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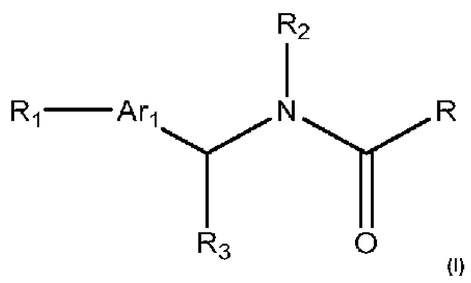
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(54) Title: TRICYCLIC CARBOXAMIDE DERIVATIVES AS PRMT5 INHIBITORS



(I)

(57) Abstract: Described herein are compounds of Formula (I) and pharmaceutically acceptable salts thereof, as well as pharmaceutical compositions thereof. Compounds of the present invention are useful for inhibiting PRMT5 activity and may have use in treating proliferative, such as cancer, metabolic and blood disorders. Compounds of Formula (I) have the following structure of Formule (I).

[Continued on next page]

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NOVEL PRMT5 INHIBITORS

CROSS-REFERENCE TO RELATED APPLICATION

[001] This application claims priority from U.S. Provisional Application No. 63/117,937, having a filing date of November 24, 2020.

BACKGROUND OF THE INVENTION

[002] Epigenetic regulation of gene expression is an important biological determinant of protein production and cellular differentiation and plays a significant pathogenic role in a number of human diseases.

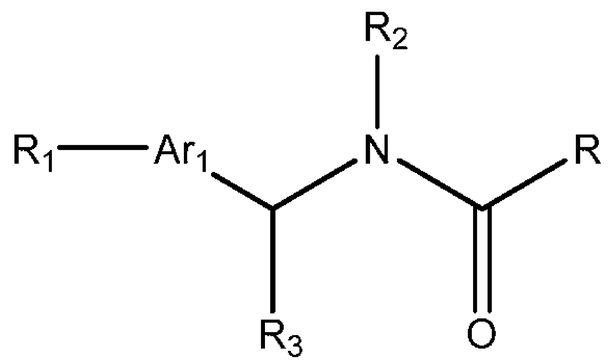
[003] Epigenetic regulation involves heritable modification of genetic material without changing its nucleotide sequence. Typically, epigenetic regulation is mediated by selective and reversible modification (*e.g.*, methylation) of DNA and proteins (*e.g.*, histones) that control the conformational transition between transcriptionally active and inactive states of chromatin. These covalent modifications can be controlled by enzymes such as methyltransferases (*e.g.*, PRMT5), many of which are associated with specific genetic alterations that can cause human disease. PRMT5 plays a role in diseases such as proliferative disorders, metabolic disorders, and blood disorders.

[004] The homozygous deletion of tumor suppressor genes is a key driver of cancer, frequently resulting in the collateral loss of passenger genes located in close genomic proximity to the tumor suppressor. Deletion of these passenger genes can create therapeutically tractable vulnerabilities that are specific to tumor cells. Homozygous deletion of the chromosome 9p21 locus, which harbors the well-known tumor suppressor CDKN2A (cyclin dependent kinase inhibitor 2A), occurs in 15% of all tumors and frequently includes the passenger gene MTAP (methylthioadenosine phosphorylase), a key enzyme in the methionine and adenine salvage pathways. Deletion of MTAP results in accumulation of its substrate, methylthioadenosine (MTA). MTA shares close structural similarity to S-adenosylmethionine (SAM), the substrate methyl donor for the type II methyltransferase PRMT5. Elevated MTA levels, driven by loss of MTAP, selectively compete with SAM for binding to PRMT5, placing the methyltransferase in a hypomorphic state, vulnerable to further PRMT5 inhibition. Multiple genome scale shRNA drop out screens performed in large tumor cell line panels have identified a strong correlation between MTAP loss and cell line dependency on PRMT5, further highlighting the strength of this metabolic vulnerability. However, PRMT5 is a known cell essential gene and conditional PRMT5 knockout and siRNA knockdown studies suggest that significant liabilities could be associated with inhibiting PRMT5 in normal tissues (*e.g.*, pan-cytopenia, infertility, skeletal muscle loss, cardiac hypertrophy). Therefore,

novel strategies are required to exploit this metabolic vulnerability and preferentially target PRMT5 in MTAP null tumors while sparing PRMT5 in normal tissues (MTAP WT). Targeting PRMT5 with an MTA-cooperative small molecule inhibitor could preferentially target the MTA bound state of PRMT5, enriched in MTAP null tumor cells, while providing an improved therapeutic index over normal cells where MTAP is intact and MTA levels are low.

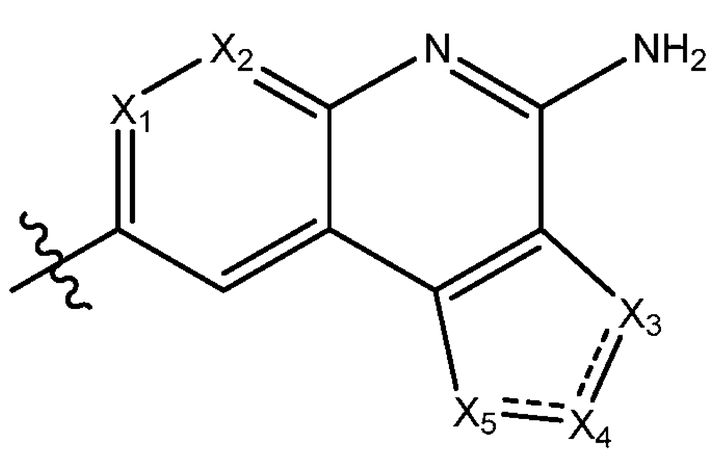
SUMMARY OF THE INVENTION

[005] In one aspect, the invention provides a compound of Formula **I**



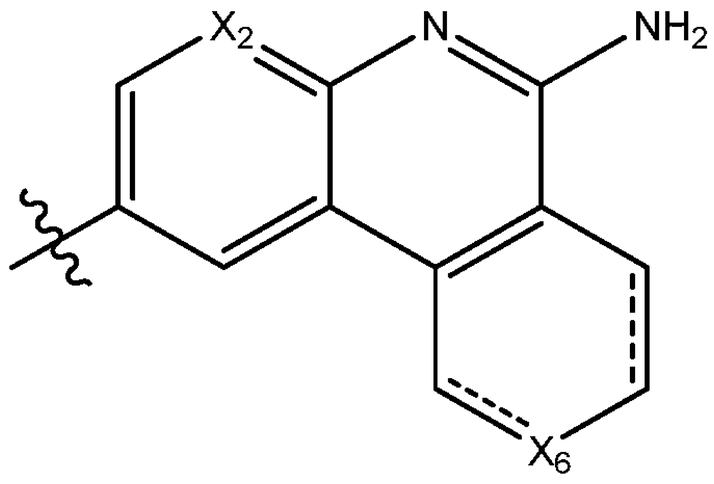
I

a tautomer thereof, a stereoisomer thereof, or a pharmaceutically acceptable salt of any of the foregoing. In one aspect, R is a tricycle independently selected from the formulae IA.



IA

[006] In another aspect, R can be a tricycle independently selected from the formulae IB



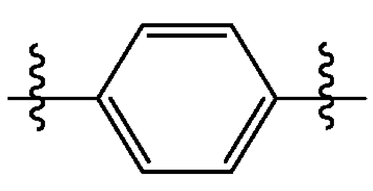
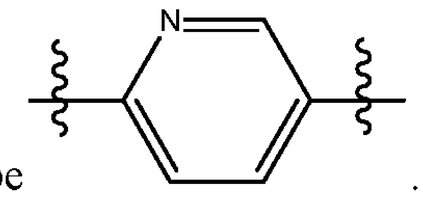
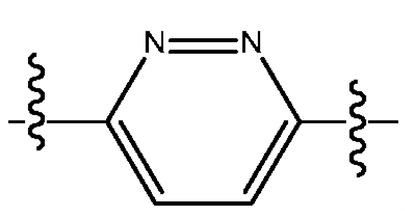
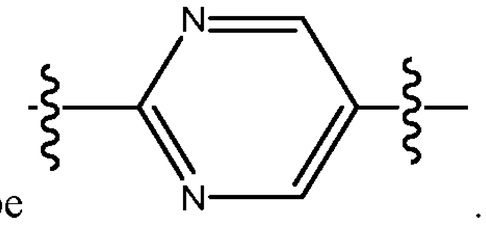
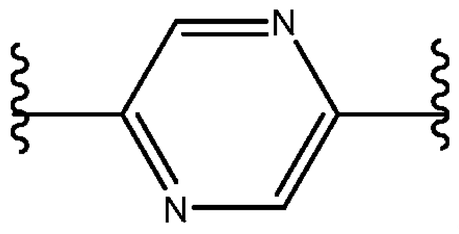
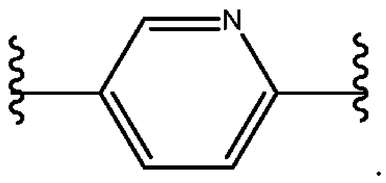
IB,

The invention provides that  can be a single or double bond.

[007] In one aspect, X^1, X^2 and X^6 can be in each instance N, provided that both X^1 and X^2 cannot be N at the same time. In another aspect X^1, X^2 and X^6 can be C. In one embodiment, if X^1 is C, it can be optionally substituted with halo. In a further aspect, halo could be Cl.

The invention further provides that X^3, X^4 and X^5 can be at each instance optionally substituted C. In another aspect, X^3, X^4 and X^5 can be at each instance optionally substituted O. In a further aspect, X^3, X^4 and X^5 can be at each instance optionally substituted N. In a further aspect, X^3, X^4 and X^5 can be at each instance optionally substituted and S. The invention provides that the substituents can be independently selected from $C_{1\text{-}3}$ alkyl, $C_{1\text{-}3}$ alkyl(OH), wherein alkyl can be optionally substituted with halo;

[008] In one aspect of the invention, R^3 in each instance can be H. In another aspect of the invention, R^3 in each instance can be $C_{1\text{-}3}$ alkyl. In a further aspect, R^3 can be methyl.

[009] The invention provides that Ar^1 can be a six membered optionally substituted aryl. In another aspect, Ar^1 can be a six membered optionally substituted heteroaryl. In one embodiment, Ar^1 can be  . In another embodiment, Ar^1 can be  . In a further aspect, Ar^1 can be  . In another aspect, Ar^1 can be  . In yet another embodiment, Ar^1 can be  . In another embodiment, Ar^1 can be  . The invention provides that the Ar^1 substituents can be independently selected from $C_{1\text{-}3}$ alkyl. In another aspect, the substituents can be independently selected from -$OC_{1\text{-}3}$ alkyl. In a further aspect, the substituents can be independently selected from halo.

[010] The invention provides that R^1 in each instance can be H. In another aspect, R^1 can be halo. In a further aspect, R^1 can be an optionally substituted $C_{1\text{-}3}$ alkyl. The substituents can be selected from halo and -CN. In a further aspect, R^1 can be an optionally substituted -O-$C_{1\text{-}3}$ alkyl. The substituents can be halo. In a further aspect, R^1 can be an optionally substituted -C(O)$OC_{1\text{-}3}$ alkyl, wherein $C_{1\text{-}3}$ alkyl can be optionally substituted with halo, and morpholinyl.

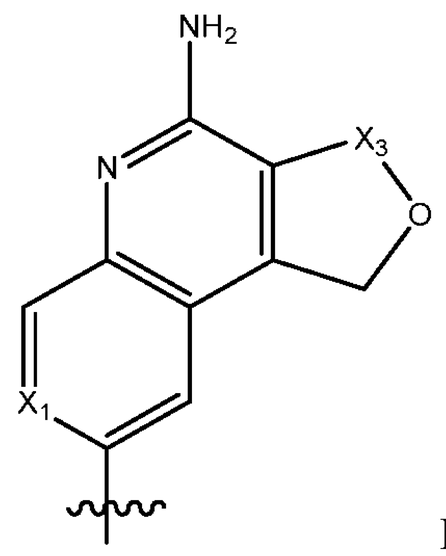
[011] The invention provides that R^2 in each instance can be an optionally substituted $C_{1\text{-}8}$ alkyl. The $C_{1\text{-}8}$ alkyl substituents can be selected from halo, hydroxy, amino, -O- $C_{1\text{-}3}$ alkyl or -CN.

[012] In a further aspect, R^2 in each instance can be an optionally substituted 5 or 6 membered cycle or heterocycle. The 5 or 6 membered cycle or heterocycle substituents can be hydroxy, amino, an optionally substituted C_{1-6} alkyl, wherein the substituents are selected from halo. In a further aspect, R^2 can be an optionally substituted C_{1-6} alkyl-O- C_{1-3} alkyl, wherein the substituents are selected from halo. In another aspect, R^2 can be an optionally substituted 5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridinyl. In another aspect, R^2 can be an C_{1-3} alkyl-heterocyclyl, wherein the heterocyclyl can be an optionally substituted 3,4-dihydro-2H-pyrano[2,3-c]pyridinyl or pyradazinyl or triazolyl or pyrimidinyl or tetrahydrofuranyl or1H-pyrrolo[2,3-b]pyridinyl or cyclohexyl. The substituents in each instance can be C_{1-3} alkyl, -CN, or halo, or an optionally substituted C_{1-6} alkyl-O- C_{1-3} alkyl. In the latter case the substituents can be selected from halo; optionally substituted phenyl, wherein in turn the phenyl substituents can be selected from halo or C_{1-3} alkyl.

[013] The invention provides compounds of, the tautomer thereof, the stereoisomer thereof, or the pharmaceutically acceptable salt of any of the foregoing, wherein R^1 can be a tricycle of formulae IA. In another aspect, R^1 can be a tricycle of formulae IB.

In one aspect, when the compound is a tricycle of formulae IA, X^1 and X^2 can be both C. In another aspect, one of X^1 and X^2 can be C and another N. In the following embodiment, if X^1 is C, it can be unsubstituted or substituted with halo. In a further aspect, X^2 can be N.

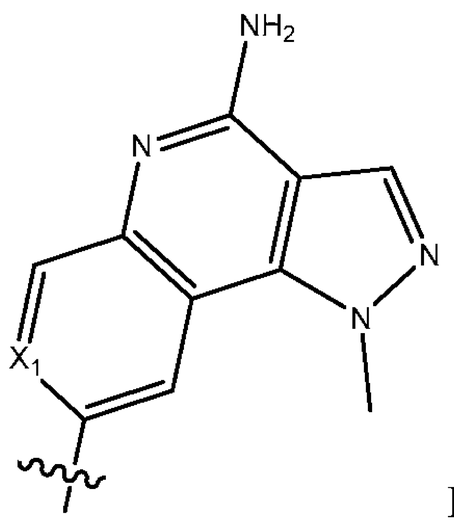
[014] The invention further provides compounds, the tautomer thereof, the stereoisomer thereof, or the pharmaceutically acceptable salt of any of the foregoing, wherein R can be a tricycle of the formulae **IA1**



IA1

[015] In one aspect, X^3 can be C, unsubstituted or substituted with one or more methyl.

[016] The invention further provides compounds, the tautomer thereof, the stereoisomer thereof, or the pharmaceutically acceptable salt of any of the foregoing, wherein R can be a tricycle of the formula **IA2**



IA2

[017] In one aspect of the compounds of the invention R^3 can be H. in another aspect, R^3 can be methyl.

[018] The invention further provides compounds, the tautomer thereof, the stereoisomer thereof, or the pharmaceutically acceptable salt of any of the foregoing, wherein R^2 is an optionally substituted $C_{1\text{-}8}$ alkyl. In one embodiment, R^2 can be an optionally substituted methyl, ethyl, isopropyl, or cyclo$C_{1\text{-}6}$alkyl.

[019] All possible combinations between aspects and embodiments as disclosed above are comprised in the present invention.

[020] The invention further provides compounds, the tautomer thereof, the stereoisomer thereof, or the pharmaceutically acceptable salt of any of the foregoing, wherein the compound is selected from the following:

[021] In one aspect, the compound can be selected from

4-amino-N-(cyclopropylmethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-N-((6-cyclopropyl-3-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-N-((2R)-1-methoxy-2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-N-((2S)-1-methoxy-2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3R)-4-amino-N-((2R)-1-methoxy-2-propanyl)-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3R)-4-amino-N-((2S)-1-methoxy-2-propanyl)-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-N-((6-chloro-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-chloro-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-((6-chloro-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((6-chloro-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-3-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3S)-4-amino-N-(bicyclo[1.1.1]pentan-1-yl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-3-methyl-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-(bicyclo[1.1.1]pentan-1-yl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-N,3-dimethyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-3-methyl-N-(2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-((2R)-1-methoxy-2-propanyl)-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-((2S)-1-methoxy-2-propanyl)-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-cyclopropyl-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-cyclopropyl-3-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N,3-dimethyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3S)-4-amino-N-cyclopropyl-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
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4-amino-N-(cyclopropylmethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide;
4-amino-N-((2R)-1-methoxy-2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide;
4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-(cyclopropylmethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
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4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((5-bromo-2-pyridinyl)methyl)-N,3-dimethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((6-cyclopropyl-3-pyridazinyl)methyl)-3-methyl-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-bromo-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-(cyclopropylmethyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((6-bromo-3-pyridazinyl)methyl)-3-methyl-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-(cyclopropylmethyl)-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-(cyclopropylmethyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(cyclopropylmethyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1-methylcyclopropyl)methyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-(2,2-dimethylpropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3R)-4-amino-3-methyl-N-((1-methylcyclopropyl)methyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(2,2-dimethylpropyl)-3,3-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-3,3-dimethyl-N-((1-methylcyclopropyl)methyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(2,2-dimethylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-N-((5-cyclopropyl-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-7-fluoro-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-cyclopropyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-cyclopropyl-N-((5-cyclopropyl-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-((6-cyclopropyl-3-pyridinyl)methyl)-3-methyl-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-cyclopropyl-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-cyclopropyl-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-cyclopropyl-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3R)-4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-N,3-dimethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-7-fluoro-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-(2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-ethyl-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-ethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-ethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-cyclopropyl-3-pyridinyl)methyl)-7-fluoro-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-cyclopropyl-N-((5-cyclopropyl-2-pyridinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-7-fluoro-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-N-((5-cyclopropyl-2-pyridinyl)methyl)-7-fluoro-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-7-fluoro-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-7-fluoro-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-N-((6-ethoxy-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((6-ethoxy-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N,3-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-3-methyl-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(bicyclo[1.1.1]pentan-1-yl)-N-((6-ethoxy-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-7-chloro-N-((5-cyclopropyl-2-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-(bicyclo[1.1.1]pentan-1-yl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(bicyclo[1.1.1]pentan-1-yl)-7-fluoro-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((6-cyclopropyl-3-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-3-methyl-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-N,3-dimethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(bicyclo[1.1.1]pentan-1-yl)-N-((6-ethoxy-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-ethoxy-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-7-chloro-N-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-N-((2R)-1-methoxy-2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((2S)-1-methoxy-2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-((5-cyano-2-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-(2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-(2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(bicyclo[1.1.1]pentan-1-yl)-7-chloro-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-(cyclopropylmethyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-((6-ethoxy-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-3-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((1-methylcyclopropyl)methyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-methyl-N-(4-(trifluoromethyl)benzyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-methyl-N-((6-(trifluoromethyl)-3-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-((6-cyclopropyl-3-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-(cyclopropylmethyl)-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3S)-4-amino-N-((6-cyclopropyl-3-pyridinyl)methyl)-3-methyl-N-(2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-N-(2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-cyclopropyl-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;

(3R)-4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-3-methyl-N-(2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3S)-4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-3-methyl-N-(2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-ethyl-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-(bicyclo[1.1.1]pentan-1-yl)-N-((6-ethoxy-3-pyridazinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-3-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N,3-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-((6-cyclopropyl-3-pyridinyl)methyl)-3-methyl-N-(2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
methyl 4-(6-((((4-amino-1,3-dihydrofuro[3,4-c]quinolin-8-yl)carbonyl)(methyl)amino)methyl)-3-pyridinyl)-1-piperazinecarboxylate;
(3S)-4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-N,3-dimethyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-N,3-dimethyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-cyclopropyl-N-((5-cyclopropyl-2-pyridinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3S)-4-amino-N-cyclopropyl-N-((5-cyclopropyl-2-pyridinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(cyclopropylmethyl)-N-((6-(difluoromethoxy)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-ethyl-7-fluoro-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-ethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((5-chloro-2-pyridinyl)methyl)-N-ethyl-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-ethyl-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;

(3R)-4-amino-N-((5-chloro-2-pyridinyl)methyl)-3-methyl-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-(cyclopropylmethyl)-N-((6-(difluoromethoxy)-3-pyridazinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3S)-4-amino-N-(cyclopropylmethyl)-N-((6-(difluoromethoxy)-3-pyridazinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(cyclopropylmethyl)-N-((6-(difluoromethoxy)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-ethyl-7-fluoro-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
5-amino-N-ethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)benzo[c][2,6]naphthyridine-9-carboxamide;
4-amino-N-((5-(3,6-dihydro-2H-pyran-4-yl)-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
methyl 6-((((4-amino-1,3-dihydrofuro[3,4-c]quinolin-8-yl)carbonyl)(methyl)amino)methyl)-3',6'-dihydro[3,4'-bipyridine]-1'(2'H)-carboxylate;
5-oxo-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-5,6-dihydropyrazolo[1,5-c]quinazoline-9-carboxamide;
4-amino-1,3-dimethyl-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((5-bromo-2-pyridinyl)methyl)-N,3-dimethyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3S)-4-amino-N-((5-bromo-2-pyridinyl)methyl)-N,3-dimethyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-3-methyl-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyrazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-7-fluoro-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-7-fluoro-N-((1R)-1-(3-fluoro-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-(difluoromethyl)-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-N-((5-chloro-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1S)-1-(2-pyrimidinyl)ethyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1R)-1-(3-fluoro-2-pyridinyl)ethyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(1,3-dimethoxy-2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((2R)-1-methoxy-2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-methoxy-3-pyridazinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((8R)-5,6,7,8-tetrahydro[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((8S)-5,6,7,8-tetrahydro[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((8R)-5,6,7,8-tetrahydro[1,2,4]triazolo[1,5-a]pyridin-8-yl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((8S)-5,6,7,8-tetrahydro[1,2,4]triazolo[1,5-a]pyridin-8-yl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(4-(3-oxetanyl)benzyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(4-(3-oxetanyl)benzyl)-N-((1S)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(cyclopropylmethyl)-N-((6-(4-morpholinyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((6-(2,2,2-trifluoroethoxy)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-cyclopropyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-bromo-2-pyridinyl)methyl)-N-cyclopropyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-N-((5-(difluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1-cyanocyclopropyl)methyl)-N-((5-cyano-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-cyclopropyl-3-pyridazinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((3R,4S)-3-methoxytetrahydro-2H-pyran-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((3S,4R)-3-methoxytetrahydro-2H-pyran-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((3R,4R)-4-methoxytetrahydro-2H-pyran-3-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((3S,4S)-4-methoxytetrahydro-2H-pyran-3-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-((5-cyano-2-pyridinyl)methyl)-N-cyclopropyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-chloro-5-methoxy-2-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-(cyclopropylmethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-(2-propanyl)-N-((5-(trifluoromethoxy)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((5-(difluoromethyl)-2-pyridinyl)methyl)-3-methyl-N-((1R)-1-(1-methyl-1H-1,2,4-triazol-3-yl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3R)-4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(3,4-dihydro-2H-pyrano[2,3-c]pyridin-6-ylmethyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(bicyclo[1.1.1]pentan-1-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-((5-cyano-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((2R)-1-fluoro-2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((2S)-1-fluoro-2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-((5-cyano-2-pyridinyl)methyl)-N-(cyclopropylmethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-cyclopropyl-7-fluoro-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-7-fluoro-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-((5-cyclopropyl-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-7-fluoro-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-cyclopropyl-N-((5-cyclopropyl-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-(2,2,2-trifluoroethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-(bicyclo[1.1.1]pentan-1-yl)-N-((6-ethoxy-3-pyridazinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(2,2,2-trifluoroethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-7-chloro-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N,3-dimethyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(2,2,2-trifluoroethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-7-chloro-N-((2R)-1-methoxy-2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-((2S)-1-methoxy-2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((2R)-1-methoxy-2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((2S)-1-methoxy-2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-(tetrahydro-2H-pyran-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-cyclopropyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
6-amino-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-8,9-dihydro-7H-cyclopenta[c][1,7]naphthyridine-2-carboxamide;
6-amino-N-((5-(difluoromethyl)-2-pyridinyl)methyl)-N-(1-methyl-1H-pyrazol-4-yl)-8,9-dihydro-7H-cyclopenta[c][1,7]naphthyridine-2-carboxamide;
4-amino-3-methyl-N-(1-methylcyclopropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
4-amino-3-methyl-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyrazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-ethyl-7-fluoro-N-((5-(trifluoromethyl)-2-pyrazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-ethyl-N-((5-(trifluoromethyl)-2-pyrazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyrazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3R)-4-amino-N-ethyl-3-methyl-N-((5-(trifluoromethyl)-2-pyrazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-cyclobutyl-7-fluoro-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-methoxy-N-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N,7-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-cyclobutyl-7-fluoro-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-cyclobutyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-3-methyl-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
4-amino-1-methyl-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-cyclopropyl-7-fluoro-3-methyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
4-amino-N-cyclobutyl-N-((6-(difluoromethoxy)-3-pyridazinyl)methyl)-7-fluoro-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-methyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-methyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-7-fluoro-N-methyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-methyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N,3-dimethyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N,3-dimethyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-fluoro-2-pyridinyl)methyl)-N,1,7-trimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;

4-amino-N-((6-cyclopropyl-3-pyridazinyl)methyl)-7-fluoro-N,3-dimethyl-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-cyclopropyl-3-pyridazinyl)methyl)-7-fluoro-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-((6-cyclopropyl-3-pyridazinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N,3,7-trimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
4-amino-N,1,7-trimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-7-fluoro-3-methyl-N-(2-propanyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-chloro-2-pyridinyl)methyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-((5-(difluoromethyl)-2-pyridinyl)methyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-((5-(difluoromethyl)-2-pyridinyl)methyl)-7-fluoro-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-(3-fluoro-4-(trifluoromethyl)benzyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-((3-fluoro-5-(trifluoromethyl)-2-pyridinyl)methyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((3-fluoro-5-(trifluoromethyl)-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N,1-dimethyl-N-((6-(1-(trifluoromethyl)-1H-pyrazol-4-yl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N,1-dimethyl-N-((6-(4-(trifluoromethyl)phenyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N,1-dimethyl-N-((1R)-1-(4'-(trifluoromethyl)[biphenyl]-4-yl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N,1-dimethyl-N-((1R)-1-(6-(4-(trifluoromethyl)phenyl)-3-pyridazinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N,1-dimethyl-N-((1R)-1-(4'-(pentafluoro-lambda~6~-sulfanyl)[biphenyl]-4-yl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;

4-amino-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-2,3-dihydrofuro[3,2-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(2-(5-chloro-2-pyridinyl)-2,2-difluoroethyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-2,3-dihydrofuro[3,2-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-ethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide;
4-amino-7-fluoro-1,3-dimethyl-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-N-ethyl-1-methyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-N-ethyl-1-methyl-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-N-ethyl-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N,1-dimethyl-N-(4-(trifluoromethyl)benzyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N,1-dimethyl-N-(4-(trifluoromethyl)benzyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-N-ethyl-7-fluoro-1-methyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-ethyl-1-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-ethyl-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)[1,2]oxazolo[4,5-c]quinoline-8-carboxamide;
4-amino-N-ethyl-1-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-ethyl-1-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-ethyl-1-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-ethyl-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-7-fluoro-N,1-dimethyl-N-(4-(trifluoromethyl)benzyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-ethyl-1,3-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-ethyl-7-fluoro-1-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-ethyl-7-fluoro-1-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
(3R)-4-amino-N-ethyl-7-fluoro-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-ethyl-7-fluoro-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N,1-dimethyl-N-(4-(trifluoromethyl)benzyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
(3R)-4-amino-N-ethyl-7-fluoro-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-ethyl-7-fluoro-1,3-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N,1-dimethyl-N-(4-(pentafluoroethyl)benzyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N,1-dimethyl-N-(4-(pentafluoroethyl)benzyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide;
4-amino-7-fluoro-N,1-dimethyl-N-(4-(pentafluoroethyl)benzyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-ethyl-1-methyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-ethyl-1-methyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-ethyl-7-fluoro-1-methyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N,1-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N,1-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide;

4-amino-N-cyclopropyl-1-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-7-fluoro-1-(2,2,2-trifluoroethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N,1-dimethyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-methyl-7-(trifluoromethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N,1-dimethyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N,1-dimethyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide;
4-amino-7-fluoro-N,1-dimethyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-(2-hydroxy-4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((2R)-1-fluoro-2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((2S)-1-fluoro-2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-(hydroxymethyl)-N-(2-methylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-(hydroxymethyl)-N-(2-methylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1R)-2-cyano-1-cyclopropylethyl)-N-((5-cyano-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1S)-2-cyano-1-cyclopropylethyl)-N-((5-cyano-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-6-methyl-2-pyridinyl)methyl)-N-((3R,4R)-4-methoxytetrahydro-2H-pyran-3-yl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-6-methyl-2-pyridinyl)methyl)-N-((3S,4S)-4-methoxytetrahydro-2H-pyran-3-yl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((3S,4R)-3-methoxytetrahydro-2H-pyran-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-N-((3R,4S)-3-methoxytetrahydro-2H-pyran-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((3R,4R)-4-methoxytetrahydro-2H-pyran-3-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((3S,4S)-4-methoxytetrahydro-2H-pyran-3-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-6-methyl-2-pyridinyl)methyl)-N-((3R,4R)-4-methoxytetrahydro-2H-pyran-3-yl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-cyclopropyl-3-methyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3S)-4-amino-N-cyclopropyl-3-methyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((1S)-1-(5-fluoro-2-pyridinyl)ethyl)-N,1,7-trimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-((1R)-1-(5-fluoro-2-pyridinyl)ethyl)-N,1,7-trimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-((1R)-1-(5-fluoro-2-pyridinyl)ethyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-((1S)-1-(5-fluoro-2-pyridinyl)ethyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((1R)-1-(3-fluoro-5-(trifluoromethyl)-2-pyridinyl)ethyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-ethyl-3-(fluoromethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((5-bromo-2-pyridinyl)methyl)-N,3-dimethyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N,1-dimethyl-N-((1R)-1-(4-(trifluoromethyl)phenyl)ethyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide;
4-amino-N,1-dimethyl-N-((1S)-1-(4-(trifluoromethyl)phenyl)ethyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide;
4-amino-N,1-dimethyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N,1-dimethyl-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;

4-amino-7-fluoro-N,1-dimethyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N,1-dimethyl-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-((1R)-1-(5-fluoro-2-pyridinyl)ethyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N,1-dimethyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
6-amino-N-(2-methylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-8,9-dihydro-7H-cyclopenta[c][1,8]naphthyridine-2-carboxamide;
4-amino-N-(cyclopropylmethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide;
4-amino-N-((2R)-1-methoxy-2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide;
4-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-2,3-dihydro-1H-cyclopenta[c]quinoline-8-carboxamide;
4-amino-N-(2-methylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-2,3-dihydro-1H-cyclopenta[c]quinoline-8-carboxamide;
4-amino-N-(2-methylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide;
4-amino-N-(2-methylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-2,3-dihydro-1H-cyclopenta[c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((1S)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-3-methyl-N-(2-methylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)[1,2]oxazolo[4,5-c]quinoline-8-carboxamide;

4-amino-3-methyl-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
4-amino-3-methyl-N-((1S)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
4-amino-3-methyl-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)[1,2]oxazolo[4,5-c]quinoline-8-carboxamide;
4-amino-3-methyl-N-((1S)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)[1,2]oxazolo[4,5-c]quinoline-8-carboxamide;
4-amino-N-(2-methylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((5-chloro-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-2,3-dihydro-1H-cyclopenta[c]quinoline-8-carboxamide;
4-amino-N-((5-(difluoromethyl)-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-2,3-dihydro-1H-cyclopenta[c]quinoline-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((1R)-1-(3-fluoro-2-pyridinyl)ethyl)-2,3-dihydro-1H-cyclopenta[c]quinoline-8-carboxamide;
6-amino-N-((5-(difluoromethyl)-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-8,9-dihydro-7H-cyclopenta[c][1,8]naphthyridine-2-carboxamide;
6-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-8,9-dihydro-7H-cyclopenta[c][1,8]naphthyridine-2-carboxamide;
6-amino-N-((5-chloro-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-8,9-dihydro-7H-cyclopenta[c][1,8]naphthyridine-2-carboxamide;
6-amino-N-((1R)-1-(3-fluoro-2-pyridinyl)ethyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-8,9-dihydro-7H-cyclopenta[c][1,8]naphthyridine-2-carboxamide;
6-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-2-phenanthridinecarboxamide;
6-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-2-phenanthridinecarboxamide;
5-amino-N-(2-pyrimidinylmethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)benzo[c][2,6]naphthyridine-9-carboxamide;
5-amino-N-(2-methylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)benzo[c][2,6]naphthyridine-9-carboxamide;

5-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)benzo[c][2,6]naphthyridine-9-carboxamide;
4-amino-N-((2R)-1-methoxy-2-propanyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)[1,2]oxazolo[4,5-c]quinoline-8-carboxamide;
4-amino-N-((2S)-1-methoxy-2-propanyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)[1,2]oxazolo[4,5-c]quinoline-8-carboxamide;
4-amino-N-((3-fluoro-2-pyridinyl)methyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)thieno[2,3-c]quinoline-8-carboxamide;
4-amino-N-(2-pyrimidinylmethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)thieno[2,3-c]quinoline-8-carboxamide;
4-amino-N-(2-methylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)thieno[2,3-c]quinoline-8-carboxamide;
5-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)pyrimido[4,5-c]quinoline-9-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((1R)-1-cyclopropyl-2-methoxyethyl)thieno[2,3-c]quinoline-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((1S)-1-cyclopropyl-2-methoxyethyl)thieno[2,3-c]quinoline-8-carboxamide;
4-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1S)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1S)-1-cyclopropyl-2-methoxyethyl)-N-((6-(4-morpholinyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-ethoxy-3-pyridazinyl)methyl)-N-(2-methylpropyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)thieno[2,3-c]quinoline-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-(1-methoxy-2-methyl-2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-(1-methoxy-2-methyl-2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((6-methoxy-3-pyridazinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-2,3-dihydro-1H-cyclopenta[c]quinoline-8-carboxamide;

4-amino-N-((6-methoxy-3-pyridazinyl)methyl)-N-((1S)-1-(2-pyrimidinyl)ethyl)-2,3-dihydro-1H-cyclopenta[c]quinoline-8-carboxamide;
4-amino-N-((1S)-1-(2-pyrimidinyl)ethyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-2,3-dihydro-1H-cyclopenta[c]quinoline-8-carboxamide;
4-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-2,3-dihydro-1H-cyclopenta[c]quinoline-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((1S)-1-cyclopropyl-2-methoxyethyl)thieno[2,3-c]quinoline-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((1S)-1-cyclopropyl-2-methoxyethyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide;
4-amino-N-(cyclopropylmethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
6-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-7,8,9,10-tetrahydro-2-phenanthridinecarboxamide;
4-amino-7-chloro-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-cyclopropyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-bromo-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(3,3-difluorocyclobutyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-(difluoromethyl)-2-pyridinyl)methyl)-N-((1R)-1-(1-methyl-1H-1,2,4-triazol-3-yl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(cyclopropylmethyl)-N-((5-(trifluoromethoxy)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-N-(2-methylpropyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-(2-methylpropyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((1S)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-(difluoromethyl)-2-pyridinyl)methyl)-N-((1R)-1-(1-methyl-1H-1,2,4-triazol-3-yl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(3,3-difluorocyclobutyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-cyclobutyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(2-methylpropyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-(cyclopropylmethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((6-ethoxy-3-pyridazinyl)methyl)-N-(2-methylpropyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-(cyclopropylmethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((6-chloro-3-pyridazinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-bromo-6-methyl-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(2-propanyl)-N-((5-(trifluoromethoxy)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-chloro-5-cyano-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;

4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-(cyclopropylmethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((6-chloro-5-methoxy-2-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((5-chloro-6-methoxy-2-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(3,4-dihydro-2H-pyrano[2,3-c]pyridin-6-ylmethyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((2R)-1-fluoro-2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((2S)-1-fluoro-2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(cyclopropylmethyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(bicyclo[1.1.1]pentan-1-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(1-cyclopropyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((5-(difluoromethyl)-2-pyridinyl)methyl)-N-(1-methyl-1H-pyrazol-4-yl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-methyl-N-(4-(trifluoromethyl)benzyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-methyl-N-((6-(trifluoromethyl)-3-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((5-chloro-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-ethyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-ethyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;

4-amino-N-methyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-methyl-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-chloro-2-pyridinyl)methyl)-N-ethyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(1-methylcyclopropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-methyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide;
4-amino-N-methyl-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide;
4-amino-N-((5-chloro-2-pyridinyl)methyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-chloro-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-ethyl-N-((6-(trifluoromethyl)-3-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-ethyl-N-((6-(trifluoromethyl)-3-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-ethyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide;
4-amino-N-ethyl-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide;
4-amino-N-ethyl-N-(4-(trifluoromethyl)benzyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-ethyl-N-(4-(trifluoromethyl)benzyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-methyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-methyl-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-ethyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(1-methyl-1H-pyrazol-4-yl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;

4-amino-N-(2,2,2-trifluoroethyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(3-oxetanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N,3-dimethyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
4-amino-N,3-dimethyl-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-chloro-2-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-chloro-2-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-ethyl-7-fluoro-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-ethyl-7-fluoro-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-ethyl-3-methyl-N-((1-methyl-1H-1,2,4-triazol-3-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-cyclobutyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-cyclobutyl-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-(difluoromethoxy)-3-pyridazinyl)methyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-(difluoromethoxy)-3-pyridazinyl)methyl)-N-ethyl-7-fluoro-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((1R)-1-(5-fluoro-2-pyrimidinyl)ethyl)-N-(2-(trifluoromethoxy)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((1S)-1-(5-fluoro-2-pyrimidinyl)ethyl)-N-(2-(trifluoromethoxy)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3R)-4-amino-N-((6-(difluoromethoxy)-3-pyridazinyl)methyl)-N-ethyl-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1R)-1-(6-chloro-3-pyridinyl)ethyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1S)-1-(6-chloro-3-pyridinyl)ethyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((2R)-1-methoxy-2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-7-fluoro-N-(1-(trifluoromethyl)-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(cyclopropylmethyl)-7-fluoro-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(cyclopropylmethyl)-7-fluoro-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
4-amino-N-(1-(trifluoromethyl)-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(2-propanyl)-N-(4-(trifluoromethyl)benzyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-cyclopropyl-N-(4-(trifluoromethyl)benzyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-cyclopropyl-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-((1R)-1-(6-chloro-3-pyridinyl)ethyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-((1S)-1-(6-chloro-3-pyridinyl)ethyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-ethyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1R)-1-(6-chloro-3-pyridinyl)ethyl)-N-ethyl-7-fluoro-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1S)-1-(6-chloro-3-pyridinyl)ethyl)-N-ethyl-7-fluoro-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-1-methyl-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;

