 (m, 2H), 2.26 – 2.10 (m, 2H), 1.33 (s, 3H).
200	MS *m/z* 455.1, 457.1 $[M+1]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.77 (s, 1H), 8.08 (d, J = 1.6 Hz, 1H), 7.98 (dd, J = 2.0 Hz, J = 8.4 Hz, 1H), 7.57 (d, J = 8.4 Hz, 1H), 7.37 (s, 1H), 4.45 – 4.44 (m, 1H), 3.24 – 3.22 (m, 1H), 2.88 – 2.82 (m, 1H), 2.44 (s, 3H), 2.39 – 2.38 (m, 2H), 2.11 – 2.09 (m, 1H), 1.95 – 1.92 (m, 1H), 1.81 – 1.76 (m, 1H), 1.67 – 1.64 (m, 1H). NH not observed.
201	MS *m/z* 485.2, 487.2 $[M+1]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.81 (s, 1H), 8.08 (d, J = 1.6 Hz, 1H), 7.98 (d, J = 8.0 Hz, 1H), 7.57 (d, J = 8.0 Hz, 1H), 7.38 (s, 1H), 4.48 – 4.44 (m, 1H), 3.82 – 3.69 (m, 2H), 3.28 – 3.20 (m, 1H), 2.92 – 2.82 (m, 1H), 2.82 – 2.66 (m, 2H), 2.64 – 2.47 (m, 2H), 2.07 – 2.02 (m, 1H), 1.98 – 1.89 (m, 1H), 1.83 – 1.70 (m, 2H). NH and OH not observed.
202	MS *m/z* 389.2 $[M+1]^+$. ^{1}HNMR (400 MHz, DMSO-d_6) δ 8.82 (s, 1H), 7.67 (d, J = 7.8 Hz, 1H), 7.49 (d, J = 7.7 Hz, 1H), 7.41 (s, 1H), 7.22 (d, J = 8.1 Hz, 1H), 7.20 (s, 1H), 7.19 (t, J = 73.6 Hz, 1H), 4.27 (s, 1H), 3.06 (d, J = 10.3 Hz, 1H), 2.69 (d, J = 12.0 Hz, 1H), 2.43 (s, 3H), 2.22 (s, 3H), 2.06 – 1.89 (m, 3H), 1.84 – 1.73 (m, 1H), 1.68 – 1.53 (m, 1H), 1.50 – 1.34 (m, 1H).
203	MS *m/z* 415.3 $[M+1]^+$. ^{1}HNMR (400 MHz, DMSO-d_6) δ 8.82 (s, 1H), 7.67 (d, J = 7.8 Hz, 1H), 7.47 (d, J = 7.9 Hz, 1H), 7.41 (s, 1H), 7.21 (t, J = 73.6 Hz, 1H), 7.09 (d, J = 8.0 Hz, 1H), 7.06 (s, 1H), 4.28 (s, 1H), 3.11 – 3.00 (m, 1H), 2.75 – 2.63 (m, 1H), 2.22 (s, 3H), 2.10 – 1.89 (m, 4H), 1.82 – 1.72 (m, 1H), 1.65 – 1.53 (m, 1H), 1.49 – 1.35 (m, 1H), 1.09 – 1.00 (m, 2H), 0.84 – 0.76 (m, 2H).
204	MS *m/z* 442.2, 444.2 $[M+1]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.75 (s, 1H), 8.08 (d, J = 1.6 Hz, 1H), 7.97 (d, J = 1.6 Hz, J = 8.4 Hz, 1H), 7.57 (d, J = 8.4 Hz, 1H), 7.37 (s, 1H), 4.31 – 4.23 (m, 1H), 2.68 – 2.62 (m, 2H), 2.30 – 2.25 (m, 2H), 1.44 (s, 3H). NH and OH not observed.
205	MS *m/z* 487.1, 489.1 $[M+1]^+$. 1H NMR (400 MHz, Methanol-d_4) δ 8.65 (s, 1H), 7.98 (d, J = 1.6 Hz, 1H), 7.88 (d, J = 1.6 Hz, J = 8.0 Hz, 1H), 7.47 (d, J = 8.4 Hz, 1H), 7.28 (s, 1H), 4.97 – 4.95 (m, 1H), 4.69 – 4.63 (m, 1H), 3.03 – 2.97 (m, 1H), 2.51 – 2.46 (m, 2H), 2.37 – 2.14 (m, 4H), 1.89 – 1.73 (m, 1H), 1.04 (t, J = 7.2 Hz, 3H). NH and OH not observed.
206	MS *m/z* 391.1 $[M+1]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.75 (s, 1H), 7.72 (s, 1H), 7.60 (d, J = 8.0 Hz, 1H), 7.49 (d, J = 7.6 Hz, 1H), 7.30 (s, 1H), 4.62 – 4.37 (m, 1H), 3.20 – 3.08 (m, 1H), 2.78 – 2.68 (m, 1H), 2.53 (s, 3H), 2.35 (s, 3H), 2.32 – 2.18 (m, 2H), 2.14 – 2.04 (m, 1H), 1.94 – 1.84 (m, 1H), 1.82 – 1.68

	(m, 1H), 1.66 – 1.55 (m, 1H). NH not observed
207	MS *m/z* 417.3 $[M+1]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.74 (s, 1H), 7.59 (s, 1H), 7.49 – 7.43 (m, 2H), 7.30 (s, 1H), 4.48 – 4.40 (m, 1H), 3.17 – 3.13 (m, 1H), 2.78 – 2.68 (m, 1H), 2.36 (s, 3H), 2.32 – 2.20 (m, 2H), 2.14 – 2.06 (m, 2H), 1.94 – 1.84 (m, 1H), 1.82 – 1.70 (m, 1H), 1.70 – 1.54 (m, 1H), 1.18 – 1.04 (m, 2H), 0.88 – 0.78 (m, 2H). NH not observed
208	MS *m/z* 423.1 $[M+1]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.75 (s, 1H), 7.63 (d, J = 8.8 Hz, 1H), 7.48 (s, 1H), 7.13 (dd, J = 8.8, 2.4 Hz, 1H), 7.04 (s, 1H), 4.49 – 4.36 (m, 1H), 3.92 (s, 3H), 3.19 – 3.08 (m, 1H), 2.79 – 2.64 (m, 1H), 2.34 (s, 3H), 2.32 – 2.20 (m, 2H), 2.15 – 2.05 (m, 1H), 1.94 – 1.82 (m, 1H), 1.82 – 1.68 (m, 1H), 1.68 – 1.51 (m, 1H). NH not observed
209	MS *m/z* 437.1 $[M+1]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.74 (s, 1H), 7.63 (d, J = 8.8 Hz, 1H), 7.49 (s, 1H), 7.13 (dd, J = 8.8, 2.4 Hz, 1H), 7.05 (s, 1H), 4.52 – 4.37 (m, 1H), 3.92 (s, 3H), 3.28 – 3.18 (m, 1H), 2.88 – 2.74 (m, 1H), 2.59 – 2.48 (m, 2H), 2.34 – 2.19 (m, 2H), 2.19 – 2.08 (m, 1H), 1.94 – 1.83 (m, 1H), 1.82 – 1.69 (m, 1H), 1.69 – 1.55 (m, 1H), 1.15 (t, J = 7.2 Hz, 3H). NH not observed.
210	MS *m/z* 441.2 $[M+1]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.73 (s, 1H), 7.63 (d, J = 8.4 Hz, 1H), 7.50 (br s, 1H), 7.14 (dd, J = 8.8, 2.4 Hz, 1H), 7.05 (s, 1H), 4.71 – 4.50 (m, 1H), 3.92 (s, 3H), 3.30 – 3.22 (m, 1H), 3.07 – 2.96 (m, 1H), 2.49 – 2.42 (m, 2H), 2.40 - 2.30 (m, 1H), 2.36 (s, 3H), 2.27 – 2.18 (m, 1H), 1.97 – 1.77 (m, 1H). NH not observed.
211	MS *m/z* 453.1 $[M+1]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.79 (s, 1H), 7.63 (d, J = 8.8 Hz, 1H), 7.48 (s, 1H), 7.13 (dd, J = 8.8, 2.4 Hz, 1H), 7.04 (s, 1H), 4.51 – 4.40 (m, 1H), 3.92 (s, 3H), 3.77 – 3.66 (m, 2H), 3.17 – 3.08 (m, 1H), 2.75 – 2.67 (m, 1H), 2.67 – 2.52 (m, 2H), 2.48 – 2.36 (m, 2H), 2.10 – 1.98 (m, 1H), 1.92 – 1.81 (m, 1H), 1.81 – 1.65 (m, 2H). NH and OH not observed.
212	MS m/z 421.3 [M+H]+; ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.76 (s, 1H), 7.55 (d, J = 8.5 Hz, 1H), 7.43 – 7.29 (m, 3H), 4.63 – 4.35 (m, 1H), 3.95 (s, 3H), 3.74 – 3.45 (m, 1H), 3.21 – 3.06 (m, 1H), 3.03 – 2.81 (m, 2H), 2.77 – 2.46 (m, 2H), 2.32 – 2.13 (m, 1H), 2.10 – 1.98 (m, 1H), 1.96 – 1.66 (m, 2H), 1.27 (t, J = 6.9 Hz, 3H). NH not observed.
213	MS m/z 437.3 $[M+1]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.77 (s, 1H), 7.55 (d, J = 8.5 Hz, 1H), 7.40 (d, J = 2.4 Hz, 1H), 7.37 – 7.30 (m, 2H), 4.61 – 4.35 (m, 1H), 3.95 (s, 3H), 3.86 – 3.70 (m, 2H), 3.44 – 3.34 (m, 1H), 3.09 – 2.90 (m, 1H), 2.91 – 2.74 (m, 2H), 2.73 – 2.45 (m, 2H), 2.21 – 2.05 (m, 1H), 2.04 – 1.91 (m, 1H), 1.90 – 1.67 (m, 2H). NH and OH not observed.
214	MS m/z 394.2 $[M+1]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.80 (s, 1H), 7.55 (d, J = 8.5 Hz, 1H), 7.49 – 7.25 (m, 3H), 4.39 – 4.18 (m, 1H), 3.95 (s, 3H), 2.74 – 2.59 (m, 2H), 2.34 – 2.19 (m, 2H), 1.44 (s, 3H). NH and OH not observed.
215	MS m/z 446.3 $[M+1]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.81 (s, 1H), 8.20 (s, 1H), 8.14 (d, J = 8.0 Hz, 1H), 7.90 (d, J = 8.0 Hz, 1H), 7.43 (s, 1H), 4.46 – 4.08 (m, 1H), 3.82 – 3.50 (m, 1H), 2.67 – 2.35 (m, 1H), 2.32 – 2.12 (m, 1H), 2.08 – 1.93 (m, 1H), 1.93 – 1.74 (m, 1H), 1.52 – 1.12 (m, 4H). NH and OH not observed.
216	MS m/z 405.13 $[M+1]^+$. ^{1}HNMR (Methanol-d_4) δ: 8.74 (s, 1H), 8.35-8.59 (m,

	1H), 7.45-7.56 (m, 2H), 7.00-7.04 (m, 1H), 6.90-6.98 (m, 1H), 6.87 (s, 1H), 4.35-4.61 (m, 1H), 3.92 (s, 3H), 3.49-3.66 (m, 1H), 3.03-3.18 (m, 2H), 2.67-2.81 (m, 4H), 2.02-2.24 (m, 2H), 1.71-1.95 (m, 2H). NH not observed.
217	MS m/z 445.3 $[M+1]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.70 (s, 1H), 8.10 (s, 1H), 8.04 (d, J = 8.1 Hz, 1H), 7.79 (d, J = 8.1 Hz, 1H), 7.31 (s, 1H), 4.44 – 4.29 (m, 1H), 3.18 – 3.10 (m, 1H), 2.89 – 2.69 (m, 1H), 2.51 – 2.24 (m, 5H), 2.09 – 1.95 (m, 1H), 1.94 – 1.78 (m, 1H), 1.77 – 1.62 (m, 1H), 1.61 – 1.49 (m, 1H). NH not observed.
218	MS m/z 432.3 $[M+1]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 9.02 (s, 1H), 8.20 (s, 1H), 8.14 (d, J = 7.9 Hz, 1H), 7.89 (d, J = 8.0 Hz, 1H), 7.68 (s, 1H), 4.27 (quint., J = 8.0 Hz, 1H), 2.75 – 2.57 (m, 2H), 2.42 – 2.20 (m, 2H), 1.44 (s, 3H). NH and OH not observed.
219	MS *m/z* 410.0 $[M+1]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) 8.74 (s, 1H), 7.63 (d, J = 8.8 Hz, 1H), 7.49 (s, 1H), 7.13 (dd, J = 8.8, 2.4 Hz, 1H), 7.04 (s, 1H), 4.34 – 4.20 (m, 1H), 3.92 (s, 3H), 2.71 – 2.62 (m, 2H), 2.32 – 2.23 (m, 2H), 1.44 (s, 3H). NH and OH not observed
220	MS *m/z* 392.0 $[M+1]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.79 (s, 1H), 7.66 (d, J = 8.8 Hz, 1H), 7.62 (d, J = 2.4 Hz, 1H), 7.41 (s, 1H), 7.12 (dd, J = 8.8, 2.4 Hz, 1H), 7.04 (br s, 1H), 6.23 (d, J = 2.0 Hz, 1H), 3.92 (s, 3H). NH not observed.
221	MS *m/z* 410.0 $[M+1]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.78 (s, 1H), 7.64 (d, J = 8.4 Hz, 1H), 7.50 (s, 1H), 7.13 (dd, J = 8.4, 2.4 Hz, 1H), 7.05 (s, 1H), 4.39 – 4.29 (m, 1H), 4.29 – 4.22 (m, 1H), 3.92 (s, 3H), 2.45 – 2.30 (m, 1H), 2.15 – 1.99 (m, 1H), 1.96 – 1.66 (m, 4H). NH and OH not observed
222	MS m/z 424.1 $[M+1]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.73 (s, 1H), 7.64 (d, J = 8.4 Hz, 1H), 7.49 (s, 1H), 7.13 (dd, J = 8.8, 2.4 Hz, 1H), 7.05 (s, 1H), 4.31 – 4.16 (m, 1H), 3.92 (s, 3H), 3.78 – 3.67 (m, 1H), 2.53 – 2.42 (m, 1H), 2.23 – 2.12 (m, 1H), 2.05 – 1.95 (m, 1H), 1.92 – 1.84 (m, 1H), 1.47 – 1.38 (m, 2H), 1.33 – 1.20 (m, 2H). NH and OH not observed
223	MS m/z 424.1 $[M+1]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.76 (s, 1H), 7.63 (d, J = 8.8 Hz, 1H), 7.47 (s, 1H), 7.13 (dd, J = 8.4, 2.0 Hz, 1H), 7.05 (s, 1H), 4.26 – 4.06 (m, 1H), 3.92 (s, 3H), 3.71 – 3.58 (m, 1H), 2.30 – 2.18 (m, 1H), 2.17 – 2.05 (m, 1H), 1.89 – 1.75 (m, 2H), 1.53 – 1.35 (m, 4H). NH and OH not observed
224	MS m/z 423.1 $[M+1]^+$. ^{1}HNMR (500 MHz, Methanol-d_4) δ 8.57-8.93 (m, 1H), 7.50-7.63 (m, 2H), 6.96-7.07 (m, 2H), 6.82-6.96 (m, 2H), 5.02-5.26 (m, 1H), 4.72-4.85 (m, 1H), 3.92 (s, 3H), 3.45-3.63 (m, 1H), 2.72-2.85 (m, 1H), 2.68 (s, 1H), 2.61 (s, 3H), 2.40-2.56 (m, 2H), 1.86-2.06 (m, 1H). NH not observed.
225	MS m/z 435.15 $[M+1]^+$. ^{1}HNMR (500 MHz, Methanol-d_4) δ 8.76 (s, 1H), 7.49-7.66 (m, 2H), 6.97-7.10 (m, 2H), 6.84-6.96 (m, 2H), 4.45-4.73 (m, 1H), 3.92 (s, 3H), 3.80-3.92 (m, 2H), 3.57-3.74 (m, 1H), 3.20-3.30 (m, 2H), 3.00-3.11 (m, 2H), 2.81-2.98 (m, 2H), 2.01-2.29 (m, 2H), 1.75-2.00 (m, 2H). NH and OH not observed.
226	MS m/z 392.15 $[M+1]^+$. ^{1}HNMR (500 MHz, Methanol-d_4) δ 8.72 (s, 1H), 7.48-7.59 (m, 1H), 7.50 (s, 1H), 6.96-7.03 (m, 1H), 6.92 (s, 1H), 6.85 (s, 1H), 4.20-4.41 (m, 1H), 3.91 (s, 3H), 2.60-2.75 (m, 2H), 2.19-2.38 (m, 2H), 1.46 (s, 3H).

	NH and OH not observed.
227	MS m/z 374.05 $[M+H]^+$. ^{1}HNMR (500 MHz, Methanol-d_4) δ 8.72-8.93 (m, 1H), 7.55-7.73 (m, 2H), 7.35-7.50 (m, 1H), 6.97-7.13 (m, 1H), 6.83-6.94 (m, 2H), 6.24 (s, 1H), 5.51 (s, 1H), 3.92 (s, 3H). NH not observed.
228	MS m/z 376.1 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.68 (s, 1H), 8.44 (s, 1H, Formate), 7.56 – 7.47 (m, 2H), 7.30 – 7.26 (m, 1H), 7.25 – 7.19 (m, 1H), 7.17 – 7.11 (m, 1H), 6.16 – 6.08 (m, 1H), 3.84 (s, 3H). NH not observed.
229	MS m/z 475.1 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.78 (s, 1H), 7.93 (dd, J = 22.1, 8.5 Hz, 2H), 7.83 (s, 1H), 7.55 (s, 1H), 4.47 (s, 1H), 3.27 – 3.17 (m, 1H), 2.83 (s, 1H), 2.58 – 2.50 (m, 2H), 2.26 (s, 2H), 2.14 (s, 1H), 1.87 (s, 1H), 1.77 (d, J = 10.0 Hz, 1H), 1.64 (s, 1H), 1.15 (t, J = 7.2 Hz, 3H). NH not observed.
230	MS m/z 460.1 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.85 (s, 1H), 7.60 (d, J = 8.4 Hz, 1H), 7.49 (s, 1H), 7.25 (t, J = 8.4 Hz, 1H), 7.11 – 7.06 (m, 3H), 7.02 (s, 1H), 6.81 (dd, J = 2.0 Hz, J = 9.2 Hz, 1H), 5.52 – 5.47 (m, 1H), 3.90 (s, 3H), 3.78 (s, 3H), 1.70 (d, J = 7.2 Hz, 3H). NH not observed.
231	MS m/z 430.1 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.85 (s, 1H), 7.59 (d, J = 8.4 Hz, 1H), 7.50 (d, J = 7.6 Hz, 3H), 7.34 (t, J = 7.6 Hz, 2H), 7.24 (t, J = 7.2 Hz, 1H), 7.10 (dd, J = 2.4 Hz, J = 8.8 Hz, 1H), 7.02 (s, 1H), 5.57 – 5.49 (m, 1H), 3.90 (s, 3H), 1.71 (d, J = 6.8 Hz, 3H). NH not observed.
232	MS m/z 431.1 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.83 (s, 1H), 8.71 (d, J = 1.6 Hz, 1H), 8.44 (dd, J = 1.2 Hz, J = 4.8 Hz, 1H), 8.00 (d, J = 8.0 Hz, 1H), 7.59 (d, J = 8.8 Hz, 1H), 7.50 (s, 1H), 7.45 – 7.42 (m, 1H), 7.10 (dd, J = 2.4 Hz, J = 8.4 Hz, 1H), 7.03 (s, 1H), 5.56 – 5.54 (m, 1H), 3.90 (s, 3H), 1.76 (d, J = 6.8 Hz, 3H). NH not observed.
233	MS m/z 432.0 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.70 (s, 1H), 7.64 (d, J = 8.8 Hz, 1H), 7.50 (s, 1H), 7.19 – 7.11 (m, 2H), 7.04 (s, 1H), 6.95 – 6.92 (m, 2H), 6.74 (dd, J = 2.0 Hz, J = 8.0 Hz, 1H), 4.80 (s, 2H), 3.91 (s, 3H). NH and OH not observed.
234	MS m/z 406.0 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.69 (s, 1H), 7.65 (d, J = 8.8 Hz, 1H), 7.61 (s, 1H), 7.50 (s, 1H), 7.13 (dd, J = 2.4 Hz, J = 8.8 Hz, 1H), 7.05 (s, 1H), 6.43 (s, 1H), 4.91 (s, 2H), 3.92 (s, 3H). NH not observed.
235	MS m/z 393.2 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d4) δ 8.68 (s, 1H), 7.56 (d, J = 8.5 Hz, 1H), 7.43 – 7.28 (m, 3H), 5.13 – 5.00 (m, 1H), 3.95 (s, 3H), 3.57 – 3.42 (m, 2H), 2.86 – 2.67 (m, 1H), 2.44 – 2.24 (m, 1H). NH not observed.
236	MS m/z 408.2 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.86 (s, 1H), 7.60 (s, 1H), 7.56 (d, J = 8.5 Hz, 1H), 7.16 (s, 1H), 7.13 (dd, J = 8.5, 2.4 Hz, 1H), 4.28 – 4.18 (m, 1H), 3.91 (s, 3H), 3.77 (q, J = 10.9 Hz, 2H), 2.74 – 2.62 (m, 2H), 2.39 – 2.26 (m, 2H), 1.45 (s, 3H). 2H not observed (NH and OH).
237	MS m/z 422.2 $[M+H]+$; ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.78 (s, 1H), 7.54 (d, J = 8.4 Hz, 1H), 7.46 (s, 1H), 7.15 – 7.07 (m, 2H), 4.17 – 4.04 (m, 1H), 3.90 (s, 3H), 3.87 – 3.69 (m, 2H), 3.69 – 3.60 (m, 1H), 2.30 – 2.19 (m, 1H), 2.17 – 2.08 (m, 1H), 1.88 – 1.76 (m, 2H), 1.53 – 1.34 (m, 4H). 2H not observed (NH and OH).
238	MS m/z 407.2 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.68 (s, 1H), 7.54 (d, J = 8.4 Hz, 1H), 7.48 (s, 1H), 7.16 – 7.08 (m, 2H), 5.11 – 5.02 (m, 1H), 3.90

	(s, 3H), 3.77 (q, J = 11.0 Hz, 2H), 3.53 – 3.44 (m, 2H), 2.80 – 2.69 (m, 1H), 2.42 – 2.26 (m, 1H). 2H not observed (2NH).
239	MS m/z 491.1 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.83 (s, 1H), 7.96 (d, J = 8.1 Hz, 1H), 7.90 (d, J = 8.2 Hz, 1H), 7.83 (s, 1H), 7.55 (s, 1H), 4.56 – 4.42 (m, 1H), 3.76 – 3.68 (m, 2H), 3.16 – 3.07 (m, 1H), 2.73 – 2.66 (m, 1H), 2.64 – 2.54 (m, 2H), 2.50 – 2.40 (m, 2H), 2.08 – 2.00 (m, 1H), 1.92 – 1.83 (m, 1H), 1.80 – 1.68 (m, 2H). NH and OH not observed.
240	MS m/z 462.1 $[M+H]^+$. ^{1}HNMR (400 MHz, DMSO-d_6) δ 8.85 (s, 1H), 7.99 (s, 2H), 7.96 (s, 1H), 7.52 (s, 1H), 4.75 (s, 1H), 4.18 (s, 1H), 3.55 (t, J = 10.7 Hz, 1H), 2.31 (d, J = 11.4 Hz, 1H), 2.06 (d, J = 12.4 Hz, 1H), 1.88 (d, J = 11.6 Hz, 1H), 1.78 (d, J = 13.3 Hz, 1H), 1.34 (dd, J = 23.3, 11.8 Hz, 3H), 1.18 – 1.09 (m, 1H).
241	MS m/z 448.1 $[M+H]^+$. ^{1}HNMR (400 MHz, DMSO-d_6) δ 8.86 (s, 1H), 8.32 (d, J = 6.1 Hz, 1H), 7.99 (s, 2H), 7.96 (s, 1H), 7.53 (s, 1H), 5.12 (s, 1H), 4.25 (dd, J = 14.3, 7.8 Hz, 1H), 2.53 (s, 1H), 2.48 (s, 1H), 2.22 (dd, J = 11.3, 8.9 Hz, 2H), 1.34 (s, 3H).
242	MS m/z 462.1 $[M+H]^+$. 1H NMR (400 MHz, DMSO-d_6) δ 8.91 (s, 1H), 7.99 (s, 2H), 7.96 (s, 2H), 7.52 (s, 1H), 4.89 (d, J = 4.8 Hz, 1H), 4.09 (s, 1H), 3.57 (s, 1H), 2.09 (s, 1H), 1.99 (s, 1H), 1.72 (s, 2H), 1.33 (d, J = 5.4 Hz, 4H).
243	MS m/z 446.1 [M+H]+; 1H NMR (400 MHz, Methanol-d_4) δ 8.81 (s, 1H), 8.20 (s, 1H), 8.14 (d, J = 7.5 Hz, 1H), 7.89 (d, J = 7.7 Hz, 1H), 7.38 (s, 1H), 4.15 (s, 1H), 3.73 – 3.56 (m, 1H), 2.28 – 2.17 (m, 1H), 2.14 – 2.06 (m, 1H), 1.94 – 1.69 (m, 2H), 1.51 – 1.39 (m, 4H). NH and OH not observed.
244	MS m/z 446.1 $[M+H]^+$. ^{1}HNMR (400 MHz, DMSO-d_6) δ 8.83 (s, 1H), 8.23 (d, J = 6.1 Hz, 1H), 7.80 (d, J = 8.9 Hz, 1H), 7.46-7.40 (m, 3H), 7.28 (t, J = 72.0 Hz, 1H), 5.11 (s, 1H), 4.23 (dd, J = 13.9, 7.5 Hz, 1H), 2.50 – 2.46 (m, 2H), 2.21 (dd, J = 11.3, 8.8 Hz, 2H), 1.31 (d, J = 25.2 Hz, 3H).
245	MS m/z 460.1 $[M+H]^+$. ^{1}HNMR (400 MHz, DMSO-d_6) δ 8.85 (s, 1H), 7.89 (d, J = 7.5 Hz, 1H), 7.80 (d, J = 8.9 Hz, 1H), 7.46 – 7.40 (m, 3H), 7.28 (t, J = 73.2 Hz, 1H), 4.75 (d, J = 4.6 Hz, 1H), 4.28 – 4.05 (m, 1H), 3.54 (td, J = 6.5, 2.3 Hz, 1H), 2.31 (d, J = 11.6 Hz, 1H), 2.13 – 2.00 (m, 1H), 1.88 (d, J = 10.4 Hz, 1H), 1.77 (dd, J = 9.4, 3.7 Hz, 1H), 1.44 – 1.22 (m, 3H), 1.13 (d, J = 14.3 Hz, 1H).
246	MS m/z 460.0 $[M+H]^+$. ^{1}HNMR (400 MHz, DMSO-d_6) δ 8.85 (s, 1H), 7.80 (d, J = 8.9 Hz, 1H), 7.45 – 7.39 (m, 3H), 7.28 (t, J = 73.2 Hz, 1H), 6.0 (bs, 1H) 4.98 – 4.78 (m, 1H), 4.11 – 4.00 (m, 1H), 3.61 – 3.48 (m, 1H), 2.14 – 2.06 (m, 1H), 2.03 – 1.96 (m, 1H), 1.76 – 1.68 (m, 2H), 1.37 – 1.27 (m, 4H).
247	MS m/z 446.1 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.86 (s, 1H), 7.60 (d, J = 8.4 Hz, 1H), 7.48 (s, 1H), 7.14 (t, J = 7.6 Hz, 1H), 7.10 (dd, J = 2.0 Hz, J = 8.4 Hz, 1H), 7.03 (s, 1H), 6.94 – 6.92 (m, 2H), 6.66 (dd, J = 2.4 Hz, J = 7.2 Hz, 1H), 5.48 – 5.43 (m, 1H), 3.91 (s, 3H), 1.69 (d, J = 6.8 Hz, 3H). NH and OH not observed.
248	MS m/z 446.1 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.86 (s, 1H), 7.60 (d, J = 8.4 Hz, 1H), 7.48 (s, 1H), 7.13 (t, J = 8.4 Hz, 1H), 7.10 (dd, J = 2.0 Hz, J = 8.4 Hz, 1H), 7.02 (s, 1H), 6.93 – 6.91 (m, 2H), 6.66 (dd, J = 2.0 Hz, J = 7.2 Hz, 1H), 5.48 – 5.43 (m, 1H), 3.90 (s, 3H), 1.69 (d, J = 7.2 Hz, 3H). NH and OH not observed.

249	MS m/z 424.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 9.06 – 8.72 (m, 1H), 7.77 – 7.45 (m, 2H), 7.15 – 7.08 (m, 2H), 4.37 – 4.21 (m, 1H), 4.04 (dd, J = 11.1, 4.8 Hz, 1H), 3.98 (dd, J = 11.6, 4.1 Hz, 1H), 3.90 (s, 3H), 3.86 – 3.71 (m, 3H), 3.56 (t, J = 11.3 Hz, 1H), 3.28 (t, J = 10.6 Hz, 1H), 2.26 (d, J = 12.1 Hz, 1H), 1.77 (qd, J = 12.4, 4.4 Hz, 1H). 2H not observed (NH and OH).
250	MS m/z 421.4 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.74 (s, 1H), 8.48 (s, 1H, formic acid), 7.53 (d, J = 8.5 Hz, 1H), 7.45 (br s, 1H), 7.15 – 7.08 (m, 2H), 4.54 – 4.35 (m, 1H), 3.90 (s, 3H), 3.78 (q, J = 11.0, 2H), 3.51 – 3.38 (m, 1H), 3.14 – 2.98 (m, 1H), 2.76 – 2.54 (m, 5H), 2.28 – 1.97 (m, 2H), 1.92 – 1.62 (m, 2H). 1H not observed (NH).
251	MS m/z 430.2 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d4) δ 8.88 (s, 1H), 7.53 (d, J = 8.5 Hz, 1H), 7.42 – 7.24 (m, 3H), 7.16 (t, J = 7.9 Hz, 1H), 7.01 – 6.90 (m, 2H), 6.68 (d, J = 8.1 Hz, 1H), 5.47 (q, J = 7.2 Hz, 1H), 3.94 (s, 3H), 1.70 (d, J = 6.9 Hz, 3H). NH and OH not observed.
252	MS m/z 463.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.82 (s, 1H), 8.22 (s, 1H), 8.16 (d, J = 8.0 Hz, 1H), 7.91 (d, J = 8.0 Hz, 1H), 7.47 (s, 1H), 5.58 – 5.10 (m, 1H), 4.89 – 4.69 (m, 1H), 3.81 – 3.56 (m, 1H), 3.55 – 3.36 (m, 1H), 3.02 – 2.81 (m, 1H), 2.77 – 2.66 (m, 4H), 2.63 – 2.40 (m, 1H), 2.25 – 1.85 (m, 1H). 1H not observed (NH).
253	MS m/z 475.4 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.88 (s, 1H), 8.22 (s, 1H), 8.16 (d, J = 8.1 Hz, 1H), 7.92 (d, J = 8.0 Hz, 1H), 7.42 (s, 1H), 4.60 – 4.42 (m, 1H), 3.99 – 3.69 (m, 2H), 3.25 – 3.08 (m, 1H), 2.96 – 2.61 (m, 3H), 2.58 – 2.39 (m, 2H), 2.23 – 2.02 (m, 1H), 2.01 – 1.84 (m, 1H), 1.84 – 1.68 (m, 2H). NH and OH not observed.
254	MS m/z 432.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.95 (s, 1H), 8.22 (s, 1H), 8.16 (d, J = 8.0 Hz, 1H), 7.91 (d, J = 8.0 Hz, 1H), 7.56 (s, 1H), 4.42 – 4.34 (m, 1H), 4.27 – 4.12 (m, 1H), 4.01 – 3.81 (m, 1H), 3.71 – 3.42 (m, 2H), 2.38 – 2.18 (m, 1H), 2.06 – 1.68 (m, 3H). 1H not observed (NH).
255	MS m/z 448.1 $[M+H]^+$. ^{1}HNMR (400 MHz, DMSO-d_6) δ 8.86 (s, 1H), 8.00 (s, 2H), 7.97 (s, 1H), 7.52 (s, 1H), 4.60 – 4.52 (m, 1H), 3.44 (d, J = 5.6 Hz, 2H), 2.49 – 2.39 (m, 2H), 2.25 – 2.16 (m, 1H), 2.00 – 1.88 (m, 2H). NH and OH not observed.
256	MS m/z 447.1 [M+H]+; ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.73 (s, 1H), 7.96 (d, J = 8.0 Hz, 1H), 7.91 (d, J = 8.1 Hz, 1H), 7.84 (s, 1H), 7.59 (s, 1H), 5.10 (t, J = 9.6 Hz, 1H), 3.55 – 3.47 (m, 2H), 2.81 – 2.69 (m, 1H), 2.43 – 2.28 (m, 1H). NH not observed.
257	MS m/z 432.0 [M+H]+; ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.94 (s, 1H), 8.24 (s, 1H), 8.17 (d, J = 8.4 Hz, 1H), 7.93 (d, J = 8.0 Hz, 1H), 7.54 (s, 1H), 4.55 – 4.46 (m, 1H), 3.60 (d, J = 6.0 Hz, 2H), 2.69 – 2.62 (m, 2H), 2.38-2.34 (m, 1H), 2.12 – 2.04 (m, 2H). NH and OH not observed.
258	MS m/z 489.1 $[M+H]^+$. ^{1}HNMR (400 MHz, DMSO-d_6) δ 8.85 (s, 1H), 7.81 (d, J = 8.4 Hz, 1H), 7.75 (s, 1H), 7.46 (t, J = 73.2 Hz, 1H), 7.43 (s, 1H), 7.41 (d, J = 2.4, 1H), 4.42 – 4.40 (m, 1H), 4.30 – 4.29 (m, 1H), 3.53 (q, J = 5.6, 2H), 3.17 (d, J = 9.6 Hz, 1H), 2.82 (d, J = 10.8 Hz, 1H), 2.47-2.44 (m, 1H), 2.11-2.00 (m, 3H), 1.77-1.74 (m, 1H), 1.63-1.54 (m, 1H), 1.48-1.43 (m, 1H). NH and OH not observed.

259	MS m/z 482.1 $[M+H]^+$. ^{1}HNMR (400 MHz, DMSO-d_6) δ 8.98 (s, 1H), 7.79 (d, J = 8.0 Hz, 1H), 7.47 (s, 1H), 7.45 (t, J = 73.2 Hz, 1H), 7.41 – 7.38 (m, 2H), 7.16-7.12 (m, 1H), 6.92 – 6.88 (m, 2H), 6.65 – 6.63 (m, 1H), 5.45 – 5.43 (m, 1H), 1.61 (d, J = 6.8 Hz, 3H). NH and OH not observed.
260	MS m/z 445.0 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.70 (s, 1H), 7.77 (d, J = 8.4 Hz, 1H), 7.55 (s, 1H), 7.37 (d, J = 8.4 Hz, 1H), 7.33 (s, 1H), 7.05 (t, J = 72.8 Hz, 1H), 5.10 – 5.05 (m, 1H), 3.52 – 3.47 (m, 2H), 2.75 – 2.73 (m, 1H), 2.41 – 2.31 (m, 1H). NH not observed.
261	MS m/z 473.1 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.77 (s, 1H), 8.49 (s, 1H), 7.92 (s, 1H), 7.85 (dd, J = 19.2, 8.2 Hz, 2H), 7.50 (s, 1H), 4.63 – 4.36 (m, 1H), 3.92 (q, J = 10.9 Hz, 2H), 3.64 – 3.47 (m, 1H), 3.29 – 3.08 (m, 2H), 3.02 – 2.79 (m, 2H), 2.72 – 2.57 (m, 1H), 2.31 – 1.70 (m, 4H), 1.28 (t, J = 6.8 Hz, 3H). NH not observed.
262	MS m/z 460.0 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.77 (s, 1H), 7.92 (s, 1H), 7.85 (d, J = 4.8 Hz, 2H), 7.49 (s, 1H), 4.33 – 4.14 (m, 1H), 3.94 (q, J = 10.9 Hz, 2H), 3.85 – 3.63 (m, 1H), 2.47 (d, J = 11.4 Hz, 1H), 2.17 (d, J = 11.8 Hz, 1H), 2.00 (d, J = 12.4 Hz, 1H), 1.90 (d, J = 13.4 Hz, 1H), 1.55 – 1.19 (m, 4H). NH and OH not observed.
263	MS m/z 446.0 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.80 (s, 1H), 7.92 (s, 1H), 7.85 (q, J = 8.1 Hz, 2H), 7.51 (s, 1H), 4.33 – 4.17 (m, 1H), 3.93 (q, J = 11.0 Hz, 2H), 2.71 – 2.60 (m, 2H), 2.30 (t, J = 10.2 Hz, 2H), 1.45 (s, 3H). NH and OH not observed.
264	MS m/z 446.0 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.77 (s, 1H), 7.91 (s, 1H), 7.84 (q, J = 8.3 Hz, 2H), 7.48 (s, 1H), 4.66 – 4.54 (m, 1H), 3.94 (q, J = 11.0 Hz, 2H), 3.59 (d, J = 6.0 Hz, 2H), 2.64 (dt, J = 10.0, 3.7 Hz, 2H), 2.34 (d, J = 7.7 Hz, 1H), 1.98 (dd, J = 20.8, 9.3 Hz, 2H). NH and OH not observed.
265	MS m/z 445.0 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.72 (s, 1H), 7.97 – 7.72 (m, 3H), 7.51 (s, 1H), 5.09 (t, J = 9.5 Hz, 1H), 3.91 (q, J = 11.0 Hz, 2H), 3.58 – 3.42 (m, 2H), 2.75 (s, 1H), 2.37 (dd, J = 20.9, 10.7 Hz, 1H). NH not observed.
266	MS m/z 482.0 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.99 (s, 1H), 7.93 (s, 1H), 7.84 (dd, J = 20.5, 8.1 Hz, 2H), 7.58 (s, 1H), 7.18 (t, J = 7.9 Hz, 1H), 7.01 – 6.91 (m, 2H), 6.71 (dd, J = 7.9, 2.1 Hz, 1H), 5.43 (q, J = 6.9 Hz, 1H), 3.88 (tdd, J = 15.1, 10.9, 4.3 Hz, 2H), 1.73 (d, J = 7.0 Hz, 3H). NH and OH not observed.
267	MS m/z 428.0 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.82 (s, 1H), 7.89 (d, J = 15.4 Hz, 3H), 7.63 (d, J = 2.3 Hz, 1H), 7.40 (s, 1H), 6.24 (d, J = 2.4 Hz, 1H), 3.96 (q, J = 10.8 Hz, 2H). NH not observed.
268	MS m/z 408.4 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.64 (s, 1H), 7.32-7.51 (m, 2H), 6.90 (s, 1H), 6.67-6.85 (m, 2H), 4.03-4.35 (m, 1H), 3.86-3.99 (m, 2H), 3.81 (s, 3H), 3.59-3.72 (m, 1H), 3.31-3.58 (m, 1H), 3.10-3.19 (m, 1H), 2.08-2.31 (m, 1H), 1.51-1.77 (m, 1H). NH and OH not observed.
269	MS m/z 391.2 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.56 (s, 1H), 7.29-7.55 (m, 2H), 6.86-6.96 (m, 1H), 6.69-6.85 (m, 2H), 4.86-5.05 (m, 1H), 3.81 (s, 3H), 3.31-3.48 (m, 2H), 2.64 (s, 1H), 2.02-2.25 (m, 1H). NH not observed.
270	MS m/z 406.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.63 (s, 1H), 7.39-

	7.51 (3, 1H), 7.37 (s, 1H), 6.86-6.96 (m, 1H), 6.67-6.84 (m, 2H), 3.95-4.17 (m, 1H), 3.80 (s, 3H), 3.49-3.62 (m, 1H), 2.12-2.18 (m, 1H), 1.97-2.11 (m, 1H), 1.57-1.82 (m, 2H), 1.23-1.47 (m, 4H). NH and OH not observed.
271	MS m/z 459.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.81 (s, 1H), 8.22 (s, 1H), 8.16 (d, J = 8.1 Hz, 1H), 7.91 (d, J = 8.0 Hz, 1H), 7.42 (s, 1H), 4.54 – 4.38 (m, 1H), 2.94 – 2.83 (m, 1H), 2.83 – 2.61 (m, 2H), 2.52 – 2.31 (m, 2H), 2.22 – 2.10 (m, 1H), 2.03 – 1.89 (m, 1H), 1.87 – 1.73 (m, 1H), 1.77 – 1.58 (m, 1H), 1.45 – 1.26 (m, 1H), 1.20 (t, J = 7.2 Hz, 3H). NH not observed.
272	MS m/z 459.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.82 (s, 1H), 8.22 (s, 1H), 8.16 (d, J = 8.0 Hz, 1H), 7.92 (d, J = 8.0 Hz, 1H), 7.53 (s, 1H), 3.69 – 3.38 (m, 2H), 3.04 (s, 3H), 2.48 – 2.35 (m, 1H), 2.26 – 1.87 (m, 3H). NH not observed. 1H alpha to carbonyl and nitrogen linker is overlapping with water peak.
273	MS m/z 448.2 $[M+H]^+$. ^{1}HNMR (500 MHz, Methanol-d_4) δ 8.85 (s, 1H), 8.22 (s, 1H), 8.16 (d, J = 8.1 Hz, 1H), 7.92 (d, J = 8.0 Hz, 1H), 7.56 – 7.40 (m, 1H), 4.42 – 4.25 (m, 1H), 4.13 – 4.03 (m, 1H), 4.02 – 3.95 (m, 1H), 3.84 – 3.70 (m, 1H), 3.63 – 3.49 (m, 1H), 3.32 – 3.24 (m, 1H), 2.41 – 2.14 (m, 1H), 1.90 – 1.65 (m, 1H). NH and OH not observed.
274	MS m/z 448.2 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.85 (s, 1H), 8.22 (s, 1H), 8.16 (d, J = 8.0 Hz, 1H), 7.91 (d, J = 8.0 Hz, 1H), 7.47 (s, 1H), 4.44 – 4.15 (m, 2H), 4.07 – 3.97 (m, 1H), 3.97 – 3.91 (m, 1H), 3.61 – 3.50 (m, 1H), 3.41 – 3.34 (m, 1H), 2.16 – 2.11 (m, 1H), 1.85 – 1.70 (m, 1H). NH and OH not observed.
275	MS m/z 446.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.88 (s, 1H), 8.22 (s, 1H), 8.15 (d, J = 8.0 Hz, 1H), 7.92 (d, J = 8.0 Hz, 1H), 7.44 (s, 1H), 4.23 (p, J = 7.3 Hz, 1H), 4.06 – 3.98 (m, 1H), 2.05 – 1.87 (m, 6H), 1.85 – 1.69 (m, 2H). NH and OH not observed.
276	MS m/z 445.2 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.77 (s, 1H), 8.22 (s, 1H), 8.17 (d, J = 8.8 Hz, 1H), 7.92 (d, J = 8.0 Hz, 1H), 7.46 (s, 1H), 3.51 – 3.40 (m, 3H), 2.48 – 2.36 (m, 1H), 2.25 – 1.88 (m, 3H). 2 NH not observed.
277	MS m/z 439.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.82 (br s, 1H), 7.60 (br s, 1H), 7.53 (d, J = 8.5 Hz, 1H), 7.13 (s, 1H), 7.11 (d, J = 8.5 Hz, 1H), 5.09 (d, J = 45.7 Hz, 1H), 4.81 - 4.70 (m, 1H), 3.90 (s, 3 H), 3.78 (q, J = 11.0 Hz, 2H), 3.45 (d, J = 10.0 Hz, 1H), 3.24 (t, J = 11.9 Hz, 1H), 2.68 (dd, J = 35.1, 14.4 Hz, 1H), 2.55 (s, 3H), 2.52 – 2.42 (m, 2H), 2.06 – 1.82 (m, 1H). 1H not observed (NH).
278	MS m/z 451.2 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.76 (s, 1H, formic acid), 8.45 (s, 1H), 7.53 (d, J = 8.5 Hz, 1H), 7.46 (s, 1H), 7.13 (s, 1H), 7.13 – 7.09 (m, 1H), 4.59 – 4.41 (m, 1H), 3.90 (s, 3H), 3.88 – 3.74 (m, 4H), 3.63 – 3.44 (m, 1H), 3.23 – 3.10 (m, 1H), 3.07 – 2.92 (m, 2H), 2.92 – 2.66 (m, 2H), 2.23 – 2.11 (m, 1H), 2.10 – 2.00 (m, 1H), 1.96 – 1.69 (m, 2H). 2H not observed (NH and OH).
279	MS m/z 473.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.71 (s, 1H), 8.44-8.63 (m, 1H), 7.96 (s, 1H), 7.87 (s, 1H), 7.60-7.72 (m, 1H), 4.31-4.59 (m, 1H), 3.79-4.02 (m, 1H), 3.51-3.73 (m, 1H), 3.34-3.42 (m, 1H), 2.88-3.06 (m, 1H), 2.56 (s, 5H), 2.10-2.28 (m, 1H), 1.96 (s, 4H), 1.77-1.89 (m, 1H), 1.56-1.77 (m,

	1H). NH not observed.
280	MS m/z 474.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ: 8.60 (s, 1H), 7.84 (s, 1H), 7.74-7.79 (m, 1H), 7.51-7.59 (m, 1H), 3.94-4.10 (m, 1H), 3.69-3.94 (m, 1H), 3.45-3.61 (m, 2H), 2.07-2.22 (m, 1H), 1.98-2.07 (m, 1H), 1.85 (s, 3H), 1.61-1.77 (m, 2H), 1.24-1.40 (m, 4H). NH and OH not observed.
281	MS m/z 457.3 [M+H]+; ^{1}HNMR (400 MHz, Methanol-d_4) δ: 8.75 (s, 1H), 8.45-8.62 (m, 1H), 7.49 (s, 1H), 7.36-7.43 (m, 1H), 7.31 (s, 2H), 4.34-4.63 (m, 1H), 3.96 (s, 3H), 2.89-3.06 (m, 1H), 2.33-2.74 (ms, 5H), 2.08-2.23 (m, 1H), 1.91-2.07 (m, 1H), 1.79-1.90 (m, 2H), 1.63-1.76 (m, 1H). NH not observed.
282	MS m/z 460.1 [M+H]+; ^{1}HNMR (400 MHz, DMSO-d_6) δ 8.88 (s, 1H), 8.00 – 7.96 (m, 1H), 7.93 – 7.82 (m, 3H), 7.49 (s, 1H), 4.87 (t, J = 5.2 Hz, 1H), 4.14 (dd, J = 23.7, 10.8 Hz, 3H), 3.54 (d, J = 9.1 Hz, 1H), 2.16 – 1.93 (m, 2H), 1.81 – 1.62 (m, 2H), 1.44 – 1.24 (m, 4H).
283	MS m/z 474.0 [M+H]+; ^{1}HNMR (400 MHz, DMSO-d_6) δ 9.07 – 9.01 (m, 1H), 7.99 (s, 1H), 7.88 (t, J = 9.6 Hz, 2H), 7.55 – 7.46 (m, 1H), 7.37 – 7.30 (m, 1H), 4.72 (s, 1H), 4.43 (s, 1H), 4.18 – 4.03 (m, 2H), 1.97 – 1.89 (m, 1H), 1.73 (s, 2H), 1.67 – 1.47 (m, 3H), 1.37 (t, J = 11.4 Hz, 2H), 1.23 (s, 3H).
284	MS m/z 409.0 [M+H]+; ^{1}HNMR (400 MHz, DMSO-d_6) δ 8.81 (s, 1H), 8.36 (d, J = 7.8 Hz, 1H), 8.05 (s, 1H), 7.66 (d, J = 8.6 Hz, 1H), 7.46 (s, 1H), 7.17 (dd, J = 8.7, 2.4 Hz, 1H), 7.10 (s, 1H), 4.94 (dd, J = 17.9, 8.5 Hz, 1H), 3.89 (s, 3H), 3.31 – 3.20 (m, 2H), 2.61 – 2.55 (m, 1H), 2.22 – 2.09 (m, 1H).
285	MS m/z 414.0 [M+H]+; ^{1}HNMR (400 MHz, DMSO-d_6) δ 8.81 (s, 1H), 8.29 (d, J = 9.8 Hz, 2H), 8.07 (d, J = 7.8 Hz, 1H), 7.77 (s, 1H), 7.43 (s, 1H), 6.22 (s, 1H).
286	MS m/z 406.3 [M+H]+; ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.86 – 8.70 (m, 1H), 7.48 (d, J = 7.9 Hz, 1H), 7.44 – 7.39 (m, 2H), 7.38 – 7.33 (m, 1H), 4.21 – 4.06 (m, 1H), 3.86 – 3.69 (m, 2H), 3.69 – 3.60 (m, 1H), 2.45 (s, 3H), 2.25 (d, J = 4.1 Hz, 1H), 2.15 – 2.04 (m, 1H), 1.89 – 1.75 (m, 2H), 1.55 – 1.35 (m, 4H). NH and OH peak not observed.
287	MS m/z 412.9, 414.9 $[M+H]^+$. ^{1}HNMR (400 MHz, DMSO-d_6) δ 8.83 (s, 1H), 8.48 (brs, 1H), 8.05 (s, 1H), 7.79 – 7.76 (m, 1H), 7.76 – 7.73 (m, 1H), 7.70 – 7.66 (m, 1H), 7.54 – 7.48 (m, 1H), 5.02 – 4.88 (m, 1H), 3.34 – 3.31 (m, 2H), 2.60 – 2.55 (m, 1H), 2.20 – 2.10 (m, 1H).
288	MS m/z 391.3 $[M+H]^+$. 1H NMR (400 MHz, Methanol-d_4) δ 8.77 – 8.63 (m, 1H), 7.52 – 7.39 (m, 3H), 7.39 – 7.30 (m, 1H), 5.15 – 4.97 (m, 1H), 3.74 (q, J = 11.0 Hz, 2H), 3.58 – 3.42 (m, 2H), 2.84 – 2.67 (m, 1H), 2.46 (s, 3H), 2.40 – 2.26 (m, 1H). 2 NH peak not observed.
289	MS m/z 475.0 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 7.79 (s, 2H), 7.73 (d, J = 8.4 Hz, 1H), 7.60 (d, J = 8.0 Hz, 1H), 7.20 (s, 1H), 4.00 – 3.95 (m, 1H), 3.75 – 3.67 (m, 2H), 2.92 (dd, J = 12.0, 5.2 Hz, 1H), 2.66 – 2.61 (m, 1H), 2.52 – 2.47 (m, 1H), 2.36 (d, J = 12.0 Hz, 5H), 2.22 – 2.16 (m, 2H). NH and OH not observed.
290	MS m/z 462.1 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.80 (s, 1H), 7.93 (dd, J = 23.4, 8.2 Hz, 2H), 7.83 (s, 1H), 7.54 (s, 1H), 4.23 – 4.15 (m, 1H), 3.71 – 3.62 (m, 1H), 2.29 – 2.20 (m, 1H), 2.17 – 2.07 (m, 1H), 1.88 – 1.77 (m, 2H), 1.50 – 1.41 (m, 4H). NH and OH not observed.

291	MS m/z 410.1 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.73 (s, 1H), 7.63 (d, J = 8.8 Hz, 1H), 7.48 (s, 1H), 7.12 (dd, J = 2.0 Hz, J = 8.4 Hz, 1H), 7.04 (s, 1H), 4.62 – 4.53 (m, 1H), 3.92 (s, 3H), 3.59 (d, J = 5.6 Hz, 2H), 2.66 – 2.60 (m, 2H), 2.36 – 2.30 (m, 1H), 1.99 – 1.92 (m, 2H). NH and OH not observed.
292	MS m/z 426.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.76 (s, 1H), 7.63 (d, J = 8.6 Hz, 1H), 7.49 (s, 1H), 7.13 (dd, J = 8.6, 2.1 Hz, 1H), 7.05 (s, 1H), 4.32-4.28 (m, 1H), 4.08 – 4.01 (m, 1H), 4.00 – 3.95 (m, 1H), 3.92 (s, 3H), 3.76 (td, J = 9.7, 4.8 Hz, 1H), 3.55 (t, J = 11.1 Hz, 1H), 3.30 – 3.20 (m, 1H), 2.28-2.22 (m, 1H), 1.86 – 1.68 (m, 1H). NH and OH peak not observed.
293	MS m/z 446.1 $[M+H]^+$. ^{1}HNMR (400 MHz, DMSO-d_6) δ 8.88 (s, 1H), 8.26 (s, 1H), 8.23 (d, J = 8.3 Hz, 1H), 7.96 (d, J = 8.1 Hz, 1H), 7.86 (d, J = 7.8 Hz, 1H), 7.41 (s, 1H), 4.87 (d, J = 4.9 Hz, 1H), 4.16 – 3.96 (m, 1H), 3.63 – 3.48 (m, 1H), 2.16 – 2.06 (m, 1H), 2.03 – 1.93 (m, 1H), 1.78 – 1.61 (m, 2H), 1.41 – 1.27 (m, 4H).
294	MS m/z 431.0 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.72 (s, 1H), 8.20 (s, 1H), 8.14 (d, J = 8.2 Hz, 1H), 7.90 (d, J = 8.1 Hz, 1H), 7.43 (s, 1H), 5.16 – 5.02 (m, 1H), 3.57 – 3.42 (m, 2H), 2.83 – 2.66 (m, 1H), 2.43 – 2.22 (m, 1H). NH not observed.
295	MS m/z 459.1 $[M+H]^+$. ^{1}HNMR (400 MHz, DMSO-d_6) δ 8.88 (s, 1H), 7.81 (d, J = 8.5 Hz, 2H), 7.49 – 7.39 (m, 3H), 7.47 (t, J = 73.7 Hz, 1H), 4.37 – 4.24 (m, 1H), 3.06 (d, J = 6.7 Hz, 1H), 2.69 (d, J = 11.4 Hz, 1H), 2.22 (s, 3H), 2.06 – 1.99 (m, 1H), 1.99 – 1.89 (m, 2H), 1.84 – 1.71 (m, 1H), 1.66 – 1.54 (m, 1H), 1.47 – 1.36 (m, 1H).
296	MS m/z 428.0 $[M+H]^+$. ^{1}HNMR (400 MHz, DMSO-d_6) δ 12.78 (s, 1H), 12.65 (s, 1H), 8.79 (s, 1H), 7.86 (d, J = 8.4 Hz, 1H), 7.78 (s, 1H), 7.49 (t, J = 74 Hz, 1H), 7.52 – 7.44 (m, 4H).
297	MS m/z 428.3 $[M+H]^+$. ^{1}HNMR (500 MHz, Methanol-d_4) δ 8.89 – 8.82 (m, 1H), 7.48 – 7.41 (m, 2H), 7.39 (s, 1H), 7.34 (d, J = 7.9 Hz, 1H), 7.16 (t, J = 7.9 Hz, 1H), 6.97 (d, J = 7.8 Hz, 1H), 6.94 (s, 1H), 6.68 (d, J = 8.1 Hz, 1H), 5.54 – 5.39 (m, 1H), 3.88 – 3.60 (m, 2H), 2.44 (s, 3H), 1.74 – 1.66 (m, 3H). NH and OH peak not observed.
298	MS m/z 398.0, 400.0 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.76 (s, 1H), 7.94 (d, J = 2.0 Hz, 1H), 7.82 (dd, J = 8.3, 1.9 Hz, 1H), 7.65 (d, J = 8.2 Hz, 1H), 7.37 (s, 1H), 4.26 (s, 1H), 2.73 – 2.59 (m, 2H), 2.28 (dd, J = 11.4, 9.1 Hz, 2H), 1.44 (s, 3H). 2H not observed (NH and OH).
299	MS m/z 414.1, 416.1 $[M+H]^+$. ^{1}HNMR (400 MHz, DMSO-d_6) δ 8.83 (s, 1H), 8.25 (d, J = 6.1 Hz, 1H), 7.76 (t, J = 6.3 Hz, 2H), 7.68 (dd, J = 8.3, 1.9 Hz, 1H), 7.48 (s, 1H), 5.12 (s, 1H), 4.22 (dt, J = 15.2, 7.7 Hz, 1H), 2.48 (d, J = 2.9 Hz, 2H), 2.21 (t, J = 10.1 Hz, 2H), 1.34 (s, 3H).
300	MS m/z 428.2, 430.2 $[M+H]^+$. ^{1}HNMR (400 MHz, DMSO-d_6) δ 8.86 (s, 1H), 7.86 (d, J= 7.8 Hz, 1H), 7.79 –7.72 (m, 2H), 7.68 (dd, J= 8.3, 1.6 Hz, 1H), 7.47 (s, 1H), 4.94 –4.83 (m, 1H), 4.13 –3.99 (m, 1H), 3.61 –3.50 (m, 1H), 2.14 – 2.06 (m, 1H), 2.03 –1.94 (m, 1H), 1.76 –1.66 (m, 2H), 1.41 –1.22 (m, 4H).
301	MS m/z 489.1 $[M+H]^+$. ^{1}HNMR (400 MHz, DMSO-d_6) δ 8.88 (s, 1H), 8.17 (s, 1H), 7.99 (s, 1H), 7.89 (dd,J = 19.9, 8.1 Hz, 2H),7.49 (s, 1H), 4.31 (s, 1H), 4.18 – 4.04 (m, 2H), 3.53 (t,J = 6.1 Hz, 2H), 3.19 (s, 2H), 2.83 (d,J = 12.3 Hz,1H),

	2.47 (d,J = 6.2 Hz, 2H), 2.16 – 2.01 (m, 3H), 1.75 (s, 1H), 1.60 (d,J = 12.1 Hz, 1H), 1.46 (s, 1H).
302	MS m/z 422.1 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.80 (br s, 1H), 7.55 (d, J = 8.4 Hz, 1H), 7.52 (br s, 1H), 7.13 (s, 1H), 7.11 (d, J = 8.5 Hz, 1H), 4.24 – 4.15 (m, 1H), 3.90 (s, 3H), 3.86 – 3.69 (m, 3H), 2.47 (d, J = 11.6 Hz, 1H), 2.17 (d, J = 11.7 Hz, 1H), 2.01 (d, J = 11.4 Hz, 1H), 1.90 (d, J = 13.6 Hz, 1H), 1.54 – 1.34 (m, 3H), 1.32 – 1.22 (m, 1H). 2H not observed (NH and OH).
303	MS m/z 444.2 $[M+H]^+$. ^{1}HNMR (500 MHz, DMSO-d_6) δ 9.34 (br s, 1H), 8.95 (s, 1H), 8.20 (d, J = 7.48 Hz, 1H), 7.53 (d, J = 8.5 Hz, 1H), 7.41 (s, 1H), 7.17 – 7.05 (m, 3H), 6.90 (d, J = 7.5 Hz, 1H), 6.88 (s, 1H), 6.63 (d, J = 8.09 Hz, 1H), 5.43 (quint, J = 7.32 Hz, 1H), 4.08 – 3.94 (m, 1H), 3.88 – 3.77 (m, 4H), 1.60 (d, J = 6.9 Hz, 3H).
304	MS m/z 437.1 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.69 (s, 1H), 7.71 – 7.24 (m, 2H), 6.82 – 6.74 (m, 2H), 4.57 (q, J = 8.5 Hz, 2H), 4.42 (s, 1H), 3.88 (s, 3H), 3.20 – 3.07 (m, 1H), 2.77 – 2.64 (m, 1H), 2.33 (s, 3H), 2.31 – 1.99 (m, 3H), 1.95 – 1.81 (m, 1H), 1.80 – 1.67 (m, 1H), 1.67 – 1.51 (m, 1H). NH not observed.
305	MS m/z 424.1 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.67 (s, 1H), 7.52 – 7.41 (m, 2H), 6.82 – 6.74 (m, 2H), 4.57 (q, J = 8.5 Hz, 2H), 4.30 – 4.20 (m, 1H), 3.88 (s, 3H), 2.72 – 2.60 (m, 2H), 2.33 – 2.18 (m, 2H), 1.43 (s, 3H). NH and OH not observed.
306	MS m/z 453.9, 455.9 [M+H]+; ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.75 (s, 1H), 7.62 –7.53 (m, 3H), 7.49 (s, 1H), 6.89 (t, J= 73.2Hz, 1H), 4.23 –4.10 (m, 1H), 3.71 –3.58 (m, 1H), 2.29 –2.06 (m, 2H), 1.87 –1.75 (m, 2H), 1.50 –1.37 (m, 4H). NH and OH not observed.
307	MS m/z 472.1, 474.1 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.77 (s,1H), 7.75 (d, J = 8.0, 2H), 7.64 (d, J = 8.0, 1H), 7.51 (s, 1H), 4.15 –4.17 (m, 1H),3.62 –3.64 (m, 1H), 2.10 –2.23 (m,2H), 1.80 –1.81 (m, 2H), 1.43 – 1.48 (m, 4H). NH and OH not observed.
308	MS m/z 431.1 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.83 (s, 1H), 8.71 (d, J = 1.6 Hz, 1H), 8.44 (d, J = 4.0 Hz, 1H), 8.01 (d, J = 7.6 Hz, 1H), 7.59 (d, J= 8.8 Hz, 1H), 7.51 (s, 1H), 7.45 – 7.41 (m, 1H), 7.10 (dd, J = 2.4Hz, J = 8.8 Hz, 1H), 7.02 (s, 1H), 5.58 – 5.53 (m, 1H), 3.90 (s, 3H), 1.76 (d, J = 7.2 Hz, 3H). NH not observed.
309	MS m/z 431.0 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.85 (s, 1H), 8.72(s, 1H), 8.44 (d, J = 4.0 Hz, 1H), 8.01 (d, J = 8.0 Hz, 1H), 7.59 (d, J = 8.8 Hz, 1H), 7.50 (s, 1H), 7.45 – 7.42 (m, 1H), 7.10 (dd, J = 2.4 Hz, J = 8.8 Hz, 1H), 7.02 (s, 1H), 5.56 – 5.54 (m, 1H), 3.90 (s, 3H), 1.76(d, J = 7.2 Hz, 3H). NH not observed.
310	MS m/z 438.1 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.86 (s, 1H), 7.62 (d, J = 8.8 Hz, 1H), 7.49 (s, 1H), 7.12 (dd, J = 8.4, J = 2.0 Hz, 1H), 7.04 (s, 1H), 4.58 –4.33 (m, 1H), 3.91 (s, 3H), 2.07 –1.96 (m, 1H), 1.88 –1.79 (m, 2H), 1.77 –1.60 (m, 3H),1.53 –1.42 (m, 2H), 1.31 (s, 3H). NH and OH not observed.
311	MS m/z 438.1 [M+H]+; ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.86 (s, 1H), 7.62 (d, J= 8.8Hz, 1H), 7.48 (s, 1H), 7.12 (dd, J= 8.4, J= 2.4 Hz, 1H), 7.04 (s, 1H), 4.51 –4.31 (m, 1H), 3.91 (s, 3H), 2.06 –1.95 (m, 1H), 1.91 –1.80 (m, 2H), 1.76