4-amino-7-chloro-N-(cyclopropylmethyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-ethyl-N-((1R)-1-(2-fluoro-4-(trifluoromethyl)phenyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-ethyl-N-((1R)-1-(4-(trifluoromethyl)phenyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-cyclobutyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-cyclobutyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-cyclopropyl-3-methyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-ethoxy-3-pyridazinyl)methyl)-N-ethyl-7-fluoro-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((S)-cyclopropyl(5-(trifluoromethyl)-2-pyridinyl)methyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-ethoxy-3-pyridazinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-7-fluoro-N-(1-methyl-1H-pyrazol-4-yl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-(1-methyl-1H-pyrazol-4-yl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(cyclopropylmethyl)-N-((6-ethoxy-3-pyridazinyl)methyl)-7-fluoro-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(cyclopropylmethyl)-N-((6-ethoxy-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
5-amino-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)benzo[c][2,6]naphthyridine-9-carboxamide;
5-amino-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)pyrimido[4,5-c]quinoline-9-carboxamide;
5-amino-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)pyrido[4,3-c][1,7]naphthyridine-9-carboxamide;
4-amino-1-methyl-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;

4-amino-N-((6-ethoxy-3-pyridazinyl)methyl)-3-methyl-N-((1R)-1-(2-pyrimidinyl)ethyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
4-amino-N-ethyl-N-(2-(4-(trifluoromethyl)phenyl)-2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
5-amino-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)pyrimido[4,5-c][1,7]naphthyridine-9-carboxamide;
4-amino-N-ethyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)propyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-ethyl-7-fluoro-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-ethyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((R)-cyclopropyl(5-(trifluoromethyl)-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((S)-cyclopropyl(5-(trifluoromethyl)-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(cyclopropylmethyl)-N-((6-ethoxy-3-pyridazinyl)methyl)-7-fluoro-3-methyl-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-(cyclopropylmethyl)-N-((6-ethoxy-3-pyridazinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((R)-cyclopropyl(6-(trifluoromethyl)-3-pyridazinyl)methyl)-N-ethyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-3-methyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N,1-dimethyl-N-((5-methyl-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((5-fluoro-2-pyridinyl)methyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-((2,6-difluoro-3-pyridinyl)methyl)-7-fluoro-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-((1R)-1-(5-fluoro-2-pyridinyl)ethyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-((1S)-1-(5-fluoro-2-pyridinyl)ethyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-N-((1R)-1-(5-(difluoromethyl)-2-pyridinyl)ethyl)-N-ethyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-methyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyrazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1R)-1-(5-(difluoromethyl)-2-pyridinyl)ethyl)-N-ethyl-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N,1-dimethyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyrazinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
(3R)-4-amino-N-ethyl-3-methyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-ethyl-3-methyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N,3-dimethyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N,1-dimethyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyrazinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-ethyl-7-fluoro-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((2-fluoro-6-(trifluoromethyl)-3-pyridinyl)methyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-((R)-cyclopropyl(6-(trifluoromethyl)-3-pyridazinyl)methyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-ethyl-7-fluoro-3-methyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-ethyl-7-fluoro-3-methyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N,3-dimethyl-N-((1R)-1-(4-(pentafluoroethyl)phenyl)ethyl)-3H-pyrazolo[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-7-fluoro-N,1-dimethyl-N-((1S)-1-(4-(pentafluoroethyl)phenyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N,1-dimethyl-N-((1R)-1-(4-(pentafluoroethyl)phenyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N,1-dimethyl-N-((5-(1-(trifluoromethyl)-1H-pyrazol-4-yl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;

4-amino-N-cyclopropyl-1-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-chloro-N,1-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-chloro-N,1-dimethyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-ethyl-1-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-ethyl-1-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-cyclopropyl-1-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-cyclopropyl-1-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-1-methyl-N-(2,2,2-trifluoroethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-cyclobutyl-1-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-cyclobutyl-1-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-1-methyl-N-(2,2,2-trifluoroethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-cyclobutyl-7-fluoro-1-methyl-N-(1,3-oxazol-4-ylmethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N,1-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-7-fluoro-1-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-7-fluoro-1-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-1-methyl-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((2-methoxy-6-(trifluoromethyl)-3-pyridinyl)methyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;

4-amino-N-cyclobutyl-7-fluoro-1-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-cyclopropyl-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-7-fluoro-N-((3-fluoro-5-(trifluoromethyl)-2-pyridinyl)methyl)-1-methyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N,1-dimethyl-7-(trifluoromethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N,1-dimethyl-7-(trifluoromethyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-1-methyl-7-(trifluoromethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-1-methyl-7-(trifluoromethyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-((1R)-1-cyclopropylethyl)-7-fluoro-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1S)-1-cyclopropylethyl)-7-fluoro-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(cyclopropylmethyl)-7-fluoro-N-((6-(2,2,2-trifluoroethoxy)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(cyclopropylmethyl)-7-fluoro-3-methyl-N-((6-(2,2,2-trifluoroethoxy)-3-pyridazinyl)methyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-(cyclopropylmethyl)-7-fluoro-3-methyl-N-((6-(2,2,2-trifluoroethoxy)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-ethyl-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-ethyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-ethyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-ethyl-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(1-methyl-1H-pyrazol-4-yl)-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;

4-amino-N-(1-methyl-1H-pyrazol-4-yl)-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3S)-4-amino-3-methyl-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-3-methyl-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3S)-4-amino-N-cyclobutyl-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-cyclobutyl-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(2-propanyl)-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(2-propanyl)-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((1S)-1-(5-fluoro-2-pyrimidinyl)ethyl)-N-(2-(trifluoromethoxy)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((1R)-1-(5-fluoro-2-pyrimidinyl)ethyl)-N-(2-(trifluoromethoxy)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1R)-1-(4-cyanophenyl)ethyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1S)-1-(4-cyanophenyl)ethyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1S)-1-(5-cyano-2-pyridinyl)ethyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1R)-1-(5-cyano-2-pyridinyl)ethyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-(2-propanyl)-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-(2-propanyl)-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-(2-propanyl)-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-(2-propanyl)-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1S)-1-(5-cyano-2-pyridinyl)ethyl)-N-ethyl-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1R)-1-(5-cyano-2-pyridinyl)ethyl)-N-ethyl-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-7-chloro-N-(2-propanyl)-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-7-chloro-N-(2-propanyl)-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-N-(2-propanyl)-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;

4-amino-N-(2-propanyl)-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;

4-amino-N-methyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)propyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;

4-amino-N-methyl-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)propyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;

(3R)-4-amino-N,3-dimethyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3R)-4-amino-N,3-dimethyl-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-N-((1R)-1-(3,5-difluoro-2-pyridinyl)ethyl)-7-fluoro-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;

4-amino-N-methyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;

4-amino-N,1-dimethyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;

(3R)-4-amino-N,3-dimethyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-7-fluoro-N-methyl-N-((1R)-1-(4-(trifluoromethyl)phenyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-7-fluoro-N-methyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3R)-4-amino-7-fluoro-N,3-dimethyl-N-((1S)-1-(4-(trifluoromethyl)phenyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3R)-4-amino-7-fluoro-N,3-dimethyl-N-((1R)-1-(4-(trifluoromethyl)phenyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-N-((1R)-1-(3-fluoro-5-(trifluoromethyl)-2-pyridinyl)ethyl)-N,3-dimethyl-3H-pyrazolo[3,4-c][1,7]naphthyridine-8-carboxamide;

(3R)-4-amino-7-fluoro-N,3-dimethyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((1R)-1-(3-fluoro-5-(trifluoromethyl)-2-pyridinyl)ethyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((1S)-1-(3-fluoro-5-(trifluoromethyl)-2-pyridinyl)ethyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((1R)-1-(3-fluoro-5-(trifluoromethyl)-2-pyridinyl)ethyl)-N,3-dimethyl-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((1R)-1-(3-methoxy-5-(trifluoromethyl)-2-pyridinyl)ethyl)-N,3-dimethyl-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((1R)-1-(3-methoxy-5-(trifluoromethyl)-2-pyridinyl)ethyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N,3-dimethyl-N-((1R)-1-(4-(pentafluoro-lambda~6~-sulfanyl)phenyl)ethyl)-3H-pyrazolo[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-7-fluoro-N,1-dimethyl-N-((1S)-1-(4-(pentafluoro-lambda~6~-sulfanyl)phenyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N,1-dimethyl-N-((1R)-1-(4-(pentafluoro-lambda~6~-sulfanyl)phenyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-1-methyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-N-((1R)-1-(5-pyrimidinyl)propyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide;
4-amino-1-methyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-N-((1S)-1-(5-pyrimidinyl)propyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide;
4-amino-7-fluoro-N-((1R)-1-(5-fluoro-2-pyridinyl)ethyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((1S)-1-(5-fluoro-2-pyridinyl)ethyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-ethyl-7-fluoro-N-((1R)-1-(5-fluoro-2-pyridinyl)ethyl)-1-methyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-ethyl-7-fluoro-N-((1S)-1-(5-fluoro-2-pyridinyl)ethyl)-1-methyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-7-fluoro-1-methyl-N-((1S)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-7-fluoro-1-methyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;

4-amino-N,1-dimethyl-7-(trifluoromethyl)-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-cyclopropyl-1-methyl-N-((1S)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-cyclopropyl-1-methyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-(1-methyl-1H-pyrazol-4-yl)-N-(4-(trifluoromethyl)benzyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(3-fluorophenyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide;
5-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,4-dihydro-2H-pyrano[3,4-c]quinoline-9-carboxamide;
4-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-2,3-dihydrofuro[3,2-c]quinoline-8-carboxamide;
4-amino-3,3-dimethyl-N-(2-methylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((3-fluoro-2-pyridinyl)methyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((3-fluoro-2-pyridinyl)methyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((1R)-1-(tetrahydro-2H-pyran-4-yl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((1S)-1-(tetrahydro-2H-pyran-4-yl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((1R)-1-(tetrahydro-2H-pyran-4-yl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((1S)-1-(tetrahydro-2H-pyran-4-yl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3R)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-N-((1R)-1-(tetrahydro-2H-pyran-4-yl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3R)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-N-((1S)-1-(tetrahydro-2H-pyran-4-yl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3S)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-N-((1R)-1-(tetrahydro-2H-pyran-4-yl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3S)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-N-((1S)-1-(tetrahydro-2H-pyran-4-yl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3R)-4-amino-N-((trans-4-hydroxycyclohexyl)methyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3S)-4-amino-N-((trans-4-hydroxycyclohexyl)methyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3R)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((trans-4-hydroxycyclohexyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3S)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((trans-4-hydroxycyclohexyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3R)-4-amino-3-methyl-N-(tetrahydro-2H-pyran-4-ylmethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3S)-4-amino-3-methyl-N-(tetrahydro-2H-pyran-4-ylmethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3R)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-N-(tetrahydro-2H-pyran-4-ylmethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3S)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-N-(tetrahydro-2H-pyran-4-ylmethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3R)-4-amino-N-((1R,2R)-2-cyanocyclopentyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3R)-4-amino-N-((1R,2S)-2-cyanocyclopentyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3R)-4-amino-N-((1S,2R)-2-cyanocyclopentyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3R)-4-amino-N-((1S,2S)-2-cyanocyclopentyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3S)-4-amino-N-((1R,2R)-2-cyanocyclopentyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3S)-4-amino-N-((1R,2S)-2-cyanocyclopentyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1S,2R)-2-cyanocyclopentyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1S,2S)-2-cyanocyclopentyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1R,2R)-2-cyanocyclopentyl)-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1R,2S)-2-cyanocyclopentyl)-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1S,2R)-2-cyanocyclopentyl)-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1S,2S)-2-cyanocyclopentyl)-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1R,2R)-2-cyanocyclopentyl)-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1R,2S)-2-cyanocyclopentyl)-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1S,2R)-2-cyanocyclopentyl)-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1S,2S)-2-cyanocyclopentyl)-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((3R)-tetrahydro-3-furanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((3S)-tetrahydro-3-furanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((3R)-tetrahydro-3-furanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((3S)-tetrahydro-3-furanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((1R,5S,6r)-3-oxabicyclo[3.1.0]hexan-6-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((1R,5S,6r)-3-oxabicyclo[3.1.0]hexan-6-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3R)-4-amino-3-methyl-N-((3R,4R)-3-methyltetrahydro-2H-pyran-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((3R,4S)-3-methyltetrahydro-2H-pyran-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((3S,4R)-3-methyltetrahydro-2H-pyran-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((3S,4S)-3-methyltetrahydro-2H-pyran-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((3R,4R)-3-methyltetrahydro-2H-pyran-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((3R,4S)-3-methyltetrahydro-2H-pyran-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((3S,4R)-3-methyltetrahydro-2H-pyran-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((3S,4S)-3-methyltetrahydro-2H-pyran-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((3S,4R)-3-methoxytetrahydro-2H-pyran-4-yl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((3S,4R)-3-methoxytetrahydro-2H-pyran-4-yl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((3R,4S)-3-methoxytetrahydro-2H-pyran-4-yl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((3R,4S)-3-methoxytetrahydro-2H-pyran-4-yl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1R,2R)-[1,1'-bi(cyclopropyl)]-2-yl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1R,2S)-[1,1'-bi(cyclopropyl)]-2-yl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1S,2R)-[1,1'-bi(cyclopropyl)]-2-yl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1S,2S)-[1,1'-bi(cyclopropyl)]-2-yl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1R,2R)-[1,1'-bi(cyclopropyl)]-2-yl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3S)-4-amino-N-((1R,2S)-[1,1'-bi(cyclopropyl)]-2-yl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1S,2R)-[1,1'-bi(cyclopropyl)]-2-yl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1S,2S)-[1,1'-bi(cyclopropyl)]-2-yl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((1R)-spiro[2.5]octan-1-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((1S)-spiro[2.5]octan-1-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((1R)-spiro[2.5]octan-1-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((1S)-spiro[2.5]octan-1-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1R,2R)-2-aminocyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1R,2S)-2-aminocyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1S,2R)-2-aminocyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1S,2S)-2-aminocyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1R,2R)-2-aminocyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1R,2S)-2-aminocyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1S,2R)-2-aminocyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1S,2S)-2-aminocyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1R,2R)-2-ethoxycyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1R,2S)-2-ethoxycyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3R)-4-amino-N-((1S,2R)-2-ethoxycyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1S,2S)-2-ethoxycyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1R,2R)-2-ethoxycyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1R,2S)-2-ethoxycyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1S,2R)-2-ethoxycyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1S,2S)-2-ethoxycyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1R)-2,2-dimethylcyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1S)-2,2-dimethylcyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1R)-2,2-dimethylcyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1S)-2,2-dimethylcyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((1R)-spiro[2.4]heptan-1-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((1S)-spiro[2.4]heptan-1-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((1R)-spiro[2.4]heptan-1-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((1S)-spiro[2.4]heptan-1-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((1R,2R)-2-(trifluoromethyl)cyclopropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((1S,2S)-2-(trifluoromethyl)cyclopropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((1R,2R)-2-(trifluoromethyl)cyclopropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3S)-4-amino-3-methyl-N-((1S,2S)-2-(trifluoromethyl)cyclopropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-(5,6-dihydro-2H-pyran-3-ylmethyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-(5,6-dihydro-2H-pyran-3-ylmethyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1-cyanocyclopropyl)methyl)-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1-cyanocyclopropyl)methyl)-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((2-amino-1,3-thiazol-5-yl)methyl)-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((2-amino-1,3-thiazol-5-yl)methyl)-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-(5,6-dihydro-2H-pyran-3-ylmethyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-(5,6-dihydro-2H-pyran-3-ylmethyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-(1H-pyrrolo[2,3-b]pyridin-4-ylmethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-(1H-pyrrolo[2,3-b]pyridin-4-ylmethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1-cyanocyclopropyl)methyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1-cyanocyclopropyl)methyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((2-amino-1,3-thiazol-5-yl)methyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((2-amino-1,3-thiazol-5-yl)methyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3R)-4-amino-3-methyl-N-(2-methylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-(2-methylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((2R,3R)-3-hydroxy-2-butanyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((2R,3S)-3-hydroxy-2-butanyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((2S,3R)-3-hydroxy-2-butanyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((2S,3S)-3-hydroxy-2-butanyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((2R,3R)-3-hydroxy-2-butanyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((2R,3S)-3-hydroxy-2-butanyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((2S,3R)-3-hydroxy-2-butanyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((2S,3S)-3-hydroxy-2-butanyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1R,3R)-3-hydroxycyclohexyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1R,3S)-3-hydroxycyclohexyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1S,3R)-3-hydroxycyclohexyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1S,3S)-3-hydroxycyclohexyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1R,3R)-3-hydroxycyclohexyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1R,3S)-3-hydroxycyclohexyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1S,3R)-3-hydroxycyclohexyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3S)-4-amino-N-((1S,3S)-3-hydroxycyclohexyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-(2-(cis-3-hydroxycyclobutyl)ethyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-(2-(trans-3-hydroxycyclobutyl)ethyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-(2-(cis-3-hydroxycyclobutyl)ethyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-(2-(trans-3-hydroxycyclobutyl)ethyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((2R)-2-hydroxypropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((2S)-2-hydroxypropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((2R)-2-hydroxypropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((2S)-2-hydroxypropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((2R)-3-hydroxy-2-methylpropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((2S)-3-hydroxy-2-methylpropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((2R)-3-hydroxy-2-methylpropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((2S)-3-hydroxy-2-methylpropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((2R)-3,3,3-trifluoro-2-hydroxypropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((2S)-3,3,3-trifluoro-2-hydroxypropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((2R)-3,3,3-trifluoro-2-hydroxypropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((2S)-3,3,3-trifluoro-2-hydroxypropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3R)-4-amino-3-methyl-N-((1-methyl-1H-1,2,4-triazol-3-yl)methyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((1-methyl-1H-1,2,4-triazol-3-yl)methyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((3R)-tetrahydro-3-furanylmethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((3S)-tetrahydro-3-furanylmethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((3R)-tetrahydro-3-furanylmethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((3S)-tetrahydro-3-furanylmethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((2R)-2-cyanopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((2S)-2-cyanopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((2R)-2-cyanopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((2S)-2-cyanopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N,3-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N,3-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-ethyl-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-ethyl-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N,3,3-trimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-N-ethyl-3,3-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-3,3-dimethyl-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-3,3-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide; and
4-amino-N-((1R)-1-(3-cyano-5-(trifluoromethyl)-2-pyridinyl)ethyl)-7-fluoro-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide.

In another aspect, the compound can be selected from
(3R)-4-amino-N-ethyl-7-fluoro-3-methyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N,1-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((1R)-1-(3-fluoro-5-(trifluoromethyl)-2-pyridinyl)ethyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N,1-dimethyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide;
4-amino-7-fluoro-N,1-dimethyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
(3R)-4-amino-7-fluoro-N,3-dimethyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-methyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
5-amino-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)pyrido[4,3-c][1,7]naphthyridine-9-carboxamide;
4-amino-N-ethyl-7-fluoro-1-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-((1R)-1-(5-fluoro-2-pyridinyl)ethyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-cyclobutyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-N-cyclopropyl-1-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-ethyl-7-fluoro-1-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-7-fluoro-1-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N,1-dimethyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
(3R)-4-amino-N-ethyl-3-methyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-7-fluoro-1-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N,1-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide and
4-amino-N-ethyl-1-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide.

[022] The invention further provides methods of treating cancer comprising administering to a subject an effective amount of the compound of the invention, the tautomer thereof, the stereoisomer thereof, or the pharmaceutically acceptable salt of any of the foregoing. In one aspect, the cancer is selected from ovarian, lung, lymphoid, glioblastoma, colon, melanoma, gastric, pancreatic or bladder cancer.

[023] The invention further provides pharmaceutical compositions, comprising the compounds of the invention, the tautomer thereof, the stereoisomer thereof, or the pharmaceutically acceptable salt of any of the foregoing or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable excipient.

[024] The invention also provides methods of treating a cancer, the method comprising administering to a subject an effective amount of the compound of the invention, the tautomer thereof, the stereoisomer thereof, or the pharmaceutically acceptable salt of any of the foregoing. In one aspect, the cancer can be ovarian, lung, lymphoid, glioblastoma, colon, melanoma, gastric, pancreatic or bladder cancer.

[025] The invention also provides the compound of the invention, the tautomer thereof, the stereoisomer thereof, or the pharmaceutically acceptable salt of any of the foregoing for use in a method of treating a cancer, the method comprising administering to a subject an effective amount of such compound. In one aspect, the cancer can be ovarian, lung, lymphoid, glioblastoma, colon, melanoma, gastric, pancreatic or bladder cancer.

[026] The invention also provides the use of the compound of the present invention, the tautomer thereof, the stereoisomer thereof, or the pharmaceutically acceptable salt of any of the foregoing in the manufacture of a medicament for treating a cancer. In one aspect, the cancer is selected from ovarian, lung, lymphoid, glioblastoma, colon, melanoma, gastric, pancreatic or bladder cancer.

[027] Other objects, features and advantages of the invention will become apparent to those skilled in the art from the following description and claims.

DETAILED DESCRIPTION OF THE INVENTION

Definitions

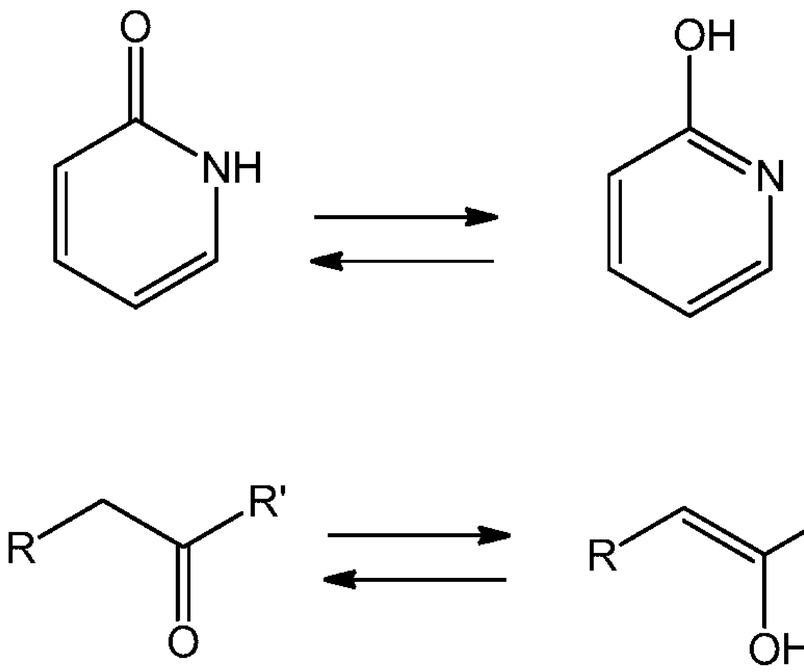
[028] As used herein, if any variable occurs more than one time in a chemical formula, its definition on each occurrence is independent of its definition at every other occurrence. If the chemical structure and chemical name conflict, the chemical structure is determinative of the identity of the compound. The compounds of the present disclosure may contain one or more chiral centers and/or double bonds and therefore, may exist as stereoisomers, such as double-bond isomers (*i.e.*, geometric isomers), enantiomers, or diastereomers. Accordingly, any chemical structures within the scope of the specification depicted, in whole or in part, with a relative configuration encompass all possible enantiomers and stereoisomers of the illustrated compounds including the stereoisomerically pure form (*e.g.*, geometrically pure, enantiomerically pure or diastereomerically pure) and enantiomeric and stereoisomeric mixtures. Enantiomeric and stereoisomeric mixtures can be resolved into the component enantiomers or stereoisomers using separation techniques or chiral synthesis techniques well known to the skilled artisan.

[029] Certain compounds of the invention may possess asymmetric carbon atoms (optical centers) or double bonds; the racemates, enantiomers, diastereomers, geometric isomers and individual isomers are all intended to be encompassed within the scope of the invention. Furthermore, atropisomers and mixtures thereof such as those resulting from restricted rotation about two aromatic or heteroaromatic rings bonded to one another are intended to be encompassed within the scope of the invention. For example, when substituent is a phenyl group and is substituted with two groups bonded to the C atoms adjacent to the point of attachment to the N atom of the triazole, then rotation of the phenyl may be restricted. In some instances, the barrier of rotation is high enough that the different atropisomers may be separated and isolated.

[030] As used herein and unless otherwise indicated, the term "stereoisomer" or "stereomerically pure" means one stereoisomer of a compound that is substantially free of other stereoisomers of that compound. For example, a stereomerically pure compound having one chiral center will be substantially free of the

mirror image enantiomer of the compound. A stereomerically pure compound having two chiral centers will be substantially free of other diastereomers of the compound. A typical stereomerically pure compound comprises greater than about 80% by weight of one stereoisomer of the compound and less than about 20% by weight of other stereoisomers of the compound, more preferably greater than about 90% by weight of one stereoisomer of the compound and less than about 10% by weight of the other stereoisomers of the compound, even more preferably greater than about 95% by weight of one stereoisomer of the compound and less than about 5% by weight of the other stereoisomers of the compound, and most preferably greater than about 97% by weight of one stereoisomer of the compound and less than about 3% by weight of the other stereoisomers of the compound. 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. A bond drawn with a wavy line indicates that both stereoisomers are encompassed. This is not to be confused with a wavy line drawn perpendicular to a bond which indicates the point of attachment of a group to the rest of the molecule.

[031] As known by those skilled in the art, certain compounds of the invention may exist in one or more tautomeric forms. Because one chemical structure may only be used to represent one tautomeric form, it will be understood that for convenience, referral to a compound of a given structural formula includes tautomers of the structure represented by the structural formula. Depending on the compound, some compounds may exist primarily in one form more than another. Also, depending on the compound and the energy required to convert one tautomer to the other, some compounds may exist as mixtures at room temperature whereas others may be isolated in one tautomeric form or the other. Examples of other tautomers associated with compounds of the invention are those with a pyridone group (a pyridinyl) for which hydroxypyridine is a tautomer and compounds with a ketone group with the enol tautomer. Examples of these are shown below.



[032] Compounds of the present disclosure include, but are not limited to, compounds of Formula I and all pharmaceutically acceptable forms thereof. Pharmaceutically acceptable forms of the compounds recited herein include pharmaceutically acceptable salts, solvates, crystal forms (including polymorphs and clathrates), chelates, non-covalent complexes, prodrugs, and mixtures thereof. In certain embodiments, the compounds described herein are in the form of pharmaceutically acceptable salts. As used herein, the term "compound" encompasses not only the compound itself, but also a pharmaceutically acceptable salt thereof, a solvate thereof, a chelate thereof, a non-covalent complex thereof, a prodrug thereof, and mixtures of any of the foregoing. In some embodiments, the term "compound" encompasses the compound itself, pharmaceutically acceptable salts thereof, tautomers of the compound, pharmaceutically acceptable salts of the tautomers, and ester prodrugs such as (C_1-C_4)alkyl esters. In other embodiments, the term "compound" encompasses the compound itself, pharmaceutically acceptable salts thereof, tautomers of the compound, pharmaceutically acceptable salts of the tautomers.

[033] Pharmaceutically acceptable salts of the compounds of the present invention include acid addition salts formed with inorganic acids such as hydrochloric, hydrobromic, hydroiodic, phosphoric, metaphosphoric, nitric and sulfuric acids, and with organic acids, such as tartaric, acetic, trifluoroacetic, citric, malic, lactic, fumaric, benzoic, formic, propionic, glycolic, gluconic, maleic, succinic, camphorsulfuric, isothionic, mucic, gentisic, isonicotinic, saccharic, glucuronic, furoic, glutamic, ascorbic, anthranilic, salicylic, phenylacetic, mandelic, embonic (pamoic), methanesulfonic, ethanesulfonic, pantothenic, stearic, sulfinilic, alginic, galacturonic and arylsulfonic, for example benzenesulfonic and p-toluenesulfonic, acids; base addition salts formed with alkali metals and alkaline earth metals and organic bases such as N,N-dibenzylethylenediamine, chloroprocaine, choline, diethanolamine, ethylenediamine, meglumaine (N-methylglucamine), lysine and procaine; and internally formed salts. Suitable salts include those described in P. Heinrich Stahl, Camille G. Wermuth (Eds.), Handbook of Pharmaceutical Salts Properties, Selection and Use; 2002. Salts having a non-pharmaceutically acceptable anion or cation are within the scope of the invention as useful intermediates for the preparation of pharmaceutically acceptable salts and/or for use in non-therapeutic, for example, *in vitro*, situations.

[034] The term "solvate" refers to the compound formed by the interaction of a solvent and a compound. Solvates of a compound includes solvates of all forms of the compound. In certain embodiments, solvents are volatile, non-toxic, and/or acceptable for administration to humans in trace amounts. Suitable solvates are pharmaceutically acceptable solvates, such as hydrates, including monohydrates and hemi-hydrates.

[035] The compounds of the invention may also contain naturally occurring or unnatural proportions of atomic isotopes at one or more of the atoms that constitute such compounds. For example, the compounds

may be radiolabeled with radioactive isotopes, such as for example tritium (^{3}H), iodine-125 (^{125}I) or carbon-14 (^{14}C). Radiolabeled compounds are useful as therapeutic or prophylactic agents, research reagents, *e.g.*, assay reagents, and diagnostic agents, *e.g.*, *in vivo* imaging agents. All isotopic variations of the compounds of the invention, whether radioactive or not, are intended to be encompassed within the scope of the invention. For example, if a variable is said or shown to be H, this means that variable may also be deuterium (D) or tritium (T).

[036] "Alkyl" refers to a saturated branched or straight-chain monovalent hydrocarbon group derived by the removal of one hydrogen atom from a single carbon atom of a parent alkane. Typical alkyl groups include, but are not limited to, methyl, ethyl, propyls such as propan-1-yl and propan-2-yl, butyls such as butan-1-yl, butan-2-yl, 2-methyl-propan-1-yl, 2-methyl-propan-2-yl, tert-butyl, and the like. In certain embodiments, an alkyl group comprises 1 to 20 carbon atoms. In some embodiments, alkyl groups include 1 to 10 carbon atoms or 1 to 6 carbon atoms whereas in other embodiments, alkyl groups include 1 to 4 carbon atoms. In still other embodiments, an alkyl group includes 1 or 2 carbon atoms. Branched chain alkyl groups include at least 3 carbon atoms and typically include 3 to 7, or in some embodiments, 3 to 6 carbon atoms. An alkyl group having 1 to 6 carbon atoms may be referred to as a (C_1-C_6)alkyl group and an alkyl group having 1 to 4 carbon atoms may be referred to as a (C_1-C_4)alkyl. This nomenclature may also be used for alkyl groups with differing numbers of carbon atoms. "Alkyl" also includes cycloalkyl, a group wherein the carbons are arranged in the form of the ring. Cycloalkyl includes, but not limited to cyclopropyl, cyclobytyl, cyclpentyl and cyclohexyl.

[037] "Alkenyl" refers to an unsaturated branched or straight-chain hydrocarbon group having at least one carbon-carbon double bond derived by the removal of one hydrogen atom from a single carbon atom of a parent alkene. The group may be in either the Z- or E- form (*cis* or *trans*) about the double bond(s). Typical alkenyl groups include, but are not limited to, ethenyl; propenyls such as prop-1-en-1-yl, prop-1-en-2-yl, prop-2-en-1-yl (allyl), and prop-2-en-2-yl; butenyls such as but-1-en-1-yl, but-1-en-2-yl, 2-methyl-prop-1-en-1-yl, but-2-en-1-yl, but-2-en-1-yl, but-2-en-2-yl, buta-1,3-dien-1-yl, and buta-1,3-dien-2-yl; and the like. In certain embodiments, an alkenyl group has 2 to 20 carbon atoms and in other embodiments, has 2 to 6 carbon atoms. An alkenyl group having 2 to 6 carbon atoms may be referred to as a (C_2-C_6)alkenyl group. "Alkenyl" also includes cycloalkenyl. Cycloalkenyl refers to alkenyls that consist of three or more carbon atoms linked together with at least one carbon-carbon double bond to form a structural ring. Examples include but not limited to cyclopropenyl, cyclobutenyl, cyclopentenyl and cyclohexanyl.

[038] "Alkynyl" refers to an unsaturated branched or straight-chain hydrocarbon having at least one carbon-carbon triple bond derived by the removal of one hydrogen atom from a single carbon atom of a parent alkyne. Typical alkynyl groups include, but are not limited to, ethynyl; propynyl; butynyl, 2-

pentynyl, 3-pentynyl, 2-hexynyl, 3-hexynyl and the like. In certain embodiments, an alkynyl group has 2 to 20 carbon atoms and in other embodiments, has 2 to 6 carbon atoms. An alkynyl group having 2 to 6 carbon atoms may be referred to as a –(C_2-C_6)alkynyl group.

[039] "Alkoxy" refers to a radical –OR where R represents an alkyl group as defined herein. Representative examples include, but are not limited to, methoxy, ethoxy, propoxy, butoxy, and the like. Typical alkoxy groups include 1 to 10 carbon atoms, 1 to 6 carbon atoms or 1 to 4 carbon atoms in the R group. Alkoxy groups that include 1 to 6 carbon atoms may be designated as –O-(C_1-C_6) alkyl or as –O-(C_1-C_6 alkyl) groups. In some embodiments, an alkoxy group may include 1 to 4 carbon atoms and may be designated as –O-(C_1-C_4) alkyl or as –O-(C_1-C_4 alkyl) groups group.

[040] "Aryl" refers to a monovalent aromatic hydrocarbon group derived by the removal of one hydrogen atom from a single carbon atom of a parent aromatic ring system. Aryl encompasses monocyclic carbocyclic aromatic rings, for example, benzene. Aryl also encompasses bicyclic carbocyclic aromatic ring systems where each of the rings is aromatic, for example, naphthalene. Aryl groups may thus include fused ring systems where each ring is a carbocyclic aromatic ring. In certain embodiments, an aryl group includes 6 to 10 carbon atoms. Such groups may be referred to as C_6-C_{10} aryl groups. Aryl, however, does not encompass or overlap in any way with heteroaryl as separately defined below. Hence, if one or more carbocyclic aromatic rings is fused with an aromatic ring that includes at least one heteroatom, the resulting ring system is a heteroaryl group, not an aryl group, as defined herein.

[041] "Carbonyl" refers to the radical –C(O) which may also be referred to as –C(=O) group.

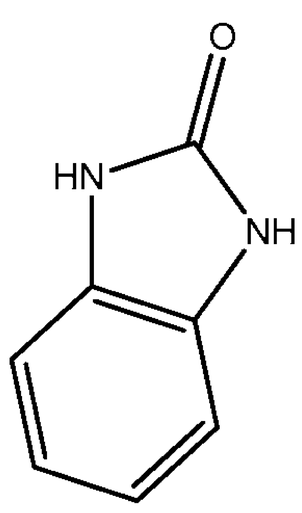
[042] "Carboxy" refers to the radical –C(O)OH which may also be referred to as –C(=O)OH.

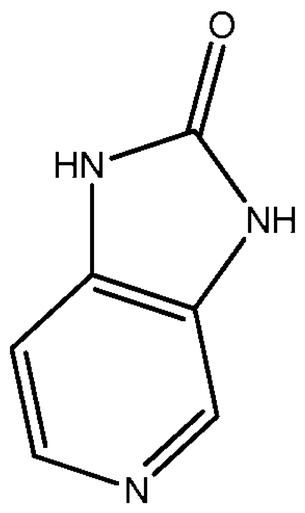
[043] "Cyano" refers to the radical –CN.

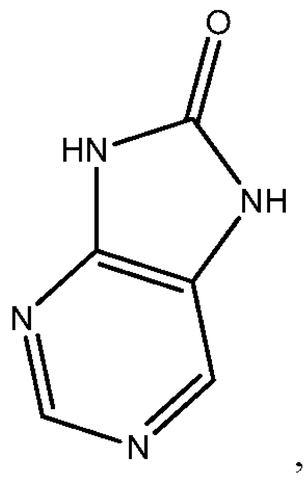
[044] "Cycloalkyl" refers to a saturated cyclic alkyl group derived by the removal of one hydrogen atom from a single carbon atom of a parent cycloalkane. Typical cycloalkyl groups include, but are not limited to, groups derived from cyclopropane, cyclobutane, cyclopentane, cyclohexane, cycloheptane, cyclooctane, and the like. Cycloalkyl groups may be described by the number of carbon atoms in the ring. For example, a cycloalkyl group having 3 to 8 ring members may be referred to as a (C_3-C_8)cycloalkyl, a cycloalkyl group having 3 to 7 ring members may be referred to as a (C_3-C_7)cycloalkyl and a cycloalkyl group having 4 to 7 ring members may be referred to as a (C_4-C_7)cycloalkyl. In certain embodiments, the cycloalkyl group can be a (C_3-C_{10})cycloalkyl, a (C_3-C_8)cycloalkyl, a (C_3-C_7)cycloalkyl, a (C_3-C_6)cycloalkyl, or a (C_4-C_7)cycloalkyl group and these may be referred to as C_3-C_{10} cycloalkyl, C_3-C_8 cycloalkyl, C_3-C_7 cycloalkyl, C_3-C_6 cycloalkyl, or C_4-C_7 cycloalkyl groups using alternative language.

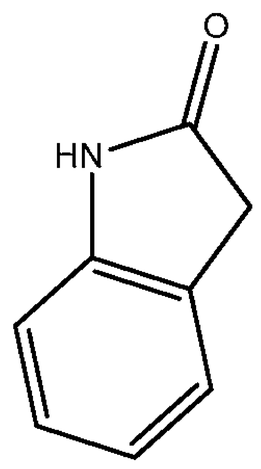
[045] "Heterocyclyl" refers to a cyclic group that includes at least one saturated, partially unsaturated, cyclic ring. Heterocyclyl groups include at least one heteroatom as a ring member. Typical heteroatoms include O, S and N and are independently chosen. Heterocyclyl groups include monocyclic ring systems

and bicyclic ring systems. Bicyclic heterocyclyl groups include at least one non-aromatic ring with at least one heteroatom ring member that may be fused to a cycloalkyl ring or may be fused to an aromatic ring where the aromatic ring may be carbocyclic or may include one or more heteroatoms. The point of attachment of a bicyclic heterocyclyl group may be at the non-aromatic cyclic ring that includes at least one heteroatom or at another ring of the heterocyclyl group. For example, a heterocyclyl group derived by removal of a hydrogen atom from one of the 9 membered heterocyclic compounds shown below may be attached to the rest of the molecule at the 5-membered ring or at the 6-membered ring.