	–1.59 (m, 3H), 1.54 –1.41 (m, 2H), 1.31 (s, 3H). NH and OH not observed.
312	MS m/z 471.1, 473.1 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.76 (s, 1H), 7.78 – 7.71 (m, 2H), 7.65 (d, J= 8.4Hz, 1H), 7.52 (s, 1H), 4.45 (s, 1H),3.12 – 3.17(m, 1H), 2.73 –2.75 (m, 1H), 2.37 (s, 3H), 2.28 –2.30 (m, 2H), 2.09 –2.11 (m, 1H), 1.86 –1.88 (m, 1H), 1.74 –1.7 7 (m, 1H), 1.60 –1.63 (m, 1H). NH not observed.
313	MS m/z 462.2 $[M+H]^+$. ^{1}HNMR (500 MHz, DMSO-d_6) δ 8.88 (s, 1H), 8.04 – 7.95 (m, 2H), 7.94 – 7.85 (m, 2H), 7.52 (s, 1H), 5.26 – 5.16 (m, 1H), 4.35 – 4.21 (m, 1H), 4.21 – 4.03 (m, 2H), 3.98 – 3.82 (m, 2H), 3.71 – 3.62 (m, 1H), 3.43 (t, J = 11.7 Hz, 1H), 3.13 (t, J = 10.5 Hz, 1H), 2.13 (d, J = 11.1 Hz, 1H), 1.70 – 1.59 (m, 1H).
314	MS m/z 408.3 $[M+H]^+$. ^{1}HNMR (500 MHz, DMSO-d_6) δ 8.83 (br s, 1H), 8.03 (d, J = 6.4 Hz, 1H), 7.54 (d, J = 8.4 Hz, 1H), 7.44 (br s, 1H), 7.13 (s, 1H), 7.09 (d, J = 9.5 Hz, 1H), 4.69 – 4.47 (m, 2H), 3.94 (q, J = 11.4 Hz, 2H), 3.84 (s, 3H), 3.43 (d, J = 5.5 Hz, 2H), 2.47 – 2.35 (m, 2H), 2.23 – 2.13 (m, 1H), 1.90 (q, J = 9.6 Hz, 2H).
315	MS m/z 444.3, $[M+H]^+$. ^{1}HNMR (500 MHz, Methanol-d_4) δ 8.55-8.69 (m, 1H), 7.335-7.40 (m, 1H), 7.22-7.32 (m, 1H), 7.19 (s, 1H), 7.13 (s, 1H), 4.15 (quin, J=8.0 Hz, 1H), 3.84 (s, 3H), 2.48-2.66 (m, 2H), 2.05-2.33 (m, 2H), 1.34 (s, 3H). NH and OH not observed.
316	MS m/z 458.3, $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ: 8.64 (s, 1H), 7.37 (s, 1H), 7.24-7.28 (m, 1H), 7.19 (s, 1H), 7.10-7.15 (m, 1H), 3.96-4.13 (m, 1H), 3.84 (s, 3H), 3.50-3.59 (m, 1H), 2.11-2.19 (m, 1H), 1.95-2.06 (m, 1H), 1.67-1.72 (m, 2H), 1.26-1.50 (m, 4H). NH and OH not observed.
317	MS m/z 405.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.81 – 8.70 (m, 1H), 7.53 – 7.48 (m, 1H), 7.43 – 7.39 (m, 2H), 7.39 – 7.34 (m, 1H), 4.54 – 4.36 (m, 1H), 3.83 – 3.67 (m, 2H), 3.61 – 3.45 (m, 1H), 3.04 – 2.88 (m, 1H), 2.65 – 2.51 (m, 5H), 2.45 (s, 3H), 2.20 – 2.09 (m, 1H), 2.06 – 1.94 (m, 1H), 1.90 – 1.79 (m, 1H), 1.76 – 1.64 (m, 1H) . NH peak not observed.
318	MS m/z 392.3 $[M+H]^+$. ^{1}HNMR (500 MHz, Methanol-d_4) δ 8.73 (s, 1H), 7.51 – 7.46 (m, 1H), 7.45 – 7.39 (m, 2H), 7.38 – 7.33 (m, 1H), 4.29 –4.24 (m, 1H), 3.77 (q, J = 11.1 Hz, 2H), 2.72 – 2.61 (m, 2H), 2.45 (s, 3H), 2.31 – 2.23 (m, 2H), 1.44 (s, 3H). NH and OH peak not observed.
319	MS m/z 366.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.71 (s, 1H), 7.41 (s, 1H), 7.32 (d, J = 8.4 Hz, 1H), 6.87 (dd, J = 8.4, 2.1 Hz, 1H), 6.61 (d, J = 1.9 Hz, 1H), 4.27 (quint, J = 8.0 Hz, 1H), 3.84 (s, 3H), 2.71 – 2.60 (m, 2H), 2.33 – 2.20 (m, 2H), 1.94 – 1.85 (m, 1H), 1.44 (s, 3H), 0.83 – 0.74 (m, 2H), 0.71 – 0.62 (m, 2H). NH and OH not observed.
320	MS m/z 365.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.67 (s, 1H), 7.44 (s, 1H), 7.33 (d, J = 8.4 Hz, 1H), 6.88 (d, J = 8.3 Hz, 1H), 6.60 (s, 1H), 5.14 – 4.96 (m, 1H), 3.84 (s, 3H), 3.57 – 3.43 (m, 2H), 2.80 – 2.65 (m, 1H), 2.44 – 2.26 (m, 1H), 1.99 – 1.81 (m, 1H), 0.89 – 0.76 (m, 2H), 0.72 – 0.58 (m, 2H). NH not observed.
321	MS m/z 380.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.74 (s, 1H), 7.40 (s, 1H), 7.32 (d, J = 8.4 Hz, 1H), 6.88 (dd, J = 8.4, 2.1 Hz, 1H), 6.60 (d, J = 1.9 Hz, 1H), 4.14 (s, 1H), 3.84 (s, 3H), 3.65 (d, J = 9.6 Hz, 1H), 2.26 (s, 1H), 2.12

	(d, J = 10.2 Hz, 1H), 1.91 (d, J = 8.8 Hz, 1H), 1.82 (d, J = 16.8 Hz, 2H), 1.44 (h, J = 12.4 Hz, 4H), 0.78 (d, J = 8.0 Hz, 2H), 0.66 (d, J = 5.0 Hz, 2H). NH and OH not observed.
322	MS m/z 464.2 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.80 (s, 1H), 7.96 (d, J = 8.1 Hz, 1H), 7.91 (d, J = 8.1 Hz, 1H), 7.83 (s, 1H), 7.57 (s, 1H), 4.38 (s, 1H), 4.05 (dd, J = 11.1, 5.0 Hz, 1H), 4.02 – 3.94 (m, 1H), 3.84 – 3.72 (m, 1H), 3.56 (t, J = 11.9 Hz, 1H), 3.27 (t, J = 10.6 Hz, 1H), 2.38 – 2.18 (m, 1H), 1.85 – 1.72 (m, 1H). NH and OH not observed.
323	MS m/z 484.2 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.90 (s, 1H), 7.93 (d, J = 8.1 Hz, 1H), 7.88 (d, J = 8.2 Hz, 1H), 7.82 (s, 1H), 7.56 (s, 1H), 7.16 (t, J = 7.9 Hz, 1H), 6.97 (d, J = 7.6 Hz, 1H), 6.94 (s, 1H), 6.68 (d, J = 8.0 Hz, 1H), 5.50 (q, J = 6.8 Hz, 1H), 1.71 (d, J = 6.9 Hz, 3H). NH and OH not observed.
324	MS m/z 462.2 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.77 (s, 1H), 7.96 (d, J = 8.0 Hz, 1H), 7.90 (d, J = 8.1 Hz, 1H), 7.83 (s, 1H), 7.55 (s, 1H), 4.62 (quint, J = 8.3 Hz, 1H), 3.45 (d, J = 5.9 Hz, 2H), 3.37 (s, 3H), 2.71 – 2.60 (m, 2H), 2.47 – 2.34 (m, 1H), 2.09 – 1.94 (m, 2H).
325	MS m/z 476.2 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.79 (s, 1H), 7.96 (d, J = 8.0 Hz, 1H), 7.90 (d, J = 8.1 Hz, 1H), 7.83 (s, 1H), 7.55 (s, 1H), 4.51 (quint, J = 8.2 Hz, 1H), 2.56 – 2.46 (m, 2H), 2.25 – 2.16 (m, 1H), 2.16 – 2.07 (m, 2H), 1.17 (s, 6H). NH and OH not observed.
326	MS m/z 422.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.73 (s, 1H), 7.53 (d, J = 8.5 Hz, 1H), 7.44 (s, 1H), 7.12 (s, 1H), 7.09 (dd, J = 8.3, 2.1 Hz, 1H), 4.57 (quint, J = 8.1 Hz, 1H), 3.89 (s, 3H), 3.80 (q, J = 11.0 Hz, 2H), 3.45 (d, J = 6.0 Hz, 2H), 3.37 (s, 3H), 2.68 – 2.58 (m, 2H), 2.48 – 2.32 (m, 1H), 2.05 – 1.93 (m, 2H).
327	MS m/z 436.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.74 (s, 1H), 7.53 (d, J = 8.5 Hz, 1H), 7.44 (s, 1H), 7.12 (s, 1H), 7.10 (dd, J = 8.6, 2.4 Hz, 1H), 4.46 (quint, J = 8.2 Hz, 1H), 3.90 (s, 3H), 3.80 (q, J = 10.9 Hz, 2H), 2.60 – 2.43 (m, 2H), 2.24 – 2.14 (m, 1H), 2.14 – 2.04 (m, 2H), 1.17 (s, 6H).
328	MS m/z 473.3 $[M+H]^+$. ^{1}HNMR (500 MHz, Methanol-d_4) δ 8.73 (s, 1H), 7.78 (d, J = 8.6 Hz, 1H), 7.54 (s, 1H), 7.38 (d, J = 8.4 Hz, 1H), 7.34 (s, 1H), 7.07 (t, J = 73.0 Hz, 1H), 4.90 – 4.82 (m, 1H), 3.62 – 3.50 (m, 1H), 3.50 – 3.41 (m, 1H), 3.03 (s, 3H), 2.48 – 2.29 (m, 1H), 2.28 – 2.14 (m, 1H), 2.14 – 2.00 (m, 2H). 1 NH is missing.
329	MS m/z 473.3 $[M+H]^+$. ^{1}HNMR (500 MHz, Methanol-d_4) δ 8.74 (s, 1H), 7.94 (s, 1H), 7.88 (d, J = 8.1 Hz, 1H), 7.84 (d, J = 8.2 Hz, 1H), 7.51 (s, 1H), 3.96 (d, J = 10.8 Hz, 1H), 3.91 (d, J = 11.0 Hz, 1H), 3.60 – 3.51 (m, 1H), 3.50 – 3.43 (m, 1H), 3.04 (s, 3H), 2.44 – 2.33 (m, 1H), 2.29 – 2.15 (m, 1H), 2.14 – 2.01 (m, 2H). the proton N-CH-carbonyl overlaps with the water peak.
330	MS m/z 435.3 $[M+H]^+$. ^{1}HNMR (500 MHz, Methanol-d_4) δ 8.82 (s, 1H), 7.60 (s, 1H), 7.54 (d, J = 8.4 Hz, 1H), 7.15 (s, 1H), 7.11 (d, J = 8.2 Hz, 1H), 4.89 – 4.81 (m, 1H), 3.91 (s, 3H), 3.81 (d, J = 11.2 Hz, 1H), 3.77 (d, J = 11.2 Hz, 1H), 3.61 – 3.50 (m, 1H), 3.50 – 3.41 (m, 1H), 3.03 (s, 3H), 2.55 – 2.32 (m, 1H), 2.30 – 1.95 (m, 3H). NH not observed.
331	MS m/z 462.1 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.79 (br s, 1H), 7.77 (d, J = 8.5 Hz, 1H), 7.53 (br s, 1H), 7.37 (d, J = 8.8 Hz, 1H), 7.33 (s, 1H),

	7.05 (t, J = 72.7 Hz, 1H), 4.40 – 4.27 (m, 1H), 4.04 (dd, J = 11.1, 4.8 Hz, 1H), 3.98 (dd, J = 11.6, 4.0 Hz, 1H), 3.76 (td, J = 9.5, 5.0 Hz, 1H), 3.56 (t, J = 11.7 Hz, 1H), 3.26 (t, J = 10.6 Hz, 1H), 2.26 (d, J = 12.9 Hz, 1H), 1.78 (qd, J = 12.4, 4.4 Hz, 1H). 2H not observed (NH and OH).
332	MS m/z 394.4 $[M+H]^+$. ^{1}HNMR (500 MHz, Methanol-d_4) δ 8.85 (s, 1H), 7.81 – 7.50 (m, 2H), 7.39 (d, J = 7.8 Hz, 1H), 7.36 (s, 1H), 4.53 – 4.11 (m, 1H), 2.74 – 2.62 (m, 2H), 2.51 (s, 3H), 2.40 – 2.25 (m, 2H), 1.46 (s, 3H). 1 NH and 1 OH not observed.
333	MS m/z 403.2 [M+H]+; ^{1}HNMR (500 MHz, Methanol-d_4) δ 8.70 (s, 1H), 7.61-7.57 (m, 2H), 7.51 – 7.42 (m, 1H), 7.35 (s, 1H), 5.13 – 5.02 (m, 1H), 3.57 – 3.45 (m, 2H), 2.84 – 2.68 (m, 1H), 2.44 – 2.28 (m, 1H), 2.04 – 1.89 (m, 1H), 0.89 (d, J = 7.3 Hz, 2H), 0.74 (d, J = 5.2 Hz, 2H). NH peak not observed.
334	MS m/z 420.3 $[M+H]^+$. ^{1}HNMR (500 MHz, Methanol-d_4) δ 8.78 (s, 1H), 7.63 - 7.61 (m, 2H), 7.45 (s, 1H), 7.36 (s, 1H), 4.45 – 4.23 (m, 1H), 4.09 – 4.01 (m, 1H), 4.01 – 3.93 (m, 1H), 3.81 – 3.72 (m, 1H), 3.58-3.53 (m, 1H), 3.29 – 3.22 (m, 1H), 2.36 – 2.21 (m, 1H), 1.99-1.97 (m, 1H), 1.79-1.74 (m, 1H), 0.88 (d, J = 8.4 Hz, 2H), 0.74 (d, J = 5.2 Hz, 2H). NH and OH peaks were not observed.
335	MS m/z 462.2 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d4) δ 8.85 (s, 1Hx2, cis and trans), 8.00 – 7.95 (m, 1Hx2, cis and trans), 7.94 – 7.89 (m, 1Hx2, cis and trans), 7.85 (s, 1Hx2, cis and trans), 7.62 (s, 1Hx2, cis and trans), 4.81 – 4.70 (m, 1H, cis/trans), 4.70 – 4.55 (m, 1H, cis/trans), 3.57 (s, 2H, cis/trans), 3.44 (s, 2H, cis/trans), 2.65 – 2.54 (m, 2H, cis/trans), 2.33 – 2.25 (m, 2H, cis/trans), 2.24 – 2.16 (m, 2H, cis/trans), 1.99 (t, J = 10.3 Hz, 2H, cis/trans), 1.29 (s, 3H, cis/trans), 1.24 (s, 3H, cis/trans). A mixture of cis/trans with ratio ~1:1. NH and OH not observed.
336	MS m/z 422.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d4) δ 8.78 (s, 1H), 7.55 (d, J = 8.5 Hz, 1H), 7.48 (s, 1H), 7.14 (s, 1H), 7.12 (d, J = 10.2 Hz, 1H), 4.69 – 4.54 (m, 1H), 3.91 (s, 3H), 3.81 (q, J = 11.0 Hz, 2H), 3.57 (s, 2H), 2.62 – 2.54 (m, 2H), 2.02 – 1.92 (m, 2H), 1.24 (s, 3H). NH and OH not observed.
337	MS m/z 422.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.68 (s, 1Hx2, cis and trans), 7.49 – 7.28 (m, 1Hx2, cis and trans), 7.05 – 6.96 (m, 1Hx2, cis and trans), 4.66 – 4.55 (m, 1H, cis/trans), 4.54 – 4.43 (m, 1H, cis/trans), 3.79 (s, 3Hx2, cis and trans), 3.70 (q, J = 10.4 Hz, 4H, cis and trans), 3.45 (s, 2H, cis/trans), 3.32 (s, 2H, cis/trans), 2.51 – 2.42 (m, 2H, cis/trans), 2.20 – 2.11 (m, 2H, cis/trans), 2.11 – 2.02 (m, 2H, cis/trans), 1.90 – 1.79 (m, 2H, cis/trans), 1.17 (s, 3H, cis/trans), 1.12 (s, 3H, cis/trans). A mixture of cis/trans with ratio ~1:1. NH and OH not observed.
338	MS m/z 438.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 1H NMR (400 MHz, Methanol-d4) δ 8.76 (s, 1H), 7.63 (d, J = 8.6 Hz, 1H), 7.50 (s, 1H), 7.12 (d, J = 8.7 Hz, 1H), 7.04 (s, 1H), 4.47 (quint, J = 7.8 Hz, 1H), 3.92 (s, 3H), 2.57 – 2.42 (m, 2H), 2.24 – 1.99 (m, 3H), 1.17 (s, 6H). NH and OH not observed.
339	MS m/z 474.2 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.79 (s, 1H), 7.92 (s, 1H), 7.89 – 7.80 (m, 2H), 7.49 (s, 1H), 4.57 – 4.39 (m, 1H), 3.95 (q, J = 10.9 Hz, 2H), 2.60 – 2.40 (m, 2H), 2.28 – 2.02 (m, 3H), 1.17 (s, 6H). NH and OH not observed.
340	MS m/z 462.2 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.79 (s, 1H), 7.96

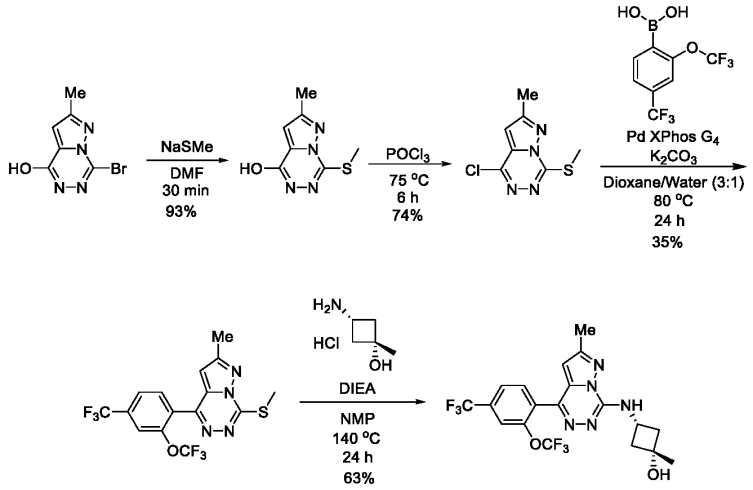
	(d, J = 8.1 Hz, 1H), 7.90 (d, J = 8.3 Hz, 1H), 7.83 (s, 1H), 7.55 (s, 1H), 4.80 – 4.66 (m, 1H), 3.42 (s, 2H), 2.31 – 2.23 (m, 2H), 2.22 – 2.13 (m, 2H), 1.27 (s, 3H). NH and OH not observed.
341	MS m/z 422.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.80 (s, 1H), 7.70 – 7.35 (m, 2H), 7.15 – 7.05 (m, 2H), 4.71 (quint, J = 8.1 Hz, 1H), 3.89 (s, 3H), 3.80 (q, J = 11.0 Hz, 2H), 3.42 (s, 2H), 2.32 – 2.22 (m, 2H), 2.20 – 2.12 (m, 2H), 1.27 (s, 3H). NH and OH not observed.
342	MS m/z 424.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.80 (s, 1H), 7.63 (d, J = 8.6 Hz, 1H), 7.55 (s, 1H), 7.12 (d, J = 8.6 Hz, 1H), 7.04 (s, 1H), 4.72 (quint, J = 8.2 Hz, 1H), 3.92 (s, 3H), 3.42 (s, 2H), 2.31 – 2.21 (m, 2H), 2.21 – 2.12 (m, 2H), 1.26 (s, 3H). NH and OH not observed.
343	MS m/z 460.2 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.80 (s, 1H), 7.92 (s, 1H), 7.89 – 7.78 (m, 2H), 7.51 (s, 1H), 4.74 (quint, J = 7.9 Hz, 1H), 3.95 (q, J = 10.9 Hz, 2H), 3.43 (s, 2H), 2.31 – 2.23 (m, 2H), 2.23 – 2.14 (m, 2H), 1.27 (s, 3H). NH and OH not observed.
344	MS m/z 375.3 $[M+H]^+$. ^{1}HNMR (500 MHz, Methanol-d_4) δ 8.61 (s, 1H), 7.35-7.42 (m, 2H), 7.03-7.16 (3, 2H), 6.46-6.93 (m, 1H), 4.15 (quin, J=7.9 Hz, 1H), 2.46-2.72 (m, 2H), 2.37 (s, 3H), 2.00-2.23 (m, 2H), 1.34 (s, 3H). NH and OH not observed.
345	MS m/z 402.3, $[M+H]^+$. ^{1}HNMR (500 MHz, Methanol-d_4) δ 8.51-8.76 (m, 1H), 7.29-7.50 (m, 2H), 6.94-7.08 (m, 2H), 6.44-6.91 (m, 1H), 4.15 (quin, J=7.9 Hz, 1H), 2.45-2.67 (m, 2H), 2.08-2.27 (m, 2H), 1.85-2.05 (m, 1H), 1.34 (s, 3H), 0.90-1.11 (m, 2H), 0.61-0.78 (m, 2H). NH and OH not observed.
346	MS m/z 420.5 $[M+H]^+$. ^{1}HNMR (500 MHz, Methanol-d_4) δ 8.86 (s, 1H), 7.87 – 7.48 (m, 2H), 7.25 (d, J = 7.9 Hz, 1H), 7.22 (s, 1H), 4.41 – 4.10 (m, 1H), 2.80 – 2.56 (m, 2H), 2.45 – 2.21 (m, 2H), 2.19 – 1.93 (m, 1H), 1.46 (s, 3H), 1.20 – 1.04 (m, 2H), 0.98 – 0.71 (m, 2H). 1 NH and 1 OH not observed.
347	MS m/z 394.6 $[M+H]^+$. ^{1}HNMR (500 MHz, Methanol-d_4) δ 8.86 (s, 1H), 7.96 – 7.46 (m, 2H), 7.39 (d, J = 7.7 Hz, 1H), 7.36 (s, 1H), 4.68 – 4.49 (m, 1H), 3.63 – 3.58 (m, 2H), 2.82 – 2.59 (m, 2H), 2.50 (s, 3H), 2.42 – 2.26 (m, 1H), 2.13 – 1.86 (m, 2H). 1 NH and 1 OH not observed.
348	MS m/z 418.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.77 (br s, 1H), 7.56 – 7.39 (m, 2H), 7.29 (s, 1H), 7.22 (d, J = 8.0 Hz, 1H), 4.25 (quint, J = 8.0 Hz, 1H), 3.77 (q, J = 11.1 Hz, 2H), 2.70 – 2.63 (m, 2H), 2.32 – 2.24 (m, 2H), 2.06 – 1.98 (m, 1H), 1.44 (s, 3H), 1.11 – 1.04 (m, 2H), 0.83 – 0.76 (m, 2H). 2H not observed (NH and OH).
349	MS m/z 418.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.76 (br s, 1H), 7.56 – 7.39 (m, 2H), 7.29 (s, 1H), 7.22 (d, J = 7.88 Hz, 1H), 4.57 (quint, J = 8.1 Hz, 1H), 3.77 (q, J = 10.9 Hz, 2H), 3.59 (d, J = 6.0 Hz, 2H), 2.69 – 2.58 (m, 2H), 2.44 – 2.26 (m, 1H), 2.06 – 1.92 (m, 3H), 1.07 (q, J = 6.2 Hz, 2H), 0.86 – 0.76 (m, 2H). 2H not observed (NH and OH).
350	MS m/z 417.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.68 (br s, 1H), 7.50 – 7.41 (m, 2H), 7.30 (s, 1H), 7.22 (d, J = 7.88 Hz, 1H), 5.06 (t, J = 9.6 Hz, 1H), 3.75 (q, J = 11.0 Hz, 2H), 3.60 – 3.39 (m, 2H), 2.81 – 2.69 (m, 1H), 2.42 – 2.31 (m, 1H), 2.07 – 1.98 (m, 1H), 1.12 – 1.03 (m, 2H), 0.82 – 0.76 (m, 2H). 2H not observed (2 NH).

351	MS m/z 434.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.77 (br s, 1H), 7.50 – 7.40 (m, 2H), 7.29 (s, 1H), 7.22 (d, J = 8.1 Hz, 1H), 4.39 – 4.23 (m, 1H), 4.04 (dd, J = 11.1, 4.9 Hz, 1H), 3.98 (dd, J = 11.6, 3.9 Hz, 1H), 3.85 – 3.67 (m, 3H), 3.55 (t, J = 11.3 Hz, 1H), 3.26 (t, J = 10.3 Hz, 1H), 2.26 (br d, J = 12.5 Hz, 1H), 2.11 – 1.93 (m, 1H), 1.78 (qd, J = 12.4, 4.5 Hz, 1H), 1.11 – 1.04 (m, 2H), 0.86 – 0.74 (m, 2H). 2H not observed (NH and OH).
352	MS m/z 431.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.75 (br s, 1H), 7.49 – 7.38 (m, 2H), 7.29 (s, 1H), 7.23 (d, J = 7.9 Hz, 1H), 4.57 – 4.34 (m, 1H), 3.76 (q, J = 11.1 Hz, 2H), 3.43 – 3.32 (m, 1H), 3.09 – 2.92 (m, 1H), 2.71 – 2.42 (m, 5H), 2.26 – 2.06 (m, 1H), 2.06 – 1.94 (m, 2H), 1.91 – 1.62 (m, 2H), 1.13 – 1.03 (m, 2H), 0.82 – 0.76 (m, 2H). 1H not observed (NH).
353	MS m/z 432.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.74 (br s, 1H), 7.54 – 7.39 (m, 2H), 7.29 (s, 1H), 7.22 (d, J = 8.0 Hz, 1H), 4.27 – 4.13 (m, 1H), 3.83 – 3.69 (m, 3H), 2.47 (br d, J = 11.3 Hz, 1H), 2.17 (br d, J = 12.1 Hz, 1H), 2.06 – 1.96 (m, 2H), 1.96 – 1.84 (m, 1H), 1.55 – 1.20 (m, 4H), 1.11 – 1.03 (m, 2H), 0.83 – 0.76 (m, 2H). 2H not observed (NH and OH).
354	MS m/z 454.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.93 (br s, 1H), 7.47 – 7.47 (m, 2H), 7.27 (s, 1H), 7.23 – 7.13 (m, 2H), 6.97 (d, J = 7.9 Hz, 1H), 6.93 (s, 1H), 6.68 (d, J = 7.9 Hz, 1H), 5.53 – 5.39 (m, 1H), 3.85 – 3.61 (m, 2H), 2.05 – 1.97 (m, 1H), 1.70 (d, J = 6.8 Hz, 3H), 1.12 – 1.00 (m, 2H), 0.82 – 0.75 (m, 2H). 2H not observed (NH and OH).
355	MS m/z 437.1 $[M+H]^+$. ^{1}HNMR (500 MHz, Methanol-d_4) δ 8.95 (s, 1H), 8.10 – 7.52 (m, 2H), 7.40 (d, J = 7.8 Hz, 1H), 7.37 (s, 1H), 4.78 – 4.49 (m, 1H), 4.11 – 3.83 (m, 2H), 3.86 – 3.78 (m, 1H), 3.54 – 3.43 (m, 1H), 3.31 – 3.23 (m, 2H), 3.22 – 3.10 (m, 2H), 2.51 (s, 3H), 2.32 – 2.11 (m, 2H), 2.03 – 1.95 (m, 1H), 1.95 – 1.85 (m, 1H). 1 NH and 1 OH not observed.
399	MS m/z 404.3 $[M+H]^+$. ^{1}HNMR (500 MHz, Methanol-d_4) δ 8.75 (s, 1H), 7.66 – 7.56 (m, 2H), 7.44 (s, 1H), 7.36 (s, 1H), 4.35 – 4.18 (m, 1H), 2.73 – 2.59 (m, 2H), 2.28 (t, J = 9.8 Hz, 2H), 2.05 – 1.89 (m, 1H), 1.44 (s, 3H), 0.93 – 0.83 (m, 2H), 0.73-0.71 (m, 2H), NH and OH peak not observed.
400	MS m/z 462.3 $[M+H]^+$. ^{1}HNMR (500 MHz, Methanol-d_4) δ 8.88 (s, 1H), 7.94 (s, 1H), 7.89 (d, J = 8.3 Hz, 1H), 7.85 (d, J = 8.1 Hz, 1H), 7.60 (s, 1H), 4.43 – 4.22 (m, 2H), 4.09 – 3.79 (m, 4H), 3.63 – 3.47 (m, 1H), 3.40 – 3.35 (m, 1H), 2.30 – 2.03 (m, 1H), 1.96 – 1.64 (m, 1H). 1 NH and 1 OH not observed.
401	MS m/z 460.1 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.94 (s, 1H), 7.92 (s, 1H), 7.85 (dd, J= 8.2 Hz, 2H), 7.49 (s, 1H), 4.33 (s, 1H), 4.31 – 4.25 (m, 1H), 4.00 – 3.89 (m, 2H), 2.06 –1.91 (m, 2H), 1.89 – 1.81 (m, 2H), 1.71 – 1.68 (m, 2H), 1.51 – 1.49 (m, 2H). NH and OH peak not observed.
402	MS m/z 408.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.82 – 8.71 (m, 1H), 7.53 – 7.46 (m, 1H), 7.46 – 7.39 (m, 2H), 7.39 – 7.33 (m, 1H), 4.43 – 4.24 (m, 1H), 4.10 – 4.01 (m, 1H), 4.01 – 3.93 (m, 1H), 3.83 – 3.68 (m, 3H), 3.61 – 3.50 (m, 1H), 3.28 – 3.22 (m, 1H), 2.45 (s, 3H), 2.34 – 2.20 (m, 1H), 1.86 – 1.67 (m, 1H). NH and OH peak not observed.

Example 3

Preparation of Compound 3

(1s,3s)-1-Methyl-3-((2-methyl-4-(2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl)pyrazolo[1,5-d][1,2,4]triazin-7-yl)amino)cyclobutan-1-ol



Step 1. **2-Methyl-7-(methylthio)pyrazolo[1,5-d][1,2,4]triazin-4-ol**

A cold solution of 7-bromo-2-methyl-pyrazolo[1,5-d][1,2,4]triazin-4-ol (Intermediate 1f, 600.0 mg, 2.620 mmol) in dry DMF (2.6 mL) at 0°Cwas treated with sodium thiomethoxide (386.6 mg, 5.239 mmol). The mixture was then stirred at room temperature for 30 minutes. Upon completion, the DMF was evaporated, and the resulting oily residue was precipitated with water. The mixture was then cooled at 0 °C and the precipitate was filtered while cold. The collected precipitate was washed with water and dried overnight to afford 2-methyl-7-(methylthio)pyrazolo[1,5-d][1,2,4]triazin-4-ol (476.0 mg, 93% yield) as white solid. MS *m/z* 197.1 $[M+H]^+$.

Step 2. **4-Chloro-2-methyl-7-(methylthio)pyrazolo[1,5-d][1,2,4]triazine**

A mixture of 2-methyl-7-(methylthio)pyrazolo[1,5-d][1,2,4]triazin-4-ol (476.0 mg, 2.426 mmol) and phosphoryl oxychloride (7.44 g, 4.51 mL, 48.51 mmol) was heated at 75 °C for 6 hours, upon which the solution became clear. The excess $POCl_3$ was then evaporated, and the resulting residue was precipitated with water. The pH of the aqueous solution was adjusted to neutral (pH ~7) using saturated $NaHCO_3$ solution. The precipitate was filtered, washed with water, and dried overnight to yield 4-chloro-2-methyl-7-(methylthio)pyrazolo[1,5-d][1,2,4]triazine (383 mg, 74% yield) as white solid. MS *m/z* 215.1 $[M+H]^+$.

Step 3. **2-Methyl-7-(methylthio)-4-(2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl)-pyrazolo[1,5-d][1,2,4]triazine**

A mixture of 4-chloro-2-methyl-7-(methylthio)pyrazolo[1,5-d][1,2,4]triazine (38.8 mg, 0.181 mmol), [2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]boronic acid (64.4 mg, 0.235 mmol), XPhos Pd G4 (16.4 mg, 0.0181 mmol) and potassium carbonate (74.9 mg, 0.542 mmol) was dissolved in dioxane (2.1 mL) and water (0.4 mL). The reaction vessel was vacuumed and backflushed with nitrogen (3x), and the mixture was stirred at 80 °C under nitrogen atmosphere for 4 hours. Upon completion, the mixture was diluted with EtOAc, washed with water and brine, dried over Na_2SO_4 and evaporated in vacuo. The resulting crude product was purified by flash column chromatography eluting with 0-80% EtOAc in hexane to afford 2-methyl-7-(methylthio)-4-(2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl)-pyrazolo[1,5-d][1,2,4]triazine (25.5 mg, 35% yield) as brown solid. MS *m/z* 409.1 $[M+H]^+$.

Step 4. (1*s*,3*s*)-1-Methyl-3-((2-methyl-4-(2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl)pyrazolo[1,5-d][1,2,4]triazin-7-yl)amino)cyclobutan-1-ol

To a solution of 2-ethyl-7-(methylthio)-4-(2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl)pyrazolo[1,5-d][1,2,4]triazine (25.5 mg, 0.0625 mmol) in NMP (0.50 mL) was added (1*s*,3*s*)-3-amino-1-methylcyclobutan-1-ol hydrochloride (25.8 mg, 0.187 mmol) and *N*,*N*-diisopropylethylamine (48.4 mg, 65.4 µL, 0.375 mmol). The mixture was heated under nitrogen atmosphere at 130 °C for 24 hours, upon which partial conversion was achieved. Additional (1*s*,3*s*)-3-amino-1-methylcyclobutan-1-ol hydrochloride (25.8 mg, 0.187 mmol) was then added and the reaction was stirred and heated further at 140 °C for 24 hours. Upon full conversion to product, the solution was diluted with small amount of water (0.50 mL). The black solution was purified by reverse phase chromatography (0.1% formic acid in MeCN:0.1% formic acid in H_2O, 5 to 100%) to provide (1*s*,3*s*)-1-methyl-3-((2-methyl-4-(2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl)pyrazolo[1,5-*d*][1,2,4]triazin-7-yl)amino)cyclobutan-1-ol (18.2 mg, 63% yield) as white solid. MS *m/z* 462.1 $[M+H]^+$; ^{1}H NMR (500 MHz, Methanol-d4) δ 7.95 (d, *J* = 8.1 Hz, 1H), 7.89 (d, *J* = 8.1 Hz, 1H), 7.81 (s, 1H), 6.51 (s, 1H), 4.39 – 4.31 (m, 1H), 2.71 – 2.61 (m, 2H), 2.54 (s, 3H), 2.36 – 2.26 (m, 2H), 1.44 (s, 3H).

The compounds below were prepared according to the procedure of Example 3 by substituting the appropriate starting materials, reagents and reaction conditions.

Compound#	Spectral Data
356	MS *m/z* 489.2 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 7.89 – 7.80 (m, 1H), 7.77 – 7.70 (m, 1H), 7.67 (s, 1H), 6.94 (t, J = 73.0 Hz, 1H), 6.51 (s, 1H), 5.04 (d, J = 47.9 Hz, 1H), 4.83 – 4.77 (m, 1H), 3.23 – 3.07 (m, 1H), 2.80 – 2.59

	(m, 3H), 2.57 – 2.47 (m, 4H), 2.45 – 2.31 (m, 1H), 2.20 – 1.97 (m, 1H), 1.20 (t, J = 7.1 Hz, 3H). 2 H not observed (NH and a CH obscured by the signal of Methanol-d_4).
357	MS *m/z* 499.0, 501.0 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.55 (s, 1H, formate CH), 7.82 – 7.69 (m, 2H), 7.64 (d, J = 8.3 Hz, 1H), 6.49 (s, 1H), 4.57 – 4.44 (m, 1H), 3.23 – 3.15 (m, 1H), 2.92 – 2.76 (m, 1H), 2.63 (q, J = 7.5 Hz, 2H), 2.58 – 2.34 (m, 5H), 2.15 – 2.01 (m, 1H), 1.97 – 1.84 (m, 1H), 1.84 – 1.67 (m, 2H), 1.18 (t, J = 7.4 Hz, 3H). NH not observed.
358	MS *m/z* 423.1, 425.0 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.51 (s, 1H, formic acid), 7.61 (d, J = 9.13 Hz, 1 H), 7.47 – 7.42 (m, 2H), 6.88 (t, J = 73.54 Hz, 1H), 6.48 (s, 1H), 4.54 – 4.46 (m, 1H), 3.28 – 3.20 (m, 1H), 2.97 – 2.82 (m, 1H), 2.71 – 2.61 (m, 1H), 2.60 – 2.56 (m, 1 H), 2.53 (s, 3H), 2.52 (s, 3 H), 2.15 – 2.02 (m, 1H), 2.02 – 1.89 (m, 1H), 1.89 – 1.67 (m, 2H). 1H not observed (NH).
359	MS *m/z* 441.5 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.48 (s, 1H, formic acid), 8.12 (s, 1H), 8.01 (d, J = 7.63 Hz, 1 H), 7.94 (d, J = 8.88 Hz, 1 H), 7.17 (t, J = 54.41 Hz, 1 H), 6.58 (s, 1H), 4.59 – 4.47 (m, 1H), 3.42 – 3.34 (m, 1H), 3.08 – 2.92 (m, 1H), 2.82 – 2.64 (m, 2H), 2.61 (s, 3H), 2.54 (s, 3H), 2.19 – 2.05 (m, 1H), 2.05 – 1.94 (m, 1H), 1.91 – 1.74 (m, 2H). 1H not observed (NH).
360	MS *m/z* 429.2 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.45 (s, 1H, formic acid), 7.47 (d, J = 8.63 Hz, 1H), 7.12 (d, J = 8.63 Hz, 1H), 7.07 (s, 1H), 6.79 (t, J = 75.67 Hz, 1H), 6.47 (s, 1H), 4.59 – 4.46 (m, 1H), 3.58 - 3.43 (m, 1H), 3.22 – 3.06 (m, 1H), 2.99 – 2.77 (m, 2H), 2.72 (s, 3H), 2.52 (s, 3H), 2.24 – 2.11 (m, 1H), 2.11 – 1.97 (m, 2H), 1.97 – 1.70 (m, 2H), 1.16 – 1.03 (m, 2H), 0.86 – 0.74 (m, 2H). 1H not observed (NH).
361	MS *m/z* 403.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.42 (s, 1H, formic acid), 7.48 (d, J = 7.8 Hz, 1H), 7.24 (d, J = 8.0 Hz, 1H), 7.21 (s, 1H), 6.80 (t, J = 74.29 Hz, 1H), 6.48 (s, 1H), 4.62 – 4.50 (m, 1H), 3.68 – 3.55 (m, 1H), 3.30 – 3.22 (m, 1H), 3.10 – 2.85 (m, 2H), 2.81 (s, 3H), 2.52 (s, 3H), 2.47 (s, 3H), 2.24 – 2.05 (m, 2H), 1.97 – 1.81 (m, 2H). 1H not observed (NH).
362	MS *m/z* 407.1, 409.0 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 7.83 (s, 1H), 7.74 – 7.66 (m, 2H), 7.08 (t, J = 55.7 Hz, 1H), 6.53 (s, 1H), 4.49 – 4.41 (m, 1H), 3.09 – 2.88 (m, 1H), 2.73 – 2.57 (m, 1H), 2.53 (s, 3H), 2.47 – 2.27 (m, 5H), 2.09 – 1.94 (m, 1H), 1.94 – 1.81 (m, 1H), 1.80 – 1.63 (m, 2H). 1H not observed (NH).
363	MS *m/z* 413.4 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.48 (br s, 1H, formic acid), 7.57 – 7.52 (m, 2H), 7.37 (d, J = 8.4 Hz, 1H), 7.00 (t, J = 55.66 Hz, 1H), 6.51 (s, 1H), 4.56 – 4.44 (m, 1H), 3.42 – 3.34 (m, 1H), 3.10 – 2.95 (m, 1H), 2.82 – 2.65 (m, 2H), 2.63 (s, 3H), 2.52 (s, 3H), 2.16 – 1.94 (m, 3H), 1.92 – 1.70 (m, 2H), 1.14 – 1.07 (m, 2H), 0.87 – 0.77 (m, 2H). 1H not observed (NH).
364	MS *m/z* 387.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.53 (br s, 1H, formic acid), 7.67 (s, 1 H), 7.56 (d, J = 8.25 Hz, 1 H), 7.49 (d, J = 8.63 Hz, 1 H), 7.01 (d, J = 55.7 Hz, 1H), 6.48 (s, 1H), 4.53 – 4.40 (m, 1H), 3.18 – 3.01 (m, 1H), 2.83 – 2.66 (m, 1H), 2.56 – 2.39 (m, 11H), 2.09 – 1.98 (m, 1H), 1.97 – 1.84 (m, 1H), 1.83 – 1.64 (m, 2H). 1H not observed (NH).
365	MS *m/z* 489.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 7.95 (d, J = 8.1 Hz,

	1H), 7.90 (d, J = 8.9 Hz, 1H), 7.82 (s, 1H), 6.51 (s, 1H), 4.56 – 4.45 (m, 1H), 3.12 – 3.03 (m, 1H), 2.80 – 2.66 (m, 1H), 2.62 – 2.48 (m, 5H), 2.48 – 2.30 (m, 2H), 2.12 – 1.99 (m, 1H), 1.93 – 1.82 (m, 1H), 1.82 – 1.65 (m, 2H), 1.15 (t, J = 7.3 Hz, 3H). NH not observed.
366	MS *m/z* 467.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.54 (s, 1H, formate CH), 7.61 (d, J = 8.1 Hz, 1H), 7.42 (dd, J = 8.1, 1.9 Hz, 1H), 7.33 (s, 1H), 6.49 (s, 1H), 4.57 – 4.47 (m, 1H), 3.00 – 2.84 (m, 1H), 2.79 – 2.65 (m, 2H), 2.65 – 2.40 (m, 7H), 2.16 – 2.04 (m, 1H), 2.02 – 1.89 (m, 1H), 1.87 – 1.72 (m, 2H), 1.20 (t, J = 7.3 Hz, 3H). 2 CH signals overlap with Methanol-d_4 peak; NH not observed.
367	MS *m/z* 397.4 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 7.32 (s, 1H), 7.30 (d, J = 7.8 Hz, 1H), 7.13 (d, J = 7.8 Hz, 1H), 6.34 (s, 1H), 4.52 – 4.40 (m, 1H), 3.17 – 3.03 (m, 1H), 2.77 – 2.65 (m, 1H), 2.59 – 2.48 (m, 5H), 2.48 – 2.31 (m, 8H), 2.08 – 1.97 (m, 1H), 1.91 – 1.81 (m, 1H), 1.78 – 1.66 (m, 2H), 1.14 (t, J = 7.3 Hz, 3H). NH not observed.
368	MS *m/z* 429.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.06 (s, 1H), 7.70 (d, J = 8.0 Hz, 1H), 7.56 (d, J = 7.9 Hz, 1H), 6.36 (s, 1H), 4.64 – 4.52 (m, 1H), 3.99 – 3.89 (m, 1H), 3.70 – 3.55 (m, 1H), 3.45 – 3.34 (m, 1H), 3.29 – 3.25 (m, 2H), 3.03 – 2.85 (m, 2H), 2.56 (s, 3H), 2.50 (s, 3H), 2.37 – 2.26 (m, 1H), 2.23 – 2.14 (m, 1H), 2.06 – 1.75 (m, 2H), 1.40 (t, J = 7.3 Hz, 3H). 2 CH signals overlap with Methanol-d_4 peak; NH not observed.
369	MS *m/z* 499.2 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.16 (dd, J = 8.1, 1.7 Hz, 1H), 8.10 (s, 1H), 8.00 (d, J = 8.0 Hz, 1H), 6.58 (s, 1H), 4.69 – 4.59 (m, 1H), 4.00 – 3.92 (m, 1H), 3.69 – 3.61 (m, 1H), 3.28 – 3.23 (m, 5H), 2.95 (t, J = 11.8 Hz, 2H), 2.55 (s, 3H), 2.35 – 2.28 (m, 1H), 2.24 – 2.16 (m, 1H), 2.00 – 1.83 (m, 2H), 1.40 (t, J = 7.3 Hz, 3H). NH not observed.
370	MS *m/z* 427.4 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 7.19 (d, J = 8.6 Hz, 1H), 6.93 (d, J = 8.6 Hz, 1H), 6.44 (s, 1H), 4.52 – 4.41 (m, 1H), 3.92 (s, 3H), 3.90 (s, 3H), 3.69 (s, 3H), 3.20 – 3.14 (m, 1H), 2.86 – 2.70 (m, 1H), 2.66 – 2.55 (m, 2H), 2.51 (s, 3H), 2.48 – 2.32 (m, 2H), 2.12 – 2.00 (m, 1H), 1.93 – 1.82 (m, 1H), 1.82 – 1.65 (m, 2H), 1.16 (t, J = 7.3 Hz, 3H). NH not observed.
371	MS *m/z* 451.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 7.61 (d, J = 8.6 Hz, 1H), 7.12 (dd, J = 8.6, 2.5 Hz, 1H), 7.03 (dq, J = 2.9, 1.5 Hz, 1H), 6.45 (s, 1H), 4.52 – 4.41 (m, 1H), 3.91 (s, 3H), 3.18 – 3.03 (m, 1H), 2.78 – 2.65 (m, 1H), 2.60 – 2.47 (m, 5H), 2.47 – 2.28 (m, 2H), 2.10 – 1.99 (m, 1H), 1.93 – 1.81 (m, 1H), 1.80 – 1.66 (m, 2H), 1.14 (t, J = 7.3 Hz, 3H). NH not observed.
372	MS *m/z* 448.3 $[M+H]^+$. ^{1}HNMR (400 MHz, DMSO-d_6) δ 8.18 (s, 1H, formate CH), 8.10 (s, 1H), 8.03 – 7.91 (m, 2H), 7.85 (d, J = 7.9 Hz, 1H), 7.63 – 7.54 (m, 1H), 7.47 (s, 1H), 6.51 (s, 1H), 4.43 – 4.25 (m, 1H), 2.88 (d, J = 8.5 Hz, 1H), 2.66 – 2.58 (m, 1H), 2.46 (s, 3H), 2.40 (q, J = 7.1 Hz, 2H), 2.31 – 2.21 (m, 1H), 2.20 – 2.05 (m, 1H), 1.91 – 1.78 (m, 1H), 1.78 – 1.63 (m, 2H), 1.63 – 1.46 (m, 1H), 1.02 (t, J = 7.1 Hz, 3H).
373	MS *m/z* 435.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 7.51 (d, J = 8.4 Hz, 1H), 7.38 (d, J = 2.6 Hz, 1H), 7.32 (dd, J = 8.6, 2.7 Hz, 1H), 6.29 (s, 1H), 4.51 – 4.43 (m, 1H), 3.94 (s, 3H), 3.15 – 3.05 (m, 1H), 2.79 – 2.66 (m, 1H), 2.61 – 2.48 (m, 5H), 2.48 – 2.32 (m, 2H), 2.10 – 1.99 (m, 1H), 1.92 – 1.81 (m, 1H),

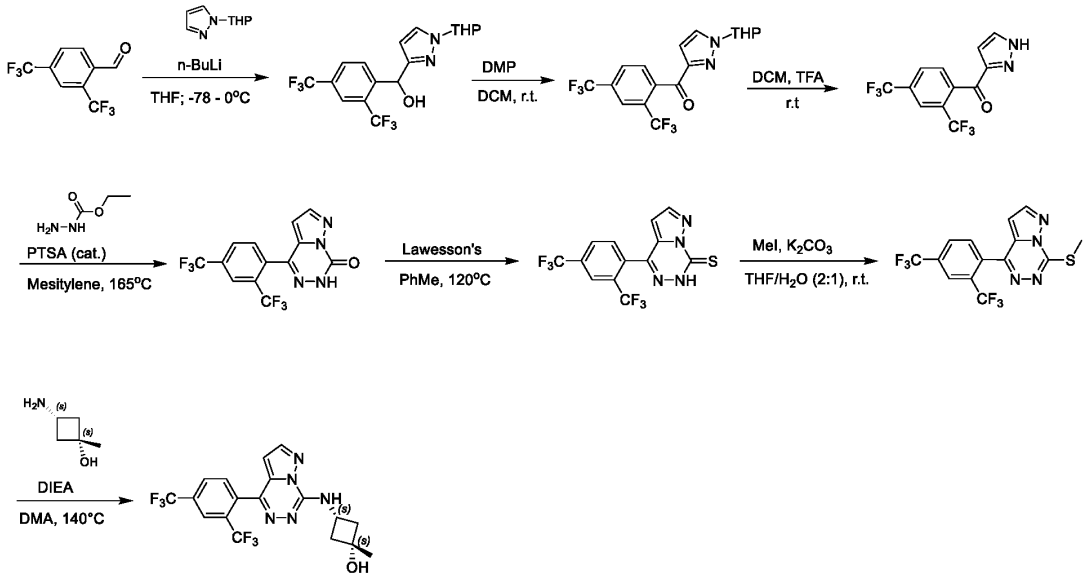
	1.78 – 1.67 (m, 2H), 1.15 (t, J = 7.3 Hz, 3H). NH not observed.
374	MS *m/z* 401.3, 403.3 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 7.46 (d, J = 8.6 Hz, 1H), 7.16 (d, J = 2.5 Hz, 1H), 7.05 (dd, J = 8.6, 2.6 Hz, 1H), 6.39 (s, 1H), 4.53 – 4.43 (m, 1H), 3.89 (s, 3H), 3.23 – 3.15 (m, 1H), 2.88 – 2.75 (m, 1H), 2.68 – 2.56 (m, 2H), 2.54 – 2.39 (m, 5H), 2.10 – 2.01 (m, 1H), 1.95 – 1.85 (m, 1H), 1.83 – 1.68 (m, 2H), 1.17 (t, J = 7.3 Hz, 3H). NH not observed.
375	MS *m/z* 439.2, 441.2 $[M+H]^+$. ^{1}HNMR (500 MHz, Methanol-d_4) δ 7.95 (d, J = 1.8 Hz, 1H), 7.82 (dd, J = 8.2, 1.9 Hz, 1H), 7.78 (d, J = 7.9 Hz, 1H), 6.44 (s, 1H), 4.55 – 4.48 (m, 1H), 3.25 – 3.18 (m, 1H), 2.90 – 2.79 (m, 1H), 2.71 – 2.59 (m, 2H), 2.59 – 2.36 (m, 5H), 2.14 – 2.04 (m, 1H), 1.96 – 1.87 (m, 1H), 1.84 – 1.71 (m, 2H), 1.18 (t, J = 7.2 Hz, 3H). NH not observed.
376	MS *m/z* 405.2, 407.2, 409.2 $[M+H]^+$. ^{1}HNMR (500 MHz, Methanol-d_4) δ 7.69 (d, J = 2.0 Hz, 1H), 7.55 (d, J = 8.2 Hz, 1H), 7.52 (dd, J = 8.2, 2.0 Hz, 1H), 6.42 (s, 1H), 4.57 – 4.46 (m, 1H), 3.29 – 3.23 (m, 1H), 2.99 – 2.81 (m, 1H), 2.77 – 2.66 (m, 2H), 2.61 – 2.46 (m, 5H), 2.14 – 2.04 (m, 1H), 1.99 – 1.89 (m, 1H), 1.85 – 1.72 (m, 2H), 1.20 (t, J = 7.2 Hz, 3H). NH not observed.
377	MS *m/z* 371.3, 373.3 $[M+H]^+$. ^{1}HNMR (500 MHz, Methanol-d_4) δ 7.99 – 7.86 (m, 2H), 7.62 – 7.52 (m, 2H), 6.87 (s, 1H), 4.56 – 4.47 (m, 1H), 3.42 – 3.34 (m, 1H), 3.10 – 3.00 (m, 1H), 2.89 – 2.75 (m, 2H), 2.75 – 2.60 (m, 2H), 2.56 (s, 3H), 2.16 – 2.08 (m, 1H), 2.04 – 1.95 (m, 1H), 1.88 – 1.75 (m, 2H), 1.24 (t, J = 7.2 Hz, 3H). NH not observed.
378	MS m/z 428.3 $[M+H]^+$. ^{1}HNMR (500 MHz, Methanol-d_4) δ 7.82 (d, J = 8.4 Hz, 1H), 7.80 – 7.70 (m, 2H), 6.93 (t, J = 72.8 Hz, 1H), 6.49 (s, 1H), 4.52 – 4.46 (m, 1H), 3.15 – 3.08 (m, 1H), 2.76 – 2.69 (m, 1H), 2.62 – 2.31 (m, 7H), 2.09 – 2.01 (m, 1H), 1.92 – 1.83 (m, 1H), 1.78 – 1.69 (m, 2H), 1.15 (d, J = 7.3 Hz, 3H). NH not observed.
379	MS *m/z* 407.3 $[M+H]^+$. ^{1}HNMR (500 MHz, Methanol-d_4) δ 7.30 (d, J = 8.5 Hz, 1H), 6.86 (dd, J = 8.4, 2.6 Hz, 1H), 6.61 (d, J = 2.7 Hz, 1H), 6.39 (s, 1H), 4.49 – 4.42 (m, 1H), 3.83 (s, 3H), 3.15 – 3.06 (m, 1H), 2.78 – 2.67 (m, 1H), 2.54 (q, J = 7.9 Hz, 2H), 2.50 (s, 3H), 2.45 – 2.31 (m, 2H), 2.08 – 1.99 (m, 1H), 1.92 – 1.81 (m, 2H), 1.79 – 1.66 (m, 2H), 1.15 (t, J = 7.2 Hz, 3H), 0.77 (dt, J = 6.6, 1.9 Hz, 2H), 0.67 – 0.61 (m, 2H). NH not observed.
380	MS *m/z* 444.2 $[M+H]^+$. ^{1}HNMR (500 MHz, Methanol-d_4) δ 7.84 (d, J = 7.9 Hz, 1H), 7.74 (d, J = 8.1 Hz, 1H), 7.66 (s, 1H), 6.93 (t, J = 72.7 Hz, 1H), 6.48 (s, 1H), 4.34 (p, J = 7.9 Hz, 1H), 2.70 – 2.62 (m, 2H), 2.53 (s, 3H), 2.35 – 2.26 (m, 2H), 1.43 (s, 3H). NH and OH not observed.
381	MS *m/z* 458.2 $[M+H]^+$. ^{1}HNMR (500 MHz, Methanol-d_4) δ 7.85 (d, J = 7.8 Hz, 1H), 7.74 (d, J = 8.1 Hz, 1H), 7.66 (s, 1H), 6.93 (d, J = 72.6 Hz, 1H), 6.48 (s, 1H), 4.10 (td, J = 10.2, 4.3 Hz, 1H), 3.73 – 3.64 (m, 1H), 2.52 (s, 3H), 2.29 – 2.21 (m, 1H), 2.14 – 2.07 (m, 1H), 1.85 – 1.76 (m, 2H), 1.59 – 1.37 (m, 4H). NH and OH not observed.
382	MS *m/z* 476.2 $[M+H]^+$. ^{1}HNMR (500 MHz, Methanol-d_4) δ 7.95 (d, J = 8.1 Hz, 1H), 7.89 (d, J = 8.1 Hz, 1H), 7.81 (s, 1H), 6.50 (s, 1H), 4.12 (td, J = 10.2, 4.2 Hz, 1H), 3.73 – 3.64 (m, 1H), 2.53 (s, 3H), 2.29 – 2.21 (m, 1H), 2.15 – 2.07 (m, 1H), 1.85 – 1.76 (m, 2H), 1.58 – 1.37 (m, 4H). NH and OH not observed.
383	MS *m/z* 480.3 [M+H]; ^{1}HNMR (500 MHz, Methanol-d_4) δ 7.82 (d, J = 7.9 Hz,

	1H), 7.72 (d, J = 8.1 Hz, 1H), 7.65 (s, 1H), 7.16 (t, J = 7.9 Hz, 1H), 6.97 (d, J = 7.5 Hz, 1H), 6.93 (s, 1H), 6.91 (t, JCF = 73.6 Hz, 1H), 6.68 (dd, J = 8.0, 2.7 Hz, 1H), 6.49 (s, 1H), 5.47 (q, J = 7.2 Hz, 1H), 2.54 (s, 3H), 1.70 (d, J = 7.0 Hz, 3H). NH and OH not observed.
384	MS *m/z* 438.3 $[M+H]^+$. ^{1}HNMR (500 MHz, Methanol-d_4) δ 7.50 (d, J = 8.4 Hz, 1H), 7.12 (d, J = 3.1 Hz, 1H), 7.09 (dd, J = 8.5, 2.8 Hz, 1H), 6.44 (s, 1H), 4.27 (td, J = 9.9, 4.6 Hz, 1H), 4.03 (dd, J = 11.1, 5.0 Hz, 1H), 3.97 (dd, J = 11.5, 4.0 Hz, 1H), 3.89 (s, 3H), 3.85 – 3.71 (m, 3H), 3.56 (td, J = 12.0, 2.2 Hz, 1H), 3.29 – 3.23 (m, 1H), 2.52 (s, 3H), 2.29 – 2.22 (m, 1H), 1.89 – 1.78 (m, 1H). NH and OH not observed.
385	MS *m/z* 436.3 $[M+H]^+$. ^{1}HNMR (500 MHz, Methanol-d_4) δ 7.50 (d, J = 8.5 Hz, 1H), 7.11 (s, 1H), 7.08 (dd, J = 8.5, 2.7 Hz, 1H), 6.43 (s, 1H), 4.10 – 4.03 (m, 1H), 3.89 (s, 3H), 3.84 – 3.73 (m, 2H), 3.73 – 3.63 (m, 1H), 2.52 (s, 3H), 2.32 – 2.21 (m, 1H), 2.17 – 2.05 (m, 1H), 1.88 – 1.74 (m, 2H), 1.58 – 1.36 (m, 4H). NH and OH not observed.
386	MS *m/z* 421.3 $[M+H]^+$. ^{1}HNMR (500 MHz, Methanol-d_4) δ 7.50 (d, J = 8.5 Hz, 1H), 7.12 (d, J = 2.9 Hz, 1H), 7.09 (dd, J = 8.4, 2.7 Hz, 1H), 6.45 (s, 1H), 5.06 – 4.97 (m, 1H), 3.89 (s, 3H), 3.76 (q, J = 11.1 Hz, 2H), 3.54 – 3.43 (m, 2H), 2.79 – 2.69 (m, 1H), 2.52 (s, 3H), 2.44 – 2.33 (m, 1H). NH not observed.
387	MS *m/z* 422.3 $[M+H]^+$. ^{1}HNMR (500 MHz, Methanol-d_4) δ 7.50 (d, J = 8.5 Hz, 1H), 7.11 (d, J = 2.9 Hz, 1H), 7.08 (dd, J = 8.5, 2.5 Hz, 1H), 6.43 (s, 1H), 4.32 (p, J = 8.2 Hz, 1H), 3.89 (s, 3H), 3.79 (q, J = 11.1 Hz, 2H), 2.73 – 2.59 (m, 2H), 2.52 (s, 3H), 2.35 – 2.23 (m, 2H), 1.43 (s, 3H).
388	MS *m/z* 460.1 $[M+H]^+$. ^{1}HNMR (400 MHz, DMSO-d_6) δ 8.30 (s, 1H), 8.00 (s, 1H), 7.92 (d, J = 8.2 Hz, 1H), 7.84 (d, J = 8.1 Hz, 1H), 6.55 (s, 1H), 4.98 (s, 1H), 4.35 – 4.24 (m, 1H), 4.15 – 4.06 (m, 2H), 2.47 (s, 3H), 2.46 – 2.40 (m, 2H), 2.35 – 2.27 (m, 2H), 1.31 (s, 3H).
389	MS *m/z* 474.1 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 7.90 (s, 1H), 7.84 (d, J = 8.4 Hz, 1H), 7.80 (d, J = 8.4 Hz, 1H), 6.46 (s, 1H), 4.14 – 4.06 (m, 1H), 4.00 – 3.89 (m, 2H), 3.73 – 3.64 (m, 1H), 2.52 (s, 3H), 2.26 – 2.23 (m, 1H), 2.12 – 2.09 (m, 1H), 1.83 – 1.80 (m, 2H), 1.55 – 1.38 (m, 4H). NH and OH not observed.
390	MS *m/z* 406.3 $[M+H]^+$. ^{1}HNMR (500 MHz, Methanol-d_4) δ 7.45 (d, J = 7.8 Hz, 1H), 7.39 (s, 1H), 7.35 (br d, J = 7.8 Hz, 1H), 6.43 (s, 1H), 4.32 (quint, J = 7.9 Hz, 1H), 3.77 (q, J = 11.0 Hz, 2H), 2.69 – 2.62 (m, 2H), 2.52 (s, 3H), 2.45 (s, 3H), 2.30 (t, J = 9.8 Hz, 2H), 1.43 (s, 3H). 2H not observed (NH and OH).
391	MS *m/z* 424.3 $[M+H]^+$. ^{1}HNMR (400 MHz, DMSO-d_6) δ 8.16 (d, J = 6.9 Hz, 1H), 7.64 (d, J = 8.6 Hz, 1H), 7.16 (dd, J = 8.7, 2.5 Hz, 1H), 7.09 (s, 1H), 6.45 (s, 1H), 4.97 (s, 1H), 4.25 (dd, J = 15.1, 7.5 Hz, 1H), 3.89 (s, 3H), 2.47 (s, 3H), 2.46 – 2.39 (m, 2H), 2.33 – 2.26 (m, 2H), 1.31 (s, 3H).
392	MS *m/z* 438.3 $[M+H]^+$. ^{1}HNMR (400 MHz, DMSO-d_6) δ 7.64 (d, J = 8.6 Hz, 1H), 7.60 (d, J = 8.1 Hz, 1H), 7.17 (dd, J = 8.7, 2.5 Hz, 1H), 7.09 (s, 1H), 6.44 (s, 1H), 4.76 (d, J = 5.4 Hz, 1H), 4.09 – 3.92 (m, 1H), 3.89 (s, 3H), 3.71 – 3.56 (m, 1H), 2.47 (s, 3H), 2.09 – 2.01 (m, 1H), 1.99 – 1.91 (m, 1H), 1.72 – 1.64 (m, 2H), 1.39 – 1.18 (m, 4H).