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[046] In some embodiments, a heterocyclyl group includes 5 to 10 ring members of which 1, 2, 3 or 4 or 1, 2, or 3 are heteroatoms independently selected from O, S, or N. In other embodiments, a heterocyclyl group includes 3 to 7 ring members of which 1, 2, or 3 heteroatom are independently selected from O, S, or N. In such 3-7 membered heterocyclyl groups, only 1 of the ring atoms is a heteroatom when the ring includes only 3 members and includes 1 or 2 heteroatoms when the ring includes 4 members. In some embodiments, a heterocyclyl group includes 3 or 4 ring members of which 1 is a heteroatom selected from O, S, or N. In other embodiments, a heterocyclyl group includes 5 to 7 ring members of which 1, 2, or 3 are heteroatoms independently selected from O, S, or N. Typical heterocyclyl groups include, but are not limited to, groups derived from epoxides, aziridine, azetidine, imidazolidine, morpholine, piperazine, piperidine, hexahydropyrimidine, 1,4,5,6-tetrahydropyrimidine, pyrazolidine, pyrrolidine, quinuclidine, tetrahydrofuran, tetrahydropyran, benzimidazolone, pyridinone, and the like. Heterocyclyl groups may be fully saturated but may also include one or more double bonds. Examples of such heterocyclyl groups include, but are not limited to, 1,2,3,6-tetrahydropyridinyl, 3,6-dihydro-2H-pyranyl, 3,4-dihydro-2H-pyranyl, 2,5-dihydro-1H-pyrolyl, 2,3-dihydro-1H-pyrolyl, 1H-azirinyl, 1,2-dihydroazetenyl, and the like. Substituted heterocyclyl also includes ring systems substituted with one or more oxo (=O) or oxide ($-O^-$) substituents, such as piperidinyl N-oxide, morpholinyl-N-oxide, 1-oxo-1-thiomorpholinyl, pyridinonyl, benzimidazolonyl, benzo[d]oxazol-2(3H)-onyl, 3,4-dihydroisoquinolin-1(2H)-onyl, indolin-onyl, 1H-imidazo[4,5-c]pyridin-2(3H)-onyl, 7H-purin-8(9H)-onyl, imidazolidin-2-onyl, 1H-imidazol-2(3H)-onyl, 1,1-dioxo-1-thiomorpholinyl, and the like.

[047] The term "comprising" is meant to be open ended, *i.e.*, all-encompassing and non-limiting. It may be used herein synonymously with "having" or "including". Comprising is intended to include each and every indicated or recited component or element(s) while not excluding any other components or elements.

[048] "Disease" refers to any disease, disorder, condition, symptom, or indication.

[049] "Halo" or "halogen" refers to a fluoro, chloro, bromo, or iodo group.

[050] "Haloalkyl" refers to an alkyl group in which at least one hydrogen is replaced with a halogen. Thus, the term "haloalkyl" includes monohaloalkyl (alkyl substituted with one halogen atom) and polyhaloalkyl (alkyl substituted with two or more halogen atoms). Representative "haloalkyl" groups include difluoromethyl, 2,2,2-trifluoroethyl, 2,2,2-trichloroethyl, and the like. The term "perhaloalkyl" means, unless otherwise stated, an alkyl group in which each of the hydrogen atoms is replaced with a halogen atom. For example, the term "perhaloalkyl", includes, but is not limited to, trifluoromethyl, pentachloroethyl, 1,1,1-trifluoro-2-bromo-2-chloroethyl, and the like.

[051] "Heteroaryl" refers to a monovalent heteroaromatic group derived by the removal of one hydrogen atom from a single atom of a parent heteroaromatic ring system. Heteroaryl groups typically include 5- to 14-membered, but more typically include 5- to 10-membered aromatic, monocyclic, bicyclic, and tricyclic rings containing one or more, for example, 1, 2, 3, or 4, or in certain embodiments, 1, 2, or 3, heteroatoms chosen from O, S, or N, with the remaining ring atoms being carbon. In monocyclic heteroaryl groups, the single ring is aromatic and includes at least one heteroatom. In some embodiments, a monocyclic heteroaryl group may include 5 or 6 ring members and may include 1, 2, 3, or 4 heteroatoms, 1, 2, or 3 heteroatoms, 1 or 2 heteroatoms, or 1 heteroatom where the heteroatom(s) are independently selected from O, S, or N. In bicyclic aromatic rings, both rings are aromatic. In bicyclic heteroaryl groups, at least one of the rings must include a heteroatom, but it is not necessary that both rings include a heteroatom although it is permitted for them to do so. For example, the term "heteroaryl" includes a 5- to 7-membered heteroaromatic ring fused to a carbocyclic aromatic ring or fused to another heteroaromatic ring. In tricyclic aromatic rings, all three of the rings are aromatic and at least one of the rings includes at least one heteroatom. For fused, bicyclic and tricyclic heteroaryl ring systems where only one of the rings contains one or more heteroatoms, the point of attachment may be at the ring including at least one heteroatom or at a carbocyclic ring. When the total number of S and O atoms in the heteroaryl group exceeds 1, those heteroatoms are not adjacent to one another. In certain embodiments, the total number of S and O atoms in the heteroaryl group is not more than 2. In certain embodiments, the total number of S and O atoms in the aromatic heterocycle is not more than 1. Heteroaryl does not encompass or overlap with aryl as defined above. Examples of heteroaryl groups include, but are not limited to, groups derived from acridine, carbazole, cinnoline, furan, imidazole, indazole, indole,

indolizine, isobenzofuran, isochromene, isoindole, isoquinoline, isothiazole, 2H-benzo[d][1,2,3]triazole, isoxazole, naphthyridine, oxadiazole, oxazole, perimidine, phenanthridine, phenanthroline, phenazine, phthalazine, pteridine, purine, pyrazine, pyrazole, pyridazine, pyridine, pyrimidine, pyrrole, pyrrolizine, quinazoline, quinoline, quinolizine, quinoxaline, tetrazole, thiadiazole, thiazole, thiophene, triazole, and the like. In certain embodiments, the heteroaryl group can be between 5 to 20 membered heteroaryl, such as, for example, a 5 to 14 membered or 5 to 10 membered heteroaryl. In certain embodiments, heteroaryl groups can be those derived from thiophene, pyrrole, benzothiophene, 2H-benzo[d][1,2,3]triazole benzofuran, indole, pyridine, quinoline, imidazole, benzimidazole, oxazole, tetrazole, and pyrazine.

[052] "Pharmaceutically acceptable" refers to generally recognized for use in animals, and more particularly in humans.

[053] "Pharmaceutically acceptable salt" refers to a salt of a compound that is pharmaceutically acceptable and that possesses the desired pharmacological activity of the parent compound.

[054] "Pharmaceutically acceptable excipient" refers to a broad range of ingredients that may be combined with a compound or salt of the present invention to prepare a pharmaceutical composition or formulation. Typically, excipients include, but are not limited to, diluents, colorants, vehicles, anti-adherants, glidants, disintegrants, flavoring agents, coatings, binders, sweeteners, lubricants, sorbents, preservatives, and the like.

[055] "Stereoisomer" refers to an isomer that differs in the arrangement of the constituent atoms in space. Stereoisomers that are mirror images of each other and optically active are termed "enantiomers," and stereoisomers that are not mirror images of one another and are optically active are termed "diastereomers."

[056] "Subject" includes mammals and humans. The terms "human" and "subject" are used interchangeably herein.

[057] "Therapeutically effective amount" refers to the amount of a compound that, when administered to a subject for treating a disease, or at least one of the clinical symptoms of a disease or disorder, is sufficient to affect such treatment for the disease, disorder, or symptom. As those skilled in the art will recognize. this amount is typically not limited to a single dose but may comprise multiple dosages over a significant period of time as required to bring about a therapeutic or prophylactic response in the subject. Thus, a "therapeutically effective amount" is not limited to the amount in a single capsule or tablet, but may include more than one capsule or tablet, which is the dose prescribed by a qualified physician or medical care provider. The "therapeutically effective amount" can vary depending on the compound, the disease, disorder, and/or symptoms of the disease or disorder, severity of the disease, disorder, and/or symptoms of the disease or disorder, the age of the subject to be treated, and/or the weight of the subject

to be treated. An appropriate amount in any given instance can be readily apparent to those skilled in the art or capable of determination by routine experimentation.

[058] "Treating" or "treatment" of any disease or disorder refers to arresting or ameliorating a disease, disorder, or at least one of the clinical symptoms of a disease or disorder, reducing the risk of acquiring a disease, disorder, or at least one of the clinical symptoms of a disease or disorder, reducing the development of a disease, disorder or at least one of the clinical symptoms of the disease or disorder, or reducing the risk of developing a disease or disorder or at least one of the clinical symptoms of a disease or disorder. "Treating" or "treatment" also refers to inhibiting the disease or disorder, either physically, (e.g., stabilization of a discernible symptom), physiologically, (e.g., stabilization of a physical parameter), or both, or inhibiting at least one physical parameter which may not be discernible to the subject. Further, "treating" or "treatment" refers to delaying the onset of the disease or disorder or at least symptoms thereof in a subject which may be exposed to or predisposed to a disease or disorder even though that subject does not yet experience or display symptoms of the disease or disorder.

[059] In some aspects, the compound may be in a form of a salt. Such salts may be anhydrous or associated with water as a hydrate. In some embodiments, the compound may be in a neutral form as a base or an acid.

[060] Also provided are pharmaceutical compositions that include the compound or the pharmaceutically acceptable salt thereof, the tautomer thereof, the pharmaceutically acceptable salt of the tautomer, the stereoisomer of any of the foregoing, or the mixture thereof according to any one of the examples and at least one pharmaceutically acceptable excipient, carrier or diluent. In some such examples, the compound or the pharmaceutically acceptable salt thereof, the tautomer thereof, the pharmaceutically acceptable salt of the tautomer, the stereoisomer of any of the foregoing, or the mixture thereof according to any one of the aspects is present in an amount effective for the treatment of PRMT5-dependent cancers. In some aspects, the pharmaceutical composition is formulated for oral delivery whereas in other embodiments, the pharmaceutical composition is formulated for intravenous delivery. In some embodiments, the pharmaceutical composition is formulated for oral administration once a day or QD, and in some such formulations is a tablet where the effective amount of the active ingredient ranges from 1 mg to 100 mg, from 5 mg to 80 mg, from 10 mg to 50 mg or from 15 to 30 mg.

[061] In some aspects, the subject is a mammal. In some such aspects, the mammal is a rodent. In other aspects, the mammal is a canine. In still other embodiments, the subject is a primate and, in some such embodiments, is a human.

[062] The pharmaceutical compositions or formulations for the administration of the compounds of this invention may conveniently be presented in unit dosage form and may be prepared by any of the methods well known in the art. All methods include the step of bringing the active ingredient into association with

the carrier which constitutes one or more accessory ingredients. In general, the pharmaceutical compositions are prepared by uniformly and intimately bringing the active ingredient into association with a liquid carrier or a finely divided solid carrier or both, and then, if necessary, shaping the product into the desired formulation. In the pharmaceutical composition, the active object compound is included in an amount sufficient to produce the desired effect upon the process or condition of diseases.

[063] The compounds of the invention may be administered via oral, mucosal (including sublingual, buccal, rectal, nasal, or vaginal), parenteral (including subcutaneous, intramuscular, bolus injection, intra-arterial, or intravenous), transdermal, or topical administration. In some aspects, the compounds of the invention are administered via mucosal (including sublingual, buccal, rectal, nasal, or vaginal), parenteral (including subcutaneous, intramuscular, bolus injection, intra-arterial, or intravenous), transdermal, or topical administration. In other aspects, the compounds of the invention are administered via oral administration. In still other embodiments, the compounds of the invention are not administered via oral administration.

[064] The compounds of the invention, the pharmaceutically acceptable salt thereof, the tautomer thereof, the pharmaceutically acceptable salt of the tautomer, the stereoisomer of any of the foregoing, or the mixture thereof may find use in treating a number of conditions.

[065] Compounds and compositions described herein are generally useful for the inhibition of PRMT5. In some aspects, methods of treating PRMT5-mediated disorder in a subject are provided which comprise administering an effective amount of a compound described herein (*e.g.*, a compound of Formula I or a pharmaceutically acceptable salt thereof), to a subject in need of treatment. In certain aspects, the effective amount is a therapeutically effective amount. In certain aspects, the effective amount is a prophylactically effective amount. In certain aspects, the subject is suffering from a PRMT5-mediated disorder (*e.g.*, a cancer, for example a lymphoma, breast cancer, or pancreatic cancer). In other aspects, the subject is susceptible to a PRMT5-mediated disorder (*e.g.*, a cancer, for example a lymphoma, breast cancer, or pancreatic cancer).

[066] As used herein, the term "PRMT5-mediated disorder" means any disease, disorder, or other pathological condition in which PRMT5 is known to play a role. Accordingly, in some aspects, the present disclosure relates to treating or lessening the severity of one or more diseases in which PRMT5 is known to play a role.

[067] In some aspects, herein provided is a method of inhibiting PRMT5 activity in a subject in need thereof comprising administering to the subject an effective amount of a compound described herein (*e.g.*, a compound of Formula I, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition thereof.

[068] In further aspects, a compound contemplated by the present invention is useful in treating a proliferative disorder, such as cancer. In certain embodiment, compounds described herein are useful for treating lymphoma. In some embodiments, the lymphoma is mantle cell lymphoma (MCL). In some embodiments, the lymphoma is acute myeloid lymphoma (AML). In some embodiments, the cancer compounds described herein are useful for treating pancreatic cancer. In some aspects, the cancer compounds described herein are useful for treating multiple myeloma (MM). In further embodiments, the cancer compounds described herein are useful for treating breast cancer. The breast cancer can be estrogen receptor negative (ER-) or the breast cancer can be progesterone receptor negative (PR-). In further embodiments, the breast cancer can be HER2 negative. In some embodiments, the breast cancer is estrogen receptor negative, progesterone receptor negative and HER2 negative, also referred to herein as "triple negative breast cancer".

[069] In further aspects, a breast cancer can be a lobular carcinoma in situ (LCIS), a ductal carcinoma in situ (DCIS), an invasive ductal carcinoma (IDC), inflammatory breast cancer, Paget disease of the nipple, Phyllodes tumor, Angiosarcoma, adenoid cystic carcinoma, low-grade adenosquamous carcinoma, medullary carcinoma, mucinous carcinoma, papillary carcinoma, tubular carcinoma, metaplastic carcinoma, micropapary carcinoma, mixed carcinoma, or another breast cancer, including but not limited to triple negative, HER positive, estrogen receptor positive, progesterone receptor positive, HER and estrogen receptor positive, HER and progesterone receptor positive, estrogen and progesterone receptor positive, and HER and estrogen and progesterone receptor positive.

[070] In one embodiment, compounds of the invention are useful for treating pancreatic cancer.

[071] In another embodiment, compounds of the invention are useful for treating NSCLC (non-small cell lung carcinoma. In one embodiment, the NSCLC can be squamous NSCLC. In another embodiment, it can be adenocarcinoma.

[072] In a further aspect, cancer can be GBM. In a further aspect, cancer can be mesothelioma. In one aspect, cancer can be bladder cancer. In another aspect, cancer can be esophageal cancer. In a further aspect, cancer can be melanoma. In one aspect, cancer can be DLBCL, HNSCC or cholangiocarcinoma.

[073] In some aspects, one or more compounds described herein are useful for treating any PRMT5-mediated or PRMT5-responsive proliferative cell disorder, for example a cancer that is PRMT5 responsive.

[074] In one aspect, a cancer that lacks p53 (*e.g.*, a p53 null cancer) is less sensitive to PRMT5 inhibition than a cancer that is p53 positive. Accordingly, a cancer that is PRMT5 responsive can be a p53 positive cancer. The term "p53 positive" refers to a cancer that does not lack p53 expression and/or activity. In some embodiments, one or more compounds described herein are useful for treating a p53

positive cancer. In some aspects, a greater amount of one or more compounds described herein may be required to treat a p53 negative cancer (*e.g.* , a p53 null cancer) than a p53 positive cancer.

[075] In some aspects, the disclosure provides a method for identifying subjects having a cancer that is sensitive to treatment with a PRMT5 inhibitor. In some embodiments, the method comprises obtaining a sample from the subject; detecting the presence or absence of p53; and, identifying the subject as having a cancer that is sensitive to treatment with a PRMT5 inhibitor if p53 is present in the sample. Accordingly, in some embodiments, a subject having a p53 positive cancer is identified as a subject for treatment with a PRMT5 inhibitor. In some embodiments, the method further comprises administering to the subject a composition comprising a PRMT5 inhibitor.

[076] In some embodiments, aspects of the disclosure relate to a method for identifying subjects having a cancer that is insensitive (or that has low sensitivity) to treatment with a PRMT5 inhibitor. In some embodiments, the method comprises obtaining a sample from the subject; detecting the presence or absence of p53; and, identifying the subject as having a cancer that is not sensitive (for example, a cancer that is less sensitive than a p53 positive cancer) to treatment with a PRMT5 inhibitor if p53 is absent from the sample (*e.g.*, if the cancer is a p53 null cancer). In some embodiments, a p53 negative cancer (*e.g.*, a p53 null cancer) is treated with a PRMT5 inhibitor, but a greater amount of PRMT5 inhibitor may be required to treat the p53 negative cancer than a p53 positive cancer. However, in some embodiments, a subject having a p53 negative cancer (*e.g.* , a p53 null cancer) is treated with a therapeutic agent that is not a PRMT5 inhibitor.

[077] By "sample" is meant any biological sample derived from the subject, includes but is not limited to, cells, tissues samples, body fluids (including, but not limited to, mucus, blood, plasma, serum, urine, saliva, and semen), cancer cells, and cancer tissues. Detection of the presence or absence of p53 in the sample may be achieved by any suitable method for detecting p53 nucleic acid or protein, for example, nucleic acid sequencing (*e.g.*, DNA or RNA sequencing), quantitative PCR, Western blotting, etc., or any combination of thereof.

[078] It should be appreciated that in some aspects, one or more of the compounds described herein may be useful for treating other types of cancer, including, but not limited to, acoustic neuroma, adenocarcinoma, adrenal gland cancer, anal cancer, angiosarcoma (*e.g.*, lymphangiosarcoma, lymphangioendotheliosarcoma, hemangio sarcoma), appendix cancer, benign monoclonal gammopathy, biliary cancer (e.g. , cholangiocarcinoma), bladder cancer, brain cancer (e.g., meningioma; glioma, e.g. , astrocytoma, oligodendroglioma; medulloblastoma), bronchus cancer, carcinoid tumor, cervical cancer (e.g. , cervical adenocarcinoma), choriocarcinoma, chordoma, craniopharyngioma, colorectal cancer (e.g., colon cancer, rectal cancer, colorectal adenocarcinoma), epithelial carcinoma, ependymoma, endothelio sarcoma (e.g., Kaposi's sarcoma, multiple idiopathic hemorrhagic sarcoma), endometrial cancer (e.g.,

uterine cancer, uterine sarcoma), esophageal cancer (e.g. , adenocarcinoma of the esophagus, Barrett' s adenocarinoma), Ewing sarcoma, eye cancer (e.g., intraocular melanoma, retinoblastoma), familiar hypereosinophilia, gall bladder cancer, gastric cancer (e.g. , stomach adenocarcinoma), gastrointestinal stromal tumor (GIST), head and neck cancer (e.g., head and neck squamous cell carcinoma, oral cancer (e.g., oral squamous cell carcinoma (OSCC), throat cancer (e.g., laryngeal cancer, pharyngeal cancer, nasopharyngeal cancer, oropharyngeal cancer)), hematopoietic cancers (e.g., leukemia such as acute lymphocytic leukemia (ALL) (e.g., B-cell ALL, T-cell ALL), acute myelocytic leukemia (AML) (e.g. , B-cell AML, T-cell AML), chronic myelocytic leukemia (CML) (e.g. , B-cell CML, T-cell CML), and chronic lymphocytic leukemia (CLL) (e.g. , B-cell CLL, T- cell CLL), follicular lymphoma, chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), marginal zone B-cell lymphomas (e.g. , mucosa-associated lymphoid tissue (MALT) lymphomas, nodal marginal zone B-cell lymphoma, splenic marginal zone B-cell lymphoma), primary mediastinal B-cell lymphoma, Burkitt lymphoma, lymphoplasmacytic lymphoma (e.g., "Waldenstrom's macro globulinemia"), hairy cell leukemia (HCL), immunoblastic large cell lymphoma, precursor B -lymphoblastic lymphoma and primary central nervous system (CNS) lymphoma; and T-cell NHL such as precursor T-lymphoblastic lymphoma/leukemia, peripheral T-cell lymphoma (PTCL) (e.g., cutaneous T-cell lymphoma (CTCL) (e.g. , mycosis fungiodes, Sezary syndrome), angioimmunoblastic T-cell lymphoma, extranodal natural killer T-cell lymphoma, enteropathy type T-cell lymphoma, subcutaneous panniculitis-like T-cell lymphoma, anaplastic large cell lymphoma); a mixture of one or more leukemia/lymphoma as described above; and multiple myeloma (MM)), heavy chain disease (e.g., alpha chain disease, gamma chain disease, mu chain disease), hemangioblastoma, inflammatory myofibroblastic tumors, immunocytic amyloidosis, kidney cancer (e.g., nephroblastoma a.k.a. Wilms' tumor, renal cell carcinoma), liver cancer (e.g. , hepatocellular cancer (HCC), malignant hepatoma), lung cancer (e.g., bronchogenic carcinoma, small cell lung cancer (SCLC), non-small cell lung cancer (NSCLC), adenocarcinoma of the lung), leiomyosarcoma (LMS), mastocytosis (e.g. , systemic mastocytosis), myelodysplasia syndrome (MDS), mesothelioma, myeloproliferative disorder (MPD) (e.g., polycythemia Vera (PV), essential thrombocytosis (ET), agnogenic myeloid metaplasia (AMM) a.k.a. myelofibrosis (MF), chronic idiopathic myelofibrosis, chronic myelocytic leukemia (CML), chronic neutrophilic leukemia (CNL), hypereosinophilic syndrome (HES)), neuroblastoma, neurofibroma (e.g. , neurofibromatosis (NF) type 1 or type 2, schwannomatosis), neuroendocrine cancer (e.g., gastroenteropancreatic neuroendoctrine tumor (GEP-NET), carcinoid tumor), osteosarcoma, ovarian cancer (e.g. , cystadenocarcinoma, ovarian embryonal carcinoma, ovarian adenocarcinoma), papillary adenocarcinoma, penile cancer (e.g., Paget' s disease of the penis and scrotum), pinealoma, primitive neuroectodermal tumor (PNT), prostate cancer (e.g., prostate adenocarcinoma), rectal cancer, rhabdomyosarcoma, salivary gland cancer, skin cancer (e.g. , squamous

cell carcinoma (SCC), keratoacanthoma (KA), melanoma, basal cell carcinoma (BCC)), small bowel cancer (e.g. , appendix cancer), soft tissue sarcoma (*e.g.*, malignant fibrous histiocytoma (MFH), liposarcoma, malignant peripheral nerve sheath tumor (MPNST), chondrosarcoma, fibrosarcoma, myxosarcoma), sebaceous gland carcinoma, sweat gland carcinoma, synovioma, testicular cancer (*e.g.*, seminoma, testicular embryonal carcinoma), thyroid cancer (*e.g.*, papillary carcinoma of the thyroid, papillary thyroid carcinoma (PTC), medullary thyroid cancer), urethral cancer, vaginal cancer and vulvar cancer (*e.g.* , Paget' s disease of the vulva).

[079] In some aspects, the method of treating cancer in a subject comprises administering a composition comprising a PRMT5 inhibitor to the subject, wherein treatment with the PRMT5 inhibitor inhibits tumor growth of the cancer by more than about 25%, more than about 50%, more than about 75%, more than about 90% (e.g., 25%-50%, 50%-75%, 75%- 90%, or 90%-100% for example). In some embodiments, the method of treating cancer in a subject comprises administering a composition comprising a PRMT5 inhibitor to the subject, wherein methyl mark of the cancer is reduced more than about 50%, more than about 75%, more than about 80% (e.g., 50%-75%, 50%-80%, 80%-90%, 80%-100%, or 90%-100% for example). A methyl mark refers to protein methylation, for example a histone methylation (e.g., methylation of one or more lysines and/or arginines of a histone protein), or DNA methylation (e.g., epigenetic DNA methylation, for example methylated CpG sites). In some embodiments, the methyl mark level of a cell is a measure of the extent to which histones are methylated in the cell (*e.g.*, at one or more particular lysine and/or arginine positions).

[080] Some methods of the invention comprise the administration of a compound of the invention and an additional therapeutic agent (*i.e.*, a therapeutic agent other than a compound of the invention). Thus, the compounds of the invention can be used in combination with at least one other therapeutic agent. Examples of additional therapeutic agents include, but are not limited to, antibiotics, anti-emetic agents, antidepressants, antifungal agents, anti-inflammatory agents, antineoplastic agents, antiviral agents, cytotoxic agents, and other anticancer agents, immunomodulatory agents, alpha-interferons, β-interferons, alkylating agents, hormones, and cytokines. In one embodiment, the invention encompasses administration of an additional therapeutic agent that is used to treat subjects with chronic heart failure or hypertension.

[081] As described above some methods of the invention comprise the administration of a compound of the invention and an additional therapeutic agent (*i.e.*, a therapeutic agent other than a compound of the invention). In some embodiments, the invention encompasses administration of an additional therapeutic agent that is used to treat subjects with acceptable salt thereof, the tautomer thereof, the pharmaceutically acceptable salt of the tautomer, the stereoisomer of any of the foregoing, or the mixture thereof and an

additional therapeutic agent such as an inhibitor of the funny current. In some embodiments, the method of use may include two or more additional therapeutic agents.

[082] The invention is further described by reference to the following examples, which are intended to exemplify the claimed invention but not to limit it in any way.

EXAMPLES

[083] Unless otherwise noted, all materials were obtained from commercial suppliers and were used without further purification.

[084] The following abbreviations are used to refer to various reagents and solvents:

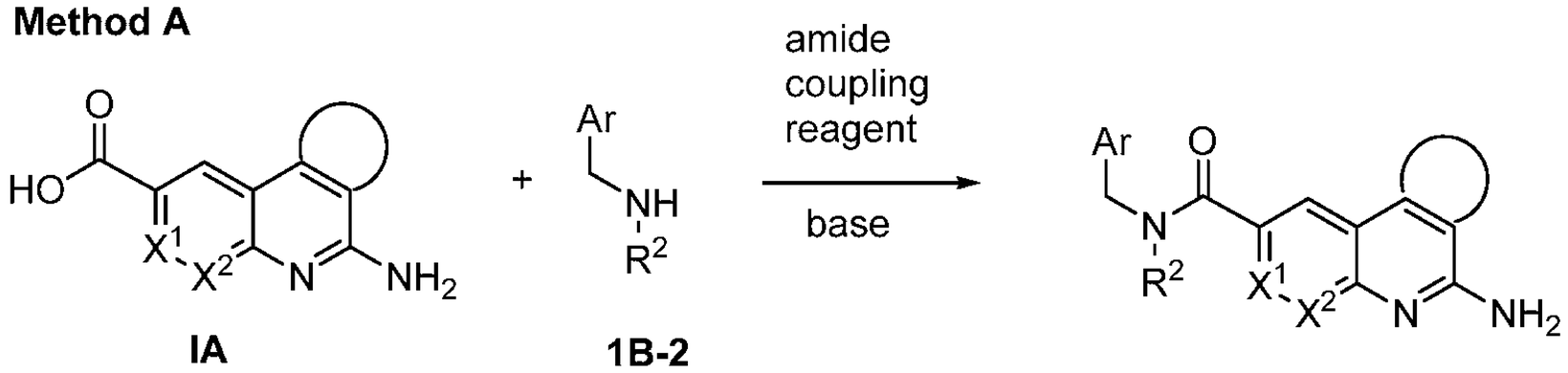
AcOH	acetic acid
aq or aq.	aqueous
Boc	*tert*-butyloxycarbonyl
CLND	chemiluminescent nitrogen detection
CMPI	2-Chloro-1-methylpyridinium iodide
DAD	diode array detector
DCE	1,2-dichloroethane
DCM	dichloromethane
DEA	diethylamine
DIAD	diisopropyl azodicarboxylate
DMA or DMAc	*N,N*-dimethylacetamide
DMF	*N,N*-dimethylformamide
DMSO	dimethyl sulfoxide
dppf	1,1'-bis(diphenylphosphino)ferrocene
EDC·HCl or EDCI	3-((ethylimino)methyleneamino)-*N,N*-dimethylpropan-1-amonium chloride
ESI or ES	electrospray ionization
Et	ethyl
Et_2O	diethyl ether
EtOH	ethyl alcohol
EtOAc	ethyl acetate

g	grams
h	hour
HPLC	high pressure liquid chromatography
HATU	1-[bis(dimethylamino)methylene]-1*H*-1,2,3-triazolo[4,5-*b*]pyridinium 3-oxid hexafluorophosphate
HBTU	N,N,N′,N′-Tetramethyl-O-(1H-benzotriazol-1-yl)uronium hexafluorophosphate, O-(Benzotriazol-1-yl)-N,N,N′,N′-tetramethyluronium hexafluorophosphate
HOAt	1-hydroxy-7-azabenzotriazole
iPr	isopropyl
iPr_2NEt or DIPEA	*N*-ethyl diisopropylamine (Hünig's base)
LC MS, LCMS, LC-MS or LC/MS	liquid chromatography mass spectroscopy
LG	leaving group (e.g., halogen, mesylate, triflate)
LiHMDS	lithium bis(trimethylsilyl)amide
m/z	mass divided by charge
Me	methyl
MeCN/ACN	acetonitrile
MeOH	methanol
Met	metal species for cross-coupling (e.g., MgX, ZnX, SnR_3, SiR_3, $B(OR)_2$)
mg	milligrams
min	minutes
mL	milliliters
MS	mass spectra
MsCl	methanesulfonyl chloride
MTBE	*tert*-butyl methyl ether
NMP	1-methyl-2-pyrrolidine
n-BuLi	n-butyllithium
NMR	nuclear magnetic resonance
$Pd_2(dba)_3$	tris(dibenzylideneacetone)dipalladium(0)
$Pd(dppf)Cl_2 \cdot DCM$	[1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with DCM
$Pd(PPh_3)_4$	tetrakis(triphenylphosphine)palladium(0)

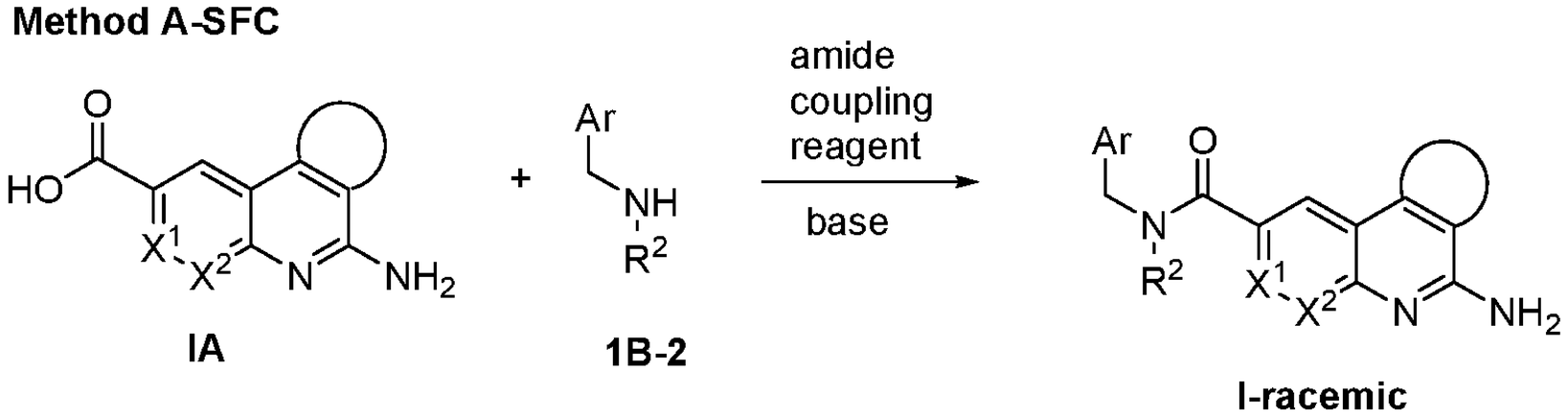
Ph	phenyl
PG or Prot. group	protecting group
Prep	preparative
PyBrOP	bromotripyrrolidinophosphonium hexafluorophosphate
rbf	round-bottom flask
RP-HPLC	reverse phase high pressure liquid chromatography
RT or rt	room temperature
R.T.	retention time
RuPhos	2-dicyclohexylphosphino-2′,6′-diisopropoxybiphenyl
sat. or sat'd	saturated
SFC	supercritical fluid chromatography
t-BuOH	*tert*-butanol
TEA or Et_3N	triethylamine
TEOS	tetraethyl orthosilicate
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TBTU	N,N,N′,N′-Tetramethyl-O-(benzotriazol-1-yl)uronium tetrafluoroborate
TOF	time of flight
UHPLC	ultra-high-performance liquid chromatography
Xantphos	4,5-bis(diphenylphosphino)-9,9-dimethylxanthene

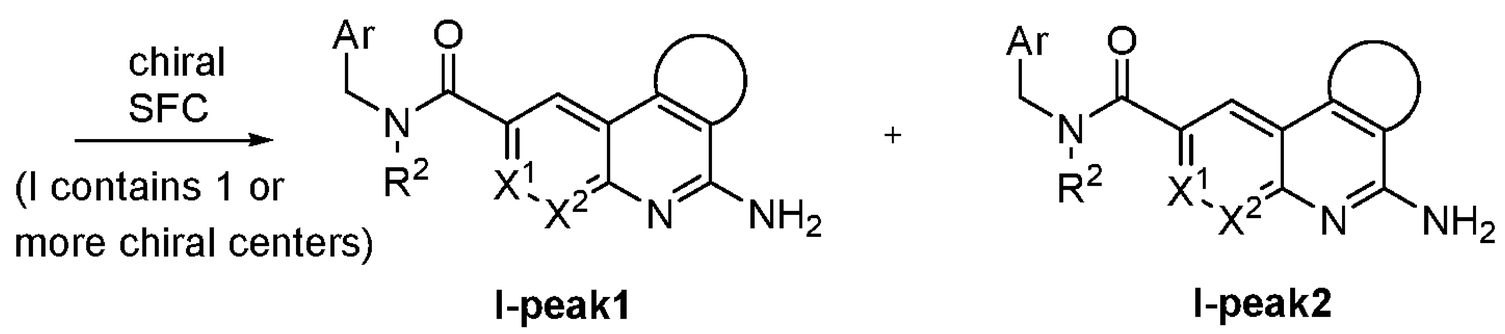
General Synthetic Schemes

Method A

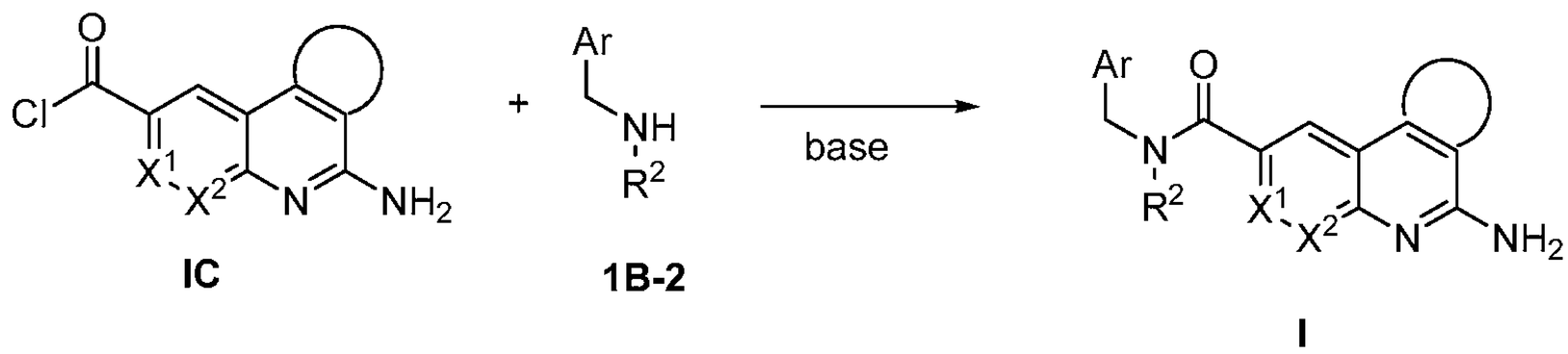


Method A-SFC

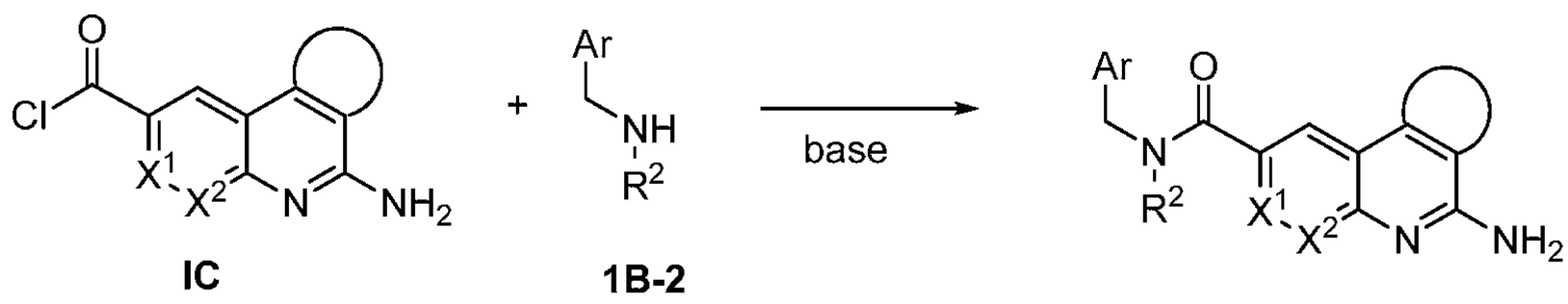


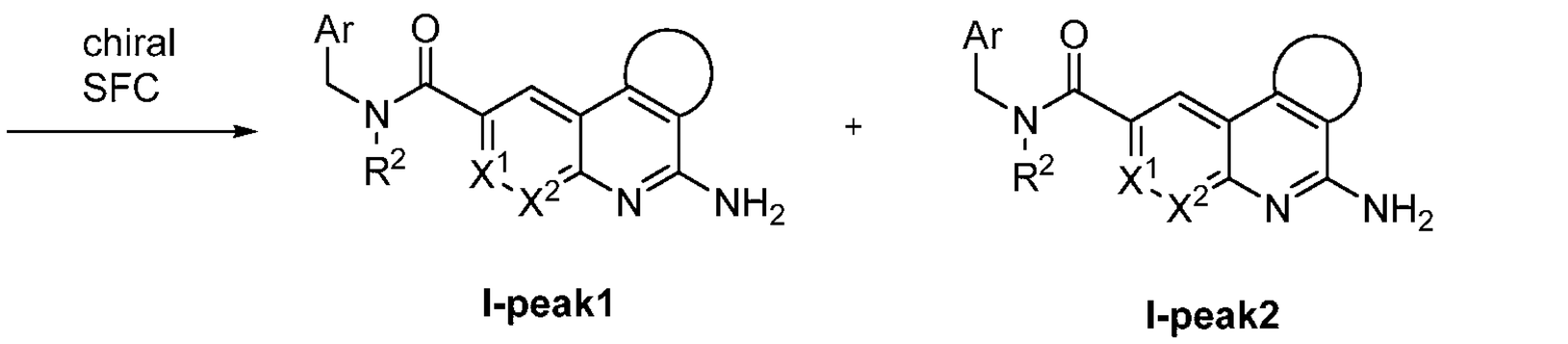


Method B

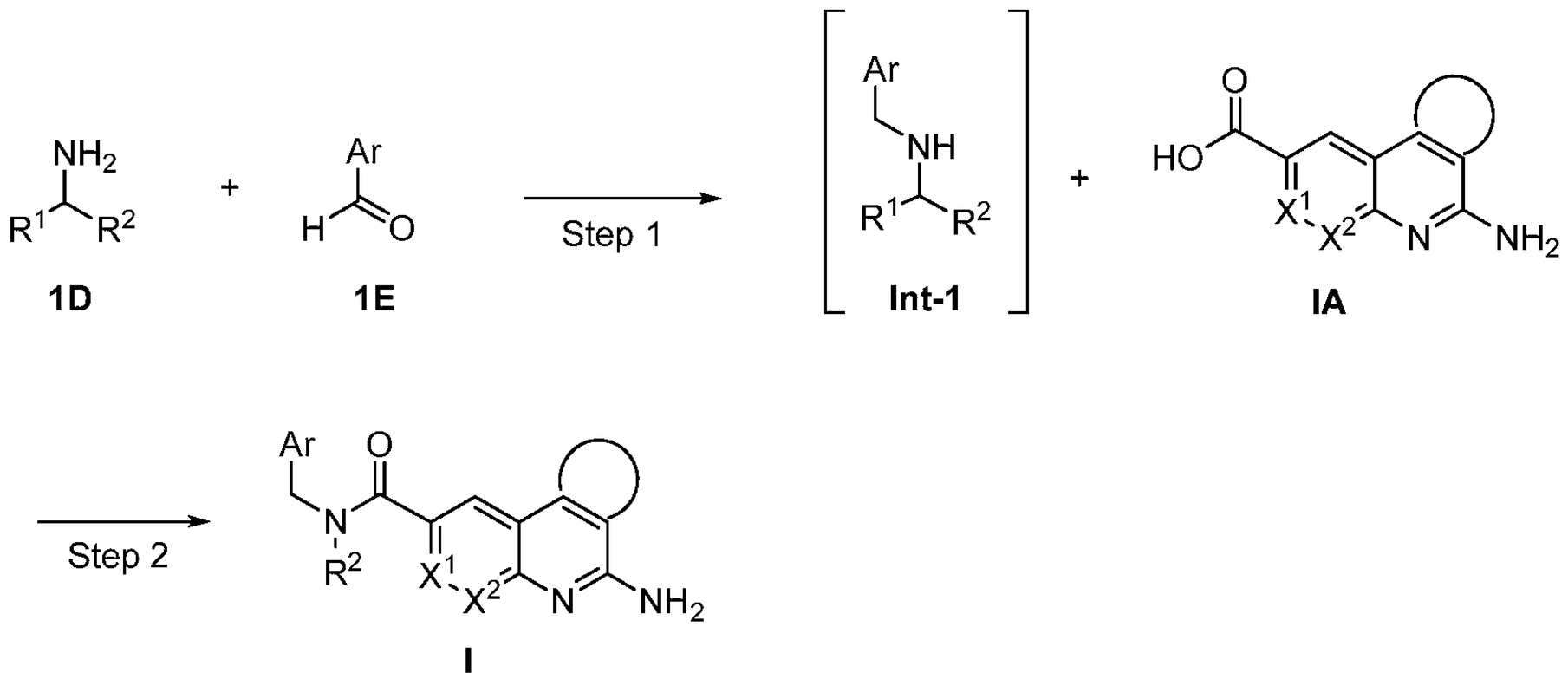


Method B-SFC





Method C: One pot, two steps synthesis



Method A: Compound **I** can be prepared from the reaction of acid **IA** and secondary amine **IB-1** in the presence of a base such as Et_3N or DIPEA, an activating reagent such as HATU or PyBrOP, in a solvent such as DMF or DMAc. If racemic amine or acid is employed in Method A, chiral SFC can be used to separate the stereoisomers, in which case stereochemistry was arbitrarily assigned to each isomer.