Example 4

Preparation of Compound 4

(1s,3s)-3-((4-(2,4-Bis(trifluoromethyl)phenyl)pyrazolo[1,5-d][1,2,4]triazin-7-yl)amino)-1-methylcyclobutan-1-ol



Step 1. (2,4-Bis(trifluoromethyl)phenyl)(1-(tetrahydro-2*H*-pyran-2-yl)-1*H*-pyrazol-3-yl) methanol

To a solution of 1-(tetrahydro-2*H*-pyran-2-yl)-1*H*-pyrazole (5.3 g, 35.0 mmol, 1.0 eq.) in tetrahydrofuran (170 mL) was added n-butyl lithium (16.8 mL, 1.2 eq., 2.5 M in hexane) dropwise at -78 °C. The reaction mixture was stirred at -78 °C for 30 min, then 2,4-bis(trifluoromethyl)benzaldehyde (11.02 g, 1.3 eq.) was added. The mixture was then warmed to room temperature and stirred for 2 hours before quenching with water (200 mL). The resulting mixture was extracted with ethyl acetate (3 x 100 mL). The organic phase was dried with sodium sulfate, filtered and concentrated under reduced pressure to afford crude (2,4-bis(trifluoromethyl)phenyl)(1-(tetrahydro-2*H*-pyran-2-yl)-1*H*-pyrazol-3-yl) methanol (15.0 g, crude) as a dark yellow oil, which was used in the next step without further purification.

Step 2. (2,4-Bis(trifluoromethyl)phenyl)(1-(tetrahydro-2*H*-pyran-2-yl)-1*H*-pyrazol-3-yl) methanone

To a solution of (2,4-bis(trifluoromethyl)phenyl)(1-(tetrahydro-2*H*-pyran-2-yl)-1*H*-pyrazol-3-yl) methanol (15.0 g, crude) in dichloromethane (170 mL) at 0 °C was added Dess-

Martin periodinane (19.3 g, mmol, 1.3 eq.) in portions. The reaction mixture was stirred at room temperature for 2 hours then washed with sat. $Na_2S_2O_3$ solution (2 x 100 mL), sat. $NaHCO_3$ solution (100 mL) and brine (100 mL). The organic phase was dried with sodium sulfate, filtered and concentrated under reduced pressure to afford (2,4-bis(trifluoromethyl)phenyl)(1-(tetrahydro-2*H*-pyran-2-yl)-1*H*-pyrazol-3-yl) methanone (15 g, crude) as a dark yellow oil, which was used in the next step without further purification. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.26 (s, 1H), 8.23 (d, *J* = 8.4 Hz, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.68 (d, *J* = 2.0 Hz, 1H), 6.66 (d, *J* = 2.0 Hz, 1H), 6.17 (dd, *J* = 10.0, 2.0 Hz, 1H), 3.95 (d, J = 11.6 Hz, 1H), 3.71 – 3.57 (m, 1H), 2.38 – 2.27 (m, 1H), 2.07 – 1.93 (m, 2H), 1.78 – 1.64 (m, 1H), 1.61 – 1.51 (m, 2H).

Step 3. (2,4-Bis(trifluoromethyl)phenyl)(1*H*-pyrazol-3-yl)methanone

(2,4-Bis(trifluoromethyl)phenyl)(1-(tetrahydro-2*H*-pyran-2-yl)-1*H*-pyrazol-3-yl) methanone (15 g, crude) was dissolved in a solution of dichloromethane (300 mL) and trifluoroacetic acid (30 mL). The resulting mixture was stirred at room temperature for 16 h. Upon completion, the reaction mixture was adjusted to pH ~ 7 by addition of sat. $NaHCO_3$ solution. The organic phase was partitioned, dried with sodium sulfate, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography eluting with 0-50% EtOAc in hexanes to afford (2,4-bis(trifluoromethyl)phenyl)(1*H*-pyrazol-3-yl)methanone (6.50 g, 60.2% yield over 3 steps) as a yellow solid. MS *m/z* 309.0 $[M+H]^+$; ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.68 (s, 1H), 8.21 (s, 1H), 8.18 (d, *J* = 8.4 Hz, 1H), 7.99 (s, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 6.98 (s, 1H).

Step 4. 4-(2,4-Bis(trifluoromethyl)phenyl)pyrazolo[1,5-*d*][1,2,4]triazin-7(6*H*)-one

A mixture of (2,4-bis(trifluoromethyl)phenyl)(1*H*-pyrazol-3-yl)methanone (3.0 g, 9.7 mmol, 1.0 eq.) and ethyl hydrazine carboxylate (1.01 g, 1.0 eq.) in mesitylene (100 mL) was heated at 165 °C for 4 h. Upon completion, the reaction mixture was cooled to room temperature, then directly purified by silica gel column chromatography eluting with 0-40% EtOAc in hexanes to afford 4-(2,4-bis(trifluoromethyl)phenyl)pyrazolo[1,5-*d*][1,2,4]triazin-7(6*H*)-one (1.50 g, 44.4% yield) as a light yellow solid. MS *m/z* 349.1 $[M+H]^+$; ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.68 (s, 1H), 8.21 (s, 1H), 8.18 (d, *J* = 8.0 Hz, 1H), 7.99 (dd, *J* = 2.8, 1.6 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 6.98 (dd, *J* = 2.4, 2.0 Hz, 1H).

Step 5. 4-(2,4-Bis(trifluoromethyl)phenyl)pyrazolo[1,5-d][1,2,4]triazine-7(6H)-thione

A mixture of 4-(2,4-bis(trifluoromethyl)phenyl)pyrazolo[1,5-*d*][1,2,4]triazin-7(6*H*)-one (1.50 g, 4.31 mmol, 1.0 eq.) and Lawesson's reagent (3.49 g, 2.0 eq.) in toluene (40 mL) was heated at 120 °C for 16 h. Upon completion, the reaction mixture was cooled to room temperature, then filtered through a pad of Celite. The filtrate was washed with water (80 mL). The organic phase was dried with sodium sulfate, filtered and concentrated under reduced pressure to afford 4-(2,4-bis(trifluoromethyl)phenyl)pyrazolo[1,5-*d*][1,2,4]triazine-7(6*H*)-thione (1.30 g, crude) as a light yellow solid, which was used in the next step without further purification.

Step 6. 4-(2,4-Bis(trifluoromethyl)phenyl)-7-(methylthio)pyrazolo[1,5-d][1,2,4]triazine

To a mixture of 4-(2,4-bis(trifluoromethyl)phenyl)pyrazolo[1,5-*d*][1,2,4]triazine-7(6*H*)-thione (1.30 g, 1.0 eq.) and K_2CO_3 (1.49 g, 2.5 eq.) in THF (12 mL) and water (6 mL) was added iodomethane (0.4 mL, 1.5 eq.) dropwise. The mixture was stirred at room temperature for 1 hour, then diluted with water (50 mL) and extracted with ethyl acetate (3 x 50 mL). The organic layer was dried over sodium sulfate, filtered and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography eluting with 0-30% EtOAc in hexanes to afford 4-(2,4-bis(trifluoro-methyl)phenyl)-7-(methylthio)pyrazolo[1,5-d][1,2,4]triazine (1.08 g, 66.2% yield over 2 steps) as a light yellow solid. MS *m/z* 379.3 $[M+H]^+$.

Step 7. (1*s*,3*s*)-3-((4-(2,4-Bis(trifluoromethyl)phenyl)pyrazolo[1,5-*d*][1,2,4]triazin-7-yl) amino)-1-methylcyclobutan-1-ol

A mixture of 4-(2,4-bis(trifluoro-methyl)phenyl)-7-(methylthio)pyrazolo[1,5-d][1,2,4]triazine (200 mg, 0.53 mmol, 1.0 eq.), (1*s*,3*s*)-3-amino-1-methylcyclobutan-1-ol hydrochloride (180.9 mg, 2.5 eq.) and DIEA (1.20 mL, 13.0 eq.) in DMAc (0.75 mL) was heated at 140°C for 4 h. Upon completion, the reaction mixture was cooled to room temperature and diluted with water (50 mL) and extracted with EtOAc (3 x 50 mL). The organic phase was washed with brine (100 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by reverse phase chromatography to afford (1*s*,3*s*)-3-((4-(2,4-bis(trifluoromethyl)phenyl)pyrazolo[1,5-*d*][1,2,4]triazin-7-yl)amino)-1-methylcyclobutan-1-ol (68.9 mg, 30.1 % yield) as a white solid. MS *m/z* 432.1 $[M+H]^+$. ^{1}H NMR (400 MHz, Methanol-d_4) δ 8.21 – 8.18 (m, 2H), 8.14 (d, J = 8.4 Hz, 1H), 7.88 (d, J = 8.0 Hz, 1H), 6.56 (d, J = 2.0 Hz, 1H), 4.36 (quin, J = 8.0 Hz, 1H), 2.71 – 2.62 (m, 2H), 2.37 – 2.29 (m, 2H), 1.44 (s, 3H).

The compounds below were prepared according to the procedure of Example 4 by substituting the appropriate starting materials, reagents and reaction conditions.

Compound#	Spectral Data
393	MS *m/z* 447.1 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.26 (d, J = 2.0 Hz, 1H), 8.00 (d, J = 7.6 Hz, 1H), 7.93 (d, J = 8.0 Hz, 1H), 7.85 (s, 1H), 6.76 (d, J = 2.0 Hz, 1H), 5.15 – 5.06 (m, 1H), 3.56 – 3.47 (m, 2H), 2.81 - 2.70 (m, 1H), 2.52 – 2.38 (m, 1H). NH not observed.
394	MS *m/z* 446.1 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.21 - 8.17 (m, 2H), 8.14 (d, J = 8.0 Hz, 1H), 7.88 (d, J = 8.0 Hz, 1H), 6.56 (d, J = 2.0 Hz, 1H), 4.20 - 4.07 (m, 1H), 3.75 – 3.65 (m, 1H), 2.30 - 2.22 (m, 1H), 2.16 - 2.06 (m, 1H), 1.85 - 1.76 (m, 2H), 1.58 - 1.42 (m, 4H). NH and OH not observed.
395	MS *m/z* 468.0 [$[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.21 (d, J = 2.4 Hz, 1H), 8.18 (s, 1H), 8.12 (d, J = 8.0 Hz, 1H), 7.86 (d, J = 8.0 Hz, 1H), 7.16 (t, J = 8.0 Hz, 1H), 7.01 - 6.96 (m, 1H), 6.95 - 6.93 (m, 1H), 6.68 (dd, J = 8.0, 2.0 Hz, 1H), 6.56 (d, J = 2.0 Hz, 1H), 5.50 (q, J = 7.2 Hz, 1H), 1.72 (d, J = 7.2 Hz, 3H). NH and OH not observed.
396	MS *m/z* 431.0 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.25 – 8.18 (m, 2H), 8.15 (d, J = 8.0 Hz, 1H), 7.89 (d, J = 8.0 Hz, 1H), 6.59 (d, J = 2.0 Hz, 1H), 5.13 – 5.02 (m, 1H), 3.57 – 3.42 (m, 2H), 2.79 – 2.67 (m, 1H), 2.51 – 2.34 (m, 1H). NH not observed.
397	MS *m/z* 448.0 $[M+H]^+$. ^{1}HNMR (400 MHz, Methanol-d_4) δ 8.22 (d, J = 2.0 Hz, 1H), 7.97 (d, J = 8.0 Hz, 1H), 7.90 (d, J = 8.4 Hz, 1H), 7.82 (s, 1H), 6.71 (d, J = 2.0 Hz, 1H), 4.42 – 4.32 (m, 1H), 2.71 – 2.64 (m, 2H), 2.37 – 2.29 (m, 2H), 1.44 (s, 3H). NH and OH not observed.
398	MS *m/z* 462.1$[M+H]^+$. 1H NMR (400 MHz, Methanol-d_4) δ 8.22 (d, J = 2.0 Hz, 1H), 7.97 (d, J = 8.0 Hz, 1H), 7.90 (d, J = 8.4 Hz, 1H), 7.82 (s , 1H), 6.71 (d, J = 2.0 Hz, 1H), 4.16 - 4.10 (m, 1H), 3.75 – 3.66 (m, 1H), 2.25 - 2.20 (m, 1H), 2.15 - 2.08 (m, 1H), 1.84 - 1.75 (m, 2H), 1.61 – 1.38 (m, 4H). NH and OH not observed.

BIOLOGICAL ASSAYS

IL-1β Secretion Assay:

Monocytic THP-1 cells (ATCC: TIB-202) were maintained in growth media consisting of RPMI 1640 medium (ThermoFisher, Cat# 11875-085), 10% FBS (ThermoFisher) and 0.05mM β-mercaptoethanol (ThermoFisher, Cat# 21985-023), according to the provider's instructions. The cell concentration was adjusted to $7.5x10^5$cells/mL, and plated in complete growth media with a final concentration of 100ng/mL phorbol 12-myristate 13-acetate (PMA, Sigma #P8139). Cells were seeded at 100µL/well into a 96-well cell culture plate (ThermoFisher

Cat#165305) and allowed to differentiate for 24 h in a cell culture incubator at 37°C with 5% CO_2. Cells were washed 1x with 100ul PBS and replaced with fresh RPMI + 5% FBS. Compounds were serial diluted in DMSO with 3 fold dilution for a total of 7 concentrations. Diluted compounds were added to the cells at a ratio of 1:200 and incubated for 20 h. The NLRP3 inflammasome was activated with the addition of 2.5µM Nigericin (Sigma: Cat# SML1779-1ml), for 3 h. After incubation, 15µL of conditioned media was removed and assayed for levels of IL-1β using the HTRF IL-1β assay kit (Cisbio: Cat# 62HIL1BPEH) as per the manufacturer's instructions.

Compounds, once produced and prepared according to the present invention, can be assessed in variety of assays to characterize their activities. For example, NLRP3-dependent IL1β secretion was evaluated in THP1 cells. IC50 values of IL1β inhibition were calculated from the plot of percentage of inhibition versus the inhibitor concentration by a logistics fit. TABLE I depict examples of compounds according to generic Formula I. Data which is < 1nM is listed as *****; data 1 - 10nM is listed as ****; data 10 - 100nM is listed as ***, data 100 - 300nM is listed as **, data ≥300 nM is listed as *. The data obtained from the THP1 NLRP3-dependent IL-1β secretion assay demonstrate that the compounds of the present invention could be used to treat diseases mediated through NLRP3 activation.

TABLE I

Compound #	IC50 IL-1β Inhibition	Compound #	IC50 IL-1β Inhibition	Compound #	IC50 IL-1β Inhibition
1	****	137	****	273	****
2	*****	138	****	274	***
3	****	139	****	275	***
4	****	140	*****	276	***
5	****	141	****	277	****
6	***	142	****	278	*****
7	***	143	***	279	*****
8	****	144	****	280	****
9	****	145	*****	281	****
10	****	146	****	282	*****
11	***	147	****	283	****
12	****	148	**	284	***
13	****	149	****	285	***
14	****	150	**	286	****
15	****	151	****	287	****
16	***	152	****	288	****
17	****	153	****	289	****

Compound #	IC50 IL-1β Inhibition
18	****
19	***
20	****
21	***
22	*****
23	****
24	*****
25	****
26	***
27	****
28	****
29	****
30	****
31	****
32	****
33	****
34	****
35	***
36	****
37	*****
38	***
39	****
40	*****
41	****
42	****
43	***
44	*****
45	***
46	***
47	***
48	*****
49	***
50	*****
51	****
52	****
53	****
54	***
55	***
56	*****
57	***
58	***
59	*****
60	****
61	*****
62	***
63	****

Compound #	IC50 IL-1β Inhibition
154	****
155	***
156	****
157	****
158	****
159	*****
160	****
161	****
162	****
163	***
164	***
165	****
166	*****
167	***
168	****
169	*****
170	*****
171	*****
172	*****
173	*****
174	***
175	*****
176	***
177	***
178	****
179	***
180	****
181	*
182	****
183	***
184	****
185	****
186	*****
187	****
188	***
189	***
190	*****
191	*****
192	***
193	****
194	****
195	*****
196	*****
197	*****
198	*****
199	****

Compound #	IC50 IL-1β Inhibition
290	***
291	****
292	***
293	***
294	****
295	*****
296	***
297	****
298	****
299	****
300	****
301	*****
302	****
303	*****
304	****
305	***
306	****
307	****
308	**
309	***
310	*
311	****
312	*****
313	****
314	****
315	**
316	***
317	****
318	****
319	***
320	***
321	***
322	***
323	****
324	***
325	***
326	***
327	***
328	***
329	****
330	***
331	***
332	***
333	****
334	***
335	***

Compound #	IC50 IL-1β Inhibition
64	***
65	***
66	***
67	****
68	***
69	***
70	****
71	***
72	***
73	***
74	***
75	****
76	***
77	****
78	***
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80	***
81	***
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83	****
84	***
85	*****
86	*****
87	****
88	****
89	****
90	****
91	***
92	**
93	***
94	***
95	****
96	****
97	***
98	****
99	**
100	****
101	****
102	****
103	***
104	***
105	**
106	***
107	***
108	****
109	****

Compound #	IC50 IL-1β Inhibition
200	****
201	****
202	****
203	*****
204	****
205	***
206	*****
207	*****
208	*****
209	*****
210	****
211	*****
212	*****
213	****
214	****
215	***
216	****
217	*****
218	****
219	****
220	**
221	***
222	****
223	****
224	****
225	****
226	***
227	***
228	***
229	*****
230	*
231	*
232	**
233	****
234	***
235	****
236	****
237	****
238	****
239	*****
240	*****
241	*****
242	*****
243	*****
244	*****
245	****

Compound #	IC50 IL-1β Inhibition
336	***
337	***
338	**
339	***
340	****
341	***
342	***
343	*****
344	***
345	****
346	****
347	***
348	*****
349	****
350	****
351	****
352	****
353	****
354	****
355	***
356	*****
357	*****
358	*****
359	****
360	*****
361	****
362	***
363	****
364	***
365	****
366	****
367	****
368	***
369	***
370	***
371	****
372	***
373	*****
374	****
375	****
376	****
377	****
378	****
379	****
380	****
381	***

Compound #	IC50 IL-1β Inhibition
110	****
111	****
112	****
113	****
114	****
115	****
116	***
117	***
118	*****
119	*****
120	*****
121	***
122	****
123	****
124	****
125	**
126	****
127	***
128	****
129	****
130	****
131	*****
132	***
133	***
134	****
135	*****
136	****

Compound #	IC50 IL-1β Inhibition
246	*****
247	*****
248	*
249	****
250	*****
251	*****
252	****
253	****
254	***
255	****
256	*****
257	****
258	****
259	*****
260	****
261	*****
262	*****
263	*****
264	*****
265	*****
266	*****
267	****
268	****
269	****
270	****
271	*****
272	****

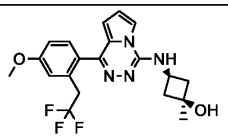
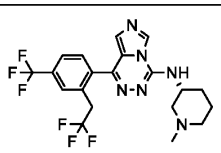
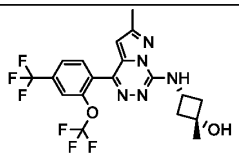
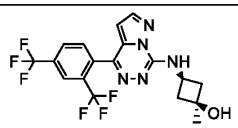
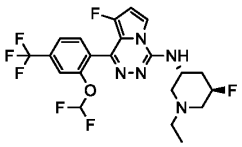
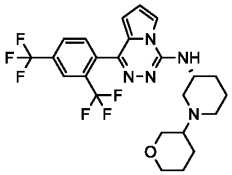
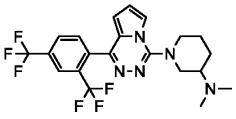
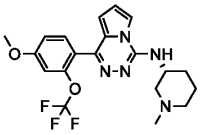
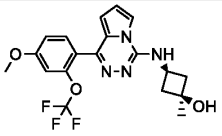
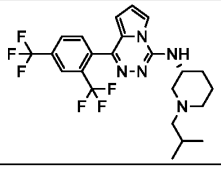
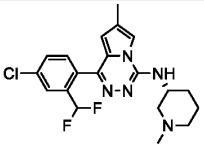
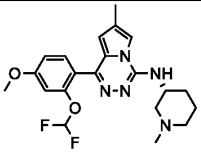
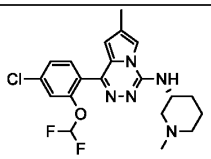
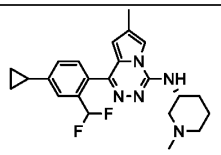
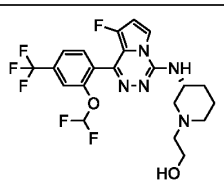
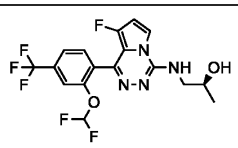
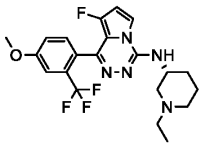
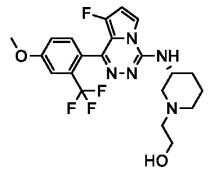
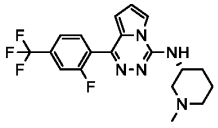
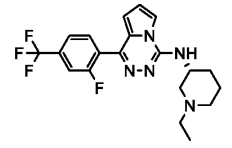
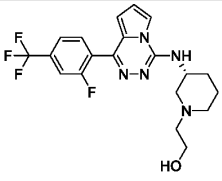
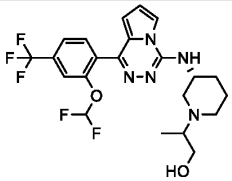
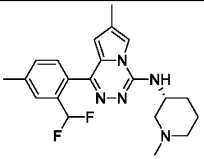
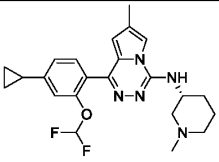
Compound #	IC50 IL-1β Inhibition
382	***
383	****
384	****
385	****
386	***
387	****
388	****
389	****
390	****
391	***
392	***
393	***
394	****
395	****
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400	***
401	***
402	***

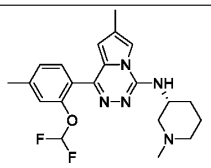
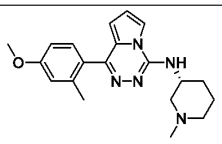
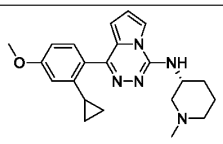
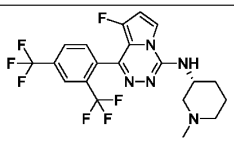
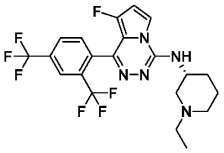
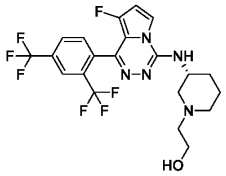
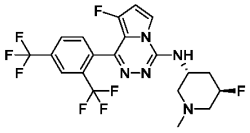
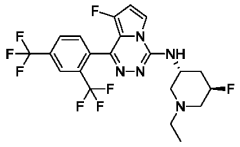
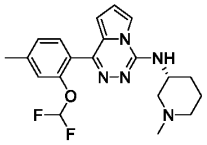
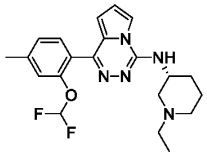
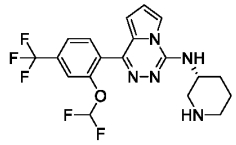
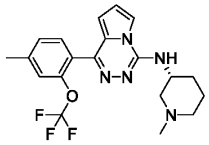
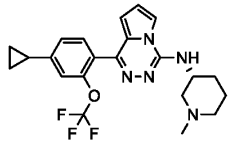
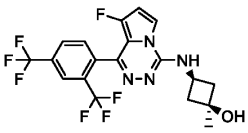
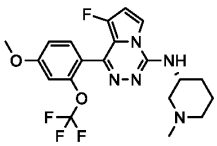
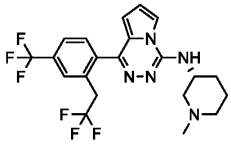
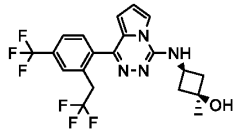
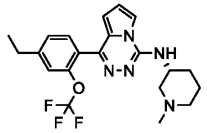
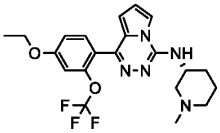
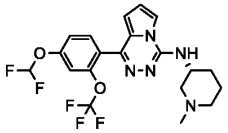
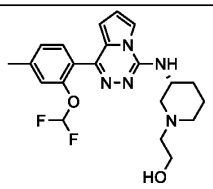
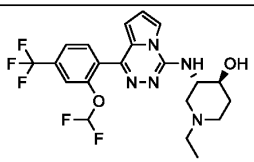
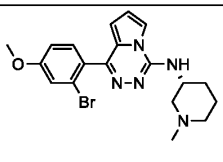
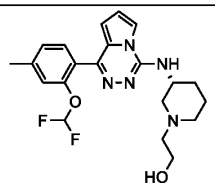
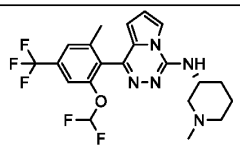
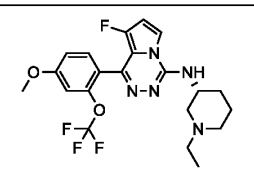
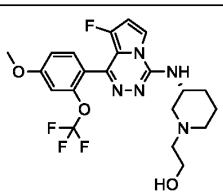
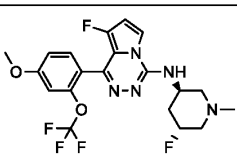
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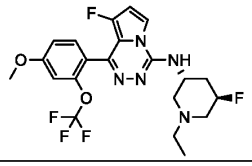
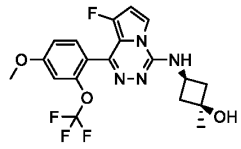
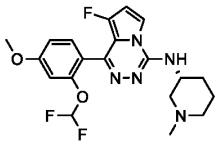
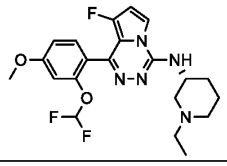
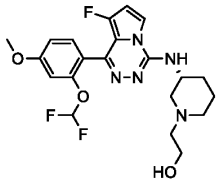
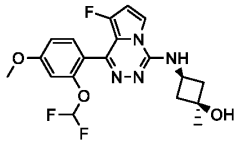
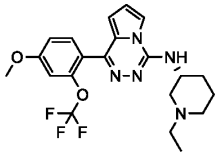
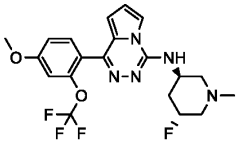
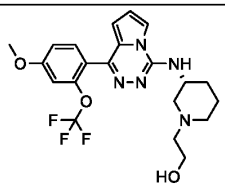
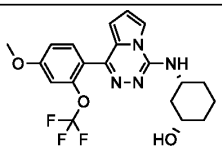
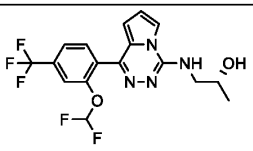
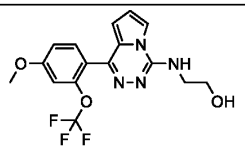
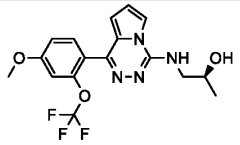
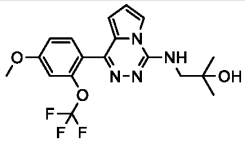
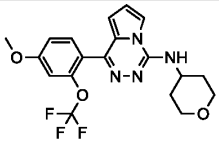
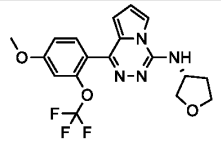
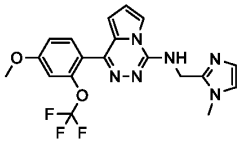
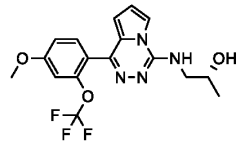
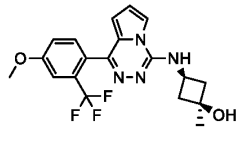
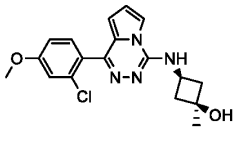
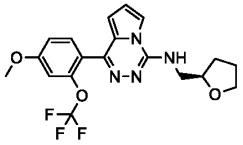
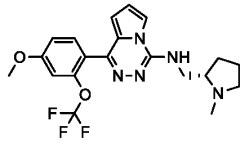
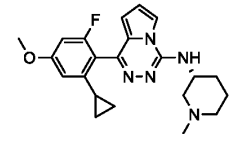
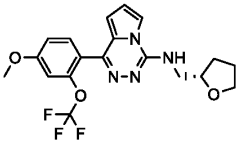
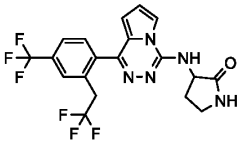
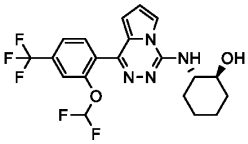
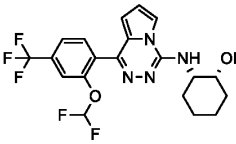
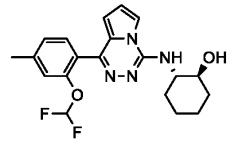
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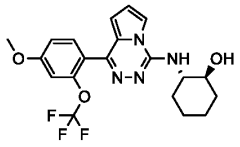
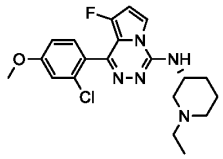
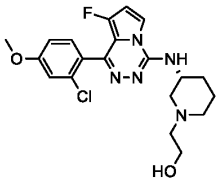
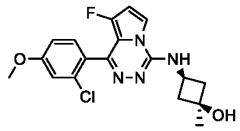
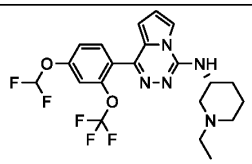
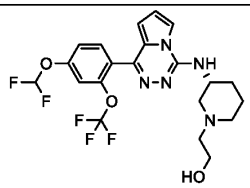
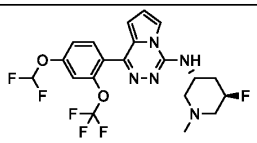
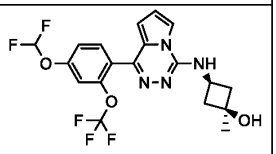
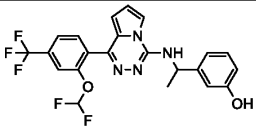
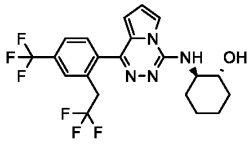
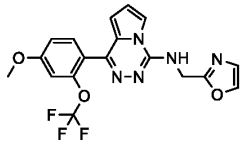
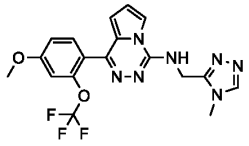
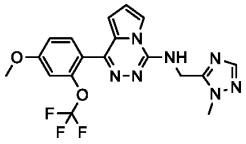
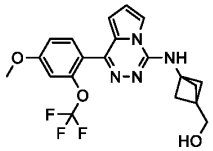
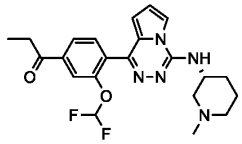
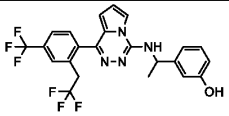
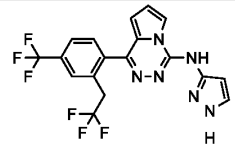
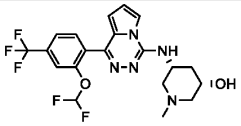
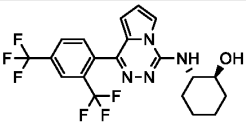
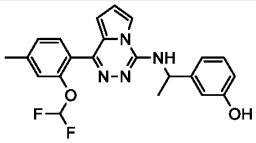
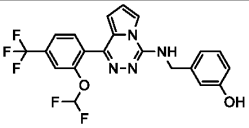
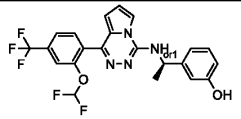
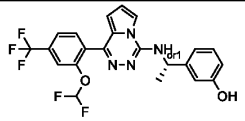
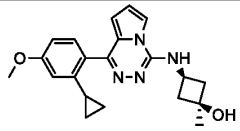
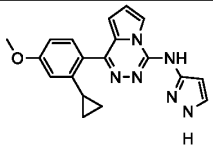
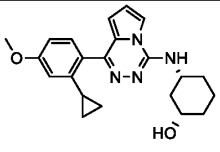
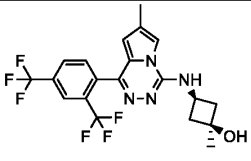
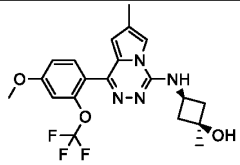
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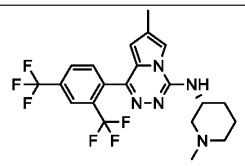
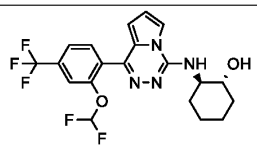
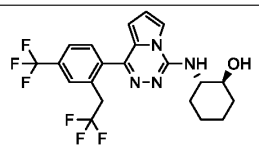
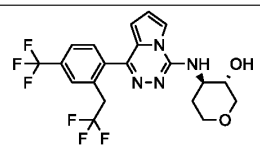
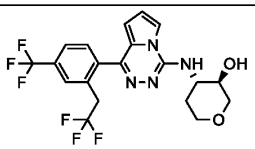
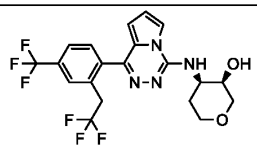
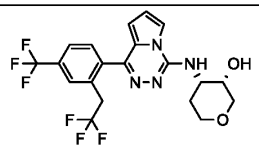
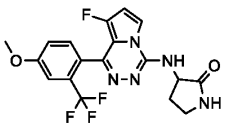
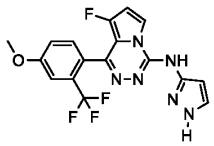
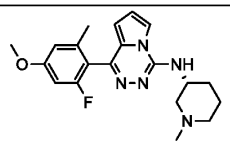
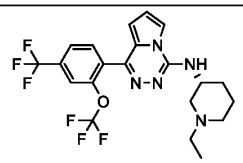
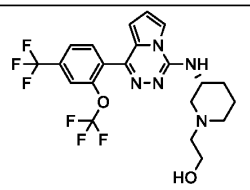
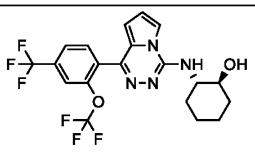
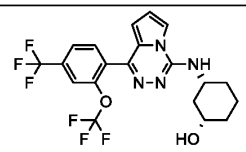
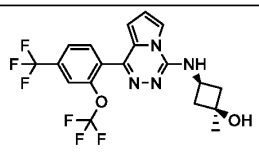
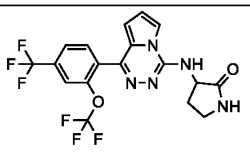
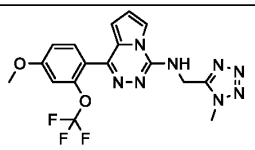
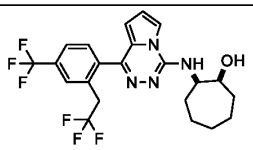
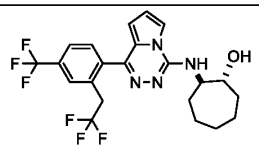
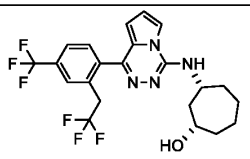
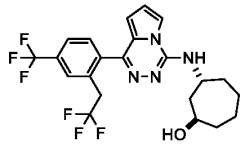
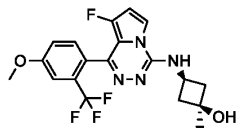
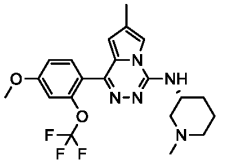
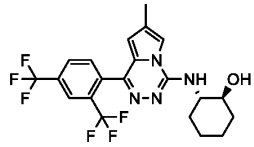
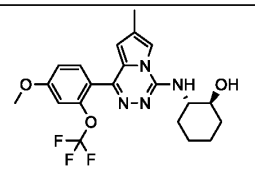
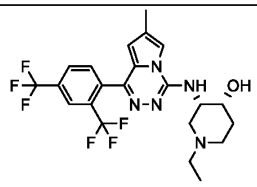
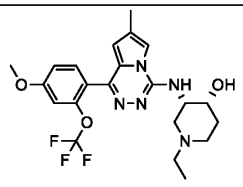
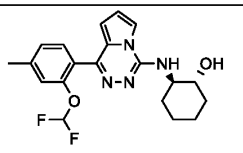
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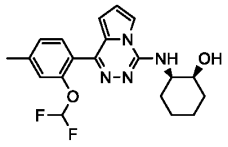
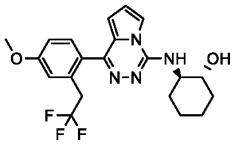
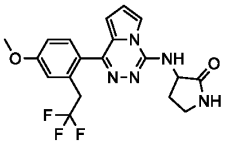
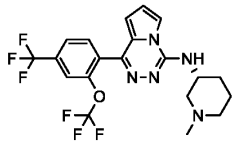
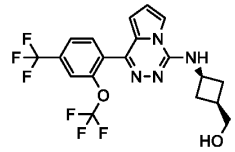
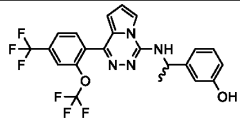
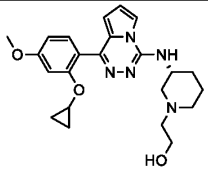
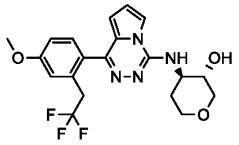
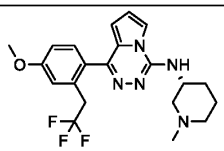
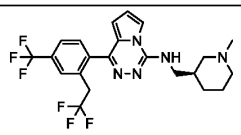
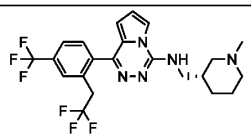
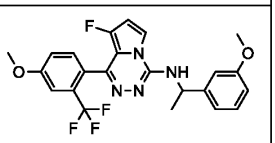
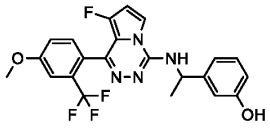
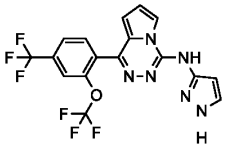
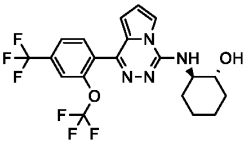
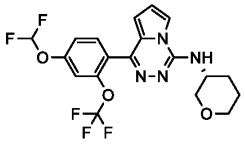
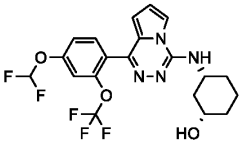
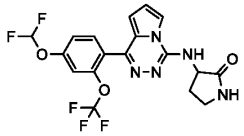
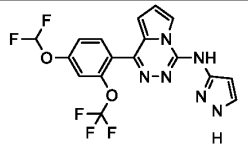
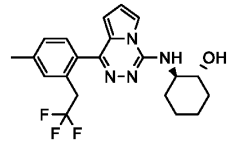
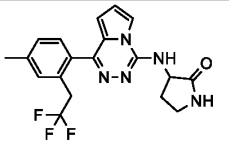
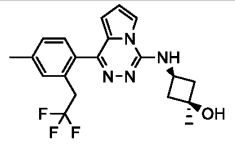
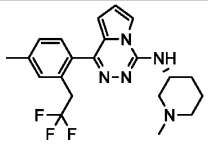
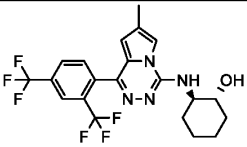
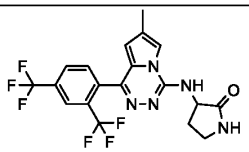
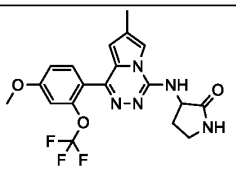
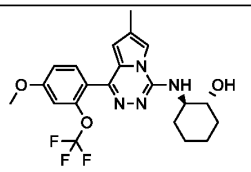
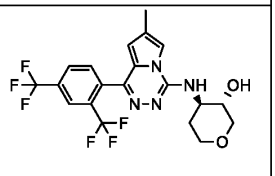
			
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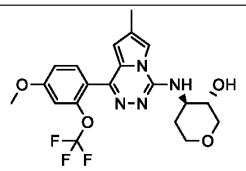
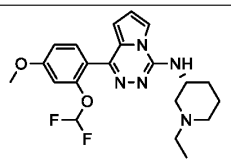
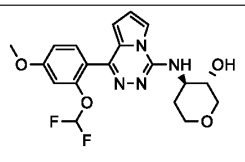
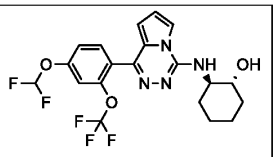
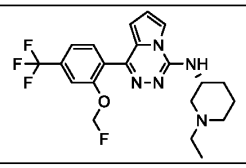
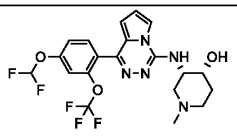
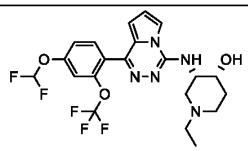
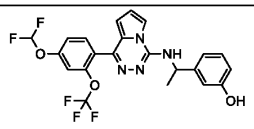
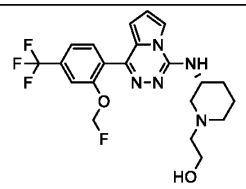
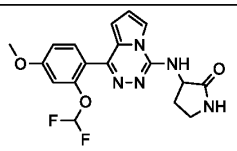
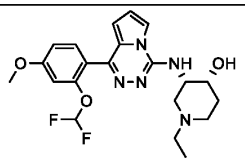
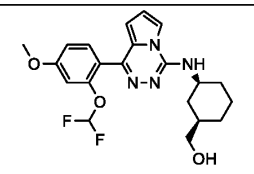
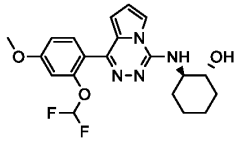
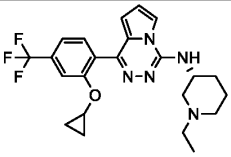
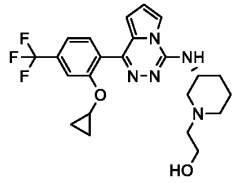
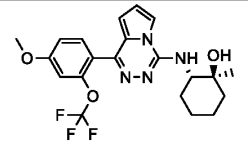
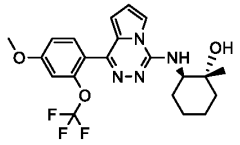
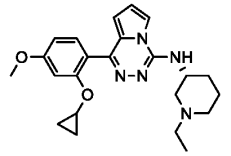
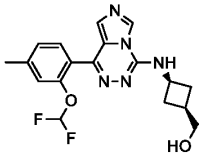
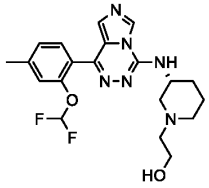
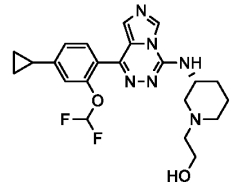
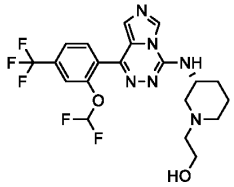
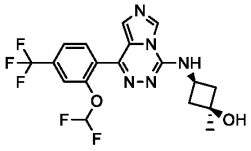
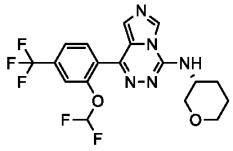
			
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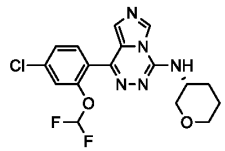
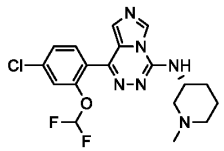
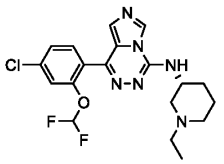
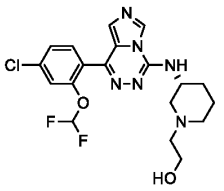
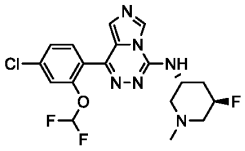
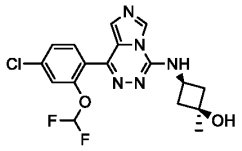
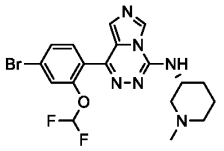
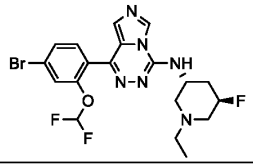
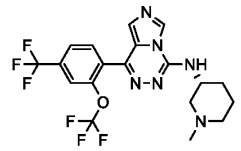
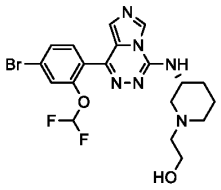
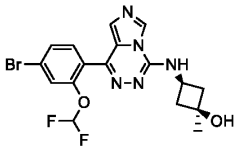
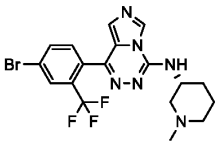
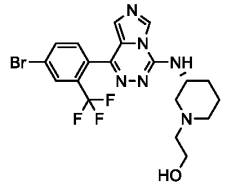
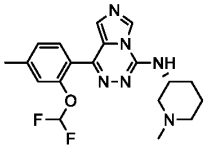
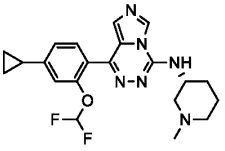
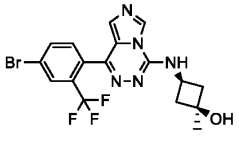
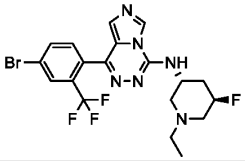
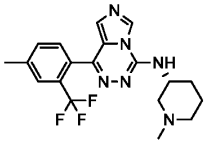
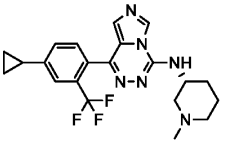
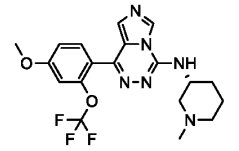
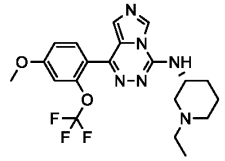
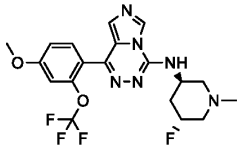
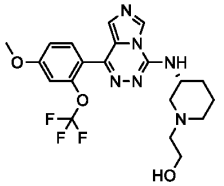
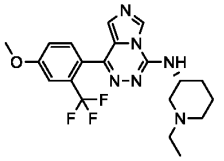
			
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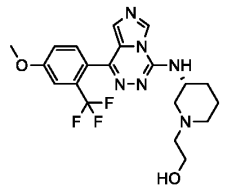
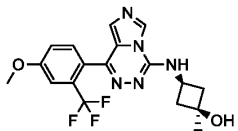
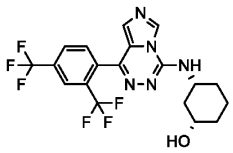
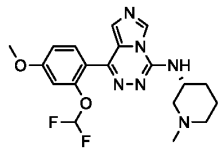
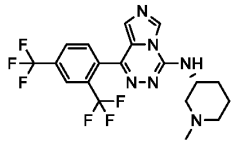
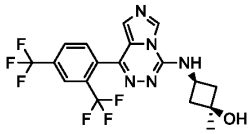
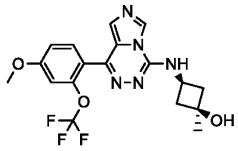
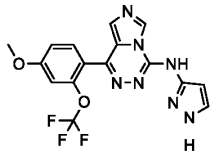
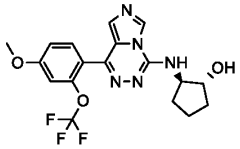
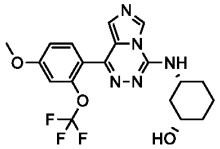
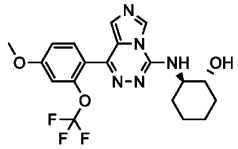
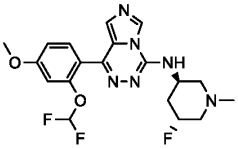
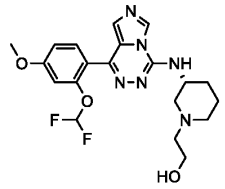
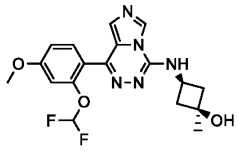
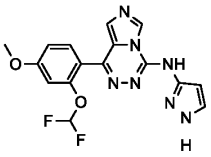
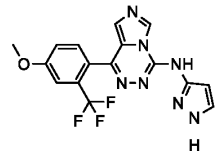
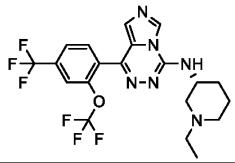
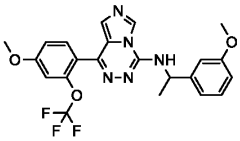
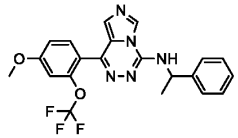
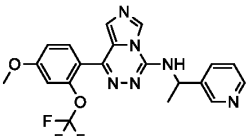
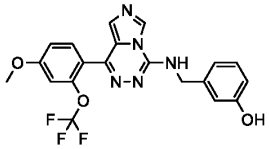
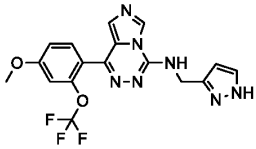
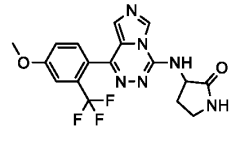
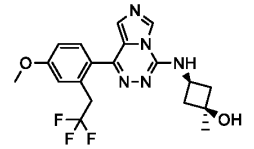
			
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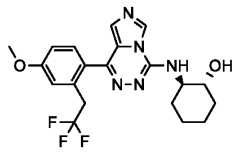
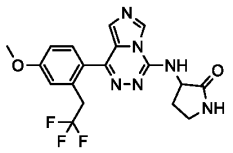
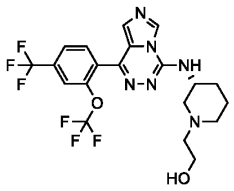
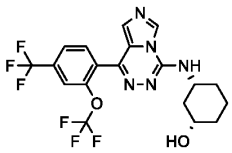
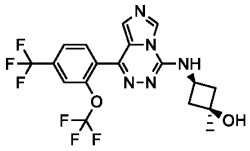
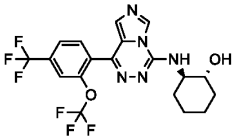
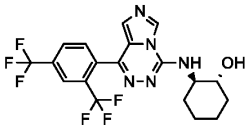
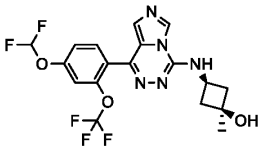
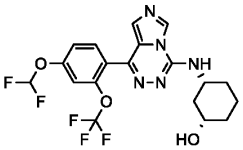
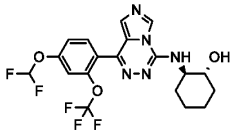
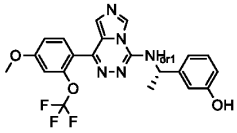
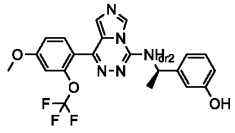
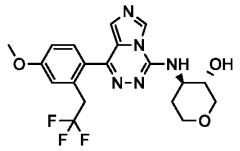
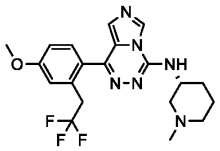
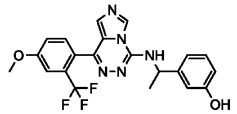
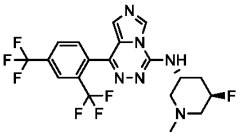
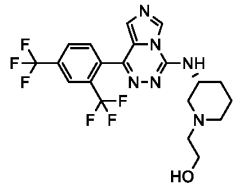
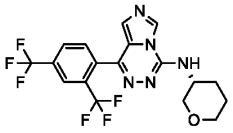
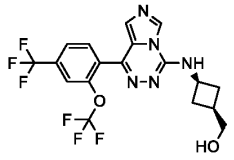
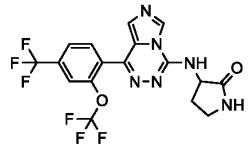
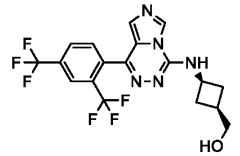
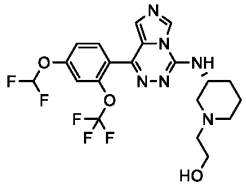
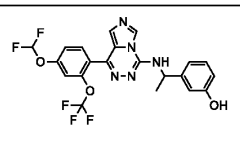
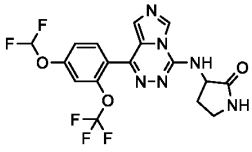
			
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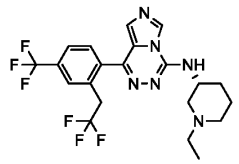
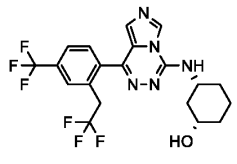
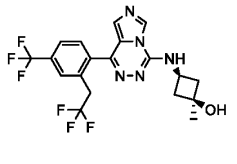
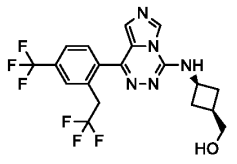
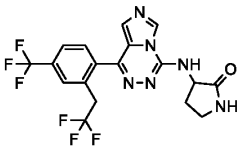
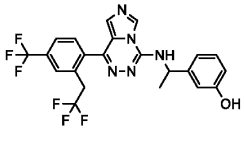
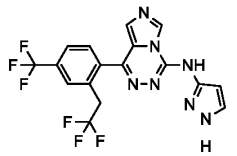
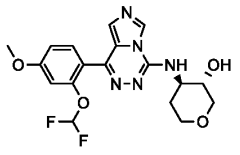
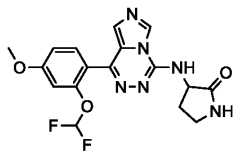
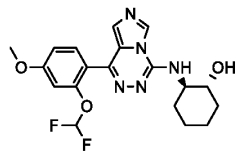
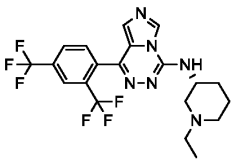
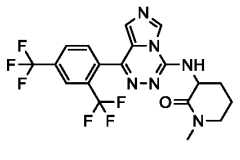
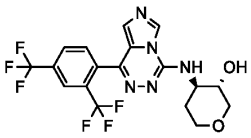
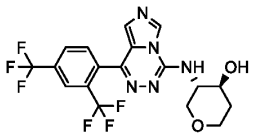
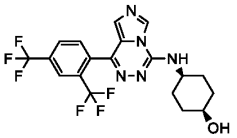
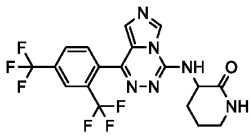
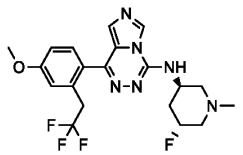
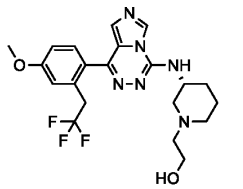
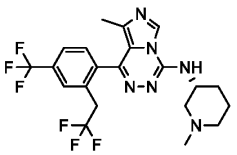
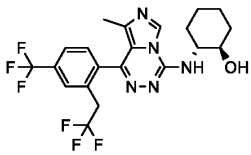
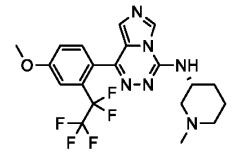
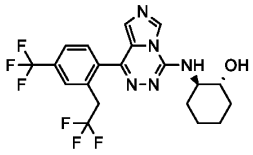
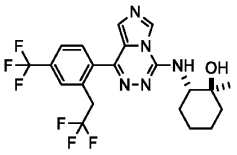
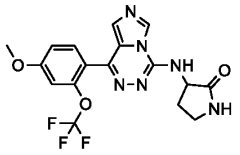
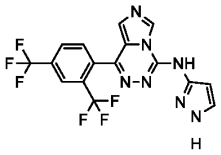
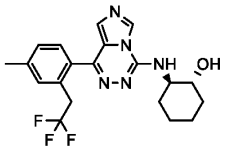
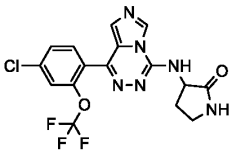
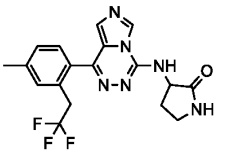
			