Method B: Compound **I** can be prepared from the reaction of acid chloride **IC** and secondary amine **IB** in the presence of a base such as Et_3N or DIPEA or pyridine, in a solvent such as THF or dioxane or DCM or DCE. Alternatively, compound **I** can be prepared from the reaction of acid chloride **IC** and secondary amine **IB** in the presence of DMAP in pyridine. If racemic amine or acid is employed in Method B, chiral SFC can be used to separate the stereoisomers, in which case stereochemistry was arbitrarily assigned to each isomer.

Method C: Compound **I** can be prepared by a small scale one pot, two step protocol as illustrated in General Scheme Method C. Primary amine **1D** can be combined with aldehyde **1E** in the method specified solvents and after imine formation and reduction will yield a secondary amine (**Int-1**) as a crude product. The secondary amine (**Int-1**) was reacted with acid **IA** with the specified coupling reagents to yield product **I** after HPLC purification.

Analytical U/HPLC

[085] The following equipment was used for analytical UHPLC:

Waters Acquity system equipped with an Acquity BEH C18 (1.7µm, 2.1 x 50 mm) with a linear gradient of a binary solvent system using a flow rate of 0.5 mL/min and DAD at ambient temperature, combined with MS detection SQD I. Linear gradients used ($H_2O/CH_3CN/HCO_2H$ (95/5/0.1% to 0/100/0.1%)).

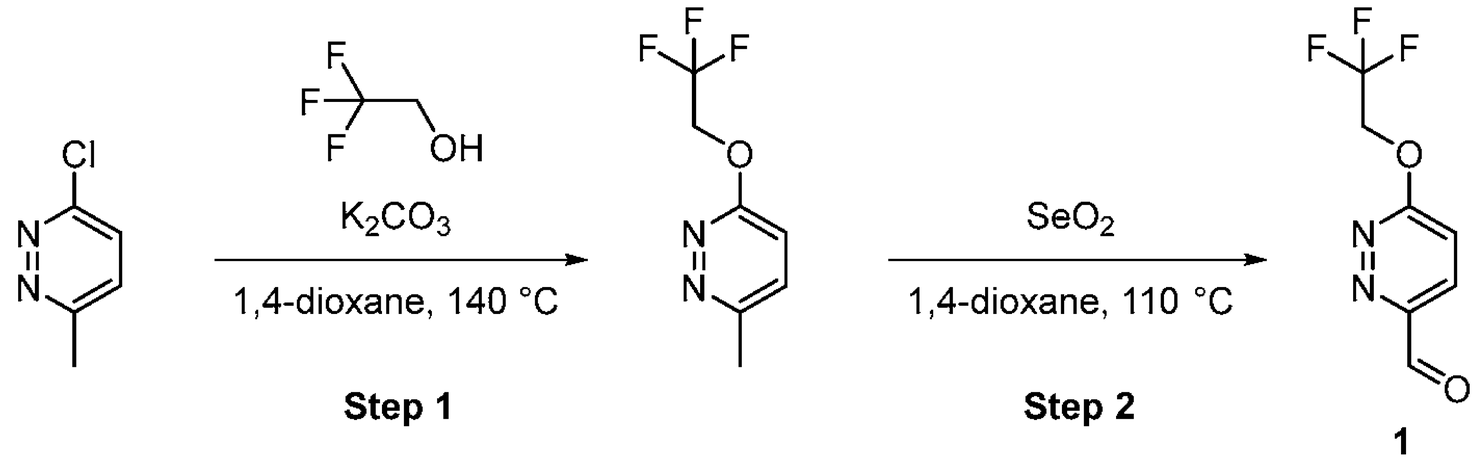
Agilent Infinity I/II -TOF6230B /CLND Antek 8060 equipped with Acquity BEH C18 (1.7µm, 2.1 x 50 mm) with a linear gradient of a binary solvent system using a flow rate of 0.75 mL/min combined with DAD. Linear gradients used (H_2O/MeOH/HCO_2H (95/5/0.1% to 0/100/0.1%)).

Preparative HPLC

[086] The following equipment was used for Prep-HPLC: Shimadzu Nexera X2 equipped with a Merck Chromolith SpeedROD RP-18E (5µm, 10 x 100 mm) with a linear gradient of a binary solvent system using a flow rate between 4 and 7 mL/min and UV detection at 254 nm, combined with MS detecting on a Shimadzu LCMS-2020. Linear gradients used (H_2O/MeOH/HCO_2H (95/5/0.1% to 0/100/0.1%)).

Intermediates

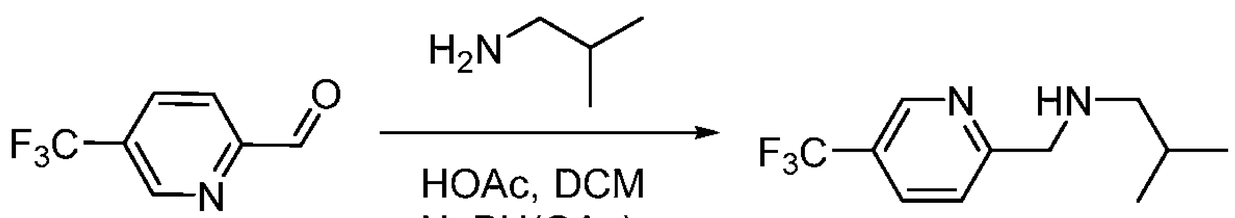
[087] Intermediate **1**: 6-(2,2,2-trifluoroethoxy)pyridazine-3-carbaldehyde



[088] Step 1. A microwave vial was charged with 3-chloro-6-methylpyridazine (1.00 g, 7.78 mmol), potassium carbonate (2.150 g, 15.56 mmol), and 1,4-dioxane (14.0 mL). To the resulting suspension was added 2,2,2-trifluoroethanol (2.334 g, 1.704 mL, 23.34 mmol) and the mixture was heated to 140 °C in the microwave for 14 h. After cooling to 23 °C, the reaction mixture was transferred to a separatory funnel with CH_2Cl_2 (30 mL), H_2O (20 mL), and sat. aq. NH_4Cl (30 mL), the layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 x 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated to dryness. The resulting crude residue was purified by flash chromatography (0 to 100% 3:1 EtOAc:EtOH in heptane) to afford 3-methyl-6-(2,2,2-trifluoroethoxy)pyridazine (662 mg, 3.45 mmol, 44.3 % yield) as a light yellow solid. m/z (ESI): 193.2 $(M+H)^+$.

[089] Step 2. A vial was charged with 3-methyl-6-(2,2,2-trifluoroethoxy)pyridazine (662 mg, 3.45 mmol), selenium dioxide (612 mg, 5.51 mmol), and 1,4-dioxane (13.8 mL). The resulting mixture was sparged with nitrogen for 10 min, and the vial was subsequently heated to 110 °C. After 1.5 h, the reaction mixture was allowed to cool to 23 °C and was filtered over a 1 cm pad of Celite (30 mL 3:1 EtOAc:EtOH eluent) and concentrated to dryness. The resulting crude residue was purified by flash chromatograpy (0 to 50% 3:1 EtOAc:EtOH in heptane) to afford 6-(2,2,2-trifluoroethoxy)pyridazine-3-carbaldehyde (**1,** 154.7 mg, 0.751 mmol, 21.8 % yield) as a light yellow solid. m/z (ESI): 207.1 $(M+H)^+$.

[090] Intermediate 2: 2-methyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)propan-1-amine.

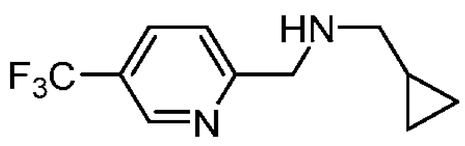
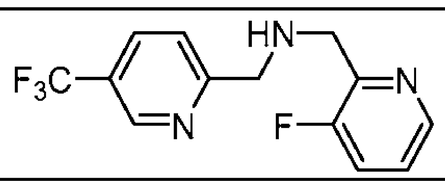
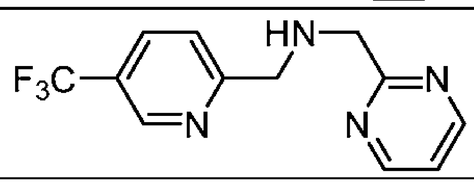
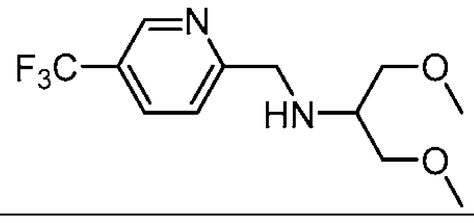
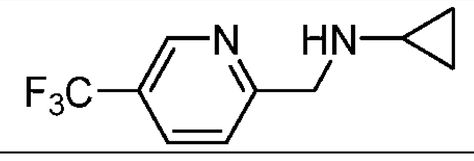


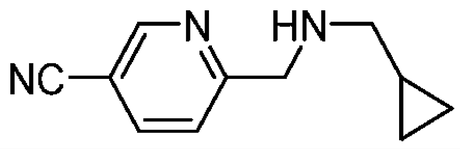
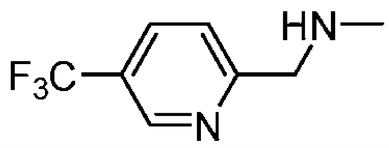
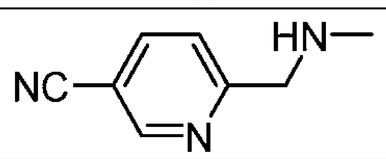
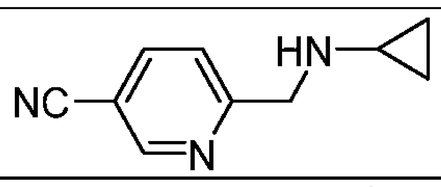
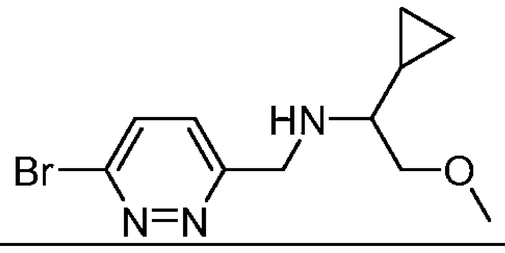
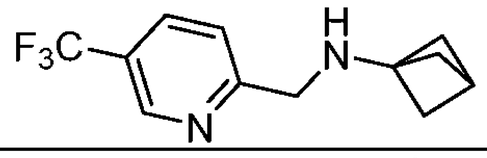
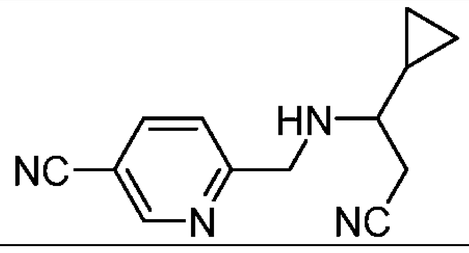
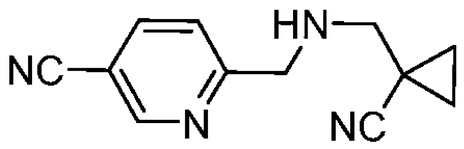
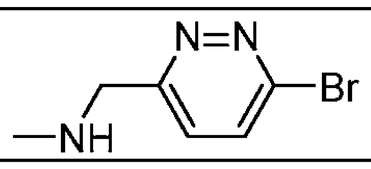
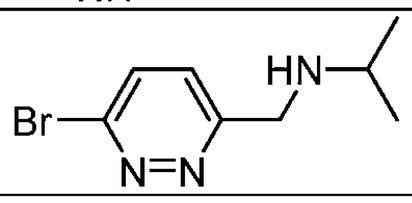
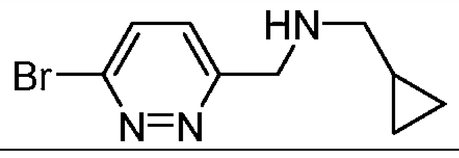
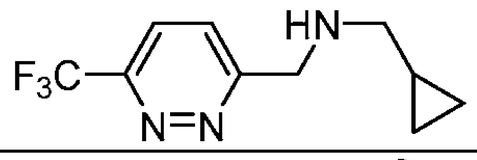
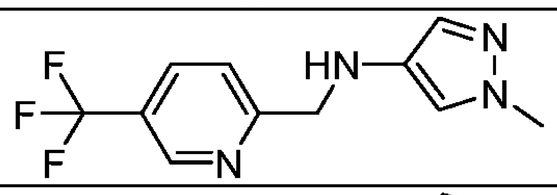
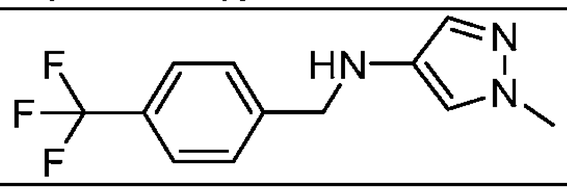
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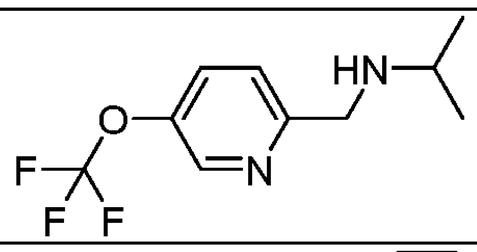
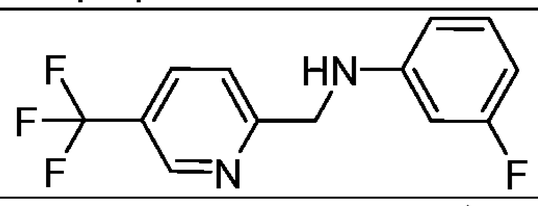
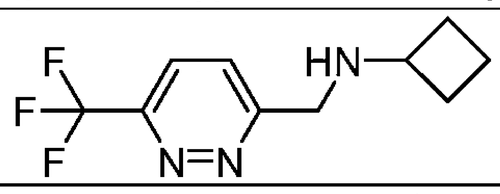
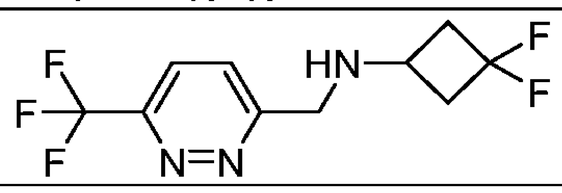
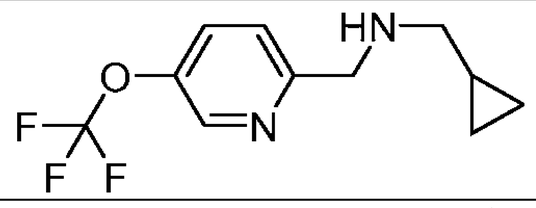
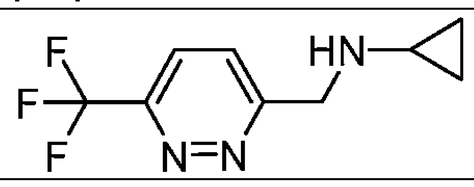
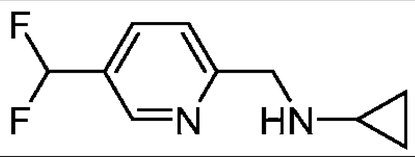
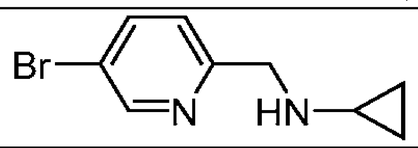
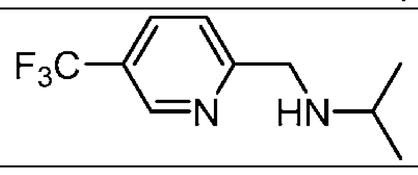
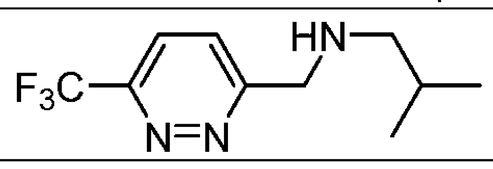
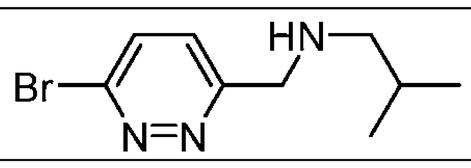
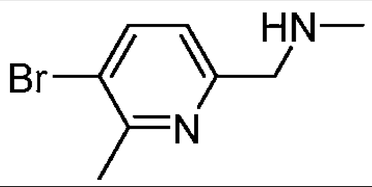
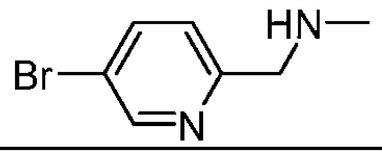
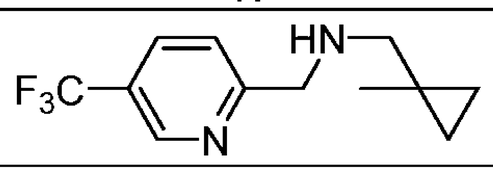
[091] To a mixture of 5-(trifluoromethyl)picolinaldehyde (3.02 g, 17.27 mmol, AstaTech Inc) and isobutylamine (1.48 g, 20.21 mmol, Combi-Blocks Inc.) in DCM (50 mL) at RT was added acetic acid (1.11 g, 18.48 mmol). The mixture was stirred at RT for 30 min then treated with sodium triacetoxyborohydride (5.49 g, 25.9 mmol, Aldrich). The mixture was stirred at RT for 1 h then neutralized with sat'd aqueous Na_2CO_3 solution. The layers were separated, and the aqueous layer was extracted with DCM. The combined organic phase was dried over Na_2SO_4 and concentrated in vacuo. The crude material was purified by silica gel chromatography (0-100% EtOAc/EtOH (3/1) in heptane) to afford 2-methyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)propan-1-amine (**2**, 2.81 g, 70% yield) as a brown oil. *m/z* (ESI): 233.0 $(M+H)^+$. ^1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.81 (s, 1 H), 7.88 (dd, *J*=8.1, 2.1 Hz, 1 H), 7.50 (d, *J*=8.1 Hz, 1 H), 3.98 (s, 2 H), 2.46 (d, *J*=6.6 Hz, 2 H), 1.73 - 1.84 (m, 2 H), 0.94 (d, *J*=6.6 Hz, 6 H). ^{19}F NMR (376 MHz, CHLOROFORM-*d*) δ ppm -62.26 (s, 3 F).

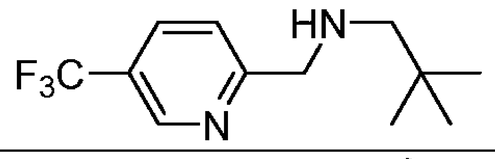
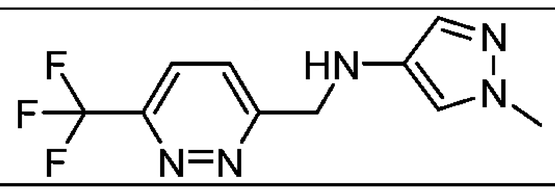
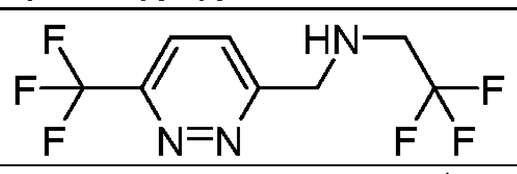
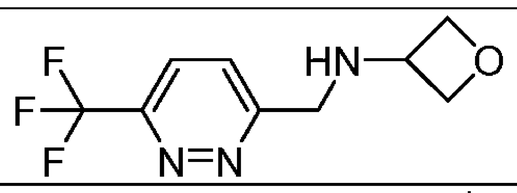
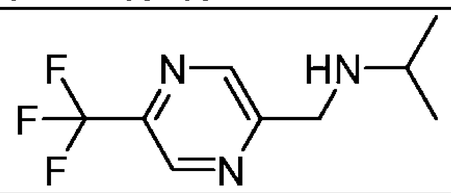
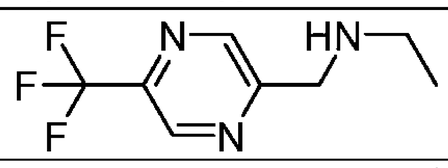
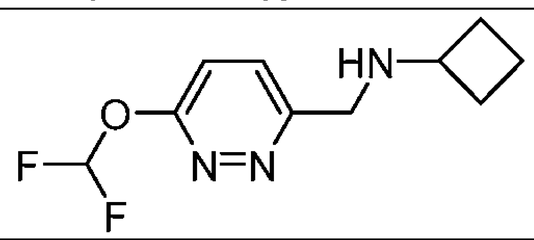
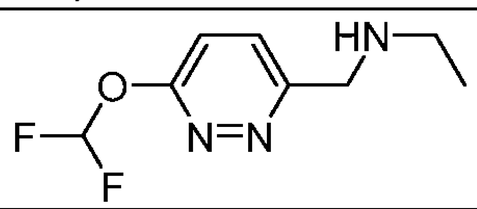
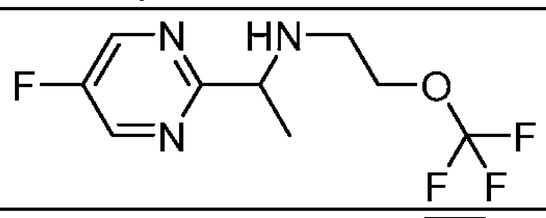
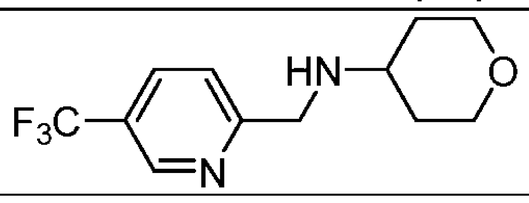
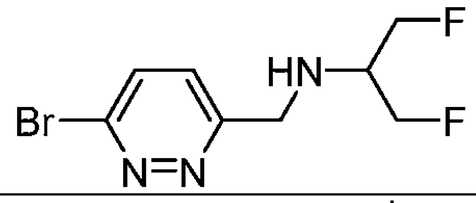
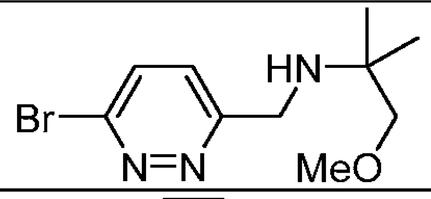
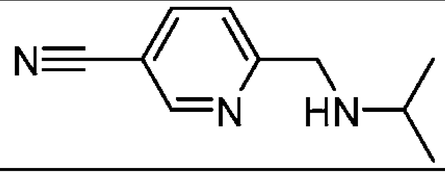
[092] Secondary amines in Table 1 were prepared in a manner similar to that described for Intermediate **2**.

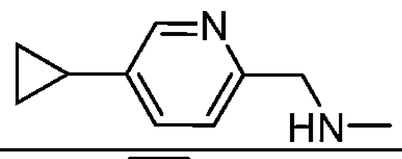
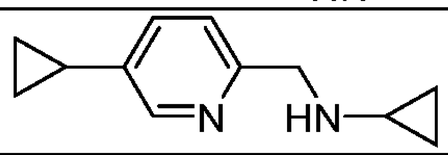
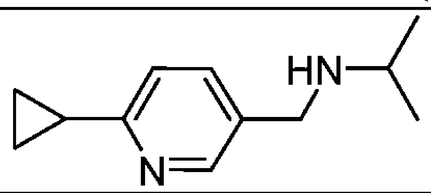
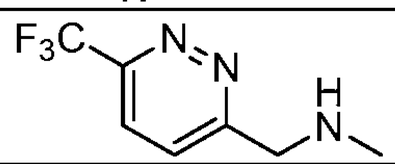
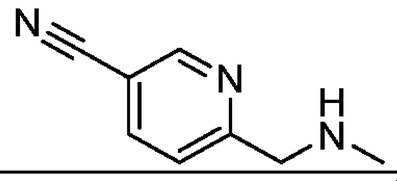
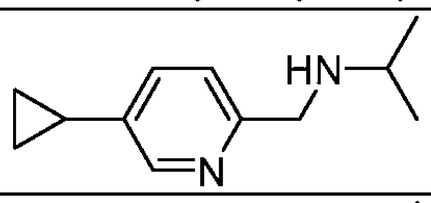
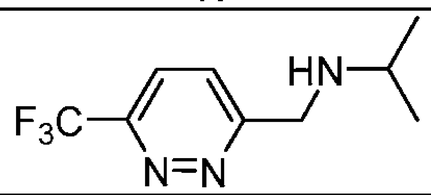
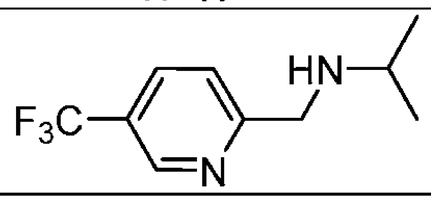
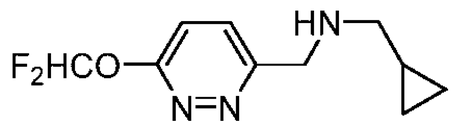
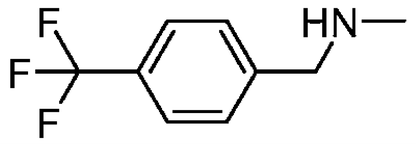
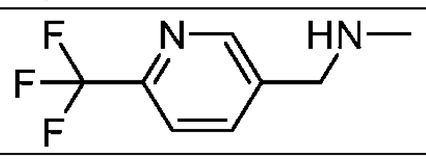
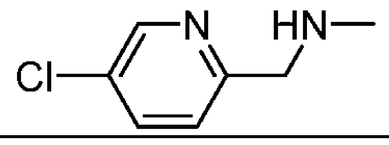
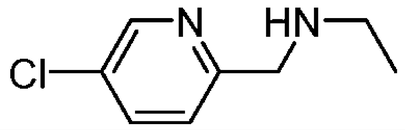
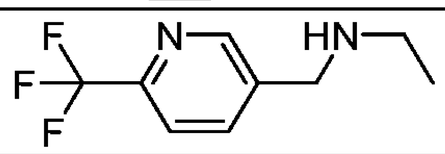
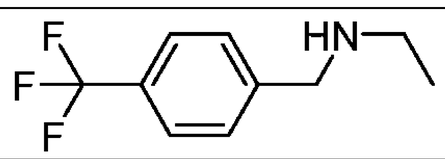
Table 1

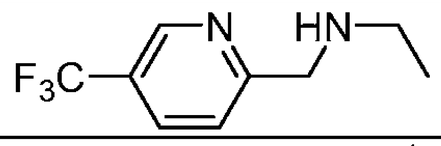
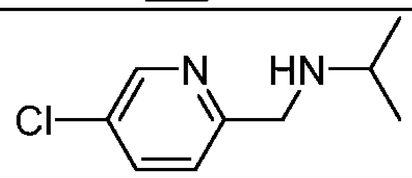
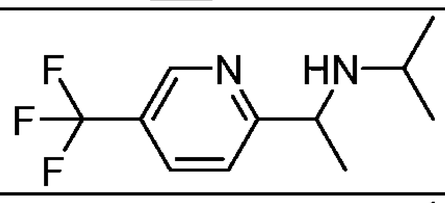
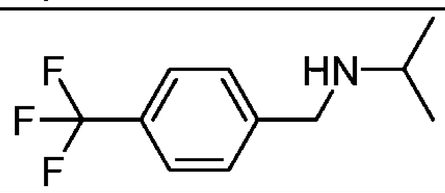
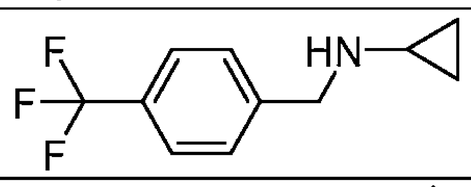
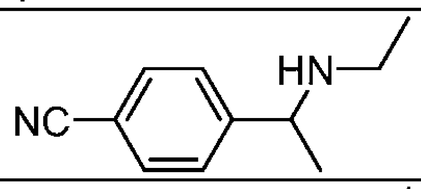
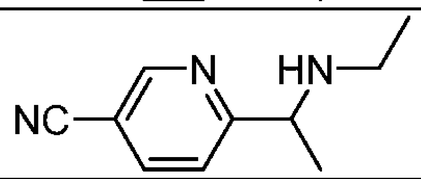
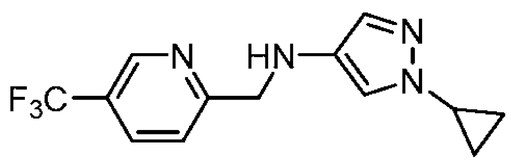
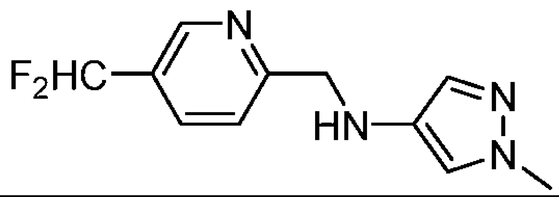
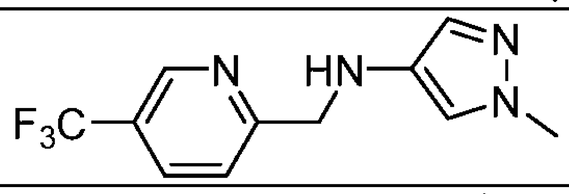
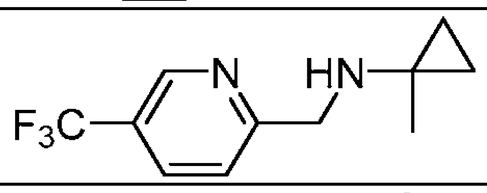
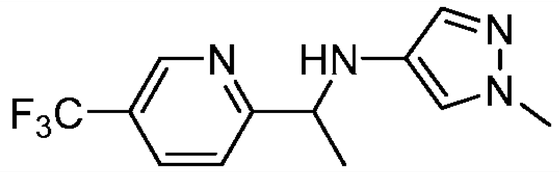
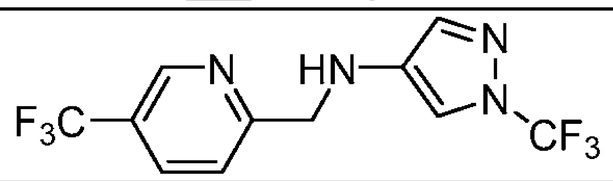
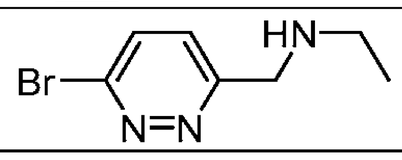
Int. #	Chemical Structure	Name	*m/z* (ESI): $(M+H)^+$
3		1-cyclopropyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)methanamine	231.0
4		1-(3-fluoropyridin-2-yl)-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)methanamine	286.0
5		1-(pyrimidin-2-yl)-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)methanamine	269.0
6		1,3-dimethoxy-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)propan-2-amine	279.2
7		N-((5-(trifluoromethyl)pyridin-2-yl)methyl)cyclopropanamine	217

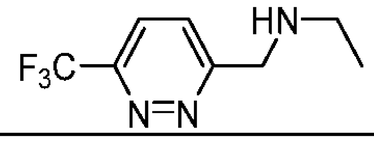
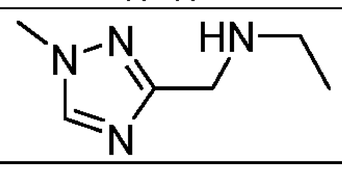
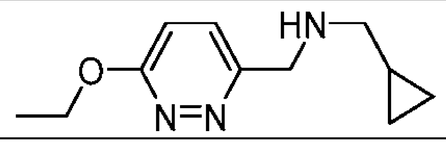
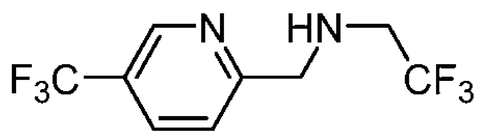
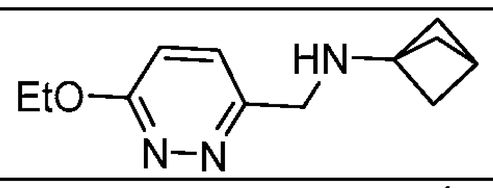
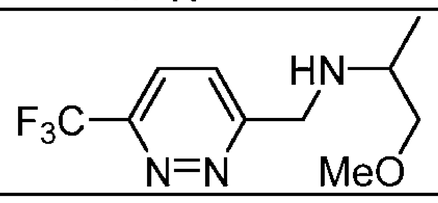
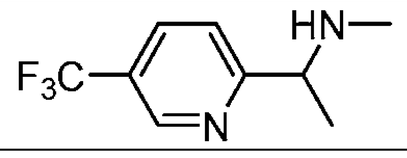
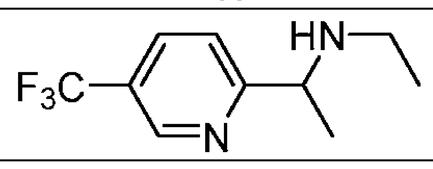
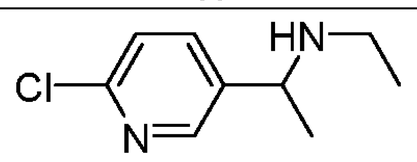
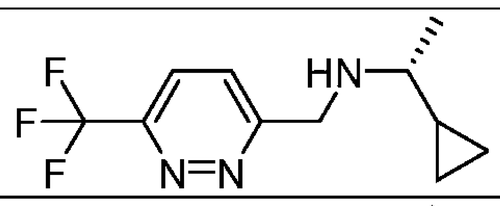
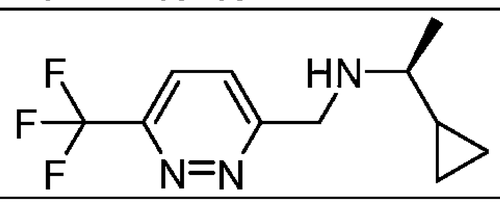
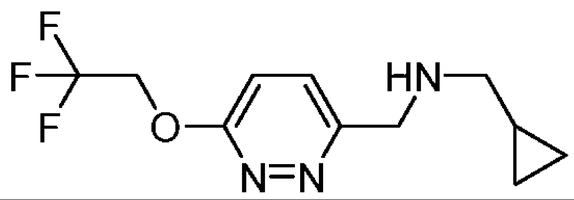
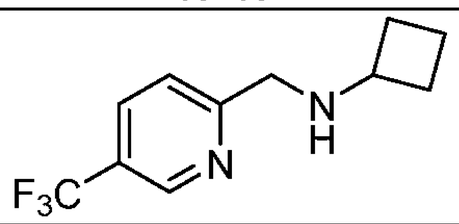
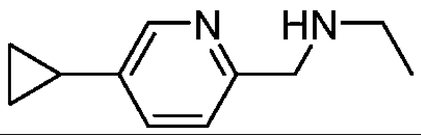
Int. #	Chemical Structure	Name	*m/z* (ESI): $(M+H)^+$
8		6-(((cyclopropylmethyl)amino)methyl)nicotinonitrile	188
9		N-methyl-1-(5-(trifluoromethyl)pyridin-2-yl)methanamine	191.2
10		6-((methylamino)methyl)nicotinonitrile	148.2
11		6-((cyclopropylamino)methyl)nicotinonitrile	174.1
12		N-((6-bromopyridazin-3-yl)methyl)-1-cyclopropyl-2-methoxyethan-1-amine	286 and 288
13		N-((5-(trifluoromethyl)pyridin-2-yl)methyl)bicyclo[1.1.1]pentan-1-amine	243.2
14		6-(((2-cyano-1-cyclopropylethyl)amino)methyl)nicotinonitrile	227.1
15		6-((((1-cyanocyclopropyl)methyl)amino)methyl)nicotinonitrile	213.2
16		1-(6-bromopyridazin-3-yl)-N-methylmethanamine	202 and 204
17		N-((6-bromopyridazin-3-yl)methyl)propan-2-amine	230 and 232
18		1-(6-bromopyridazin-3-yl)-N-(cyclopropylmethyl)methanamine	242.0
19		1-cyclopropyl-N-((6-(trifluoromethyl)pyridazin-3-yl)methyl)methanamine	232.1
20		1-methyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1H-pyrazol-4-amine	257.2
21		1-methyl-N-(4-(trifluoromethyl)benzyl)-1H-pyrazol-4-amine	256.2