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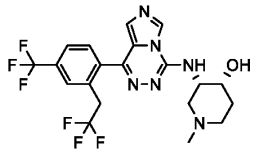
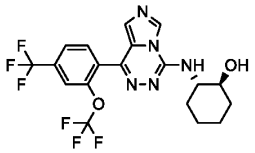
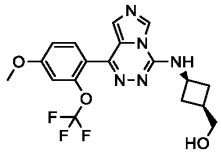
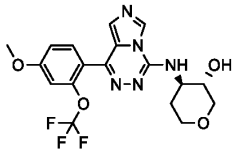
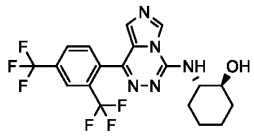
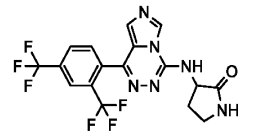
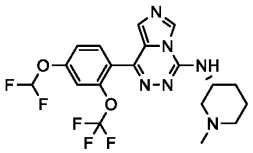
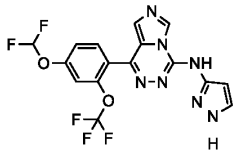
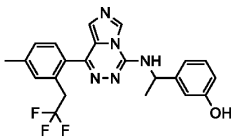
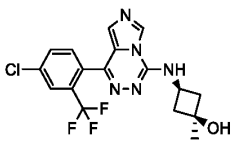
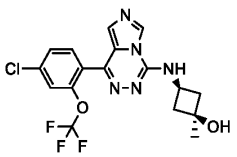
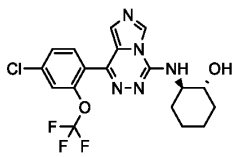
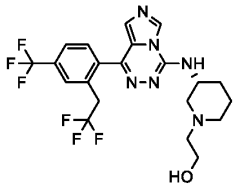
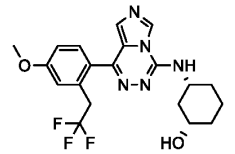
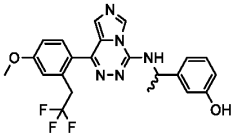
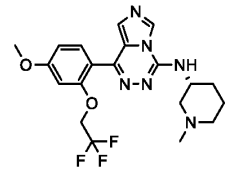
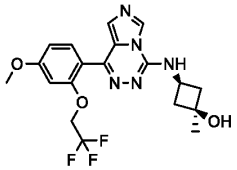
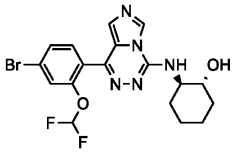
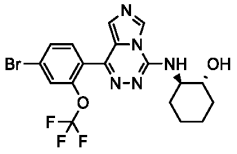
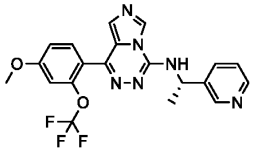
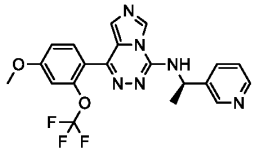
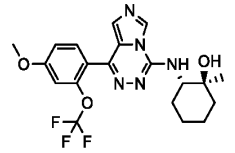
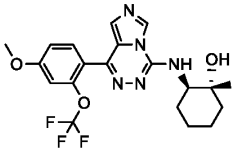
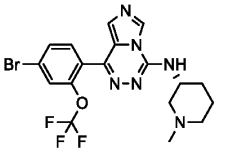
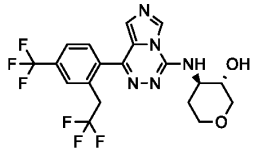
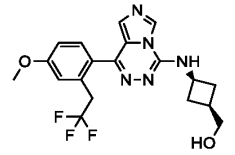
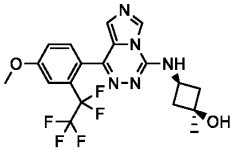
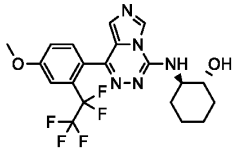
			
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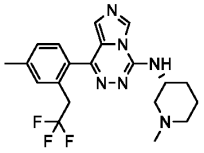
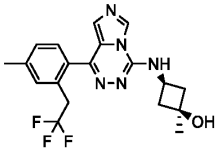
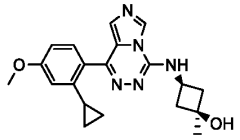
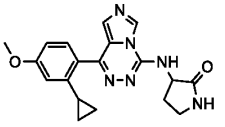
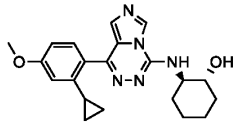
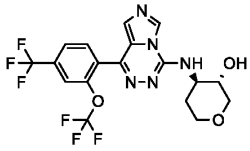
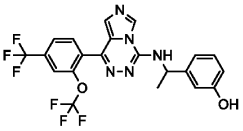
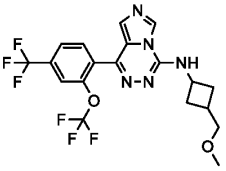
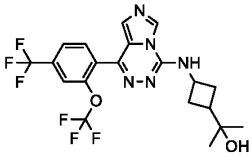
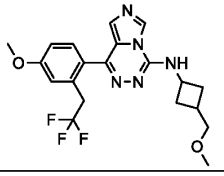
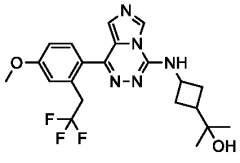
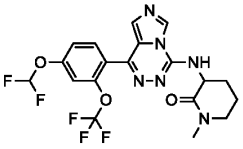
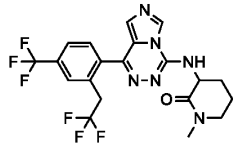
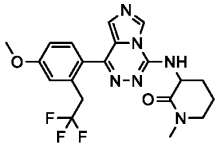
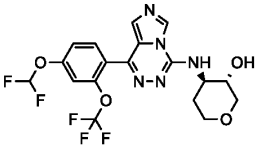
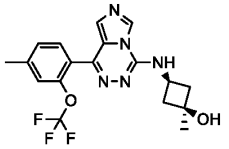
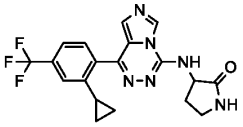
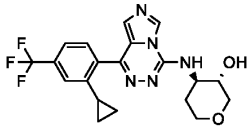
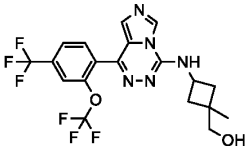
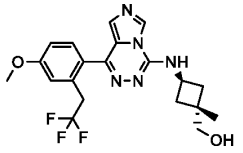
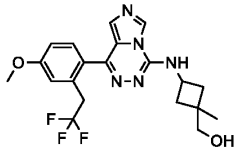
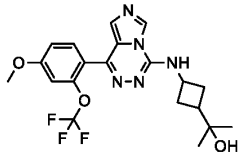
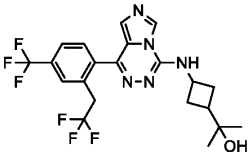
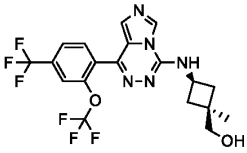
			
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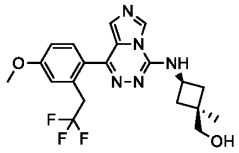
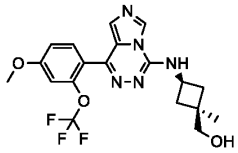
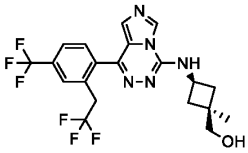
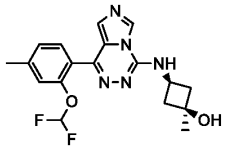
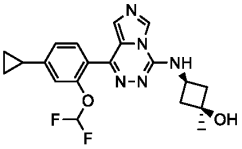
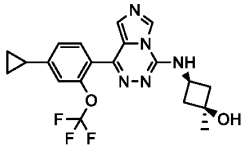
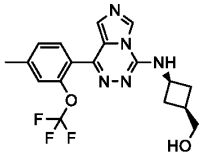
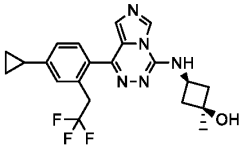
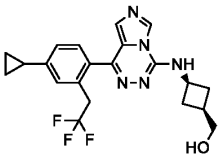
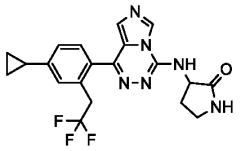
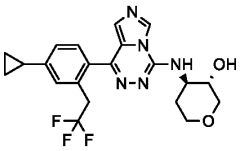
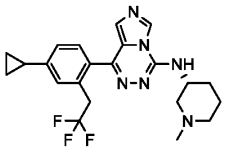
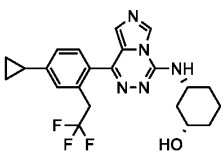
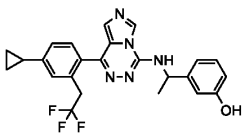
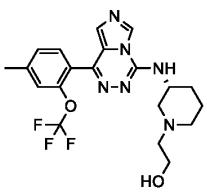
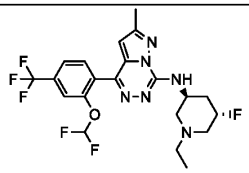
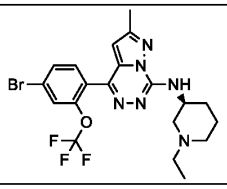
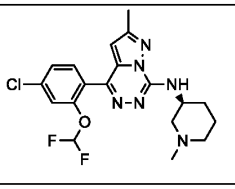
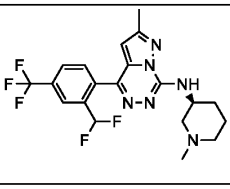
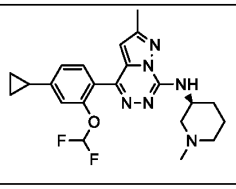
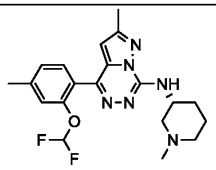
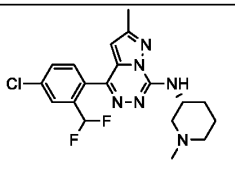
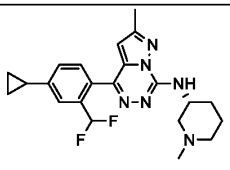
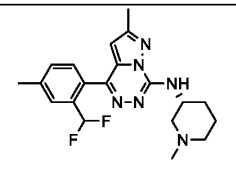
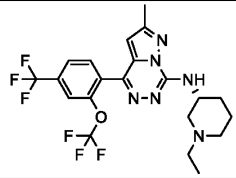
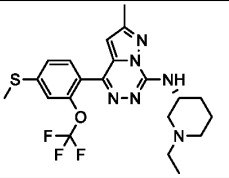
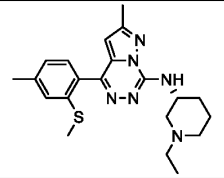
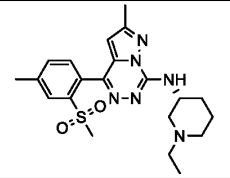
			
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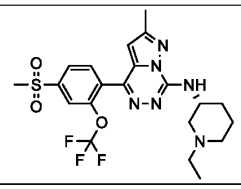
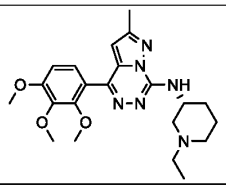
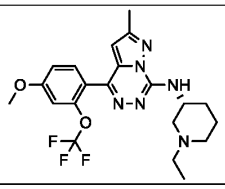
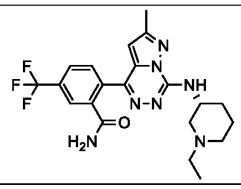
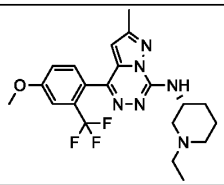
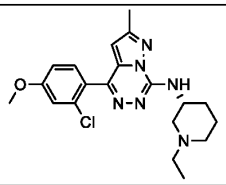
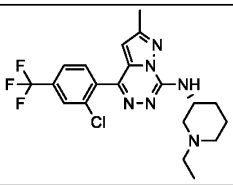
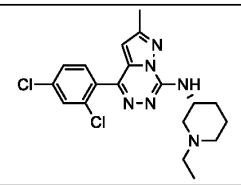
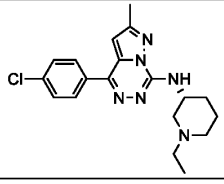
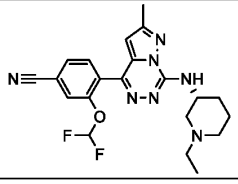
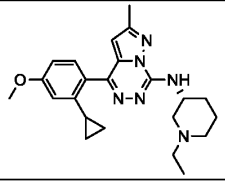
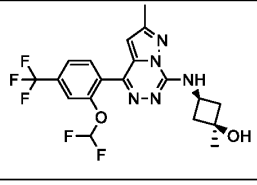
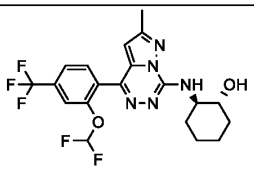
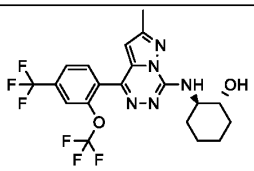
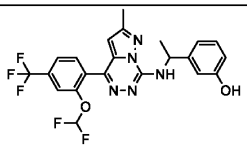
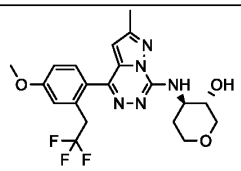
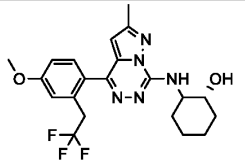
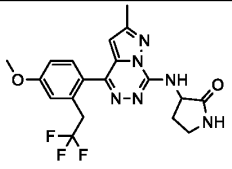
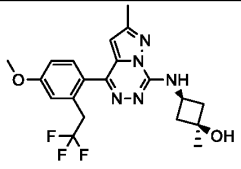
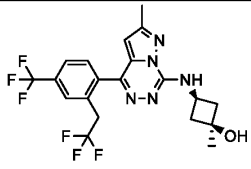
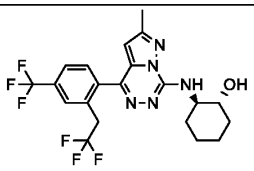
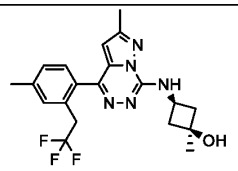
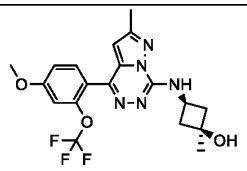
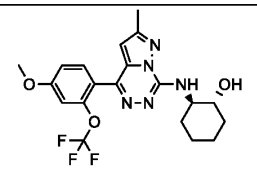
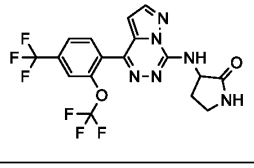
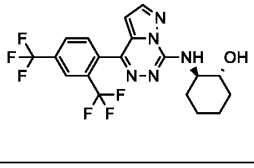
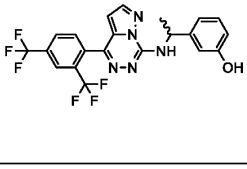
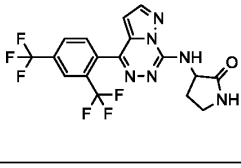
			
237	238	239	240
			
241	242	243	244
			
245	246	unassigned enantiomer	unassigned enantiomer
247	248		
			
249	250	251	252
			
253	254	255	256
			
257	258	259	260

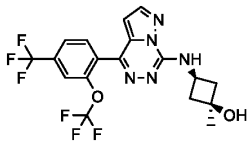
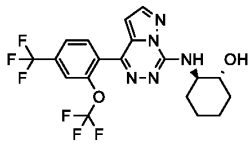
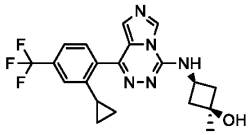
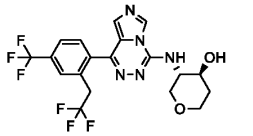
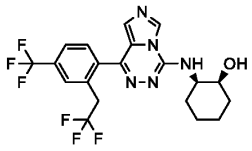
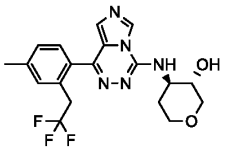
			
261	262	263	264
			
265	266	267	268
			
269	270	271	272
			
273	274	275	276
			
277	278	279	280
		 racemate	
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285	286	287	288

			
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293	294	295	296
			
297	298	299	300
			
301	302	303	304
			 unassigned enantiomer
305	306	307	308
 unassigned enantiomer	 unassigned enantiomer	 unassigned enantiomer	
309	310	311	312
			

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389	390	391	392
			
393	394	395	396

			
397	398	399	400
			
401	402		

wherein a form of the compound is selected from the group consisting of a pharmaceutically acceptable salt, hydrate, solvate, racemate, enantiomer, diastereomer, stereoisomer, tautomer, and isotope enriched form thereof.

2. A compound selected from:

Compound#	Name
1	(1s,3s)-3-({1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
2	N-[(3R)-1-methylpiperidin-3-yl]-1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine
3	(1s,3s)-1-methyl-3-({2-methyl-4-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]pyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)cyclobutan-1-ol
4	(1s,3s)-3-({4-[2,4-bis(trifluoromethyl)phenyl]pyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)-1-methylcyclobutan-1-ol
5	1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]-N-[(3R,5R)-1-ethyl-5-fluoropiperidin-3-yl]-8-fluoropyrrolo[1,2-d][1,2,4]triazin-4-amine
6	1-[2,4-bis(trifluoromethyl)phenyl]-N-[(3R)-1-(oxan-3-yl)piperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
7	1-{1-[2,4-bis(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}-N,N-dimethylpiperidin-3-amine
8	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
9	(1s,3s)-3-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
10	1-[2,4-bis(trifluoromethyl)phenyl]-N-[(3R)-1-(2-methylpropyl)piperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
11	1-[4-chloro-2-(difluoromethyl)phenyl]-7-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
12	1-[2-(difluoromethoxy)-4-methoxyphenyl]-7-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
13	1-[4-chloro-2-(difluoromethoxy)phenyl]-7-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine

14	1-[4-cyclopropyl-2-(difluoromethyl)phenyl]-7-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
15	2-[(3R)-3-({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]-8-fluoropyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
16	(2S)-1-({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]-8-fluoropyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)propan-2-ol
17	N-[(3R)-1-ethylpiperidin-3-yl]-8-fluoro-1-[4-methoxy-2-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
18	2-[(3R)-3-({8-fluoro-1-[4-methoxy-2-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
19	1-[2-fluoro-4-(trifluoromethyl)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
20	N-[(3R)-1-ethylpiperidin-3-yl]-1-[2-fluoro-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
21	2-[(3R)-3-({1-[2-fluoro-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
22	2-[(3R)-3-({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]propan-1-ol
23	1-[2-(difluoromethyl)-4-methylphenyl]-7-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
24	1-[4-cyclopropyl-2-(difluoromethoxy)phenyl]-7-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
25	1-[2-(difluoromethoxy)-4-methylphenyl]-7-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
26	1-(4-methoxy-2-methylphenyl)-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
27	1-(2-cyclopropyl-4-methoxyphenyl)-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
28	1-[2,4-bis(trifluoromethyl)phenyl]-8-fluoro-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
29	1-[2,4-bis(trifluoromethyl)phenyl]-N-[(3R)-1-ethylpiperidin-3-yl]-8-fluoropyrrolo[1,2-d][1,2,4]triazin-4-amine
30	2-[(3R)-3-({1-[2,4-bis(trifluoromethyl)phenyl]-8-fluoropyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
31	1-[2,4-bis(trifluoromethyl)phenyl]-8-fluoro-N-[(3R,5R)-5-fluoro-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
32	1-[2,4-bis(trifluoromethyl)phenyl]-N-[(3R,5R)-1-ethyl-5-fluoropiperidin-3-yl]-8-fluoropyrrolo[1,2-d][1,2,4]triazin-4-amine
33	1-[2-(difluoromethoxy)-4-methylphenyl]-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
34	1-[2-(difluoromethoxy)-4-methylphenyl]-N-[(3R)-1-ethylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
35	1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]-N-[(3R)-piperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
36	N-[(3R)-1-methylpiperidin-3-yl]-1-[4-methyl-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
37	1-[4-cyclopropyl-2-(trifluoromethoxy)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
38	(1s,3s)-3-({1-[2,4-bis(trifluoromethyl)phenyl]-8-fluoropyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol

39	8-fluoro-1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
40	N-[(3R)-1-methylpiperidin-3-yl]-1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
41	(1s,3s)-1-methyl-3-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclobutan-1-ol
42	1-[4-ethyl-2-(trifluoromethoxy)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
43	1-[4-ethoxy-2-(trifluoromethoxy)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
44	1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
45	2-[(3R)-3-({1-[2-(difluoromethoxy)-4-methylphenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
46	(3S,4S)-3-({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-ethylpiperidin-4-ol
47	1-(2-bromo-4-methoxyphenyl)-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
48	(3S,4R)-3-({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-ethylpiperidin-4-ol
49	1-[2-(difluoromethoxy)-6-methyl-4-(trifluoromethyl)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
50	N-[(3R)-1-ethylpiperidin-3-yl]-8-fluoro-1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
51	2-[(3R)-3-({8-fluoro-1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
52	8-fluoro-N-[(3R,5R)-5-fluoro-1-methylpiperidin-3-yl]-1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
53	N-[(3R,5R)-1-ethyl-5-fluoropiperidin-3-yl]-8-fluoro-1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
54	(1s,3s)-3-({8-fluoro-1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
55	1-[2-(difluoromethoxy)-4-methoxyphenyl]-8-fluoro-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
56	1-[2-(difluoromethoxy)-4-methoxyphenyl]-N-[(3R)-1-ethylpiperidin-3-yl]-8-fluoropyrrolo[1,2-d][1,2,4]triazin-4-amine
57	2-[(3R)-3-({1-[2-(difluoromethoxy)-4-methoxyphenyl]-8-fluoropyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
58	(1s,3s)-3-({1-[2-(difluoromethoxy)-4-methoxyphenyl]-8-fluoropyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
59	N-[(3R)-1-ethylpiperidin-3-yl]-1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
60	N-[(3R,5R)-5-fluoro-1-methylpiperidin-3-yl]-1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
61	2-[(3R)-3-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
62	(1S,3R)-3-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
63	(2R)-1-({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)propan-2-ol

64	2-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)ethan-1-ol
65	(2S)-1-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)propan-2-ol
66	1-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-2-methylpropan-2-ol
67	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-(oxan-4-yl)pyrrolo[1,2-d][1,2,4]triazin-4-amine
68	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-[(3R)-oxolan-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
69	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-[(1-methyl-1H-imidazol-2-yl)methyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
70	(2R)-1-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)propan-2-ol
71	(1s,3s)-3-({1-[4-methoxy-2-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
72	(1s,3s)-3-{[1-(2-chloro-4-methoxyphenyl)pyrrolo[1,2-d][1,2,4]triazin-4-yl]amino}-1-methylcyclobutan-1-ol
73	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-{[(2R)-oxolan-2-yl]methyl}pyrrolo[1,2-d][1,2,4]triazin-4-amine
74	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-{[(2S)-1-methylpyrrolidin-2-yl]methyl}pyrrolo[1,2-d][1,2,4]triazin-4-amine
75	1-(2-cyclopropyl-6-fluoro-4-methoxyphenyl)-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
76	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-{[(2S)-oxolan-2-yl]methyl}pyrrolo[1,2-d][1,2,4]triazin-4-amine
77	3-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
78	(1S,2S)-2-({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
79	(1R,2S)-2-({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
80	(1S,2S)-2-({1-[2-(difluoromethoxy)-4-methylphenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
81	(1S,2S)-2-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
82	1-(2-chloro-4-methoxyphenyl)-N-[(3R)-1-ethylpiperidin-3-yl]-8-fluoropyrrolo[1,2-d][1,2,4]triazin-4-amine
83	2-[(3R)-3-{[1-(2-chloro-4-methoxyphenyl)-8-fluoropyrrolo[1,2-d][1,2,4]triazin-4-yl]amino}piperidin-1-yl]ethan-1-ol
84	(1s,3s)-3-{[1-(2-chloro-4-methoxyphenyl)-8-fluoropyrrolo[1,2-d][1,2,4]triazin-4-yl]amino}-1-methylcyclobutan-1-ol
85	1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]-N-[(3R)-1-ethylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
86	2-[(3R)-3-({1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
87	1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]-N-[(3R,5R)-5-fluoro-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
88	(1s,3s)-3-({1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol

89	3-[1-({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)ethyl]phenol
90	(1R,2R)-2-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
91	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-[(1,3-oxazol-2-yl)methyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
92	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-[(4-methyl-4H-1,2,4-triazol-3-yl)methyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
93	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-[(1-methyl-1H-1,2,4-triazol-5-yl)methyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
94	[3-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)bicyclo[1.1.1]pentan-1-yl]methanol
95	1-[3-(difluoromethoxy)-4-(4-{[(3R)-1-methylpiperidin-3-yl]amino}pyrrolo[1,2-d][1,2,4]triazin-1-yl)phenyl]propan-1-one
96	3-[1-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)ethyl]phenol
97	N-(1H-pyrazol-3-yl)-1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
98	(3S,5R)-5-({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-methylpiperidin-3-ol
99	(1S,2S)-2-({1-[2,4-bis(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
100	3-[1-({1-[2-(difluoromethoxy)-4-methylphenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)ethyl]phenol
101	3-[({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)methyl]phenol
102	3-[(1R)-1-({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)ethyl]phenol OR 3-[(1S)-1-({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)ethyl]phenol
103	3-[(1S)-1-({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)ethyl]phenol OR 3-[(1R)-1-({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)ethyl]phenol
104	(1s,3s)-3-{[1-(2-cyclopropyl-4-methoxyphenyl)pyrrolo[1,2-d][1,2,4]triazin-4-yl]amino}-1-methylcyclobutan-1-ol
105	1-(2-cyclopropyl-4-methoxyphenyl)-N-(1H-pyrazol-3-yl)pyrrolo[1,2-d][1,2,4]triazin-4-amine
106	(1S,3R)-3-{[1-(2-cyclopropyl-4-methoxyphenyl)pyrrolo[1,2-d][1,2,4]triazin-4-yl]amino}cyclohexan-1-ol
107	(1s,3s)-3-({1-[2,4-bis(trifluoromethyl)phenyl]-7-methylpyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
108	(1s,3s)-3-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]-7-methylpyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
109	1-[2,4-bis(trifluoromethyl)phenyl]-7-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
110	(1R,2R)-2-({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
111	(1S,2S)-2-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
112	(3S,4R)-4-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)oxan-3-ol

113	(3R,4S)-4-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)oxan-3-ol
114	(3R,4R)-4-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)oxan-3-ol
115	(3S,4S)-4-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)oxan-3-ol
116	3-({8-fluoro-1-[4-methoxy-2-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
117	8-fluoro-1-[4-methoxy-2-(trifluoromethyl)phenyl]-N-(1H-pyrazol-3-yl)pyrrolo[1,2-d][1,2,4]triazin-4-amine
118	1-(2-fluoro-4-methoxy-6-methylphenyl)-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
119	N-[(3R)-1-ethylpiperidin-3-yl]-1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
120	2-[(3R)-3-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
121	(1S,2S)-2-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
122	(1S,3R)-3-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
123	(1s,3s)-1-methyl-3-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclobutan-1-ol
124	3-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
125	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-[(1-methyl-1H-tetrazol-5-yl)methyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
126	(1S,2R)-2-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cycloheptan-1-ol AND (1R,2S)-2-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cycloheptan-1-ol
127	(1R,2R)-2-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cycloheptan-1-ol AND (1S,2S)-2-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cycloheptan-1-ol
128	(1S,3R)-3-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cycloheptan-1-ol AND (1R,3S)-3-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cycloheptan-1-ol
129	(1R,3R)-3-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cycloheptan-1-ol AND (1S,3S)-3-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cycloheptan-1-ol
130	(1s,3s)-3-({8-fluoro-1-[4-methoxy-2-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
131	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-7-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
132	(1S,2S)-2-({1-[2,4-bis(trifluoromethyl)phenyl]-7-methylpyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
133	(1S,2S)-2-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]-7-methylpyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol

134	(3S,4R)-3-({1-[2,4-bis(trifluoromethyl)phenyl]-7-methylpyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-ethylpiperidin-4-ol
135	(3S,4R)-1-ethyl-3-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]-7-methylpyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)piperidin-4-ol
136	(1R,2R)-2-({1-[2-(difluoromethoxy)-4-methylphenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
137	(1S,2R)-2-({1-[2-(difluoromethoxy)-4-methylphenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
138	(1R,2R)-2-({1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
139	3-({1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
140	N-[(3R)-1-methylpiperidin-3-yl]-1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
141	[(1s,3s)-3-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclobutyl]methanol
142	3-[1-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)ethyl]phenol
143	2-[(3R)-3-({1-[2-(cyclopropyloxy)-4-methoxyphenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
144	(3S,4R)-4-({1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)oxan-3-ol
145	1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
146	N-{[(3S)-1-methylpiperidin-3-yl]methyl}-1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
147	N-{[(3R)-1-methylpiperidin-3-yl]methyl}-1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
148	8-fluoro-N-[1-(3-methoxyphenyl)ethyl]-1-[4-methoxy-2-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
149	3-[1-({8-fluoro-1-[4-methoxy-2-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)ethyl]phenol
150	N-(1H-pyrazol-3-yl)-1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
151	(1R,2R)-2-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
152	1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]-N-[(3R)-oxan-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
153	(1S,3R)-3-({1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
154	3-({1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
155	1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]-N-(1H-pyrazol-3-yl)pyrrolo[1,2-d][1,2,4]triazin-4-amine
156	(1R,2R)-2-({1-[4-methyl-2-(2,2,2-trifluoroethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
157	3-({1-[4-methyl-2-(2,2,2-trifluoroethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
158	(1s,3s)-1-methyl-3-({1-[4-methyl-2-(2,2,2-trifluoroethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclobutan-1-ol

159	N-[(3R)-1-methylpiperidin-3-yl]-1-[4-methyl-2-(2,2,2-trifluoroethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
160	(1R,2R)-2-({1-[2,4-bis(trifluoromethyl)phenyl]-7-methylpyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
161	3-({1-[2,4-bis(trifluoromethyl)phenyl]-7-methylpyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
162	3-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]-7-methylpyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
163	(1R,2R)-2-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]-7-methylpyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
164	(3S,4R)-4-({1-[2,4-bis(trifluoromethyl)phenyl]-7-methylpyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)oxan-3-ol
165	(3S,4R)-4-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]-7-methylpyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)oxan-3-ol
166	1-[2-(difluoromethoxy)-4-methoxyphenyl]-N-[(3R)-1-ethylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
167	(3S,4R)-4-({1-[2-(difluoromethoxy)-4-methoxyphenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)oxan-3-ol
168	(1R,2R)-2-({1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
169	N-[(3R)-1-ethylpiperidin-3-yl]-1-[2-(fluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
170	(3S,4R)-3-({1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-methylpiperidin-4-ol
171	(3S,4R)-3-({1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-ethylpiperidin-4-ol
172	3-[1-({1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)ethyl]phenol
173	2-[(3R)-3-({1-[2-(fluoromethoxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
174	3-({1-[2-(difluoromethoxy)-4-methoxyphenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
175	(3S,4R)-3-({1-[2-(difluoromethoxy)-4-methoxyphenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-ethylpiperidin-4-ol
176	[(1R,3S)-3-({1-[2-(difluoromethoxy)-4-methoxyphenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexyl]methanol
177	(1R,2R)-2-({1-[2-(difluoromethoxy)-4-methoxyphenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
178	1-[2-(cyclopropyloxy)-4-(trifluoromethyl)phenyl]-N-[(3R)-1-ethylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
179	2-[(3R)-3-({1-[2-(cyclopropyloxy)-4-(trifluoromethyl)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
180	(1S,2S)-2-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-methylcyclohexan-1-ol OR (1R,2R)-2-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-methylcyclohexan-1-ol
181	(1R,2R)-2-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-methylcyclohexan-1-ol OR (1S,2S)-2-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]pyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-methylcyclohexan-1-ol

182	1-[2-(cyclopropyloxy)-4-methoxyphenyl]-N-[(3R)-1-ethylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine
183	[(1s,3s)-3-({1-[2-(difluoromethoxy)-4-methylphenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutyl]methanol
184	2-[(3R)-3-({1-[2-(difluoromethoxy)-4-methylphenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
185	2-[(3R)-3-({1-[4-cyclopropyl-2-(difluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
186	2-[(3R)-3-({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
187	(1s,3s)-3-({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
188	1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]-N-[(3R)-oxan-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
189	1-[4-chloro-2-(difluoromethoxy)phenyl]-N-[(3R)-oxan-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
190	1-[4-chloro-2-(difluoromethoxy)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
191	1-[4-chloro-2-(difluoromethoxy)phenyl]-N-[(3R)-1-ethylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
192	2-[(3R)-3-({1-[4-chloro-2-(difluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
193	1-[4-chloro-2-(difluoromethoxy)phenyl]-N-[(3R,5R)-5-fluoro-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
194	(1s,3s)-3-({1-[4-chloro-2-(difluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
195	1-[4-bromo-2-(difluoromethoxy)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
196	1-[4-bromo-2-(difluoromethoxy)phenyl]-N-[(3R,5R)-1-ethyl-5-fluoropiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
197	N-[(3R)-1-methylpiperidin-3-yl]-1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine
198	2-[(3R)-3-({1-[4-bromo-2-(difluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
199	(1s,3s)-3-({1-[4-bromo-2-(difluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
200	1-[4-bromo-2-(trifluoromethyl)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
201	2-[(3R)-3-({1-[4-bromo-2-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
202	1-[2-(difluoromethoxy)-4-methylphenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
203	1-[4-cyclopropyl-2-(difluoromethoxy)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
204	(1s,3s)-3-({1-[4-bromo-2-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
205	1-[4-bromo-2-(trifluoromethyl)phenyl]-N-[(3R,5R)-1-ethyl-5-fluoropiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
206	N-[(3R)-1-methylpiperidin-3-yl]-1-[4-methyl-2-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine

207	1-[4-cyclopropyl-2-(trifluoromethyl)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
208	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
209	N-[(3R)-1-ethylpiperidin-3-yl]-1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine
210	N-[(3R,5R)-5-fluoro-1-methylpiperidin-3-yl]-1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine
211	2-[(3R)-3-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
212	N-[(3R)-1-ethylpiperidin-3-yl]-1-[4-methoxy-2-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine
213	2-[(3R)-3-({1-[4-methoxy-2-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
214	(1s,3s)-3-({1-[4-methoxy-2-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
215	(1S,3R)-3-({1-[2,4-bis(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
216	1-[2-(difluoromethoxy)-4-methoxyphenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
217	1-[2,4-bis(trifluoromethyl)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
218	(1s,3s)-3-({1-[2,4-bis(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
219	(1s,3s)-3-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
220	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-(1H-pyrazol-3-yl)imidazo[1,5-d][1,2,4]triazin-4-amine
221	(1R,2R)-2-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclopentan-1-ol
222	(1S,3R)-3-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
223	(1R,2R)-2-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
224	1-[2-(difluoromethoxy)-4-methoxyphenyl]-N-[(3R,5R)-5-fluoro-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
225	2-[(3R)-3-({1-[2-(difluoromethoxy)-4-methoxyphenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
226	(1s,3s)-3-({1-[2-(difluoromethoxy)-4-methoxyphenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
227	1-[2-(difluoromethoxy)-4-methoxyphenyl]-N-(1H-pyrazol-3-yl)imidazo[1,5-d][1,2,4]triazin-4-amine
228	1-[4-methoxy-2-(trifluoromethyl)phenyl]-N-(1H-pyrazol-3-yl)imidazo[1,5-d][1,2,4]triazin-4-amine
229	N-[(3R)-1-ethylpiperidin-3-yl]-1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine
230	N-[1-(3-methoxyphenyl)ethyl]-1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine
231	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-(1-phenylethyl)imidazo[1,5-d][1,2,4]triazin-4-amine

232	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-[1-(pyridin-3-yl)ethyl]imidazo[1,5-d][1,2,4]triazin-4-amine
233	3-[({1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)methyl]phenol
234	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-[(1H-pyrazol-3-yl)methyl]imidazo[1,5-d][1,2,4]triazin-4-amine
235	3-({1-[4-methoxy-2-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
236	(1s,3s)-3-({1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
237	(1R,2R)-2-({1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
238	3-({1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
239	2-[(3R)-3-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
240	(1S,3R)-3-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
241	(1s,3s)-1-methyl-3-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutan-1-ol
242	(1R,2R)-2-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
243	(1R,2R)-2-({1-[2,4-bis(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
244	(1s,3s)-3-({1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
245	(1S,3R)-3-({1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
246	(1R,2R)-2-({1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
247	3-[(1S)-1-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)ethyl]phenol OR 3-[(1R)-1-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)ethyl]phenol
248	3-[(1R)-1-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)ethyl]phenol OR 3-[(1S)-1-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)ethyl]phenol
249	(3S,4R)-4-({1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)oxan-3-ol
250	1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
251	3-[1-({1-[4-methoxy-2-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)ethyl]phenol
252	1-[2,4-bis(trifluoromethyl)phenyl]-N-[(3R,5R)-5-fluoro-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
253	2-[(3R)-3-({1-[2,4-bis(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
254	1-[2,4-bis(trifluoromethyl)phenyl]-N-[(3R)-oxan-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
255	[(1s,3s)-3-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutyl]methanol

256	3-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
257	[(1s,3s)-3-({1-[2,4-bis(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutyl]methanol
258	2-[(3R)-3-({1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
259	3-[1-({1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)ethyl]phenol
260	3-({1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
261	N-[(3R)-1-ethylpiperidin-3-yl]-1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine
262	(1S,3R)-3-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
263	(1s,3s)-1-methyl-3-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutan-1-ol
264	[(1s,3s)-3-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutyl]methanol
265	3-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
266	3-[1-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)ethyl]phenol
267	N-(1H-pyrazol-3-yl)-1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine
268	(3S,4R)-4-({1-[2-(difluoromethoxy)-4-methoxyphenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)oxan-3-ol
269	3-({1-[2-(difluoromethoxy)-4-methoxyphenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
270	(1R,2R)-2-({1-[2-(difluoromethoxy)-4-methoxyphenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
271	1-[2,4-bis(trifluoromethyl)phenyl]-N-[(3R)-1-ethylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
272	3-({1-[2,4-bis(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylpiperidin-2-one
273	(3S,4R)-4-({1-[2,4-bis(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)oxan-3-ol
274	(3S,4S)-3-({1-[2,4-bis(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)oxan-4-ol
275	(1s,4s)-4-({1-[2,4-bis(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
276	3-({1-[2,4-bis(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-2-one
277	N-[(3R,5R)-5-fluoro-1-methylpiperidin-3-yl]-1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine
278	2-[(3R)-3-({1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
279	8-methyl-N-[(3R)-1-methylpiperidin-3-yl]-1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine
280	(1R,2R)-2-({8-methyl-1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol

281	1-[4-methoxy-2-(pentafluoroethyl)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
282	(1R,2R)-2-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
283	(1S,2S)-1-methyl-2-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol AND (1R,2R)-1-methyl-2-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
284	3-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
285	1-[2,4-bis(trifluoromethyl)phenyl]-N-(1H-pyrazol-3-yl)imidazo[1,5-d][1,2,4]triazin-4-amine
286	(1R,2R)-2-({1-[4-methyl-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
287	3-({1-[4-chloro-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
288	3-({1-[4-methyl-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
289	(3S,4R)-1-methyl-3-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-4-ol
290	(1S,2S)-2-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
291	[(1s,3s)-3-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutyl]methanol
292	(3S,4R)-4-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)oxan-3-ol
293	(1S,2S)-2-({1-[2,4-bis(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
294	3-({1-[2,4-bis(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
295	1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
296	1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]-N-(1H-pyrazol-3-yl)imidazo[1,5-d][1,2,4]triazin-4-amine
297	3-[1-({1-[4-methyl-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)ethyl]phenol
298	(1s,3s)-3-({1-[4-chloro-2-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
299	(1s,3s)-3-({1-[4-chloro-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
300	(1R,2R)-2-({1-[4-chloro-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
301	2-[(3R)-3-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
302	(1S,3R)-3-({1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
303	3-[1-({1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)ethyl]phenol
304	1-[4-methoxy-2-(2,2,2-trifluoroethoxy)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine

305	(1s,3s)-3-({1-[4-methoxy-2-(2,2,2-trifluoroethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
306	(1R,2R)-2-({1-[4-bromo-2-(difluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
307	(1R,2R)-2-({1-[4-bromo-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
308	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-[(1S)-1-(pyridin-3-yl)ethyl]imidazo[1,5-d][1,2,4]triazin-4-amine OR 1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-[(1R)-1-(pyridin-3-yl)ethyl]imidazo[1,5-d][1,2,4]triazin-4-amine
309	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-[(1R)-1-(pyridin-3-yl)ethyl]imidazo[1,5-d][1,2,4]triazin-4-amine OR 1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-[(1S)-1-(pyridin-3-yl)ethyl]imidazo[1,5-d][1,2,4]triazin-4-amine
310	(1S,2S)-2-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclohexan-1-ol OR (1R,2R)-2-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclohexan-1-ol
311	(1R,2R)-2-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclohexan-1-ol OR (1S,2S)-2-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclohexan-1-ol
312	1-[4-bromo-2-(trifluoromethoxy)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
313	(3S,4R)-4-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)oxan-3-ol
314	[(1s,3s)-3-({1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutyl]methanol
315	(1s,3s)-3-({1-[4-methoxy-2-(pentafluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
316	(1R,2R)-2-({1-[4-methoxy-2-(pentafluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
317	N-[(3R)-1-methylpiperidin-3-yl]-1-[4-methyl-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine
318	(1s,3s)-1-methyl-3-({1-[4-methyl-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutan-1-ol
319	(1s,3s)-3-{[1-(2-cyclopropyl-4-methoxyphenyl)imidazo[1,5-d][1,2,4]triazin-4-yl]amino}-1-methylcyclobutan-1-ol
320	3-{[1-(2-cyclopropyl-4-methoxyphenyl)imidazo[1,5-d][1,2,4]triazin-4-yl]amino}pyrrolidin-2-one
321	(1R,2R)-2-{[1-(2-cyclopropyl-4-methoxyphenyl)imidazo[1,5-d][1,2,4]triazin-4-yl]amino}cyclohexan-1-ol
322	(3S,4R)-4-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)oxan-3-ol
323	3-[1-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)ethyl]phenol
324	N-[3-(methoxymethyl)cyclobutyl]-1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine
325	2-[3-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutyl]propan-2-ol

326	N-[3-(methoxymethyl)cyclobutyl]-1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine
327	2-[3-({1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutyl]propan-2-ol
328	3-({1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylpiperidin-2-one
329	1-methyl-3-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-2-one
330	3-({1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylpiperidin-2-one
331	(3S,4R)-4-({1-[4-(difluoromethoxy)-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)oxan-3-ol
332	(1s,3s)-1-methyl-3-({1-[4-methyl-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutan-1-ol
333	3-({1-[2-cyclopropyl-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one
334	(3S,4R)-4-({1-[2-cyclopropyl-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)oxan-3-ol
335	[1-methyl-3-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutyl]methanol
336	[(1r,3r)-3-({1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutyl]methanol
337	[3-({1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutyl]methanol
338	2-[3-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutyl]propan-2-ol
339	2-[3-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutyl]propan-2-ol
340	[(1s,3s)-1-methyl-3-({1-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutyl]methanol
341	[(1s,3s)-3-({1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutyl]methanol
342	[(1s,3s)-3-({1-[4-methoxy-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutyl]methanol
343	[(1s,3s)-1-methyl-3-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutyl]methanol
344	(1s,3s)-3-({1-[2-(difluoromethoxy)-4-methylphenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
345	(1s,3s)-3-({1-[4-cyclopropyl-2-(difluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
346	(1s,3s)-3-({1-[4-cyclopropyl-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
347	[(1s,3s)-3-({1-[4-methyl-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutyl]methanol
348	(1s,3s)-3-({1-[4-cyclopropyl-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
349	[(1s,3s)-3-({1-[4-cyclopropyl-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclobutyl]methanol
350	3-({1-[4-cyclopropyl-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)pyrrolidin-2-one

351	(3S,4R)-4-({1-[4-cyclopropyl-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)oxan-3-ol
352	1-[4-cyclopropyl-2-(2,2,2-trifluoroethyl)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine
353	(1S,3R)-3-({1-[4-cyclopropyl-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
354	3-[1-({1-[4-cyclopropyl-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)ethyl]phenol
355	2-[(3R)-3-({1-[4-methyl-2-(trifluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol
356	4-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]-N-[(3R,5R)-1-ethyl-5-fluoropiperidin-3-yl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-amine
357	4-[4-bromo-2-(trifluoromethoxy)phenyl]-N-[(3R)-1-ethylpiperidin-3-yl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-amine
358	4-[4-chloro-2-(difluoromethoxy)phenyl]-2-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrazolo[1,5-d][1,2,4]triazin-7-amine
359	4-[2-(difluoromethyl)-4-(trifluoromethyl)phenyl]-2-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrazolo[1,5-d][1,2,4]triazin-7-amine
360	4-[4-cyclopropyl-2-(difluoromethoxy)phenyl]-2-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrazolo[1,5-d][1,2,4]triazin-7-amine
361	4-[2-(difluoromethoxy)-4-methylphenyl]-2-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrazolo[1,5-d][1,2,4]triazin-7-amine
362	4-[4-chloro-2-(difluoromethyl)phenyl]-2-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrazolo[1,5-d][1,2,4]triazin-7-amine
363	4-[4-cyclopropyl-2-(difluoromethyl)phenyl]-2-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrazolo[1,5-d][1,2,4]triazin-7-amine
364	4-[2-(difluoromethyl)-4-methylphenyl]-2-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrazolo[1,5-d][1,2,4]triazin-7-amine
365	N-[(3R)-1-ethylpiperidin-3-yl]-2-methyl-4-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]pyrazolo[1,5-d][1,2,4]triazin-7-amine
366	N-[(3R)-1-ethylpiperidin-3-yl]-2-methyl-4-[4-(methylsulfanyl)-2-(trifluoromethoxy)phenyl]pyrazolo[1,5-d][1,2,4]triazin-7-amine
367	N-[(3R)-1-ethylpiperidin-3-yl]-2-methyl-4-[4-methyl-2-(methylsulfanyl)phenyl]pyrazolo[1,5-d][1,2,4]triazin-7-amine
368	N-[(3R)-1-ethylpiperidin-3-yl]-4-[2-(methanesulfonyl)-4-methylphenyl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-amine
369	N-[(3R)-1-ethylpiperidin-3-yl]-4-[4-(methanesulfonyl)-2-(trifluoromethoxy)phenyl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-amine
370	N-[(3R)-1-ethylpiperidin-3-yl]-2-methyl-4-(2,3,4-trimethoxyphenyl)pyrazolo[1,5-d][1,2,4]triazin-7-amine
371	N-[(3R)-1-ethylpiperidin-3-yl]-4-[4-methoxy-2-(trifluoromethoxy)phenyl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-amine
372	2-(7-{[(3R)-1-ethylpiperidin-3-yl]amino}-2-methylpyrazolo[1,5-d][1,2,4]triazin-4-yl)-5-(trifluoromethyl)benzamide
373	N-[(3R)-1-ethylpiperidin-3-yl]-4-[4-methoxy-2-(trifluoromethyl)phenyl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-amine
374	4-(2-chloro-4-methoxyphenyl)-N-[(3R)-1-ethylpiperidin-3-yl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-amine
375	4-[2-chloro-4-(trifluoromethyl)phenyl]-N-[(3R)-1-ethylpiperidin-3-yl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-amine

376	4-(2,4-dichlorophenyl)-N-[(3R)-1-ethylpiperidin-3-yl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-amine
377	4-(4-chlorophenyl)-N-[(3R)-1-ethylpiperidin-3-yl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-amine
378	3-(difluoromethoxy)-4-(7-{[(3R)-1-ethylpiperidin-3-yl]amino}-2-methylpyrazolo[1,5-d][1,2,4]triazin-4-yl)benzonitrile
379	4-(2-cyclopropyl-4-methoxyphenyl)-N-[(3R)-1-ethylpiperidin-3-yl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-amine
380	(1s,3s)-3-({4-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)-1-methylcyclobutan-1-ol
381	(1R,2R)-2-({4-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)cyclohexan-1-ol
382	(1R,2R)-2-({2-methyl-4-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]pyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)cyclohexan-1-ol
383	3-[1-({4-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)ethyl]phenol
384	(3S,4R)-4-({4-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)oxan-3-ol
385	(1R,2R)-2-({4-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)cyclohexan-1-ol
386	3-({4-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)pyrrolidin-2-one
387	(1s,3s)-3-({4-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)-1-methylcyclobutan-1-ol
388	(1s,3s)-1-methyl-3-({2-methyl-4-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)cyclobutan-1-ol
389	(1R,2R)-2-({2-methyl-4-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]pyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)cyclohexan-1-ol
390	(1s,3s)-1-methyl-3-({2-methyl-4-[4-methyl-2-(2,2,2-trifluoroethyl)phenyl]pyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)cyclobutan-1-ol
391	(1s,3s)-3-({4-[4-methoxy-2-(trifluoromethoxy)phenyl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)-1-methylcyclobutan-1-ol
392	(1R,2R)-2-({4-[4-methoxy-2-(trifluoromethoxy)phenyl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)cyclohexan-1-ol
393	3-({4-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]pyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)pyrrolidin-2-one
394	(1R,2R)-2-({4-[2,4-bis(trifluoromethyl)phenyl]pyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)cyclohexan-1-ol
395	3-[1-({4-[2,4-bis(trifluoromethyl)phenyl]pyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)ethyl]phenol
396	3-({4-[2,4-bis(trifluoromethyl)phenyl]pyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)pyrrolidin-2-one
397	(1s,3s)-1-methyl-3-({4-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]pyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)cyclobutan-1-ol
398	(1R,2R)-2-({4-[2-(trifluoromethoxy)-4-(trifluoromethyl)phenyl]pyrazolo[1,5-d][1,2,4]triazin-7-yl}amino)cyclohexan-1-ol
399	(1s,3s)-3-({1-[2-cyclopropyl-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)-1-methylcyclobutan-1-ol
400	(3S,4S)-3-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)oxan-4-ol

401	(1S,2R)-2-({1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)cyclohexan-1-ol
402	(3S,4R)-4-({1-[4-methyl-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)oxan-3-ol

wherein a form of the compound is selected from the group consisting of a pharmaceutically acceptable salt, hydrate, solvate, racemate, enantiomer, diastereomer, stereoisomer, tautomer, and isotope enriched form thereof.

3. A compound selected from:

Compound #	Name
2	N-[(3R)-1-methylpiperidin-3-yl]-1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine formate
12	1-[2-(difluoromethoxy)-4-methoxyphenyl]-7-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine formate
13	1-[4-chloro-2-(difluoromethoxy)phenyl]-7-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine formate
14	1-[4-cyclopropyl-2-(difluoromethyl)phenyl]-7-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine formate
19	1-[2-fluoro-4-(trifluoromethyl)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine formate
23	1-[2-(difluoromethyl)-4-methylphenyl]-7-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine formate
24	1-[4-cyclopropyl-2-(difluoromethoxy)phenyl]-7-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine formate
25	1-[2-(difluoromethoxy)-4-methylphenyl]-7-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine formate
34	1-[2-(difluoromethoxy)-4-methylphenyl]-N-[(3R)-1-ethylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine formate
35	1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]-N-[(3R)-piperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine hydrochloride
37	1-[4-cyclopropyl-2-(trifluoromethoxy)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine formate
42	1-[4-ethyl-2-(trifluoromethoxy)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine formate
74	1-[4-methoxy-2-(trifluoromethoxy)phenyl]-N-{[(2S)-1-methylpyrrolidin-2-yl]methyl}pyrrolo[1,2-d][1,2,4]triazin-4-amine trifluoroacetate
95	1-[3-(difluoromethoxy)-4-(4-{[(3R)-1-methylpiperidin-3-yl]amino}pyrrolo[1,2-d][1,2,4]triazin-1-yl)phenyl]propan-1-one formate
134	(3S,4R)-3-({1-[2,4-bis(trifluoromethyl)phenyl]-7-methylpyrrolo[1,2-d][1,2,4]triazin-4-yl}amino)-1-ethylpiperidin-4-ol formate
145	1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]pyrrolo[1,2-d][1,2,4]triazin-4-amine formate
184	2-[(3R)-3-({1-[2-(difluoromethoxy)-4-methylphenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol formate

185	2-[(3R)-3-({1-[4-cyclopropyl-2-(difluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol formate
186	2-[(3R)-3-({1-[2-(difluoromethoxy)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol formate
190	1-[4-chloro-2-(difluoromethoxy)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine formate
191	1-[4-chloro-2-(difluoromethoxy)phenyl]-N-[(3R)-1-ethylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine formate
192	2-[(3R)-3-({1-[4-chloro-2-(difluoromethoxy)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol formate
193	1-[4-chloro-2-(difluoromethoxy)phenyl]-N-[(3R,5R)-5-fluoro-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine formate
216	1-[2-(difluoromethoxy)-4-methoxyphenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine formate
228	1-[4-methoxy-2-(trifluoromethyl)phenyl]-N-(1H-pyrazol-3-yl)imidazo[1,5-d][1,2,4]triazin-4-amine formate
250	1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine formate
261	N-[(3R)-1-ethylpiperidin-3-yl]-1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine formate
278	2-[(3R)-3-({1-[4-methoxy-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-yl}amino)piperidin-1-yl]ethan-1-ol formate
279	8-methyl-N-[(3R)-1-methylpiperidin-3-yl]-1-[2-(2,2,2-trifluoroethyl)-4-(trifluoromethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine formate
281	1-[4-methoxy-2-(pentafluoroethyl)phenyl]-N-[(3R)-1-methylpiperidin-3-yl]imidazo[1,5-d][1,2,4]triazin-4-amine formate
317	N-[(3R)-1-methylpiperidin-3-yl]-1-[4-methyl-2-(2,2,2-trifluoroethyl)phenyl]imidazo[1,5-d][1,2,4]triazin-4-amine formate
357	4-[4-bromo-2-(trifluoromethoxy)phenyl]-N-[(3R)-1-ethylpiperidin-3-yl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-amine formate
358	4-[4-chloro-2-(difluoromethoxy)phenyl]-2-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrazolo[1,5-d][1,2,4]triazin-7-amine formate
359	4-[2-(difluoromethyl)-4-(trifluoromethyl)phenyl]-2-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrazolo[1,5-d][1,2,4]triazin-7-amine formate
360	4-[4-cyclopropyl-2-(difluoromethoxy)phenyl]-2-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrazolo[1,5-d][1,2,4]triazin-7-amine formate
361	4-[2-(difluoromethoxy)-4-methylphenyl]-2-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrazolo[1,5-d][1,2,4]triazin-7-amine formate
363	4-[4-cyclopropyl-2-(difluoromethyl)phenyl]-2-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrazolo[1,5-d][1,2,4]triazin-7-amine formate
364	4-[2-(difluoromethyl)-4-methylphenyl]-2-methyl-N-[(3R)-1-methylpiperidin-3-yl]pyrazolo[1,5-d][1,2,4]triazin-7-amine formate
368	N-[(3R)-1-ethylpiperidin-3-yl]-4-[2-(methanesulfonyl)-4-methylphenyl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-amine trifluoroacetate
369	N-[(3R)-1-ethylpiperidin-3-yl]-4-[4-(methanesulfonyl)-2-(trifluoromethoxy)phenyl]-2-methylpyrazolo[1,5-d][1,2,4]triazin-7-amine trifluoroacetate
372	2-(7-{[(3R)-1-ethylpiperidin-3-yl]amino}-2-methylpyrazolo[1,5-d][1,2,4]triazin-4-yl)-5-(trifluoromethyl)benzamide formate

wherein a form of the compound is selected from the group consisting of a pharmaceutically acceptable salt, hydrate, solvate, racemate, enantiomer, diastereomer, stereoisomer, tautomer, free-base and isotope enriched form thereof.

4. A pharmaceutical composition comprising a therapeutically effective amount of a compound according to any one of claims 1 to 3 or a pharmaceutically acceptable salt thereof and one or more pharmaceutically acceptable carriers.

5. A method for treating or ameliorating a disease modulated by NLRP3 in a subject in need thereof comprising, administering to the subject an effective amount of the compound according to any one of claims 1-3.

6. A method of treating or ameliorating a disease modulated by NLRP3 according to claim 5 selected from Alzheimer disease, Frontotemporal dementia (FTD), Huntington's disease, Parkinson's disease, Perioperative neurocognitive disorders, Post–cardiac arrest cognitive impairment, Poststroke cognitive impairment, Sepsis, Sepsis associated encephalopathy, Subarachnoid hemorrhage, Macular Degeneration, Retinal neovascularization, Uveitis, Colitis, Endothelial dysfunction, Gout, Pseudogout, Graft-versus-host-disease (GvHD), Systemic lupus erythematosus–lupus nephritis, Cryopyrin-associated periodic syndromes (CAPS), Cystic fibrosis, Sickle-cell disease, VCP-associated disease, Liver fibrosis, Nonalcoholic fatty liver disease (NASH), muscle atrophy, inherited and acquired myopathies, e.g. Duchenne Muscular Dystrophy (DMD), Hyperalgesia, Multiple sclerosis–associated neuropathic pain, Acute Kidney Injury, Chronic crystal nephropathy, Chronic Kidney Disease, asthma and allergic airway inflammation Diabetes-associated atherosclerosis, Diabetic encephalopathy, Diabetic kidney disease, Islet transplantation rejection, Obesity-associated renal disease, Oxalate-induced nephropathy, Renal fibrosis, Renal hypertension, Type I diabetes, Type II diabetes, Psoriasis, Hidradenitis suppurativa, Atherosclerosis and Cytokine Release Syndrome (CRS).

7. The method of any one of claims 5 to 6, wherein the effective amount of the compound is in a range of from about 0.001 mg/kg/day to about 500 mg/kg/day.

8. A compound according to any one of claims 1 to 3 or a pharmaceutically acceptable salt thereof, for use in treating or ameliorating a disease modulated by NLRP3 selected from Alzheimer disease, Frontotemporal dementia (FTD), Huntington's disease, Parkinson's disease, Perioperative neurocognitive disorders, Post–cardiac arrest cognitive impairment, Poststroke cognitive impairment, Sepsis, Sepsis associated encephalopathy, Subarachnoid hemorrhage, Macular Degeneration, Retinal neovascularization, Uveitis, Colitis, Endothelial dysfunction, Gout, Pseudogout, Graft-versus-host-disease (GvHD), Systemic lupus erythematosus–lupus nephritis, Cryopyrin-associated periodic syndromes (CAPS), Cystic fibrosis, Sickle-cell disease, VCP-associated disease, Liver fibrosis, Nonalcoholic fatty liver disease (NASH), muscle atrophy, inherited and acquired myopathies, Hyperalgesia, Multiple sclerosis–associated neuropathic pain, Acute Kidney Injury, Chronic crystal nephropathy, Chronic Kidney Disease, asthma and allergic airway inflammation Diabetes-associated atherosclerosis, Diabetic encephalopathy, Diabetic kidney disease, Islet transplantation rejection, Obesity-associated renal disease, Oxalate-induced nephropathy, Renal fibrosis, Renal hypertension, Type I diabetes, Type II diabetes, Psoriasis, Hidradenitis suppurativa, Atherosclerosis and Cytokine Release Syndrome (CRS).

9. Use of a compound according to claim 8, wherein the effective amount of the compound is in a range of from about 0.001 mg/kg/day to about 500 mg/kg/day.

10. Use of a compound according to any one of claims 1 to 3 in the preparation of a pharmaceutical composition for treating or ameliorating a disease modulated by NLRP3 in a subject in need thereof comprising, administering to the subject an effective amount of the compound or a form thereof in admixture with one or more of the pharmaceutically acceptable excipients.