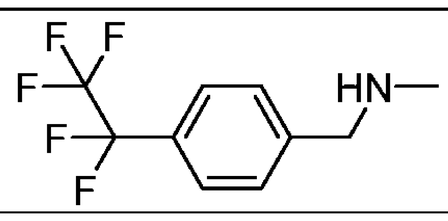
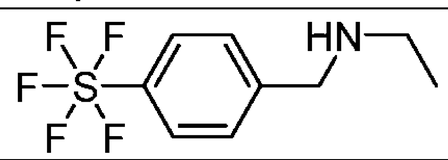
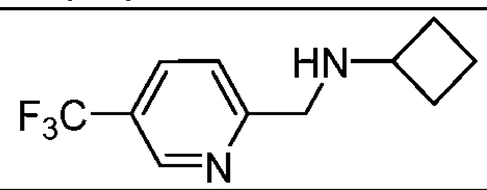
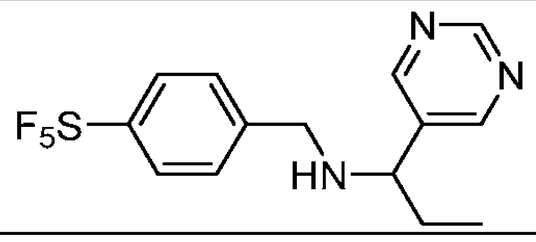
Int. #	Chemical Structure	Name	*m/z* (ESI): $(M+H)^+$
22		N-((5-(trifluoromethoxy)pyridin-2-yl)methyl)propan-2-amine	235.0
23		3-fluoro-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)aniline	271.2
24		N-((6-(trifluoromethyl)pyridazin-3-yl)methyl)cyclobutanamine	232.2
25		3,3-difluoro-N-((6-(trifluoromethyl)pyridazin-3-yl)methyl)cyclobutan-1-amine	268.2
26		1-cyclopropyl-N-((5-(trifluoromethoxy)pyridin-2-yl)methyl)methanamine	247.1
27		N-((6-(trifluoromethyl)pyridazin-3-yl)methyl)cyclopropanamine	218.2
28		N-((5-(difluoromethyl)pyridin-2-yl)methyl)cyclopropanamine	199.1
29		N-((5-bromopyridin-2-yl)methyl)cyclopropanamine	227.0
30		N-((5-(trifluoromethyl)pyridin-2-yl)methyl)propan-2-amine	219.1
31		2-methyl-N-((6-(trifluoromethyl)pyridazin-3-yl)methyl)propan-1-amine	234.2
32		N-((6-bromopyridazin-3-yl)methyl)-2-methylpropan-1-amine	244 and 246
33		1-(5-bromo-6-methylpyridin-2-yl)-N-methylmethanamine	215.0 and 216.9
34		1-(5-bromopyridin-2-yl)-N-methylmethanamine	200.9 and 203.0
35		1-(1-methylcyclopropyl)-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)methanamine	245.1

Int. #	Chemical Structure	Name	*m/z* (ESI): $(M+H)^+$
36		2,2-dimethyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)propan-1-amine	247.2
37		1-methyl-N-((6-(trifluoromethyl)pyridazin-3-yl)methyl)-1H-pyrazol-4-amine	258.1
38		2,2,2-trifluoro-N-((6-(trifluoromethyl)pyridazin-3-yl)methyl)ethan-1-amine	260.05
39		N-((6-(trifluoromethyl)pyridazin-3-yl)methyl)oxetan-3-amine	234.1
40		N-((5-(trifluoromethyl)pyrazin-2-yl)methyl)propan-2-amine	220.15
41		N-((5-(trifluoromethyl)pyrazin-2-yl)methyl)ethanamine	206.2
42		N-((6-(difluoromethoxy)pyridazin-3-yl)methyl)cyclobutanamine	230.2
43		N-((6-(difluoromethoxy)pyridazin-3-yl)methyl)ethanamine	204.2
44		1-(5-fluoropyrimidin-2-yl)-N-(2-(trifluoromethoxy)ethyl)ethan-1-amine	254.2
45		N-((5-(trifluoromethyl)pyridin-2-yl)methyl)tetrahydro-2H-pyran-4-amine	261.1
46		N-((6-bromopyridazin-3-yl)methyl)-1,3-difluoropropan-2-amine	266.0 and 268.0
47		N-((6-bromopyridazin-3-yl)methyl)-1-methoxy-2-methylpropan-2-amine	274.0 and 276.0
48		6-((isopropylamino)methyl)nicotinonitrile	

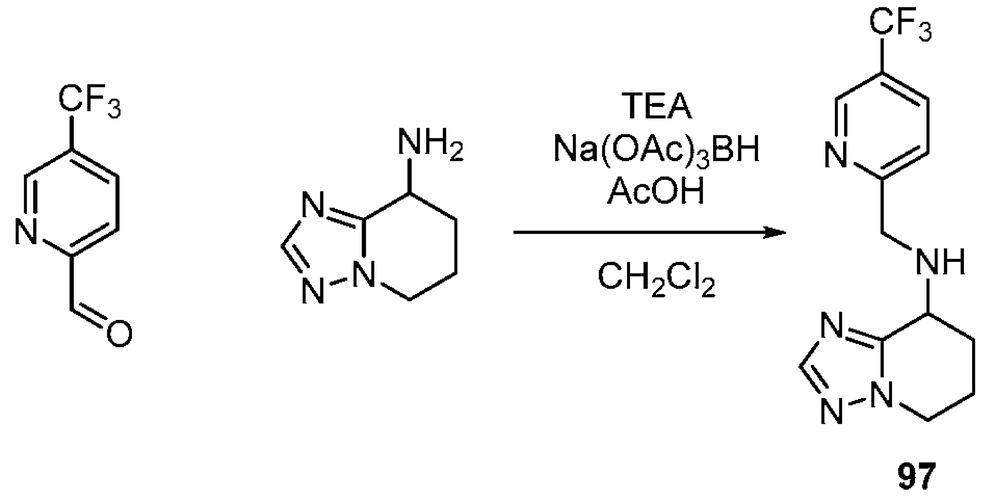
Int. #	Chemical Structure	Name	*m/z* (ESI): $(M+H)^+$
49		1-(5-cyclopropylpyridin-2-yl)-N-methylmethanamine	
50		N-((5-cyclopropylpyridin-2-yl)methyl)cyclopropanamine	
51		N-((6-cyclopropylpyridin-3-yl)methyl)propan-2-amine	
52		N-methyl-1-(6-(trifluoromethyl)pyridazin-3-yl)methanamine	
53		6-((methylamino)methyl)nicotinonitrile	
54		N-((5-cyclopropylpyridin-2-yl)methyl)propan-2-amine	
55		N-((6-(trifluoromethyl)pyridazin-3-yl)methyl)propan-2-amine	
56		N-((5-(trifluoromethyl)pyridin-2-yl)methyl)propan-2-amine	
57		1-cyclopropyl-N-((6-(difluoromethoxy)pyridazin-3-yl)methyl)methanamine	230.0
58		N-methyl-1-(4-(trifluoromethyl)phenyl)methanamine	190.0
59		N-methyl-1-(6-(trifluoromethyl)pyridin-3-yl)methanamine	191.0
60		1-(5-chloropyridin-2-yl)-N-methylmethanamine	179.0 (+Na)
61		N-((5-chloropyridin-2-yl)methyl)ethanamine	171.0
62		N-((6-(trifluoromethyl)pyridin-3-yl)methyl)ethanamine	205.0
63		N-(4-(trifluoromethyl)benzyl)ethanamine	204.0

Int. #	Chemical Structure	Name	*m/z* (ESI): $(M+H)^+$
64		N-((5-(trifluoromethyl)pyridin-2-yl)methyl)ethanamine	205.0
65		N-((5-chloropyridin-2-yl)methyl)propan-2-amine	185.0
66		N-(1-(5-(trifluoromethyl)pyridin-2-yl)ethyl)propan-2-amine	233.0
67		N-(4-(trifluoromethyl)benzyl)propan-2-amine	218.0
68		N-(4-(trifluoromethyl)benzyl)cyclopropanamine	216.0
69		4-(1-(ethylamino)ethyl)benzonitrile	175.0
70		6-(1-(ethylamino)ethyl)nicotinonitrile	176.0
71		1-cyclopropyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1H-pyrazol-4-amine	283.0
72		N-((5-(difluoromethyl)pyridin-2-yl)methyl)-1-methyl-1H-pyrazol-4-amine	239.2
73		1-methyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1H-pyrazol-4-amine	257.2
74		1-methyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)cyclopropan-1-amine	231.0
75		1-methyl-N-(1-(5-(trifluoromethyl)pyridin-2-yl)ethyl)-1H-pyrazol-4-amine	271.2
76		1-(trifluoromethyl)-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1H-pyrazol-4-amine	311.0
77		*N*-((6-bromopyridazin-3-yl)methyl)ethanamine	216.1 and 218.2

Int. #	Chemical Structure	Name	*m/z* (ESI): $(M+H)^+$
78		*N*-((6-(trifluoromethyl)pyridazin-3-yl)methyl)ethanamine	206.2
79		*N*-((6-ethoxypyridazin-3-yl)methyl)ethanamine	182.2
80		*N*-((1-methyl-1H-1,2,4-triazol-3-yl)methyl)ethanamine	141.05
81		1-cyclopropyl-*N*-((6-ethoxypyridazin-3-yl)methyl)methanamine	208.25
82		2,2,2-trifluoro-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)ethan-1-amine	
83		N-((6-ethoxypyridazin-3-yl)methyl)bicyclo[1.1.1]pentan-1-amine	
84		1-methoxy-N-((6-(trifluoromethyl)pyridazin-3-yl)methyl)propan-2-amine	
85		N-methyl-1-(5-(trifluoromethyl)pyridin-2-yl)ethan-1-amine	205.1
86		N-ethyl-1-(5-(trifluoromethyl)pyridin-2-yl)ethan-1-amine	219.1
87		1-(6-chloropyridin-3-yl)-N-ethylethan-1-amine	185.0
88		(*R*)-1-cyclopropyl-N-((6-(trifluoromethyl)pyridazin-3-yl)methyl)ethan-1-amine	246.1
89		(*S*)-1-cyclopropyl-N-((6-(trifluoromethyl)pyridazin-3-yl)methyl)ethan-1-amine	246.3
90		1-cyclopropyl-N-((6-(2,2,2-trifluoroethoxy)pyridazin-3-yl)methyl)methanamine	262.2
91		N-((5-(trifluoromethyl)pyridin-2-yl)methyl)cyclobutanamine	232.1
92		N-((5-cyclopropylpyridin-2-yl)methyl)ethanamine	177.2

Int. #	Chemical Structure	Name	*m/z* (ESI): $(M+H)^+$
93		N-methyl-1-(4-(perfluoroethyl)phenyl)methanamine	240.1
94		N-(4-(pentafluoro-l6-sulfaneyl)benzyl)ethanamine	262.0
95		N-((5-(trifluoromethyl)pyridin-2-yl)methyl)cyclobutanamine	232.1
96		N-(4-(pentafluoro-l6-sulfaneyl)benzyl)-1-(pyrimidin-5-yl)propan-1-amine	354.2

[093] Intermediate 97: N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-8-amine



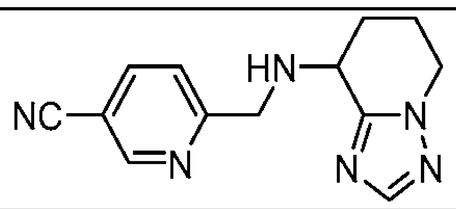
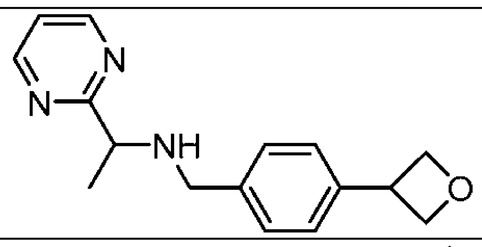
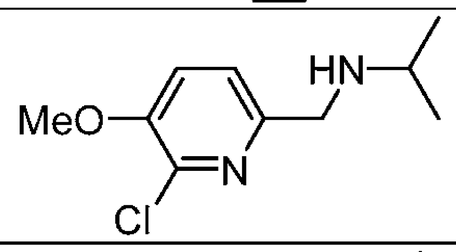
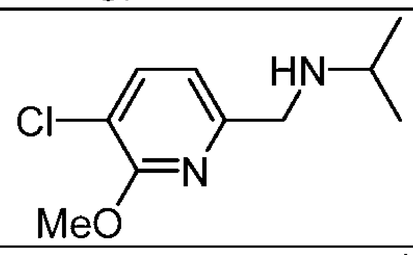
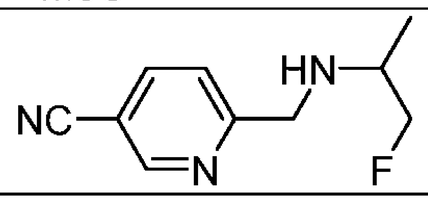
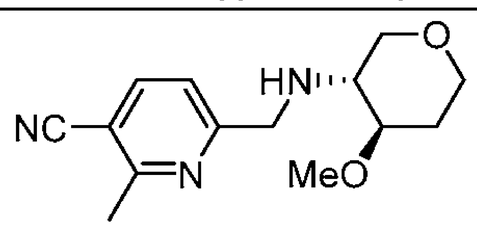
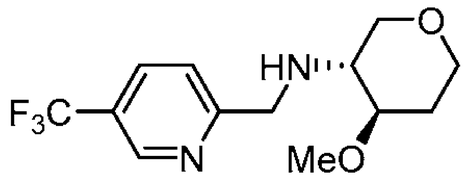
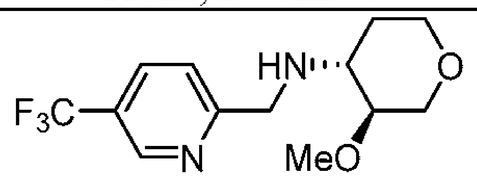
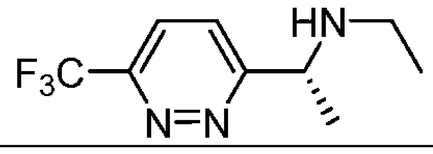
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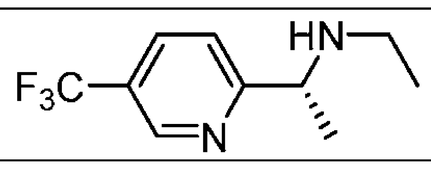
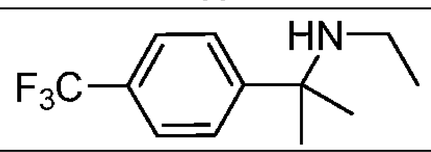
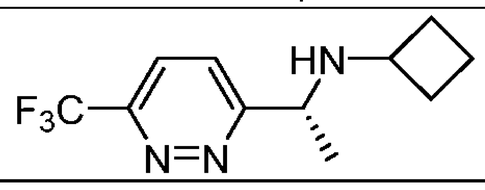
[094] To a stirred mixture of 5-(trifluoromethyl)picolinaldehyde (534 mg, 3.05 mmol, Chemshuttle) and 5,6,7,8-tetrahydro[1,2,4]triazolo[1,5-a]pyridin-8-amine (430 mg, 3.11 mmol, Enamine) in DCM (8 mL) was added triethylamine (315 mg, 0.437 mL, 3.11 mmol, Sigma-Aldrich Corporation) followed, 5 min later, by glacial acetic acid (224 mg, 0.216 mL, 3.73 mmol, Sigma-Aldrich Corporation). The resulting mixture was stirred at rt for 15 min before sodium triacetoxyborohydride (857 mg, 4.05 mmol, Sigma-Aldrich Corporation) was added in one portion as a solid. The resulting mixture was stirred at rt for 25 min. The crude mixture was directly loaded onto a silica gel precolumn (25 g) and subjected to combi-flash column chromatography with a 24-g ISCO gold column eluting with MeOH (with 0.5 % ammonium hydroxide)/DCM (1-20%) to give, after azeotroping with toluene, N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-8-amine (350 mg, 1.177 mmol, 37.8 % yield) as a colorless oil. *m/z* (ESI): 298.2 $(M+H)^+$. ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 8.78 (d, J=1.05 Hz, 1H), 7.81-7.89 (m, 2H), 7.50 (d, J=8.15 Hz, 1H), 4.09-4.29 (m,

4H), 3.97-4.06 (m, 2H), 2.12-2.33 (m, 2H), 1.83-2.04 (m, 2H). ^{19}F NMR (376 MHz, CHLOROFORM-d) δ -62.34 (s, 3F).

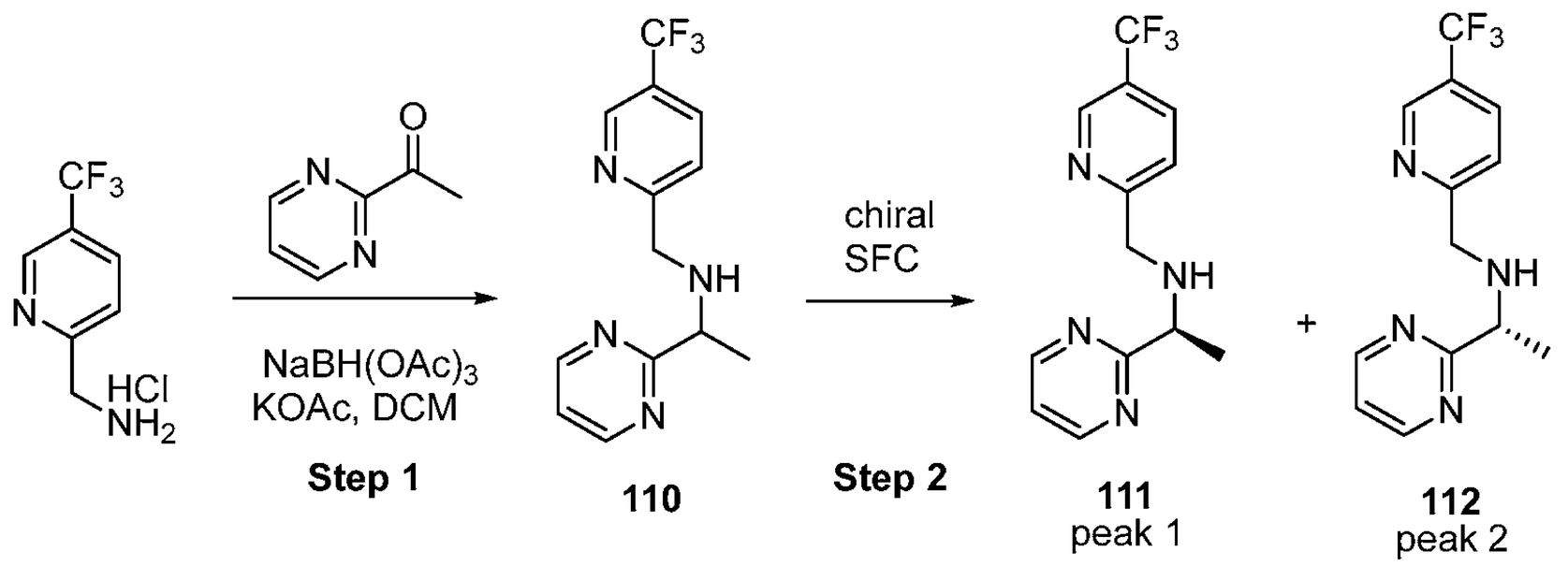
[095] Secondary amines in Table 2 were prepared in a manner similar to that described for Intermediate **97**. **106-109** were derived from commercially available, chiral amines.

Table 2

Int. #	Chemical Structure	Name	*m/z* (ESI): $(M+H)^+$
98		6-(((5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-8-yl)amino)methyl)nicotinonitrile	255.1
99		N-(4-(oxetan-3-yl)benzyl)-1-(pyrimidin-2-yl)ethan-1-amine	270.2
100		N-((6-chloro-5-methoxypyridin-2-yl)methyl)propan-2-amine	215.2
101		N-((5-chloro-6-methoxypyridin-2-yl)methyl)propan-2-amine	215.2
102		6-(((1-fluoropropan-2-yl)amino)methyl)nicotinonitrile	194.2
103	 Trans, racemate	6-((((3R,4R)-4-methoxytetrahydro-2H-pyran-3-yl)amino)methyl)-2-methylnicotinonitrile, relative	262.2
104	 Trans, racemate	(3R,4R)-4-methoxy-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)tetrahydro-2H-pyran-3-amine, relative	291.2
105	 Trans, racemate	(3S,4R)-3-methoxy-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)tetrahydro-2H-pyran-4-amine, relative	291.2
106		(R)-N-ethyl-1-(6-(trifluoromethyl)pyridazin-3-yl)ethan-1-amine	220.1

Int. #	Chemical Structure	Name	*m/z* (ESI): $(M+H)^+$
107		(R)-N-ethyl-1-(5-(trifluoromethyl)pyridin-2-yl)ethan-1-amine	219.1
108		N-ethyl-2-(4-(trifluoromethyl)phenyl)propan-2-amine	232.1
109		(R)-N-(1-(6-(trifluoromethyl)pyridazin-3-yl)ethyl)cyclobutanamine	246.0

[096] Intermediate 110: (R)-1-(pyrimidin-2-yl)-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)ethan-1-amine.



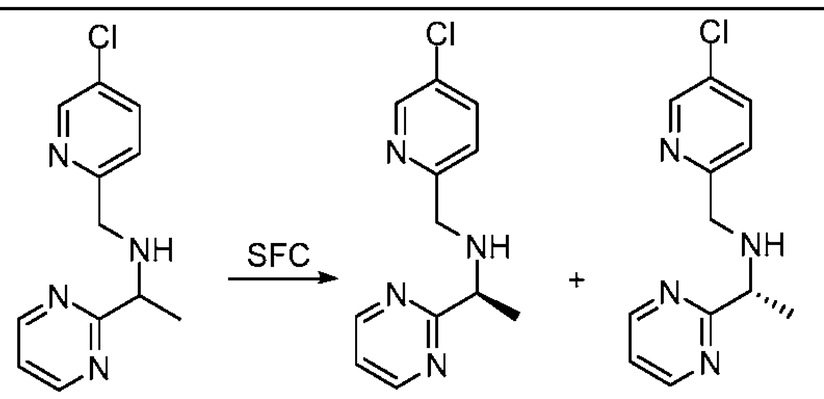
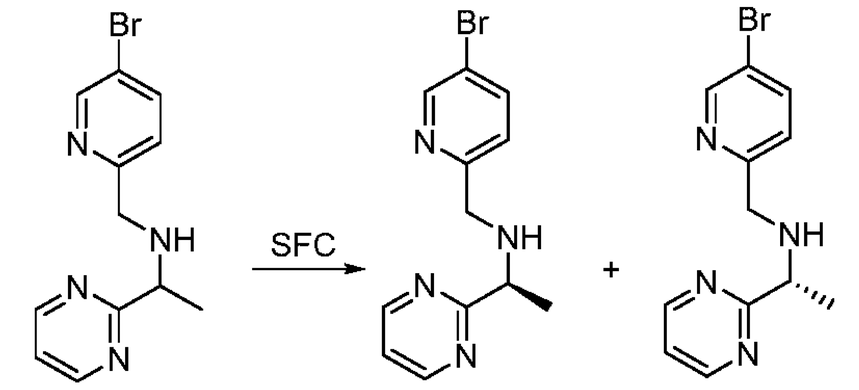
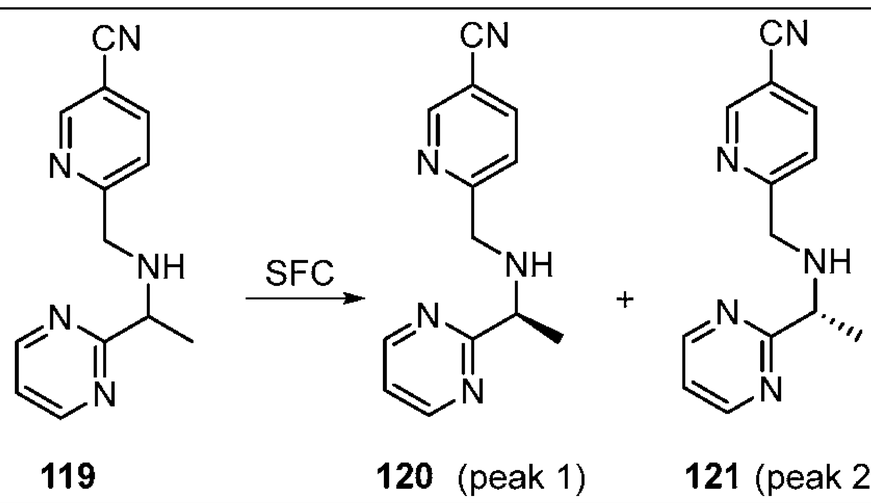
[097] Step 1. To a stirred solution of (5-(trifluoromethyl)pyridin-2-yl)methanamine hydrochloride (115 g, 541 mmol) and 1-(pyrimidin-2-yl)ethan-1-one (76 g, 622 mmol) in DCM (3.5 L) was added potassium acetate (63.7 g, 649 mmol). The mixture was stirred for 30 min then treated with sodium triacetoxyborohydride (149 g, 703 mmol). After stirring for 1.5 h, the reaction mixture was diluted with water (2 L), treated with 1 N HCl (2 L), and extracted with DCM (1 L). The layers were separated. The aqueous layer was treated with 10% sodium hydroxide to adjust the pH to 12 and extracted with DCM (3 x 2 L). The combined organic layer was dried over Na_2SO_4, filtered and concentrated. The crude material was purified by silica gel chromatography (2% MeOH in DCM) to give 1-(pyrimidin-2-yl)-*N*-((5-(trifluoromethyl)pyridin-2-yl)methyl)ethan-1-amine (**101**, 97 g, 344 mmol, 63% yield) as a brown oil. *m/z* (ESI): 283.0 $(M+H)^+$. ^{1}H NMR (400 MHz, Chloroform-*d*): δ ppm 8.81 (dt, *J* = 2.2, 1.0 Hz, 1 H), 8.74 (d, *J* = 4.9 Hz, 2 H), 7.88 (dd, *J* = 8.2, 2.3 Hz, 1 H), 7.54 (d, *J* = 8.2 Hz, 1 H), 7.20 (t, *J* = 4.9 Hz, 1 H), 4.10 (q, *J* = 6.8 Hz, 1 H), 3.94 (d, *J* = 2.9 Hz, 2 H), 1.53 (d, *J* = 6.8 Hz, 3 H).

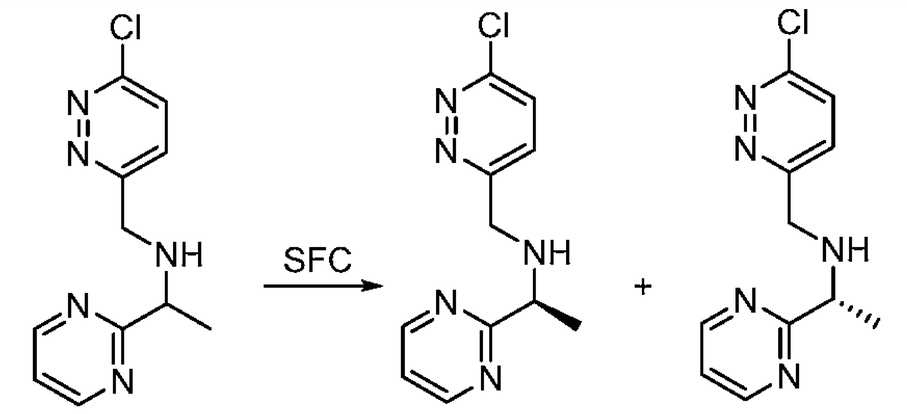
[098] Step 2. The racemic secondary amine **110** (44 g) was dissolved in 200 mL of MeOH and subjected to chiral SFC using a Chiralpak AD-H column (250 x30 mm, 5μ) with a mobile phase of 90%

Liquid CO_2 and 10% EtOH with 0.5% DEA using a flowrate of 100 mL/ min. The 1st eluting peak was (S)-1-(pyrimidin-2-yl)-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)ethan-1-amine (**111**, 18 g, > 99% *ee*) and the 2nd eluting peak was (R)-1-(pyrimidin-2-yl)-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)ethan-1-amine (**112**, 19 g, > 99% *ee*).

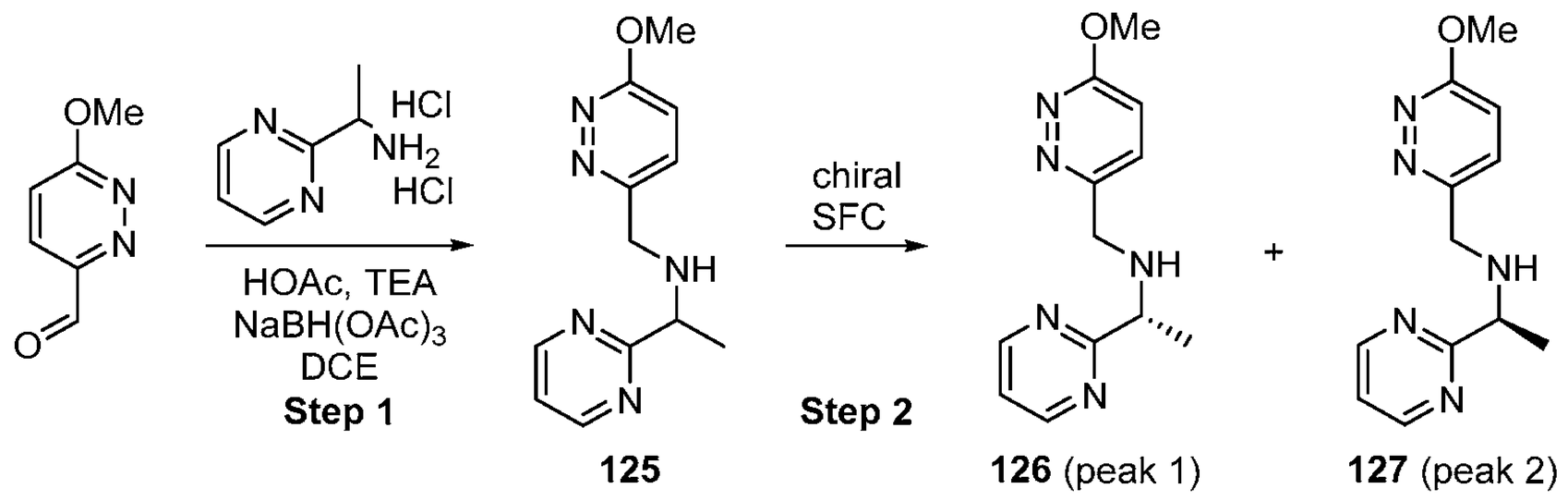
[099] Racemic amines in Table 3 were prepared in a fashion similar to that described above for amine **110**. The racemic amines were subjected to chiral SFC to provide enantiomerically pure amines (> 99% *ee*).

Table 3

Secondary Amines	SFC Conditions	*m/z* (ESI): $(M+H)^+$
 **113** **114** (peak 1) **115** (peak 2)	Chiralpak AD-H column (250×30 mm, 5 µm) using a mobile phase of 75% Liquid CO_2 and 25% EtOH with 0.3% Et_2NH	249.0
 **116** **117** (peak 1) **118** (peak 2)	ChiralPak AD-H column (250×30 mm, 5 µm) with a mobile phase of 70% Liquid CO_2 and 30% EtOH with 0.5% Et_2NH	293/295
 **119** **120** (peak 1) **121** (peak 2)	Chiral Technologies AZ column (250x 21 mm, 5 µm) with a mobile phase of 85% Liquid CO_2 and 15% MeOH with 0.2% TEA	240.0

Secondary Amines	SFC Conditions	*m/z* (ESI): $(M+H)^+$
 **122** **123** (peak 1) **124** (peak 2)	Chiral Technologies AD column (250 x 21 mm, 5 µm)with a mobile phase 85% Liquid CO_2 and 15% MeOH with 1.0% TEA using a flowrate of 100 mL/min	249.9

[0100] Intermediate 125: (R)-N-((6-methoxypyridazin-3-yl)methyl)-1-(pyrimidin-2-yl)ethan-1-amine.



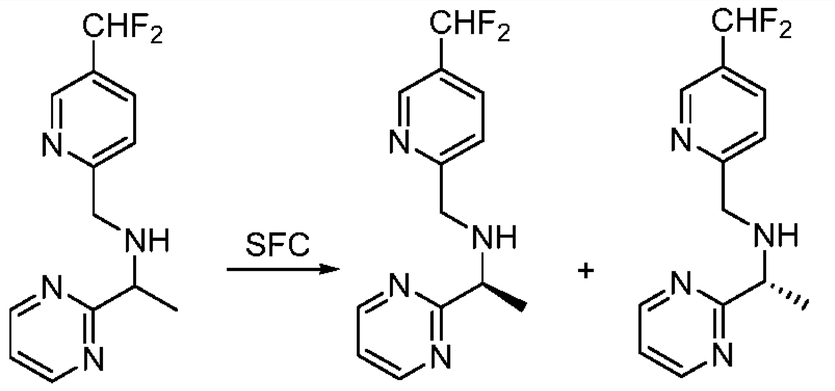
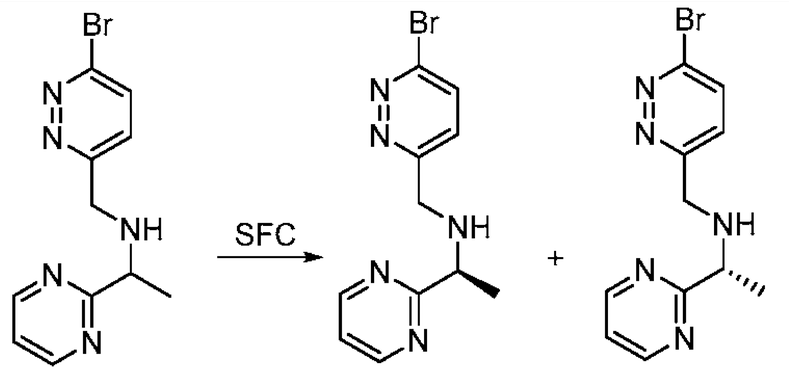
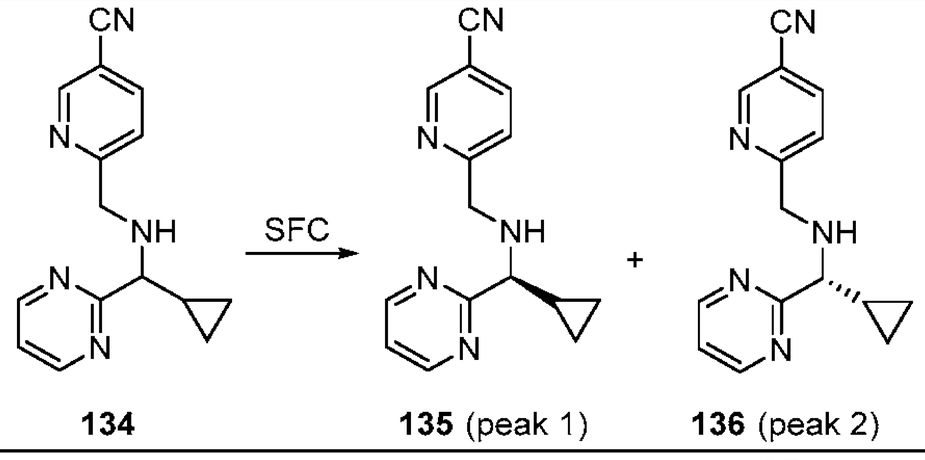
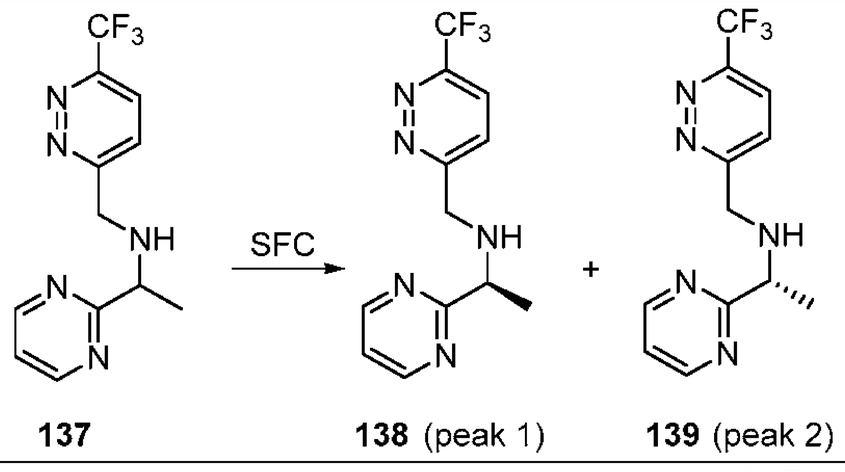
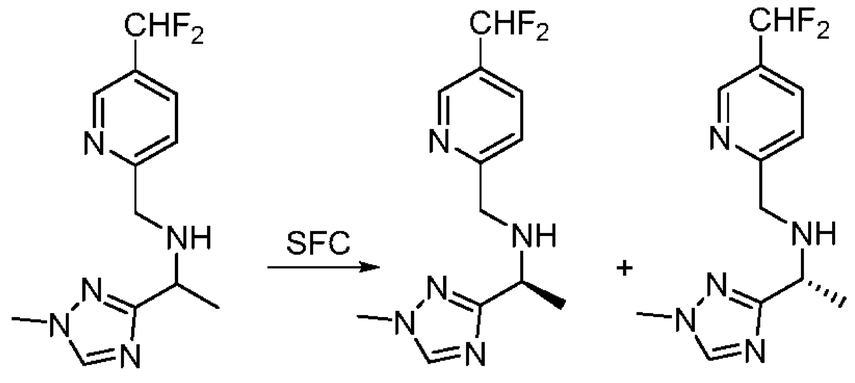
125 **126** (peak 1) **127** (peak 2)

[0101] Step 1. A mixture of 6-methoxy-pyridazine-3-carbaldehyde (0.49 g, 3.54 mmol, Princeton BioMolecular Research, Inc.), 1-(pyrimidin-2-yl)ethan-1-amine dihydrochloride (0.73 g, 3.72 mmol, Enamine), 1,2-dichloroethane (30 mL), and acetic acid (0.22 mL, 3.90 mmol) was stirred at RT for 10 min, then sodium triacetoxyborohydride (1.013 g, 4.78 mmol) was added. The mixture was stirred at RT for 30 min then neutralized with saturated aqueous Na_2CO_3 solution. The crude was extracted with DCM. The organic phase was dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel chromatography (30-100% EtOAc/EtOH (3/1) in heptane) to provide N-((6-methoxypyridazin-3-yl)methyl)-1-(pyrimidin-2-yl)ethan-1-amine (**125**, 0.84 g, 96% yield) as an orange oil. *m/z* (ESI): 246 $(M+H)^+$.

[0102] Step 2. The racemic amine **125** was subjected to chiral SFC using a Chiral Technologies IC column (250 x 30 mm, 5 µm) with a mobile phase of 70% liquid CO_2 and 30% MeOH with 0.2% TEA using a flowrate of 150 mL/min. The 1st eluting peak was (R)-N-((6-methoxypyridazin-3-yl)methyl)-1-(pyrimidin-2-yl)ethan-1-amine (**126**, 369 mg, > 99% *ee*) . The 2nd eluting peak was (S)-N-((6-methoxypyridazin-3-yl)methyl)-1-(pyrimidin-2-yl)ethan-1-amine (**127**, 374 mg, > 99% *ee*).

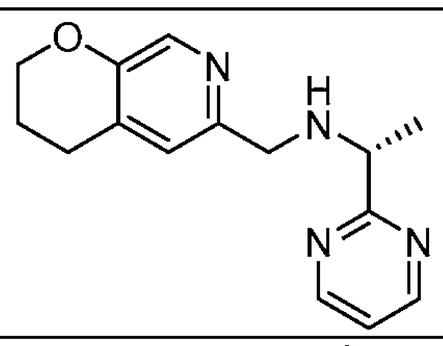
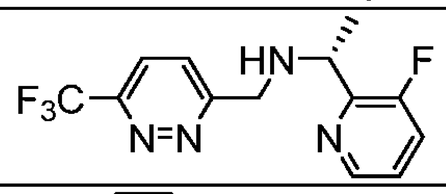
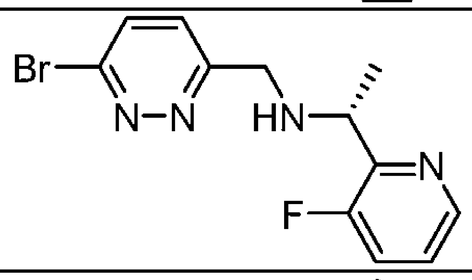
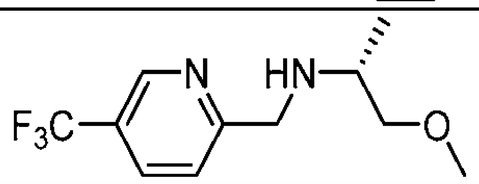
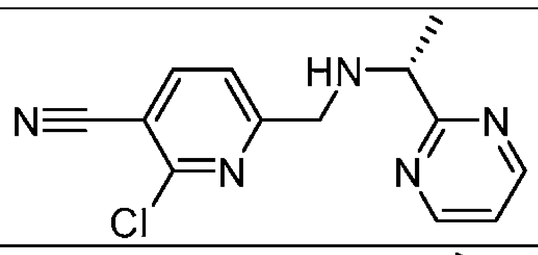
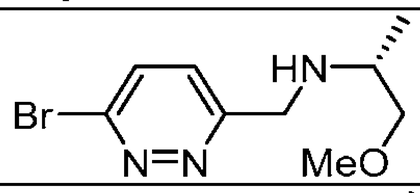
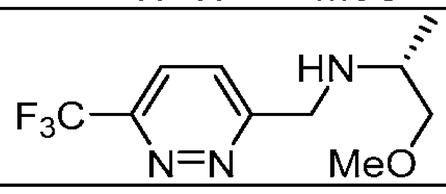
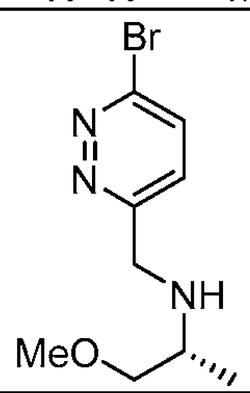
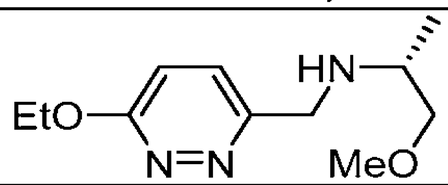
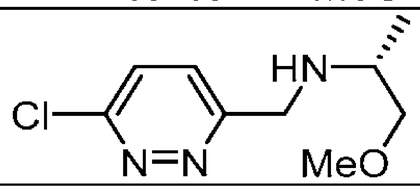
[0103] Racemic amines in Table 4 were prepared in a fashion similar to that described above for amine **125**. The racemic amines were subjected to chiral SFC to provide enantiomerically pure amines (> 99% *ee*).

Table 4

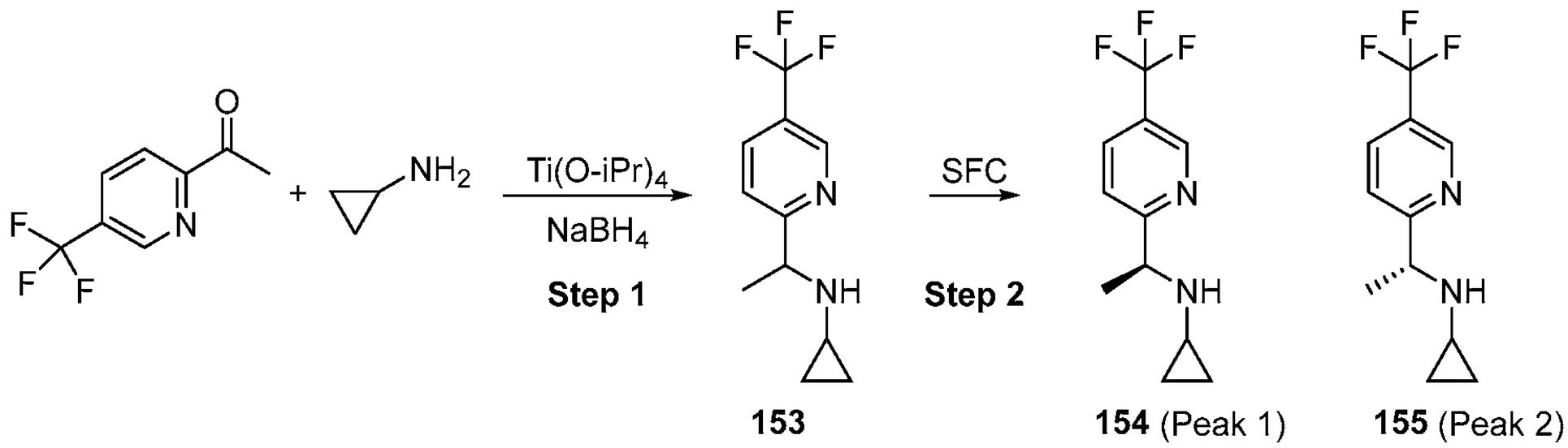
Secondary Amines	SFC Conditions	*m/z* (ESI): $(M+H)^+$
 **128** **129** (peak 1) **130** (peak 2)	Chiral Technologies AD column (250x 21 mm, 5 µm) with a mobile phase of 85% Liquid CO_2 and 15% EtOH with 0.2% TEA	265.1
 **131** **132** (peak 1) **133** (peak 2)	Chiral Technologies AD column (250 x 30 mm, 5 µm) with a mobile phase of 70% Liquid CO_2 and 30% EtOH with 0.2% TEA	293.9/ 295.9
 **134** **135** (peak 1) **136** (peak 2)	Chiral Technologies AZ column (250 x 21 mm, 5 µm) with a mobile phase of 75% Liquid CO_2 and 25% EtOH with 0.2% TEA	266.0
 **137** **138** (peak 1) **139** (peak 2)	Chiral Technologies AD column (250 X 21 mm, 5 µm) with a mobile phase of 80% Liquid CO_2 and 20% MeOH with 0.2% TEA using a flowrate of 80 mL/min	284.1
 **140** **141** (peak 1) **142** (peak 2)	Chiral IG column (250 X 20 mm, 5 µm) with a mobile phase of 80% Liquid CO_2 and 20% MeOH with 0.1% DEA using a flowrate of 80 mL/min	268.2

[0104] Secondary amines in Table 5 were prepared in a manner similar to that described for amine **125** and were derived from commercially available enantiomerically pure reagents.

Table 5

Int. #	Chemical Structure	Name	*m/z* (ESI): $(M+H)^+$
143		(R)-N-((3,4-dihydro-2H-pyrano[2,3-c]pyridin-6-yl)methyl)-1-(pyrimidin-2-yl)ethan-1-amine	271.2
144		(R)-1-(3-fluoropyridin-2-yl)-N-((6-(trifluoromethyl)pyridazin-3-yl)methyl)ethan-1-amine	301.0
145		(R)-N-((6-bromopyridazin-3-yl)methyl)-1-(3-fluoropyridin-2-yl)ethan-1-amine	311/313
146		(R)-1-methoxy-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)propan-2-amine	249.0
147		(R)-2-chloro-6-(((1-(pyrimidin-2-yl)ethyl)amino)methyl)nicotinonitrile	274.2
148		(R)-N-((6-bromopyridazin-3-yl)methyl)-1-methoxypropan-2-amine	260.1, 262.0
149		(R)-1-methoxy-N-((6-(trifluoromethyl)pyridazin-3-yl)methyl)propan-2-amine	
150		(R)-N-((6-bromopyridazin-3-yl)methyl)-1-methoxypropan-2-amine	260.1 and 262.0
151		(R)-N-((6-ethoxypyridazin-3-yl)methyl)-1-methoxypropan-2-amine	
152		(R)-N-((6-chloropyridazin-3-yl)methyl)-1-methoxypropan-2-amine	

[0105] Intermediate 153: N-(1-(5-(trifluoromethyl)pyridin-2-yl)ethyl)cyclopropanamine

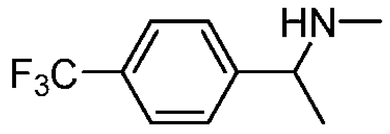
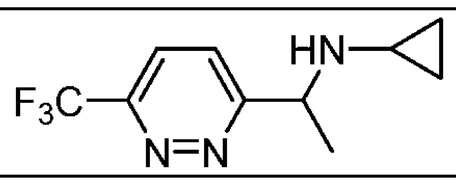


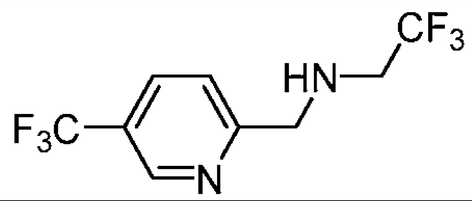
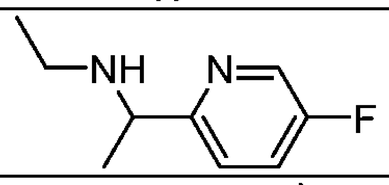
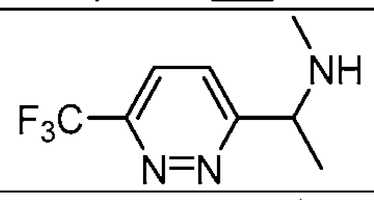
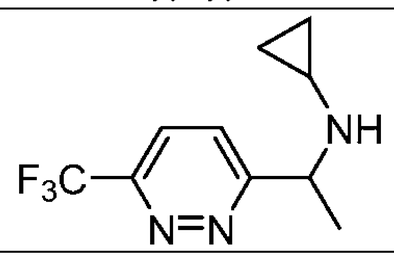
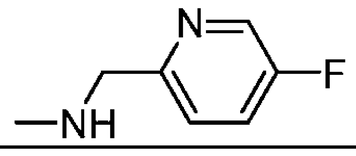
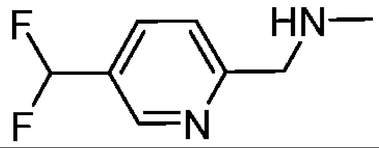
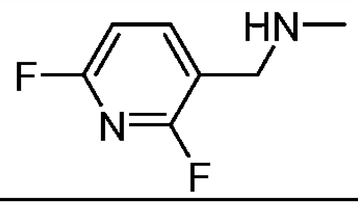
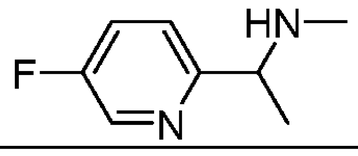
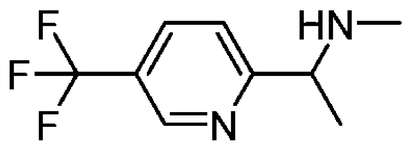
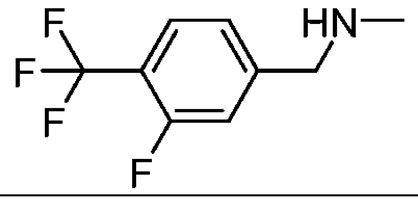
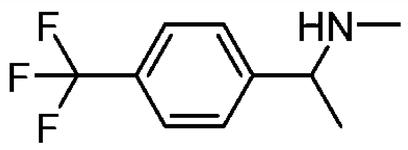
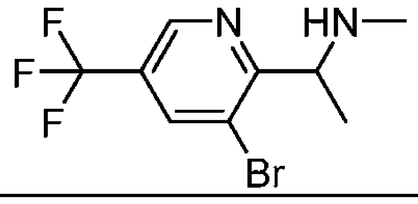
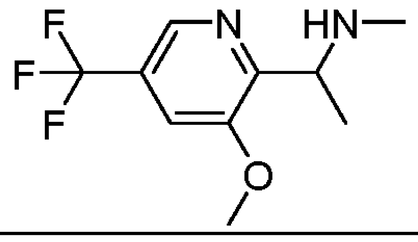
[0106] Step 1. To a mixture of 1-(5-(trifluoromethyl)pyridin-2-yl)ethan-1-one (0.71 g, 3.75 mmol, Enamine), 1,2-dichloroethane (20 mL), and cyclopropanamine (0.257 g, 4.50 mmol, Acros) was added titanium (IV) isopropoxide (1.280 g, 1.334 mL, 4.50 mmol, Aldrich). The mixture was stirred at room temperature overnight, then MeOH (2 mL) was added followed by sodium borohydride (0.142 g, 3.75 mmol, Aldrich). The mixture was stirred for 30 min until LCMS showed the product. The mixture was basified with saturated aqueous Na_2CO_3 and extracted with EtOAc. The organic phase was dried over Na_2SO_4, filtered and concentrated in vacuo. The residue was purified by silica gel chromatography: 0-100% EtOAc in heptane. The racemic product (**153**, 631 mg, 73% yield) was obtained as light-yellow oil. *m/z* (ESI): 231 $(M+H)^+$

[0107] Step 2. The oil was purified by Prep SFC using 2x Chiralpak IG column (250 X 21 mm, 5um) with a mobile phase of 90% Liquid CO_2 and 10% Heptane:EtOH (15:85, v:v) using a flowrate of 70 mL/min. The 1st eluting peak was assigned (S)-N-(1-(5-(trifluoromethyl)pyridin-2-yl)ethyl)cyclopropanamine (**154**, 198 mg, 97.72% *ee*) . The 2nd eluting peak was assigned (R)-N-(1-(5-(trifluoromethyl)pyridin-2-yl)ethyl)cyclopropanamine (**155**, 188 mg, 98.9% *ee*). Absolute stereochemistry was arbitrarily assigned.

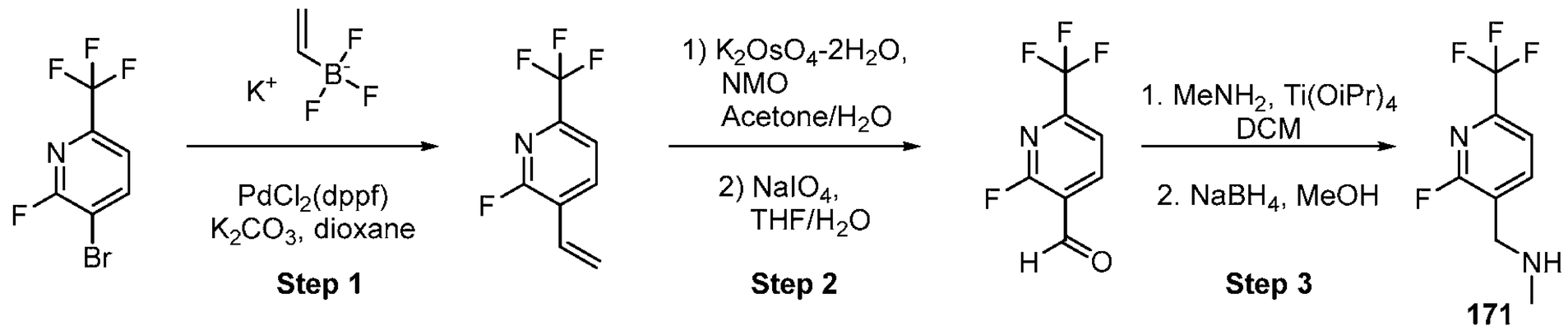
[0108] Secondary amines in Table 6 were prepared in a manner similar to that described for amine **153**

Table 6

Int. #	Chemical Structure	Name	*m/z* (ESI): $(M+H)^+$
156		N-methyl-1-(4-(trifluoromethyl)phenyl)ethan-1-amine	204.2
157		N-(1-(6-(trifluoromethyl)pyridazin-3-yl)ethyl)cyclopropanamine	231.2

Int. #	Chemical Structure	Name	*m/z* (ESI): $(M+H)^+$
158		2,2,2-trifluoro-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)ethan-1-amine	259.0
159		N-ethyl-1-(5-fluoropyridin-2-yl)ethan-1-amine	169.2
160		N-ethyl-1-(6-(trifluoromethyl)pyridazin-3-yl)ethan-1-amine	206.0
161		N-(1-(6-(trifluoromethyl)pyridazin-3-yl)ethyl)cyclopropanamine	232.2
162		1-(5-fluoropyridin-2-yl)-N-methylmethanamine	141.2
163		1-(5-(difluoromethyl)pyridin-2-yl)-N-methylmethanamine	173.0
164		1-(2,6-difluoropyridin-3-yl)-N-methylmethanamine	159.2
165		1-(5-fluoropyridin-2-yl)-N-methylethan-1-amine	155.2
166		N-methyl-1-(5-(trifluoromethyl)pyridin-2-yl)ethan-1-amine	205.0
167		1-(3-fluoro-4-(trifluoromethyl)phenyl)-N-methylmethanamine	208.1
168		N-methyl-1-(4-(trifluoromethyl)phenyl)ethan-1-amine	204.2
169		1-(3-bromo-5-(trifluoromethyl)pyridin-2-yl)-N-methylethan-1-amine	283.0
170		1-(3-methoxy-5-(trifluoromethyl)pyridin-2-yl)-N-methylethan-1-amine	235.0

[0109] Intermediate 171: 1-(2-fluoro-6-(trifluoromethyl)pyridin-3-yl)-N-methylmethanamine



[0110] Step 1. A resealable vial was charged with 3-bromo-2-fluoro-6-(trifluoromethyl)pyridine (0.600 g, 2.385 mmol, Combi-Blocks) and potassium vinyltrifluoroborate (0.639 g, 4.77 mmol, Oakwood Products, Inc.) in 1,4-dioxane (5.96 mL) and water (1.988 mL). Then, potassium carbonate (1.319 g, 9.54 mmol, Sigma-Aldrich Corporation) was added to the reaction mixture. The reaction mixture was sparged with Argon (gas) for 5 min, then [1,1'-bis(diphenylphosphino)ferrocene] dichloropalladium (II) (0.044 g, 0.060 mmol, Sigma-Aldrich Corporation) was added to the reaction mixture. The vial was sealed, then the overall reaction mixture was stirred and heated at 80 °C for 16 h. The reaction mixture was diluted with EtOAc and filtered through a pad of celite and concentrated in vacuo. The crude material was absorbed onto a plug of silica gel and purified by chromatography through a Redi-Sep pre-packed silica gel column, eluting with a gradient of 0-15% EtOAc in heptanes, to provide 2-fluoro-6-(trifluoromethyl)-3-vinylpyridine (0.206 g, 1.078 mmol, 45.2 % yield) as light-yellow oil. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.05 (t, *J*=8.4 Hz, 1 H), 7.59 (dd, *J*=7.7, 1.3 Hz, 1 H), 6.83 (dd, *J*=17.8, 11.3 Hz, 1 H), 6.05 (d, *J*=17.8 Hz, 1 H), 5.67 (d, *J*=11.3 Hz, 1 H). *m/z* (ESI): 192.3 $(M+H)^+$.

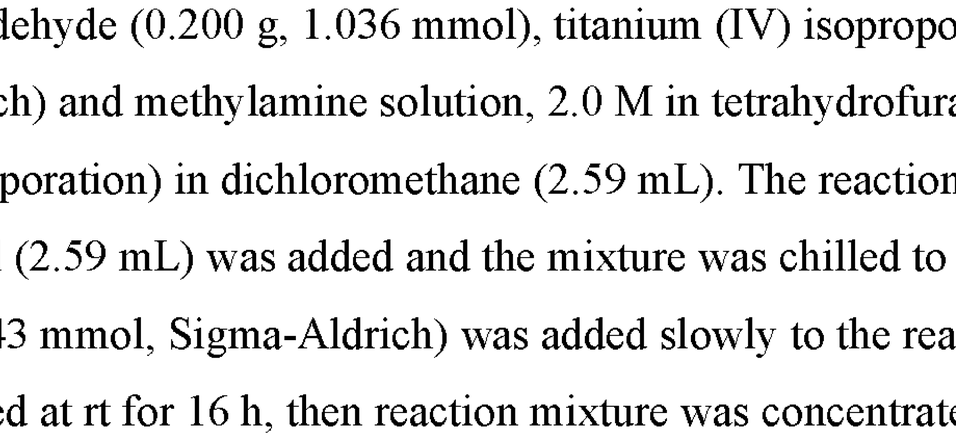
[0111] Step 2. To a 100-mL round-bottomed flask was added 2-fluoro-6-(trifluoromethyl)-3-vinylpyridine (1.176 g, 6.15 mmol) in acetone (25.6 mL)/water (5.13 mL) (5:1). To this mixture was added potassium osmate (vi) dihydrate (0.227 g, 0.615 mmol, Acros Organics) and 4-methylmorpholine n-oxide (2.52 g, 21.54 mmol, Sigma-Aldrich Corporation). The overall reaction mixture was allowed to stir under an inert (N_2) atmosphere, while at rt for 45 min. The reaction mixture was quenched with the addition of solid sodium sulfite (700 mg) and allowed the mixture to stir 15 min. The reaction mixture was partially concentrated (to remove acetone) in vacuo. The mixture was diluted with EtOAc and brine. The layers were separated and the aqueous layer was extracted with EtOAc. The organics were combined, dried over $MgSO_4$, filtered and concentrated in vacuo. The crude residue was used in the next step of the synthesis, without further purification.

[0112] The crude diol was diluted with THF (25 mL), then sodium (meta)periodate (3.95 g, 18.46 mmol, Sigma-Aldrich Corporation) and water (3 mL) was added to the mixture. The resulting reaction mixture was allowed to stir under an inert (N_2) atmosphere for 2.5 h. The reaction mixture was diluted with a mixture of EtOAc/Heptane (1:1) (36 mL). The mixture was agitated with sonicator for 1 minute. The

mixture was filtered and the filtrate was collected. The mixture was diluted with sat. aq. $NaHCO_3$ (36 mL). The layers were separated and the aqueous layer was extracted with EtOAc (3x). The combined organic extracts were washed with brine solution (2x), then dried over $MgSO_4$, filtered and concentrated in vacuo. This material was used in the next step of the synthesis, without further purification, to prevent decompostion. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 10.29 - 10.51 (m, 1 H), 8.44 - 8.66 (m, 1 H), 7.67 - 7.88 (m, 1 H).

[0113] Step 3. To an oven-dried 100-mL round-bottomed flask was added 2-fluoro-6-(trifluoromethyl)nicotinaldehyde (0.200 g, 1.036 mmol), titanium (IV) isopropoxide (0.368 g, 0.379 mL, 1.295 mmol, Sigma-Aldrich) and methylamine solution, 2.0 M in tetrahydrofuran (1.036 mL, 2.071 mmol, Sigma-Aldrich Corporation) in dichloromethane (2.59 mL). The reaction mixture was stirred at rt overnight. Then, methanol (2.59 mL) was added and the mixture was chilled to 0 °C and sodium borohydride (0.047 g, 1.243 mmol, Sigma-Aldrich) was added slowly to the reaction mixture. The overall reaction mixture was stirred at rt for 16 h, then reaction mixture was concentrated in vacuo. The crude material was absorbed onto a plug of silica gel and purified by chromatography through a Redi-Sep pre-packed silica gel column (40 g), eluting with a gradient of 0-25% MeOH in CH_2Cl_2. This afforded 1-(2-fluoro-6-(trifluoromethyl)pyridin-3-yl)-N-methylmethanamine (0.052 g, 0.250 mmol, 24.12 % yield) as tan oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.24 (t, *J*=8.3 Hz, 1 H), 7.78 - 7.93 (m, 1 H), 3.76 (s, 2 H), 3.29 (br s, 1 H), 2.21 - 2.41 (m, 3 H). *m/z* (ESI): 209.2 $(M+H)^+$

[0114] Intermediate 172: N-(oxazol-4-ylmethyl)cyclobutanamine

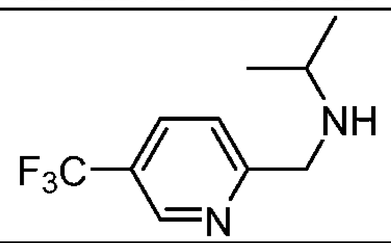
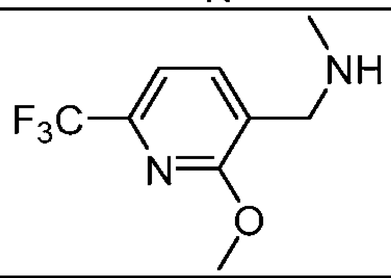
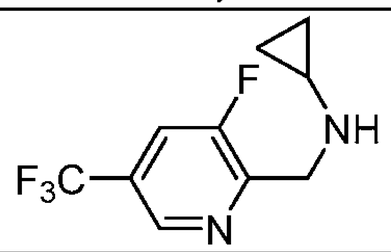


172

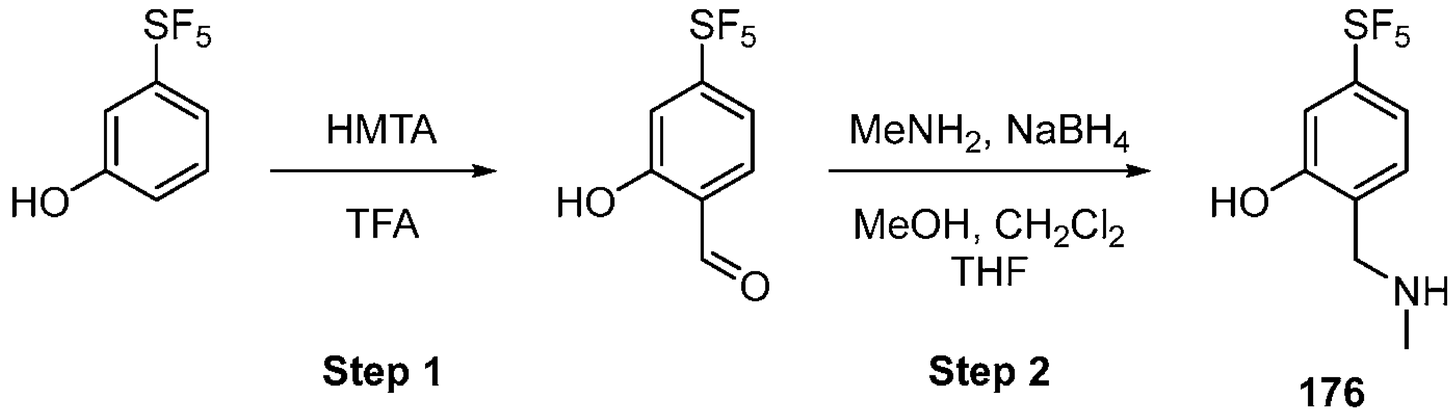
[0115] Cyclobutylamine (176 mg, 0.21 mL, 2.47 mmol) and 1,3-oxazole-4-carbaldehyde (240 mg, 2.47 mmol) were dissolved in dichloromethane (5 mL) and acetic acid glacial (29.7 mg, 0.029 mL, 0.494 mmol) was added. The mixture was stirred at rt for 30 minutes, then methanol (5.00 mL) was added and the solution cooled to 0 °C. Sodium borohydride (112 mg, 3.00 mmol) was added portionwise and the mixture was allowed to slowly warm to rt. After 16 h, volatiles were removed in vacuo, the crude product absorbed onto silica gel and the mixture was purified via column chromatography (0 - 20% MeOH/DCM in 8 minutes) to yield N-(oxazol-4-ylmethyl)cyclobutanamine (206 mg, 1.35 mmol, 54.7 % yield) as a colourless oil. *m/z* (ESI): 153.3 $(M+H)^+$.

[0116] Secondary amines in Table 7 were prepared in a manner similar to that described for amine **172**

Table 7

Int. #	Chemical Structure	Name	*m/z* (ESI): $(M+H)^+$
173		N-((5-(trifluoromethyl)pyridin-2-yl)methyl)propan-2-amine	219.1
174		1-(2-methoxy-6-(trifluoromethyl)pyridin-3-yl)-N-methylmethanamine	221.0
175		N-((3-fluoro-5-(trifluoromethyl)pyridin-2-yl)methyl)cyclopropanamine	235.0

[0117] Intermediate 176: 2-((methylamino)methyl)-5-(pentafluoro-l6-sulfaneyl)phenol



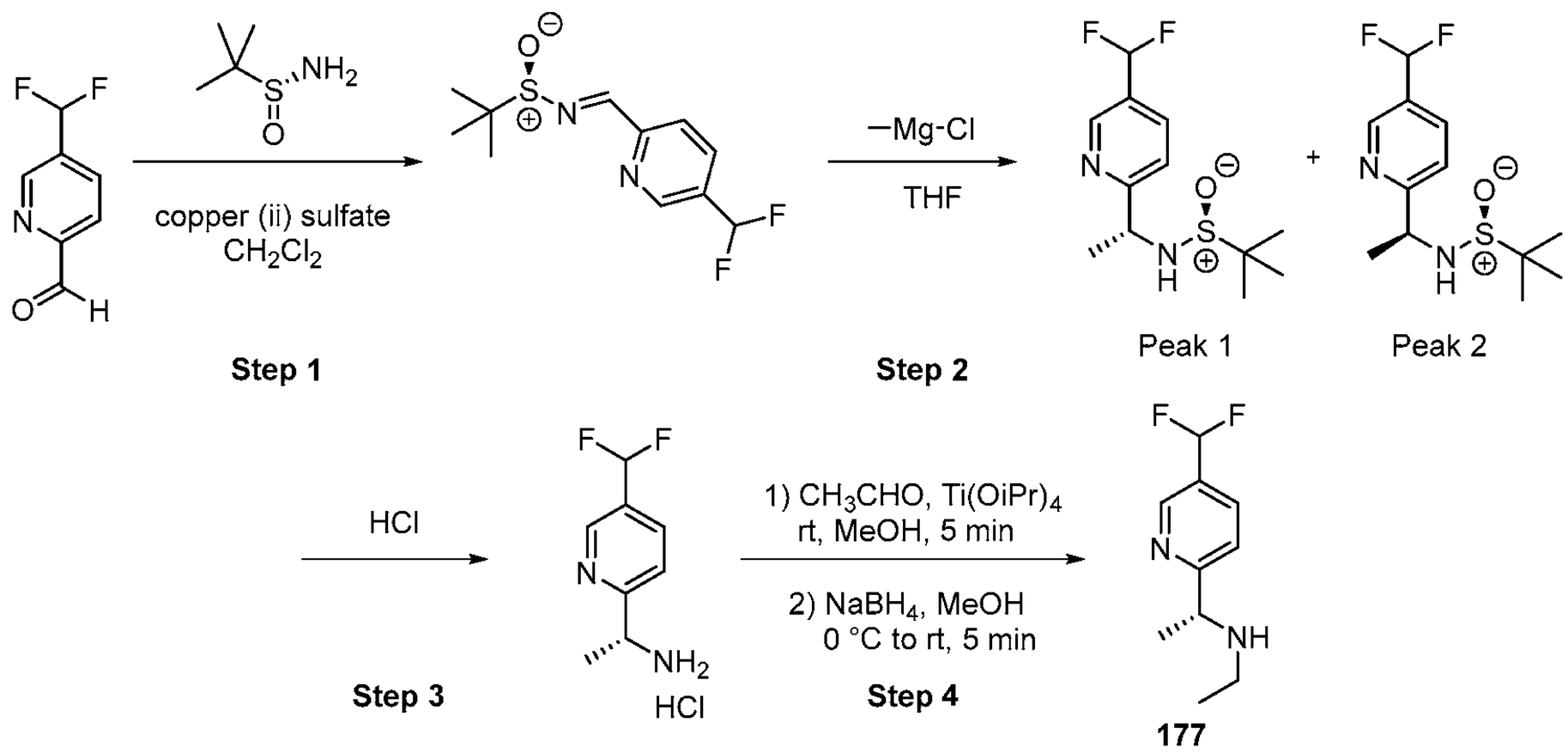
Step 1 **Step 2** **176**

[0118] Step 1. To a solution of 3-(pentafluoro-l6-sulfaneyl)phenol (2.5 g, 11.36 mmol, Aurum Pharmatech) in trifluoroacetic acid (20 mL) was add hexamethylenetetramine (HMTA) (2.229 g, 15.90 mmol, Combi-Blocks Inc.) and stirred at 80 °C for 4 h. To the reaction mixture was added water (40 mL) and the reaction was stirred at rt for another 30 min. The reaction mixture was extracted with EtOAc (2 x 40 mL).The organic extract was washed with saturated aqueous $NaHCO_3$, water and brine and dried over Na_2SO_4. The solution was filtered and concentrated in vacuo to give the crude material as a colorless oil. The crude product was absorbed onto a plug of silica gel and purified by chromatography through a Redi-Sep pre-packed silica gel column (40 g), eluting with a gradient of 0-50% EtOAc in Heptane, to obtain 2-hydroxy-4-(pentafluoro-l6-sulfaneyl)benzaldehyde (1.176 g, 4.74 mmol, 41.7 % yield) as a colorless oil. *m/z* (ESI): 248.9 $(M+H)^+$. ^1H NMR (400 MHz, $CDCl_3$) δ 11.06 (s, 1 H), 10.00 (s, 1 H), 7.71 (dd, *J*=8.2,0.8 Hz, 1 H), 7.40 - 7.45 (m, 2 H). ^{19}F NMR (376 MHz, *DMSO-d*$_6$) δ ppm 57.10 (s), 56.70 (s)

[0119] Step 2. To a solution of 2-hydroxy-4-(pentafluoro-l6-sulfaneyl)benzaldehyde (300 mg, 1.209 mmol) in dichloromethane (5 mL) was treated with methylamine solution, (2.0 M in tetrahydrofuran, 1.813 mL, 3.63 mmol, Sigma Aldrich) and stirred at rt for 3 h. The resulting mixture was concentrated to

dryness to give (E)-2-((methylimino)methyl)-5-(pentafluoro-l6-sulfaneyl)phenol as an yellow solid. The above material was dissolved in dichloromethane (5 mL)/ methanol (2 mL) and treated with sodium borohydride (45.7 mg, 1.209 mmol, Sigma Aldrich) at rt and stirred for 30 min. The reaction mixture was diluted with brine and extracted with EtOAc. The organic extract was washed with saturated aqueous NaCl and dried over Na_2SO_4. The solution was filtered and concentrated in vacuo to give the crude material as a yellow oil. The crude product was absorbed onto a plug of silica gel and purified by chromatography through a Redi-Sep pre-packed silica gel column (24 g), eluting with a gradient of 0 % to 100% EtOAc in Heptanes and then 10% MeOH (with 2 M NH_3) in DCM, to obtain 2-((methylamino)methyl)-5-(pentafluoro-l6-sulfaneyl)phenol (142 mg, 0.539 mmol, 44.6 % yield). *m/z* (ESI): 264.0 $(M+H)^+$. ^1H NMR (400 MHz, *DMSO-d_6*) δ 7.30 (d, *J*=8.4 Hz, 1 H), 7.15 - 7.23 (m, 1 H), 7.11 (d, *J*=2.3 Hz, 1 H), 6.29 (br s, 1 H), 4.14 (s, 1 H), 3.84 (s, 2 H), 2.30 (s, 3 H).

[0120] Intermediate 177: (R)-1-(5-(difluoromethyl)pyridin-2-yl)-N-ethylethan-1-amine



[0121] Step 1. To an oven-dried 100-mL round-bottomed flask was added (R)-(+)-2-methyl-2-propanesulfinamide (0.310 g, 2.56 mmol, AK Scientific, Inc.) in dichloromethane (5.12 mL). To this mixture was added copper (ii) sulfate (0.816 g, 5.12 mmol, Sigma-Aldrich Corporation) followed by 5-(difluoromethyl)-2-pyridinecarboxaldehyde (0.402 g, 2.56 mmol, Enamine). The resulting reaction mixture was stirred at rt for 24 h. The reaction mixture was filtered through a pad of Celite and the filter cake was washed with DCM. The filtrate was collected and concentrated in vacuo. The crude material was absorbed onto a plug of silica gel and purified by chromatography through a Redi-Sep pre-packed silica gel column (80 g), eluting with a gradient of 0-30% EtOAc:EtOH (3:1) in heptane, to provide (R,E)-N-((5-(difluoromethyl)pyridin-2-yl)methylene)-2-methylpropane-2-sulfinamide (0.660 g, 2.54

mmol, 99 % yield) as light-yellow solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.97 (s, 1 H), 8.54 (s, 1 H), 8.19 - 8.25 (m, 2 H), 7.25 (t, *J*=55.0 Hz, 1 H), 1.23 (s, 9 H). *m/z* (ESI): 261.0 $(M+H)^+$.

[0122] Step 2. To an oven-dried 100-mL 2-neck round-bottomed flask was added (R,E)-2-methyl-N-((5-(difluoromethyl)pyridin-2-yl)methylene)propane-2-sulfinamide (0.600 g, 2.31 mmol) in tetrahydrofuran (10.78 mL). The reaction mixture was cooled to -78 °C, then methylmagnesium chloride (3.0 M in THF) (1.294 mL, 3.88 mmol, Oakwood Chemicals) was added dropwise to the reaction mixture. After 10 min, the reaction was quenched with the addition of sat. aq. NH_4Cl (5.8 mL) and extracted with EtOAc (3 x 25 mL). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated in vacuo. The crude material was absorbed onto a plug of silica gel and purified by chromatography through a silica-gel column, eluting in a gradient of 0-80% EtOAc in heptanes, to provide both diastereomers. Peak 1 was arbitrarily assigned as N-((R)-1-(5-(difluoromethyl)pyridin-2-yl)ethyl)-2-methylpropane-2-sulfinamide (0.361 g, 1.306 mmol, 60.6 % yield) as light-yellow solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.68 - 8.74 (m, 1 H), 8.02 (d, *J*=8.5 Hz, 1 H), 7.70 (d, *J*=8.2 Hz, 1 H), 7.14 (t, *J*=55.3 Hz, 1 H), 5.83 (d, *J*=7.9 Hz, 1 H), 4.51 (quin, *J*=7.1 Hz, 1 H), 1.44 (d, *J*=6.9 Hz, 3 H), 1.14 (s, 9 H). *m/z* (ESI): 277.1 $(M+H)^+$. Peak 2 was arbitrarily assigned as N-((S)-1-(5-(difluoromethyl)pyridin-2-yl)ethyl)-2-methylpropane-2-sulfinamide (0.232 g, 0.840 mmol, 38.9 % yield) as white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.71 (s, 1 H), 8.02 (d, *J*=8.5 Hz, 1 H), 7.70 (d, *J*=8.2 Hz, 1 H), 7.14 (t, *J*=55.4 Hz, 1 H), 5.83 (d, *J*=7.7 Hz, 1 H), 4.51 (quin, *J*=7.1 Hz, 1 H), 1.44 (d, *J*=6.9 Hz, 3 H), 1.14 (s, 9 H). *m/z* (ESI): 277.1 $(M+H)^+$.

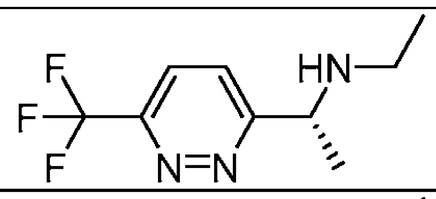
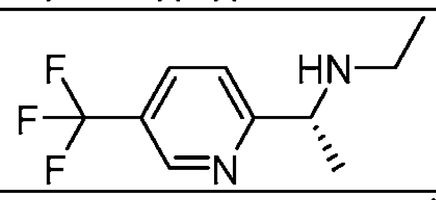
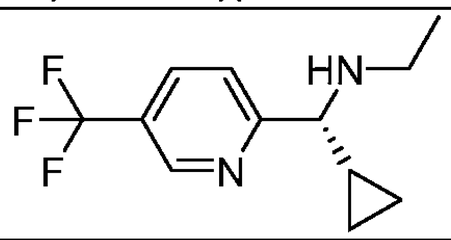
[0123] Step 3. To a 100-mL round-bottomed flask was added (S)-N-((R)-1-(5-(difluoromethyl)pyridin-2-yl)ethyl)-2-methylpropane-2-sulfinamide (0.365 g, 1.321 mmol) and hydrogen chloride solution, 4.0 M in dioxane (0.413 mL, 1.651 mmol, Sigma-Aldrich Corporation) in 1,4-dioxane (8.81 mL). The resulting reaction mixture was stirred at rt for 4 h. The reaction mixture was concentrated in vacuo. The crude residue was carried to the next step of the synthesis, without further purification. *m/z* (ESI): 173.0 $(M+H)^+$.

[0124] Step 4. To a 50-mL round-bottomed flask was added (R)-1-(5-(difluoromethyl)pyridin-2-yl)ethan-1-amine hydrochloride (0.276 g, 1.323 mmol) and acetaldehyde (0.117 g, 0.148 mL, 2.65 mmol, Acros Organics) in methanol (6.61 mL). The reaction mixture was cooled to 0 °C, then titanium (IV) isopropoxide (0.470 g, 0.485 mL, 1.654 mmol, Sigma-Aldrich) was added. The resulting mixture was stirred at rt for 5 min. Then, sodium borohydride (0.300 g, 7.94 mmol, Sigma-Aldrich) was added slowly to the reaction mixture. An additional aliquot of acetaldehyde (0.117 g, 0.148 mL, 2.65 mmol, Acros Organics) was added to the reaction mixture and stirred an additional 10 min. The reaction mixture was quenched with sat. aq. $NaHCO_3$ (0.5 mL) and stirred 5 min, then it was treated with $MgSO_4$, and filtered through a pad of Celite. The filtrate was collected and concentrated in vacuo. The crude material was absorbed onto a plug of silica gel and purified by chromatography, eluting with a gradient of 0-30%

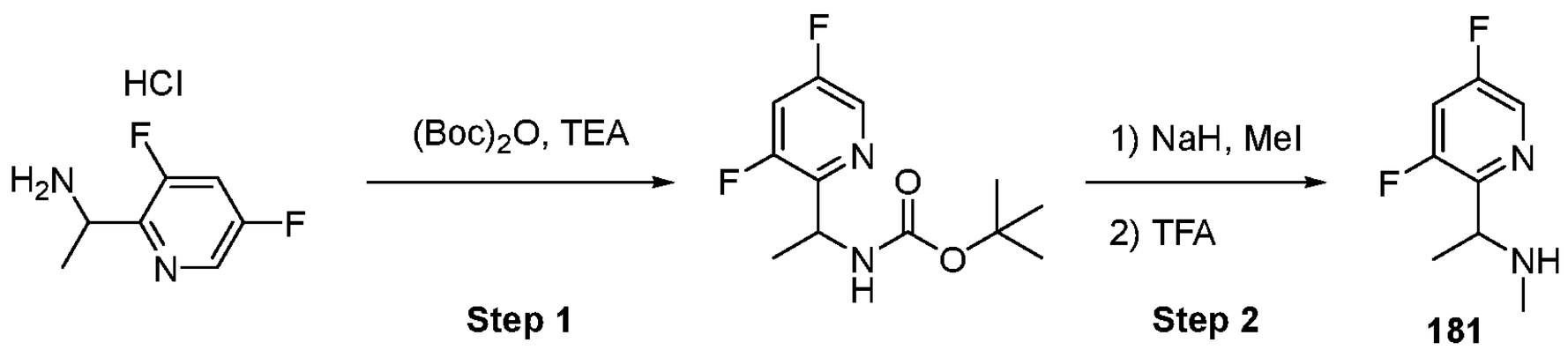
MeOH in CH_2Cl_2, to provide (R)-1-(5-(difluoromethyl)pyridin-2-yl)-N-ethylethan-1-amine (0.200 g, 0.999 mmol, 76 % yield) as off-white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.72 - 8.80 (m, 1 H), 8.00 - 8.07 (m, 1 H), 7.60 - 7.69 (m, 1 H), 7.15 (t, *J*=55.3 Hz, 1 H), 7.14 (br t, *J*=55.4 Hz, 1 H), 4.13 - 4.17 (m, 1 H), 2.56 - 2.67 (m, 1 H), 2.41 - 2.49 (m, 1 H), 1.04 - 1.10 (m, 3 H), 0.82 - 0.92 (m, 3 H). *m/z* (ESI): 201.1 $(M+H)^+$.

[0125] Secondary amines in Table 8 were prepared in a manner similar to that described for amine **177.** Secondary amines **178** and **179** were synthesized starting at Step 4 from the commercially available chiral primary amines, (R)-1-[6-(trifluoromethyl)pyridazin-3-yl]ethanamine hydrochloride (CAS# 1948236-91-6) and (R)-1-(5-(trifluoromethyl)pyridin-2-yl)ethan-1-amine hydrochloride (CAS# 1956437-55-0), respectively.

Table 8

Int. #	Chemical Structure	Name	*m/z* (ESI): $(M+H)^+$
178		(R)-N-ethyl-1-(6-(trifluoromethyl)pyridazin-3-yl)ethan-1-amine	220.1
179		(R)-N-ethyl-1-(5-(trifluoromethyl)pyridin-2-yl)ethan-1-amine	219.1
180		(R)-N-(cyclopropyl(5-(trifluoromethyl)pyridin-2-yl)methyl)ethanamine	245.1

[0126] Intermediate 181: 1-(3,5-difluoropyridin-2-yl)-N-methylethan-1-amine



[0127] Step 1. To a 100-mL round-bottomed flask was added 1-(3,5-difluoropyridin-2-yl)ethanamine hydrochloride (0.250 g, 1.285 mmol, Combi-Blocks Inc.) and di-tert-butyl dicarbonate (0.421 g, 0.447 mL, 1.927 mmol, Oakwood Products, Inc.) in 1,2-dichloroethane (6.42 mL). Then triethylamine (0.520 g, 0.722 mL, 5.14 mmol, Sigma-Aldrich Corporation) was added to the reaction mixture and the overall mixture was stirred at rt for 2 h. The reaction mixture was diluted with DCM (5 mL) and sat. aq. $NaHCO_3$ (5 mL). The layers were separated and the aqueous layer was extracted with DCM (3x). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated in vacuo. The crude material was

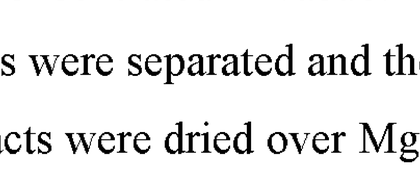
absorbed onto a plug of silica gel and purified with a gradient of 0-25% EtOAc in heptane, to afford tert-butyl (1-(3,5-difluoropyridin-2-yl)ethyl)carbamate (0.300 g, 1.162 mmol, 90 % yield) as off-white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.46 (d, *J*=1.9 Hz, 1 H), 7.87 (t, *J*=9.6 Hz, 1 H), 7.21 (br d, *J*=7.5 Hz, 1 H), 4.81 - 4.98 (m, 1 H), 1.34 (br d, *J*=5.9 Hz, 9 H), 1.31 - 1.33 (m, 3 H). *m/z* (ESI): 259.1 $(M+H)^+$.

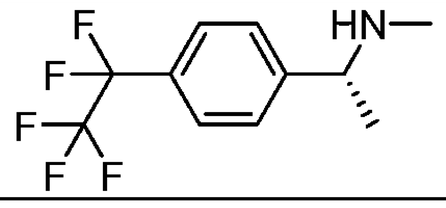
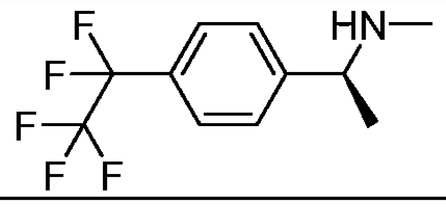
[0128] Step 2. To a 100-mL round-bottomed flask was added tert-butyl (1-(3,5-difluoropyridin-2-yl)ethyl)carbamate (0.300 g, 1.162 mmol) in tetrahydrofuran (5.81 mL). The mixture was cooled to 0 °C, then sodium hydride (60% dispersion in mineral oil) (0.058 g, 1.452 mmol, Oakwood Products, Inc.) was added to the reaction mixture. The resulting mixture was stirred at 0 °C for 20 min, then iodomethane (0.198 g, 0.198 mL, 1.394 mmol, Sigma-Aldrich Corporation) was added dropwise to the mixture. The reaction mixture was stirred an additional 20 min, while the temperature was maintained at 0 °C, then the mixture was stirred at rt overnight. The reaction mixture was quenched with MeOH and concentrated in vacuo. The crude material was absorbed onto a plug of silica gel and purified by chromatography through a Redi-Sep pre-packed silica gel column (40 g), eluting with a gradient of 0-30% EtOAc in Heptane, to provide tert-butyl (1-(3,5-difluoropyridin-2-yl)ethyl)(methyl)carbamate (0.287 g, 1.054 mmol, 91 % yield) as light-yellow oil. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.31 (d, *J*=2.3 Hz, 1 H), 7.18 (ddd, *J*=9.4, 8.3, 2.4 Hz, 1 H), 5.63 (br s, 1 H), 2.75 (br s, 3 H), 1.53 - 1.57 (m, 3 H), 1.47 (s, 9 H). *m/z* (ESI): 295.3 $(M+Na)^+$.

[0129] The residue was dissolved in dichloromethane (5.81 mL) and treated with trifluoroacetic acid (1.324 g, 0.866 mL, 11.62 mmol, Sigma-Aldrich Corporation). The reaction mixture was stirred at rt for 1 h at which time it was concentrated in vacuo. The residue was diluted with DCM, then treated with sat. aq. $NaHCO_3$. The layers were separated and the aqueous layer was extracted with DCM (3x). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated in vacuo. This afforded 1-(3,5-difluoropyridin-2-yl)-N-methylethan-1-amine (0.109 g, 0.633 mmol, 54.5 % yield) as light-yellow oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.50 (d, *J*=2.3 Hz, 1 H), 7.87 (ddd, *J*=10.0, 9.2, 2.3 Hz, 1 H), 3.98 (qd, *J*=6.7, 1.4 Hz, 1 H), 3.25 - 3.34 (m, 1 H), 2.14 (s, 3 H), 1.26 - 1.30 (m, 3 H). *m/z* (ESI): 173.2 $(M+H)^+$.

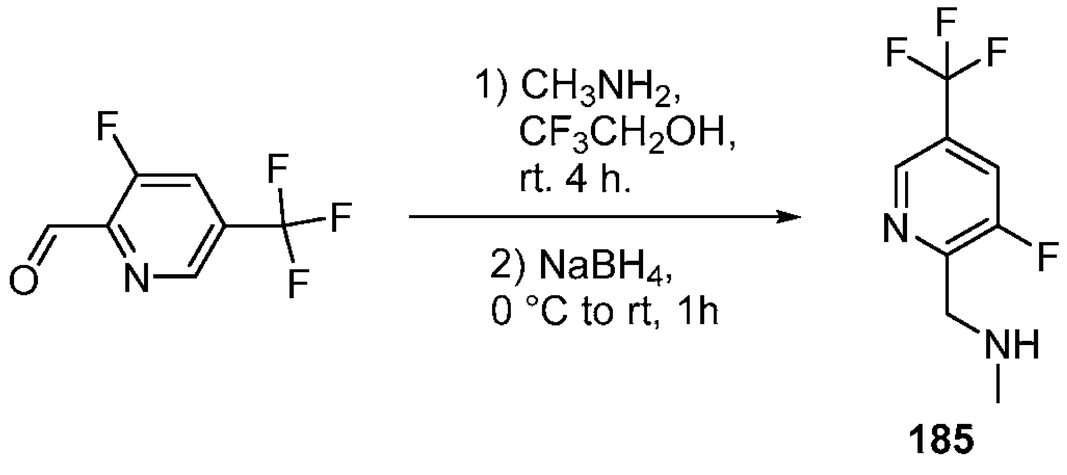
[0130] Secondary amines in Table 9 were prepared in a manner similar to Steps 1-2 described for amine **181.** The chiral primary amines used in Step 1 were synthesized in a manner similar to Step 1-3 from Example **177** above.

Table 9

Int. #	Chemical Structure	Name	*m/z* (ESI): $(M+H)^+$
182		(R)-N-methyl-1-(5-(trifluoromethyl)pyrazin-2-yl)ethan-1-amine	206.2

Int. #	Chemical Structure	Name	*m/z* (ESI): $(M+H)^+$
183		(R)-N-methyl-1-(4-(perfluoroethyl)phenyl)ethan-1-amine	254.0
184		(S)-N-methyl-1-(4-(perfluoroethyl)phenyl)ethan-1-amine	254.2

[0131] Intermediate 185: 1-(3-fluoro-5-(trifluoromethyl)pyridin-2-yl)-N-methylmethanamine

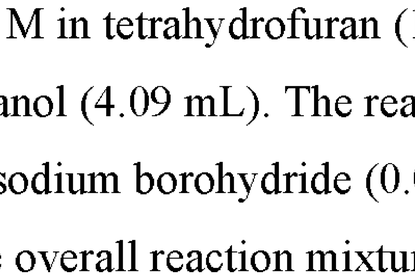
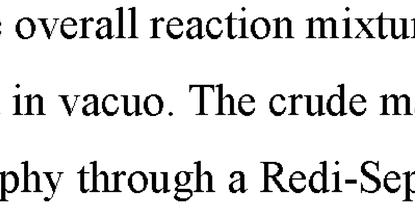


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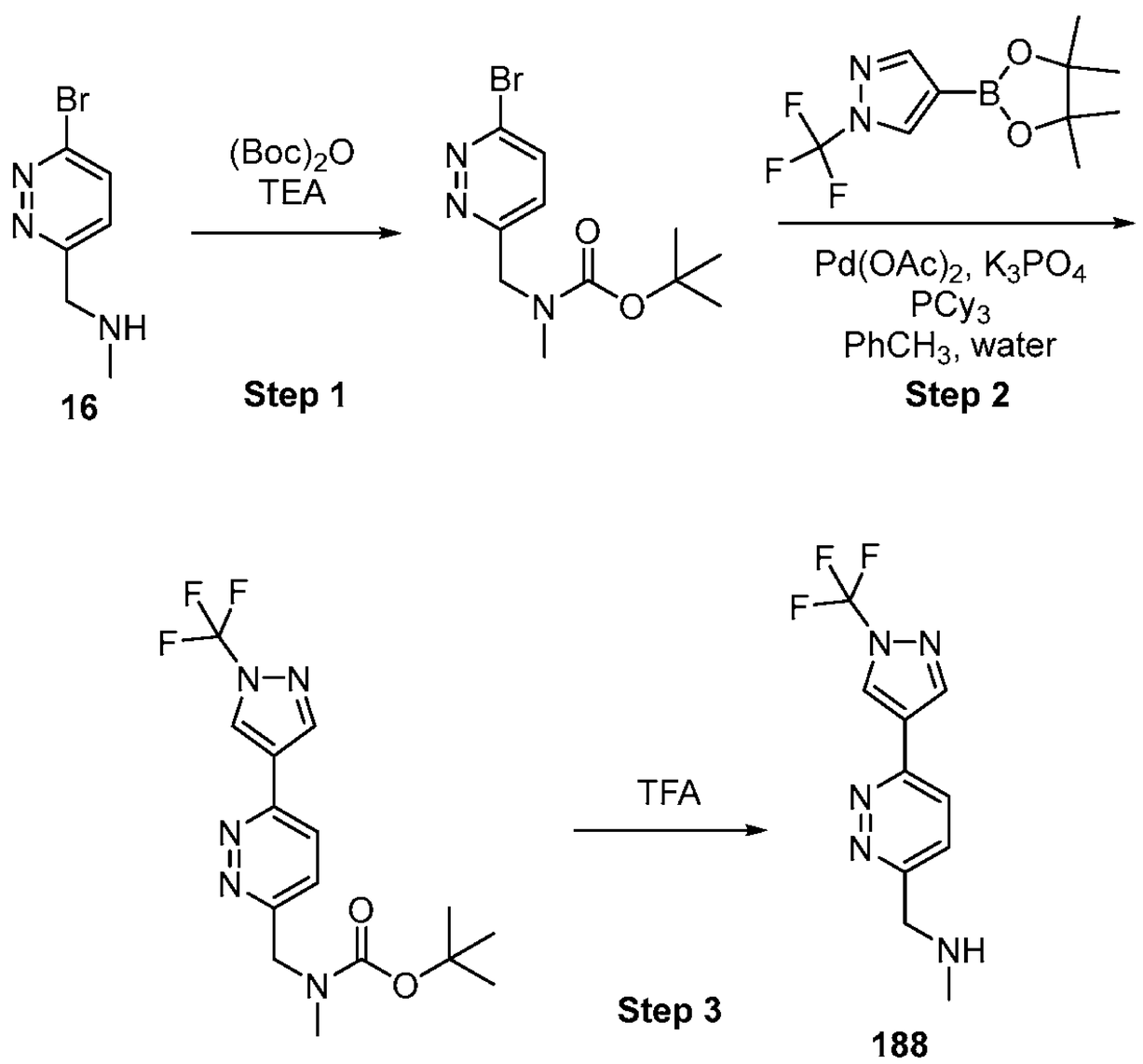
[0132] To an oven-dried 100-mL round-bottomed flask was added 3-fluoro-5-(trifluoromethyl)picolinaldehyde (0.300 g, 0.300 mL, 1.554 mmol, Combi-Blocks Inc.) and methylamine solution, 2.0 M in tetrahydrofuran (1.554 mL, 3.11 mmol, Sigma-Aldrich Corporation) in 2,2,2-Trifluoroethanol (4.09 mL). The reaction mixture was stirred at rt for 4 h. Then the mixture was cooled to 0°C, before sodium borohydride (0.071 g, 1.864 mmol, Sigma-Aldrich) was added slowly to the reaction mixture. The overall reaction mixture was stirred at rt for 2 h.. Then the reaction mixture was concentrated in vacuo. The crude material was absorbed onto a plug of silica gel and purified by chromatography through a Redi-Sep pre-packed silica gel column, eluting with a gradient of 0-20% MeOH in DCM, to provide 1-(3-fluoro-5-(trifluoromethyl)pyridin-2-yl)-N-methylmethanamine (0.190 g, 0.913 mmol, 58.8% yield) as yellow oil. *m/z* (ESI): 209.2 $(M+H)^+$.

[0133] Secondary amines in Table 10 were prepared in a manner similar to that described for amine **185.**

Table 10

Int. #	Chemical Structure	Name	*m/z* (ESI): $(M+H)^+$
186		1-(3-fluoro-5-(trifluoromethyl)pyridin-2-yl)-N-methylethan-1-amine	223.0
187		N-methyl-1-(4-(pentafluoro-l6-sulfaneyl)phenyl)ethan-1-amine	262.0

[0134] Intermediate 188: N-methyl-1-(6-(1-(trifluoromethyl)-1H-pyrazol-4-yl)pyridazin-3-yl)methanamine



[0135] Step 1. To a 100-mL round-bottomed flask was added 1-(6-bromopyridazin-3-yl)-N-methylmethanamine (0.320 g, 1.584 mmol) and di-tert-butyl dicarbonate (0.518 g, 0.552 mL, 2.376 mmol, Oakwood Products, Inc.) in 1,2-dichloroethane (7.92 mL). Then triethylamine (0.641 g, 0.890 mL, 6.33 mmol, Sigma-Aldrich Corporation) was added to the reaction mixture and the overall mixture was stirred at rt for 16 h. The reaction mixture was diluted with DCM (5 mL) and sat. aq. $NaHCO_3$ (5 mL). The layers were separated and the aqueous layer was extracted with DCM (3x). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated in vacuo. The crude material was absorbed onto a plug of silica gel and purified with a gradient of 0-60% EtOAc in heptane, to afford tert-butyl ((6-bromopyridazin-3-yl)methyl)(methyl)carbamate (0.400 g, 1.324 mmol, 84 % yield) as light-yellow oil. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 7.65 (br d, *J*=8.8 Hz, 1 H), 7.30 - 7.51 (m, 1 H), 4.71 (s, 2 H), 2.94 (br s, 3 H), 1.49 (br s, 9 H). *m/z* (ESI): 302.0 $(M+H)^+$.

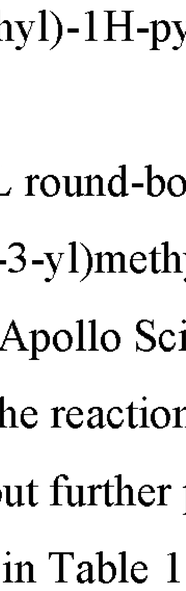
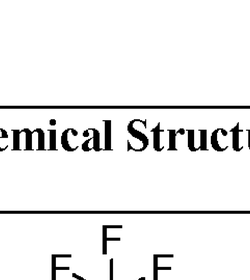
[0136] Step 2. To a resealable vial, was added tert-butyl ((6-bromopyridazin-3-yl)methyl)(methyl)carbamate (0.200 g, 0.662 mmol), 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-(trifluoromethyl)-1h-pyrazole (0.347 g, 0.347 mL, 1.324 mmol, Enamine) and potassium phosphate tribasic (0.421 g, 1.986 mmol, Sigma-Aldrich Corporation) in a mixture of toluene (2.98 mL)/water (0.331 mL). The reaction mixture was sparged with Argon (gas) for 5 min, then tricyclohexylphosphine (0.074 g, 0.265 mmol, Strem Chemicals, Inc.), followed by palladium (II) acetate (0.030 g, 0.132 mmol,

Sigma-Aldrich Corporation) was added to the reaction mixture and the vial was sealed. The reaction mixture was stirred and heated at 90 °C for 16 h at which time it was cooled to rt, then diluted with EtOAc and filtered through a pad of Celite. The organic filtrate was collected, then concentrated in vacuo. The crude material was absorbed onto a plug of silica gel and purified by chromatography through a pre-packed silica gel column, eluting with a gradient of 0-45% EtOAc in Heptane, to provide tert-butyl methyl((6-(1-(trifluoromethyl)-1H-pyrazol-4-yl)pyridazin-3-yl)methyl)carbamate (0.078 g, 0.218 mmol, 33.0 % yield) as tan oil.

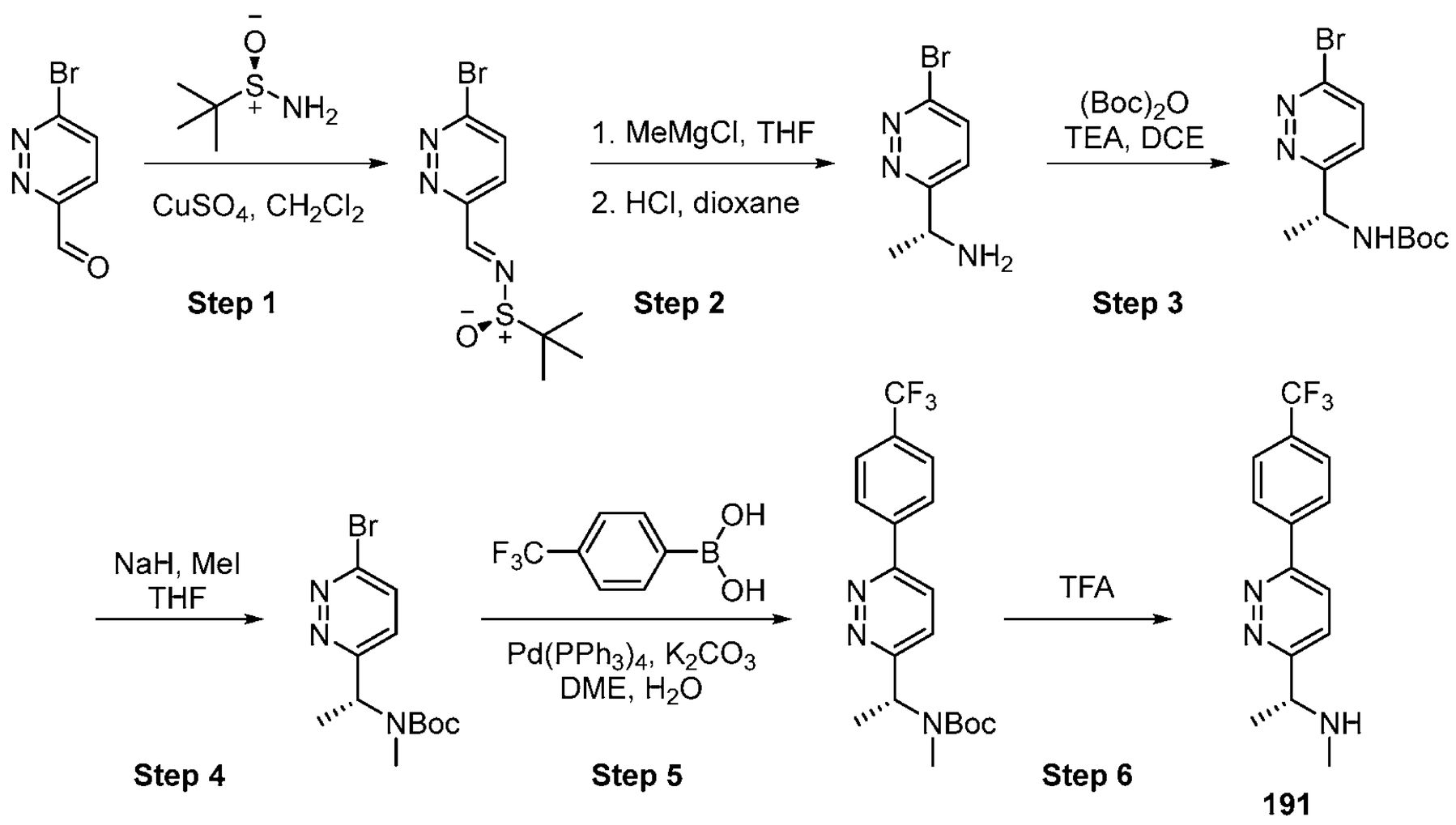
[0137] Step 3. To a 50-mL round-bottomed flask was added tert-butyl methyl((6-(1-(trifluoromethyl)-1H-pyrazol-4-yl)pyridazin-3-yl)methyl)carbamate (0.060 g, 0.168 mmol) and trifluoroacetic acid (0.191 g, 0.191 mL, 1.679 mmol, Apollo Scientific Ltd.) in 1,2-dichloroethane (1.6 mL). The overall mixture was stirred at rt for 16 h. The reaction mixture was concentrated in vacuo. The crude was used in the next step of the synthesis, without further purification. *m/z* (ESI): 258.2 $(M+H)^+$.

[0138] Secondary amines in Table 11 were prepared in a manner similar to that described for amine **188.**

Table 11

Int. #	Chemical Structure	Name	*m/z* (ESI): $(M+H)^+$
189		N-methyl-1-(6-(4-(trifluoromethyl)phenyl)pyridazin-3-yl)methanamine	268.1
190		N-methyl-1-(5-(1-(trifluoromethyl)-1H-pyrazol-4-yl)pyridin-2-yl)methanamine	257.0

[0139] Intermediate 191: (R)-N-methyl-1-(6-(4-(trifluoromethyl)phenyl)pyridazin-3-yl)ethan-1-amine



[0140] Step 1. To an oven-dried 100-mL round-bottomed flask was added (R)-(+)-2-methyl-2-propanesulfinamide (1.220 g, 10.07 mmol, AK Scientific, Inc.) in dichloromethane (20.13 mL). To this mixture was added copper (ii) sulfate (3.21 g, 20.13 mmol, Sigma-Aldrich Corporation) followed by 6-bromopyridazine-3-carbaldehyde (1.882 g, 10.07 mmol, PharmaBlock Sciences). The resulting reaction mixture was stirred at rt for 24 h at which time it was filtered through a pad of Celite and the filter cake was washed with 1:1 EtOAc:Heptane. The filtrate was collected and concentrated in vacuo. The crude material was triturated from EtOAc and heptane. The solids were collected and dried further in a reduced pressure oven for 2 h. This afforded (R,E)-N-((6-bromopyridazin-3-yl)methylene)-2-methylpropane-2-sulfinamide (1.667 g, 5.74 mmol, 57.1 % yield) as tan solid. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 9.00 (s, 1 H), 8.04 (br d, *J*=8.8 Hz, 1 H), 7.80 (br d, *J*=8.8 Hz, 1 H), 1.32 (s, 9 H). *m/z* (ESI): 314.0 $(M+Na)^+$.

[0141] Step 2. To an oven-dried 150-mL 3-neck round-bottomed flask, equipped with an internal temperature probe, was added (R,E)-N-((6-bromopyridazin-3-yl)methylene)-2-methylpropane-2-sulfinamide (1.667 g, 5.74 mmol) in tetrahydrofuran (28.7 mL). The reaction mixture was cooled to -78°C, then methylmagnesium chloride (3.45 mL, 10.34 mmol, Oakwood) was added dropwise to the reaction mixture. (Note: Addition of grignard reagent, was added slow enough where the temperature of reaction mixture did not warm past -70°C) After the addition, the overall reaction mixture was stirred an additional 20 min, while the temperature was maintained at -78°C. Then, the reaction was quenched, while at -70°C, with the addition of sat. aq. NH_4Cl (30 mL). The mixture was warmed to rt and extracted with EtOAc (3 x 100 mL). The combined organic extracts were washed with brine, then dried over

$MgSO_4$, filtered and concentrated in vacuo. The crude material was absorbed onto a plug of silica gel and purified by chromatography through a Interchim (15 micron) silica-gel column (120 grams), eluting with a gradient of 0-100% EtOAc in heptane, then with a gradient of 0-50% EtOAc:EtOH (3:1) in heptane to provide a mixture of both diasteromers (R)-N-((R)-1-(6-bromopyridazin-3-yl)ethyl)-2-methylpropane-2-sulfinamide (0.657 g, 2.146 mmol, 37.3 % yield) as tan solid and (R)-N-((S)-1-(6-bromopyridazin-3-yl)ethyl)-2-methylpropane-2-sulfinamide (0.067 g, 0.219 mmol, 3.81 % yield) as tan solid. Stereochemistry of the major isomer was assigned in analogy to Kuduk, et al. *Tet. Lett.* **2004**, 45 (35), 6641. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.90 - 8.08 (m, 1 H), 7.76 - 7.85 (m, 1 H), 5.96 (d, *J*=8.4 Hz, 1 H), 4.61 - 4.71 (m, 1 H), 1.50 (d, *J*=6.9 Hz, 3 H), 1.14 (s, 9 H). *m/z* (ESI): 306.1 $(M+H)^+$

[0142] To a 50-mL round-bottomed flask was added (R)-N-((R)-1-(6-bromopyridazin-3-yl)ethyl)-2-methylpropane-2-sulfinamide (0.650 g, 2.123 mmol) and hydrogen chloride solution, 4.0 M in dioxane (0.663 mL, 2.65 mmol, Sigma-Aldrich Corporation) in 1,4-dioxane (10.61 mL). The overall reaction mixture was stirred at rt overnight. The reaction mixture was concentrated in vacuo, and the residue was diluted with heptane and DCM (10:1), then agitated by sonication for 1 min. The precipitate was collected by filtration, then the solids were washed with heptane (3x). This afforded (R)-1-(6-bromopyridazin-3-yl)ethan-1-amine hydrochloride as black crude mixture, which was carried to the next step of the synthesis, without further purification. *m/z* (ESI): 202.1 $(M+H)^+$

[0143] Step 3. To a 100-mL round-bottomed flask was added (R)-1-(6-bromopyridazin-3-yl)ethan-1-amine hydrochloride (0.500 g, 2.096 mmol) and di-tert-butyl dicarbonate (0.686 g, 0.730 mL, 3.14 mmol, Oakwood Products, Inc.) in 1,2-dichloroethane (10.48 mL). Then, triethylamine (1.061 g, 1.473 mL, 10.48 mmol, Sigma-Aldrich Corporation) was added to the reaction mixture and the overall mixture was stirred at rt for 16 h. The reaction mixture was diluted with DCM (5 mL) and sat. aq. $NaHCO_3$ (5 mL). The layers were separated and the aqueous layer was extracted with DCM (3x). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated in vacuo. The crude material was absorbed onto a plug of silica gel and purified with a gradient of 0-80% EtOAc in heptane, to afford tert-butyl (R)-(1-(6-bromopyridazin-3-yl)ethyl)carbamate (0.182 g, 0.602 mmol, 28.7 % yield) as tan solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.90 (d, *J*=8.8 Hz, 1 H), 7.71 (d, *J*=9.0 Hz, 1 H), 7.44 - 7.66 (m, 1 H), 4.78 - 4.94 (m, 1 H), 1.38 (br d, *J*=8.8 Hz, 12 H). *m/z* (ESI): 302.0 $(M+H)^+$.

[0144] Step 4. To a 100-mL round-bottomed flask was added tert-butyl (R)-(1-(6-bromopyridazin-3-yl)ethyl)carbamate (0.170 g, 0.563 mmol) in tetrahydrofuran (5.63 mL). The mixture was cooled to 0 °C, then sodium hydride (60% dispersion in mineral oil) (0.028 g, 0.703 mmol, TCI America) was added to the reaction mixture. The resulting mixture was stirred at 0 °C for 20 min, then iodomethane (0.096 g, 0.042 mL, 0.675 mmol, Sigma-Aldrich Corporation) was added dropwise to the mixture. The reaction mixture was stirred an additional 20 min, while temperature maintained at 0 °C, then the mixture was

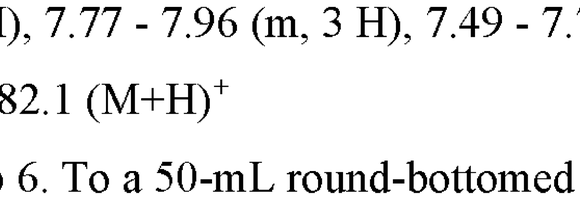
stirred at rt overnight. The reaction mixture was quenched with MeOH and concentrated in vacuo. The crude material was absorbed onto a plug of silica gel and purified by chromatography through a Redi-Sep pre-packed silica gel column (40 g), eluting with a gradient of 0-25% EtOAc in Heptane, to provide tert-butyl (R)-(1-(6-bromopyridazin-3-yl)ethyl)(methyl)carbamate (0.170 g, 0.538 mmol, 96 % yield) as light-yellow oil. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.31 (d, *J*=2.3 Hz, 1 H), 7.18 (ddd, *J*=9.4, 8.3, 2.4 Hz, 1 H), 5.63 (br s, 1 H), 2.75 (br s, 3 H), 1.53 - 1.57 (m, 3 H), 1.47 (s, 9 H). *m/z* (ESI): 216.1 (M-Boc+H)$^+$

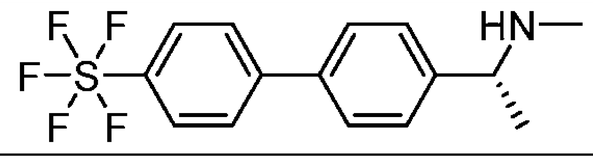
[0145] Step 5. A resealable vial was charged with tert-butyl (R)-(1-(6-bromopyridazin-3-yl)ethyl)(methyl)carbamate (0.160 g, 0.506 mmol), b-[4-(trifluoromethyl)phenyl]-boronic acid (0.288 g, 1.518 mmol, AA Blocks) and potassium carbonate (0.210 g, 1.518 mmol, Oakwood Chemicals) in 1,2-dimethoxyethane (2.300 mL)/ water (0.230 mL). The reaction mixture was sparged with Argon for 5 min. Then $Pd(PPh_3)_4$ (0.117 g, 0.101 mmol, Sigma-Aldrich) was added to the reaction mixture. The vial was sealed, then the reaction mixture was stirred and heated at 90°C for 16 h. The reaction mixture was diluted with EtOAc and brine solution. The layers were separated and the aqueous layer was extracted with EtOAc (3x). The combined organic extract was dried over $MgSO_4$, filtered and concentrated in vacuo. The crude material was absorbed onto a plug of silica gel and purified by chromatography through a Redi-Sep pre-packed silica gel column (40 g), eluting with a gradient of 0-100% EtOAc in heptane, to provide tert-butyl (R)-methyl(1-(6-(4-(trifluoromethyl)phenyl)pyridazin-3-yl)ethyl)carbamate (0.155 g, 0.406 mmol, 80 % yield) as light-yellow solid. ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.16 - 8.47 (m, 1 H), 7.77 - 7.96 (m, 3 H), 7.49 - 7.72 (m, 2 H), 5.07 (s, 1 H), 1.51 (s, 3 H), 1.28 (s, 12 H). *m/z* (ESI): 382.1 (M+H)$^+$

[0146] Step 6. To a 50-mL round-bottomed flask was added tert-butyl (R)-methyl(1-(6-(4-(trifluoromethyl)phenyl)pyridazin-3-yl)ethyl)carbamate (0.140 g, 0.367 mmol) and trifluoroacetic acid (0.419 g, 0.419 mL, 3.67 mmol, Apollo Scientific Ltd.) in 1,2-dichloroethane (3.67 mL). The overall mixture was stirred at rt for 16 h. The reaction mixture was concentrated in vacuo. The crude residue was carried to the next step of the synthesis, without further purification. *m/z* (ESI): 282.2 (M+H)$^+$

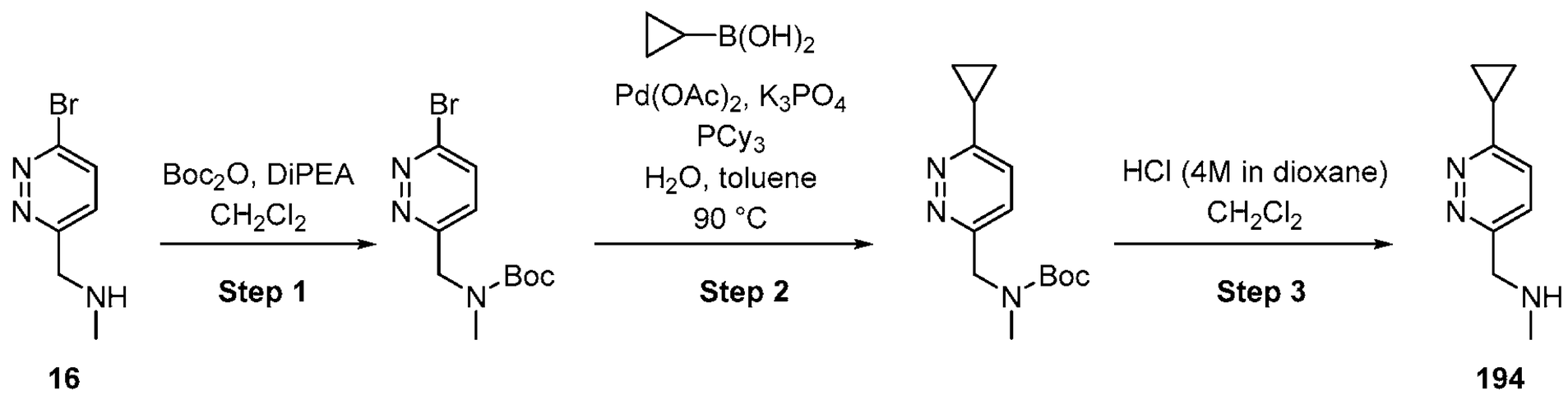
[0147] Secondary amines (**192-193**) in Table 12 were prepared in a manner similar to that described for amine **191** starting from Step 3 using the commercially available chiral amine, (R)-1-(4-Bromophenyl)ethylamine (CAS# 45791-36-4).

Table 12

Int. #	Chemical Structure	Name	*m/z* (ESI): (M+H)$^+$
192		(R)-N-methyl-1-(4'-(trifluoromethyl)-[1,1'-biphenyl]-4-yl)ethan-1-amine	280.3

Int. #	Chemical Structure	Name	*m/z* (ESI): $(M+H)^+$
193		(R)-N-methyl-1-(4'-(pentafluoro-l6-sulfaneyl)-[1,1'-biphenyl]-4-yl)ethan-1-amine	338.2

[0148] Intermediate 194: 1-(6-cyclopropylpyridazin-3-yl)-N-methylmethanamine

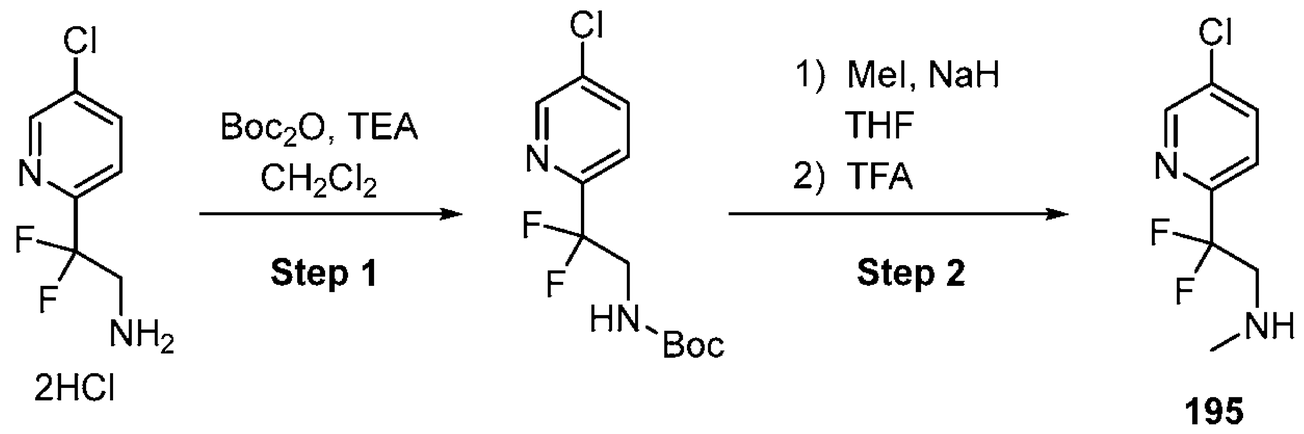


[0149] Step 1. 1-(6-bromopyridazin-3-yl)-N-methylmethanamine (**16**, 176.6 mg, 0.874 mmol) and diisopropylethylamine (226 mg, 305 µL, 1.748 mmol, Sigma-Aldrich Corporation) were stirred in dichloromethane (4370 µL) and Boc anhydride (210 mg, 0.961 mmol, Sigma-Aldrich Corporation) was added. The reaction was stirred at room temp. for 18 hours. The mixture was then partitioned between DCM and water and the layers were separated. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated. The crude product was then purified by medium pressure chromatography (silica, 10 to 100% EtOAc:Heptanes) to give tert-butyl ((6-bromopyridazin-3-yl)methyl)(methyl)carbamate (204 mg, 0.675 mmol, 77 % yield). *m/z* (ESI): 302.0, 304.2 $(M+H)^+$. ^1H NMR (400 MHz, CHLOROFORM-d) δ ppm 7.65 (br d, J=7.9 Hz, 1 H), 7.44 (br d, J=7.1 Hz, 1 H), 4.71 (s, 2 H), 2.93 (br s, 3 H), 1.48 (br d, J=5.4 Hz, 9 H)

[0150] Step 2. A mixture of tert-butyl ((6-bromopyridazin-3-yl)methyl)(methyl)carbamate (204.6 mg, 0.677 mmol), cyclopropylboronic acid (291 mg, 3.39 mmol) and toluene (2888 µL) was purged with Ar, then potassium phosphate tribasic (431 mg, 2.031 mmol, Alfa Aesar) and water (321 µL) were added and the mixture was stirred for 10 min at rt. Then, tricyclohexylphosphine (38.0 mg, 0.135 mmol, Strem Chemicals, Inc.) and palladium (II) acetate (15.20 mg, 0.068 mmol, Strem Chemicals, Inc.) were added. The mixture was stirred in a sealed vial at 90 °C for 2 hours, then it was filtered through celite and concentrated in vacuo. The crude material was purified by chromatography through a silica gel column, eluting with 0-60% 3:1 EtOAc:EtOH in heptanes and tert-butyl ((6-cyclopropylpyridazin-3-yl)methyl)(methyl)carbamate (90.4 mg, 0.343 mmol, 50.7 % yield) was obtained. *m/z* (ESI): 264.2 $(M+H)^+$. ^1H NMR (400 MHz, CHLOROFORM-d) δ ppm 7.39 (br d, J=7.5 Hz, 1 H), 7.17 - 7.27 (m, 1 H), 4.69 (s, 2 H), 2.91 (br s, 3 H), 2.11 - 2.22 (m, 1 H), 1.49 (br s, 9 H), 1.09 - 1.24 (m, 4 H)

[0151] Step 3. To a solution of tert-butyl ((6-cyclopropylpyridazin-3-yl)methyl)(methyl)carbamate (90.4 mg, 0.343 mmol) in dichloromethane (1248 µL) was added hydrogen chloride solution, 4.0 M in dioxane (687 µL, 2.75 mmol, Sigma-Aldrich Corporation). The solution became a suspension so MeOH was added to make the suspension to a solution again. The mixture was stirred was stirred at rt for 4 h until LCMS showed the product. The mixture was concentrated in vacuo. The product 1-(6-cyclopropylpyridazin-3-yl)-N-methylmethanamine hydrochloride (74.8 mg, 0.375 mmol, 109 % yield) was obtained as light brown solid and used directly in further expermiments. *m/z* (ESI): 164.2 $(M+H)^+$.

[0152] Intermediate 195: 2-(5-chloropyridin-2-yl)-2,2-difluoro-N-methylethan-1-amine

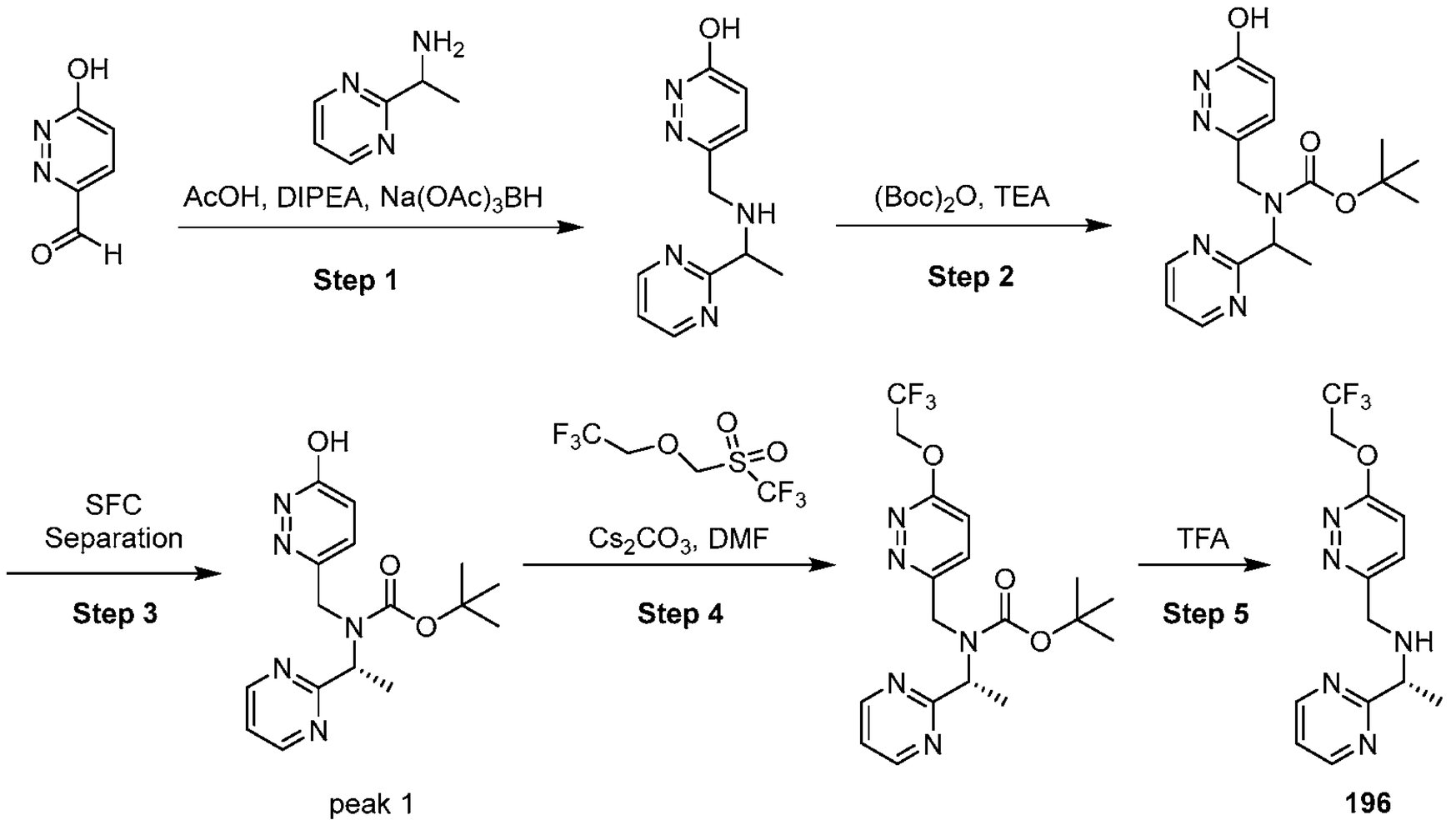


[0153] Step 1. To a stirred ice-cooled solution of 2-(5-chloropyridin-2-yl)-2,2-difluoroethan-1-amine dihydrochloride (307 mg, 1.16 mmol, 1.0 equiv, Enamine) and triethylamine (351 mg, 483 µL, 3.47 mmol, 3.0 equiv, Aldrich) in DCM (3.85 mL) was added di-tert-butyl dicarbonate (252 mg, 1.16 mmol, 1 equiv, Aldrich). The resulting mixture was stirred at 0 °C for 15 minutes then to room temperature until completion over 1.5 hours. The crude mixture was directly loaded on a silica gel column and subjected to medium pressure column chromatography eluting with EtOAc/heptane (15 min from 0 to 100%) to give tert-butyl (2-(5-chloropyridin-2-yl)-2,2-difluoroethyl)carbamate (310 mg, 1.06 mmol, 92 % yield). *m/z* (ESI): 293.1 $(M+H)^+$.

[0154] Step 2. To a stirred ice-cooled solution of tert-butyl (2-(5-chloropyridin-2-yl)-2,2-difluoroethyl)carbamate (300 mg, 1.03 mmol, 1.0 equiv) in THF (5.0 mL) was added sodium hydride (60% dispersion) (36.9 mg, 1.54 mmol,1.5 equiv) under nitrogen atmosphere. The resulting mixture was stirred at 0°C for 15 min before methyl iodide (145 mg, 64.1 µL, 1.03 mmol,1.0 equiv) was added via a syringe. The resulting mixture was stirred at 0 °C for 15 minutes and then at ambient temperature for 16 h. The reaction mixture was cooled in an ice bath before quenching with MeOH. The volatiles were removed *in vacuo* and the residue was purified by medium pressure chromatography (silica, 0 to 100% EtOAc:Heptanes) to give tert-butyl (2-(5-chloropyridin-2-yl)-2,2-difluoroethyl)(methyl)carbamate (210 mg, 0.685 mmol, 66.8 % yield). This material was then dissolved in TFA (4.0 mL) and stirred for 25 minutes to completion. The reaction mixture was then concentrated under reduced pressure on the rotovap to give the crude TFA salt. This salt was then dissolved in MeOH and loaded onto an SCX column, eluted

with 0 to 2M ammonia in MeOH, and cocentrated to give 2-(5-chloropyridin-2-yl)-2,2-difluoro-N-methylethan-1-amine (127 mg, 0.615 mmol, 60.0 % yield). *m/z* (ESI): 207.1 $(M+H)^+$.

[0155] Intermediate 196: (R)-1-(pyrimidin-2-yl)-N-((6-(2,2,2-trifluoroethoxy)pyridazin-3-yl)methyl)ethan-1-amine



peak 1 196

[0156] Step 1. To a 150-mL round-bottomed flask was added 1-(pyrimidin-2-yl)ethan-1-amine dihydrochloride (2.79 g, 14.23 mmol, Enamine) in a 1:1 mixture of methanol (21.56 mL)/dichloromethane (21.56 mL). The reaction mixture was cooled to 0 °C, then n,n'-diisopropylethylamine (3.51 g, 4.74 mL, 27.2 mmol, Sigma-Aldrich Corporation) was added to the reaction mixture and stirred 10 min. Then, 3-formyl-6-hydroxypyridazine (1.60 g, 12.93 mmol, Aurum Pharmatech LLC) and acetic acid (0.77 g, 0.74 mL, 12.93 mmol, Sigma-Aldrich Corporation) were added to the mixture, followed by acetic acid (0.77 g, 0.74 mL, 12.93 mmol, Sigma-Aldrich Corporation). The reaction mixture was warmed to rt over 15 min, Then, sodium triacetoxyborohydride (6.85 g, 32.3 mmol, Sigma-Aldrich Corporation) was added and the overall mixture was stirred for 16 h, while under an inert (N_2) atmosphere. Another aliquot of sodium triacetoxyborohydride (6.85 g, 32.3 mmol, Sigma-Aldrich Corporation) was added to the reaction mixture and stirred an additional 16 h. The reaction mixture was filtered through a pad of Celite, then the filter cake was rinsed with 1:1 MeOH:DCM (3x). The filtrate was collected and concentrated in vacuo. The crude material was absorbed onto a plug of silica gel and purified by chromatography through a Redi-Sep pre-packed silica gel column (120 g), eluting with a gradient of 0-35% MeOH in CH_2Cl_2, to provide 6-(((1-(pyrimidin-2-yl)ethyl)amino)methyl)pyridazin-3-ol (1.11 g, 4.84 mmol, 37.4 % yield) as light-yellow solid. *m/z* (ESI): 232.1 $(M+H)^+$. ^{1}H NMR (400 MHz,

METHANOL-d4) δ ppm 8.78 (d, J=5.0 Hz, 2 H), 7.54 (d, J=9.6 Hz, 1 H), 7.38 (t, J=4.9 Hz, 1 H), 6.92 (d, J=9.6 Hz, 1 H), 4.07 (q, J=6.8 Hz, 1 H), 3.72 (d, J=2.3 Hz, 2 H), 1.98 (s, 1 H), 1.48 (d, J=6.9 Hz, 3 H).

[0157] Step 2. To a 150-mL round-bottomed flask was added 6-(((1-(pyrimidin-2-yl)ethyl)amino)methyl)pyridazin-3-ol (1.11 g, 4.80 mmol) and triethylamine (1.45 g, 2.02 mL, 14.40 mmol, Sigma-Aldrich Corporation) in 1,2-dichloroethane (24.00 mL). Then di-tert-butyl dicarbonate (1.57 g, 1.67 mL, 7.20 mmol, Sigma-Aldrich Corporation) was added to the reaction mixture. The overall reaction mixture was stirred and heated at 70 °C for 2 h. The reaction mixture was quenched with sat. aq. $NaHCO_3$ and the mixture diluted with DCM. The layers were separated, and the aqueous layer was extracted with DCM (3x). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated in vacuo. The crude material was absorbed onto a plug of silica gel and purified by chromatography through a Redi-Sep pre-packed silica gel column (120 g), eluting with a gradient of 0-80% 3:1 EtOAc:EtOH in heptane, to provide tert-butyl ((6-hydroxypyridazin-3-yl)methyl)(1-(pyrimidin-2-yl)ethyl)carbamate (1.043 g, 3.15 mmol, 65.6 % yield) as white solid. *m/z* (ESI): 332.1 $(M+H)^+$. ^1H NMR (400 MHz, DMSO-d6) δ ppm 12.77 (s, 1 H), 8.75 (d, J=4.8 Hz, 2 H), 7.37 (t, J=4.8 Hz, 2 H), 6.85 (d, J=9.6 Hz, 1 H), 4.88 - 5.05 (m, 1 H), 4.42 (br s, 2 H), 1.54 (d, J=7.3 Hz, 3 H), 1.15 - 1.34 (m, 9 H).

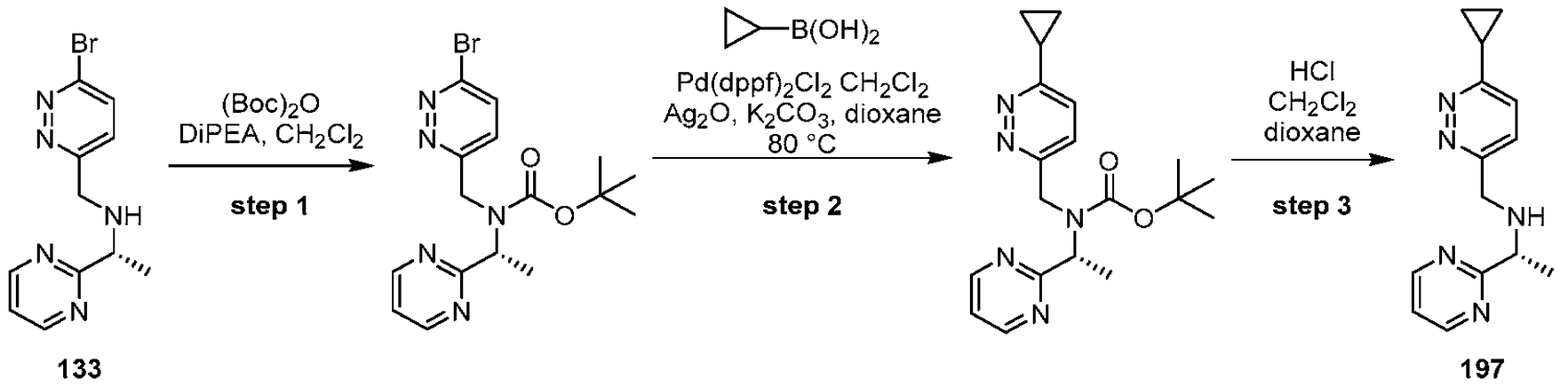
[0158] Step 3. Racemic tert-butyl ((6-hydroxypyridazin-3-yl)methyl)(1-(pyrimidin-2-yl)ethyl)carbamate (1.043 g) was purified via preparative SFC using a Chiral Technologies AD column (250 X 30 mm, 5mm) with a mobile phase of 80% Liquid CO_2 and 20% EtOH with 0.2% TEA using a flowrate of 150 mL/min. The 1st eluting peak was tert-butyl (R)-((6-hydroxypyridazin-3-yl)methyl)(1-(pyrimidin-2-yl)ethyl)carbamate (430 mg, >99% *ee*) . The 2nd eluting peak was tert-butyl (S)-((6-hydroxypyridazin-3-yl)methyl)(1-(pyrimidin-2-yl)ethyl)carbamate (455 mg, 98.8% *ee*). Peak assignment determined by SFC with AD column with 10% EtOH with 0.2% TEA. Peak 1 is the more active enantiomer.

[0159] Step 4. To a 50-mL round-bottomed flask was added tert-butyl (R)-((6-hydroxypyridazin-3-yl)methyl)(1-(pyrimidin-2-yl)ethyl)carbamate (0.20 g, 0.62 mmol) and cesium carbonate (0.25 g, 0.78 mmol, Sigma-Aldrich Corporation) in N, N-dimethylformamide (5.23 mL). Then, 2,2,2-trifluoroethyl triflate (0.18 g, 0.78 mmol, Combi-Blocks Inc.) was added to the reaction mixture over 5 min. The resulting reaction mixture was stirred at rt overnight then it was concentrated in vacuo. The crude material was absorbed onto a plug of silica gel and purified by chromatography through a Redi-Sep pre-packed silica gel column (40 g), eluting with a gradient of 0-60% MeOH in CH_2Cl_2, to provide tert-butyl (R)-(1-(pyrimidin-2-yl)ethyl)((6-(2,2,2-trifluoroethoxy)pyridazin-3-yl)methyl)carbamate (0.20 g, 0.48 mmol, 77 % yield) as light-yellow solid. *m/z* (ESI): 414.1 $(M+H)^+$.

[0160] Step 5. To a 50-mL round-bottomed flask was added tert-butyl (R)-(1-(pyrimidin-2-yl)ethyl)((6-(2,2,2-trifluoroethoxy)pyridazin-3-yl)methyl)carbamate (0.10 g, 0.25 mmol) and trifluoracetic acid (1.00 g, 0.65 mL, 8.81 mmol, Sigma-Aldrich Corporation) in dichloromethane (1.25 mL). The resulting

reaction mixture was stirred at rt for 1 h. The crude (R)-1-(pyrimidin-2-yl)-N-((6-(2,2,2-trifluoroethoxy)pyridazin-3-yl)methyl)ethan-1-amine was concentrated in vacuo and carried to the next step of the synthesis, without further purification. *m/z* (ESI): 314.0 $(M+H)^+$.

[0161] Intermediate 197: (R)-N-((6-cyclopropylpyridazin-3-yl)methyl)-1-(pyrimidin-2-yl)ethan-1-amine



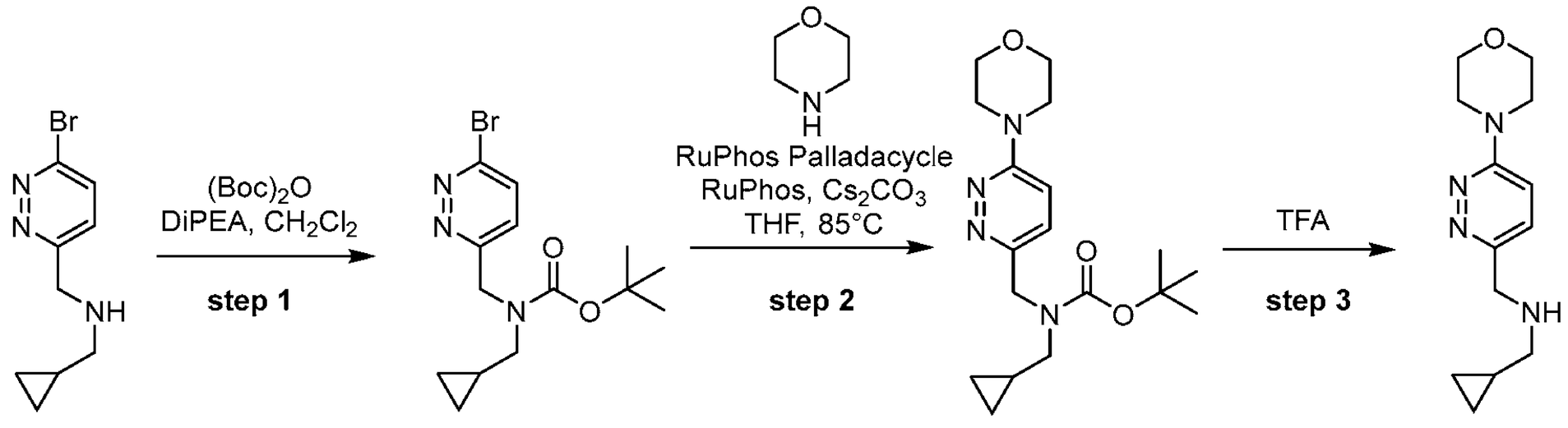
[0162] Step 1. (R)-N-((6-bromopyridazin-3-yl)methyl)-1-(pyrimidin-2-yl)ethan-1-amine (**133,** 0.8 g, 2.72 mmol) and DIPEA (0.703 g, 0.950 mL, 5.44 mmol, Aldrich) were stirred in dichloromethane (13.60 mL) and then di-tert-butyl dicarbonate (0.653 g, 0.695 mL, 2.99 mmol, Oakwood Products, Inc.) was added. The reaction was then stirred at room temp. for 4 hours. An additional 0.5 equiv of Boc_2O were added and after stirring overnight, the mixture was partitioned between 100 mL of DCM and water. The layers were separated. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The crude product was purified by flash chromatography (silica, 10 to 100% EtOAc:Heptanes) to give tert-butyl (R)-((6-bromopyridazin-3-yl)methyl)(1-(pyrimidin-2-yl)ethyl)carbamate (1.16 g, 2.94 mmol, 108 % yield). *m/z* (ESI): 394, 396 $(M+H)^+$.

[0163] Step 2. A mixture of tert-butyl (R)-((6-bromopyridazin-3-yl)methyl)(1-(pyrimidin-2-yl)ethyl)carbamate (0.2 g, 0.507 mmol), cyclopropylboronic acid (0.218 g, 2.54 mmol, Combi-Blocks), [1,1'-bis(diphenylphosphino)ferrocene]-dichloropalladium (ii) dichloromethane complex (0.041 g, 0.051 mmol, Oakwood Products, Inc.), silver (i) oxide (0.223 g, 0.964 mmol, Sigma-Aldrich Corporation), potassium carbonate (0.210 g, 1.522 mmol, Acros) and 1,4-dioxane (5 mL) was purged with Ar, then stirred in a sealed vial at 80°C for 4.5 h. Then, the mixture was filtered through Celite and concentrated in vacuo. The crude material was purified by chromatography through a silica gel column, eluting with 0-100% 3/1 EtOAc/EtOH in heptane. tert-Butyl (R)-((6-cyclopropylpyridazin-3-yl)methyl)(1-(pyrimidin-2-yl)ethyl)carbamate (149.2 mg, 0.42 mmol, 83% yield) was obtained as off-white solid and used in the next step. *m/z* (ESI): 356.3 $(M+H)^+$

[0164] Step 3. To a solution of tert-butyl (R)-((6-cyclopropylpyridazin-3-yl)methyl)(1-(pyrimidin-2-yl)ethyl)carbamate (0.14 g, 0.394 mmol) in dichloromethane (4 mL) was added HCl, 4.0 M in dioxane (0.788 mL, 3.15 mmol, Aldrich), causing the solution became a suspension. MeOH was added to make the suspension to a solution again. The mixture was stirred was stirred at rt overnight and then

concentrated in vacuo and (R)-N-((6-cyclopropylpyridazin-3-yl)methyl)-1-(pyrimidin-2-yl)ethan-1-amine (155 mg, 0.425 mmol, 108% yield) was obtained as orange solid. *m/z* (ESI): 256 $(M+H)^+$

[0165] Intermediate 198: 1-cyclopropyl-N-((6-morpholinopyridazin-3-yl)methyl)methanamine



18 198

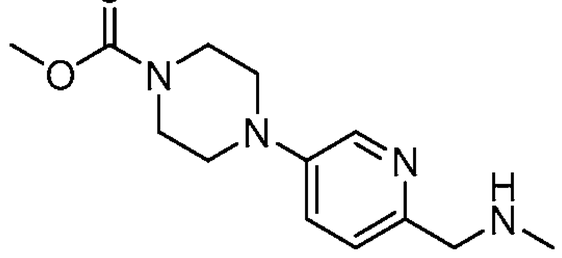
[0166] Step 1. 1-(6-bromopyridazin-3-yl)-N-(cyclopropylmethyl)methanamine (**18,** 0.84 g, 3.47 mmol) and DIPEA (0.897 g, 1.21 mL, 6.94 mmol, Aldrich) were stirred in dichloromethane (17.4 mL) and then di-tert-butyl dicarbonate (1.21 g, 1.29 mL, 5.55 mmol, Oakwood Products, Inc.) was added. The reaction was stirred at room temperature overnight. The mixture was then partitioned between 200 mL of DCM and water. The layers were separated. The organic layer was dried over Na_2SO_4 and concentrated to give crude tert-butyl ((6-bromopyridazin-3-yl)methyl)(cyclopropylmethyl)carbamate (1.31 g, 3.83 mmol, 110% yield), that is contaminated with ~30% Boc anhydride side-product. This material was used successfully in the next reaction. *m/z* (ESI): 342, 344 $(M+H)^+$ ^1H NMR (400 MHz, DMSO-d6) δ ppm 7.11 (br d, J=8.6 Hz, 1 H), 6.76 (d, J=9.0 Hz, 1 H), 4.02 (s, 1 H), 3.96 (s, 1 H), 2.40 - 2.46 (m, 1 H), 0.54 - 0.73 (m, 10 H), 0.25 - 0.29 (m, 2 H), 0.18 (br s, 1 H), -0.36 (br d, J=7.3 Hz, 1 H), -0.61 (br s, 1 H)

[0167] Step 2. RuPhos Palladacycle G1 (298 mg, 0.365 mmol, Strem), RuPhos (170 mg, 0.365 mmol, Strem), morpholine (256 µL, 255 mg, 2.92 mmol, Aldrich), cesium carbonate (1.55 g, 4.75 mmol, Aldrich), and tert-butyl ((6-bromopyridazin-3-yl)methyl)(cyclopropylmethyl)carbamate (500 mg, 1.46 mmol) were combined in THF and heated at 85 °C for 2.5 hours. The reaction mixture was then diluted with EtOAc and filtered over a pad of diatomaceous earth. The residue was purified by medium pressure chromatography (silica, 0 to 100% EtOAc:Heptanes) to give tert-butyl (cyclopropylmethyl)((6-morpholinopyridazin-3-yl)methyl)carbamate (430 mg, 1.234 mmol, 84% yield). *m/z* (ESI): 349.1 $(M+H)^+$ ^1H NMR (400 MHz, CHLOROFORM-d) δ ppm 7.29 - 7.41 (m, 1 H), 6.88 (d, J=9.4 Hz, 1 H), 4.68 (s, 2 H), 3.78 - 3.86 (m, 4 H), 3.55 - 3.63 (m, 4 H), 3.03 - 3.20 (m, 2 H), 1.46 (br s, 9 H), 0.87 - 1.00 (m, 1 H), 0.37 - 0.43 (m, 2 H), 0.17 (br s, 2 H).

[0168] Step 3. tert-butyl (cyclopropylmethyl)((6-morpholinopyridazin-3-yl)methyl)carbamate was dissolved in TFA (12.5 mL) and stirred for 15 minutes to completion. The reaction mixture was the concentrated under reduced pressure and the residue was dissolved in MeOH, eluted through an SCX

column with 0 to 2M ammonia in MeOH, and concentrated to give 1-cyclopropyl-N-((6-morpholinopyridazin-3-yl)methyl)methanamine (**198,** 90.0 mg, 0.362 mmol, 24.8 % yield). *m/z* (ESI): 249.2 $(M+H)^+$

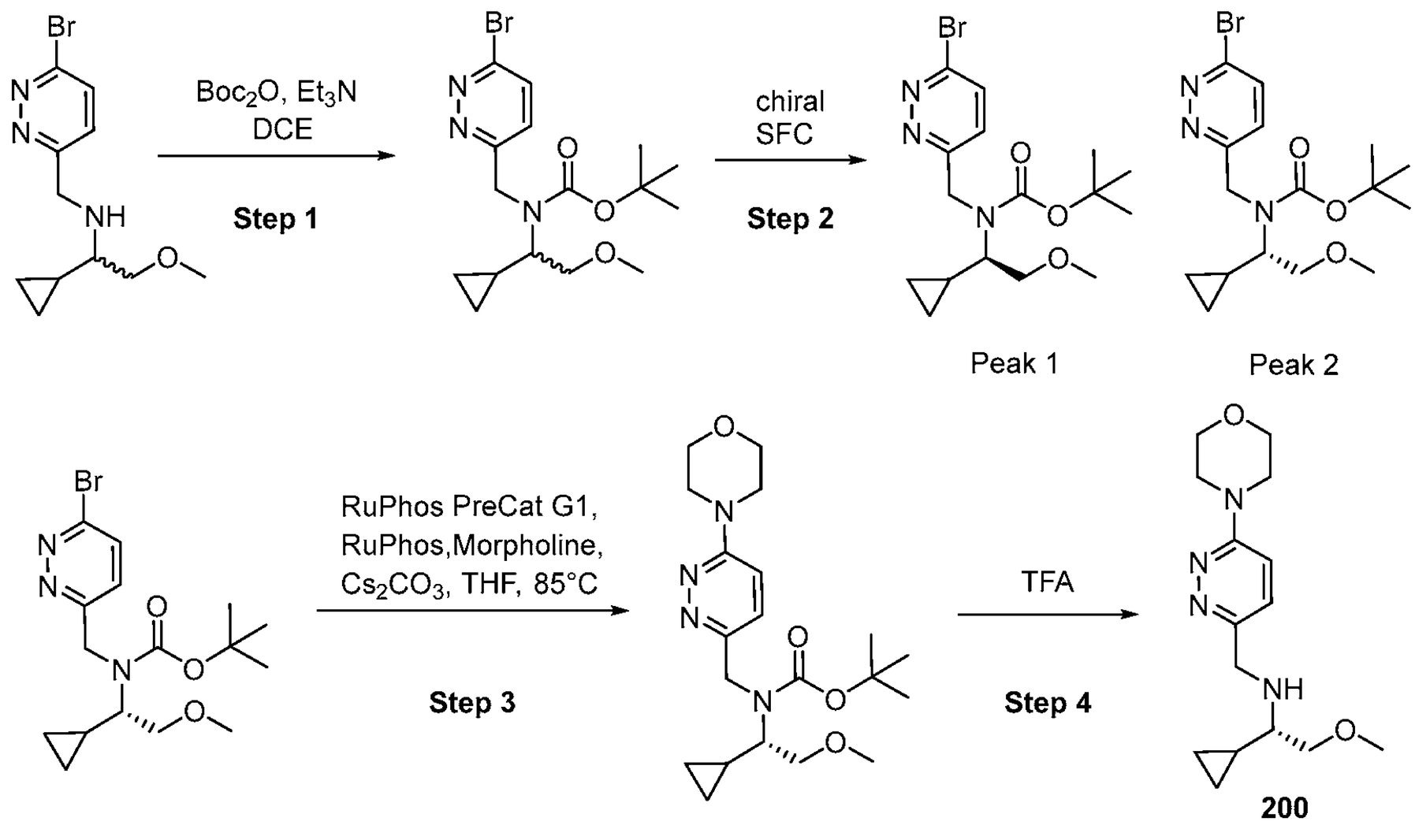
[0169] Intermediate 199: methyl 4-(6-((methylamino)methyl)pyridin-3-yl)pipe159razine-1-carboxylate



199

[0170] Intermediate 199 was prepared in a fashion similar to that described above for amine **198**. *m/z* (ESI): 265.2 $(M+H)^+$

[0171] Intermediate 200: (S)-1-Cyclopropyl-2-methoxy-N-((6-morpholinopyridazin-3-yl)methyl)ethan-1-amine



[0172] Step 1. To a 100-mL round-bottomed flask was added N-((6-bromopyridazin-3-yl)methyl)-1-cyclopropyl-2-methoxyethan-1-amine (0.075 g, 0.26 mmol) and triethylamine (0.080 g, 0.11 mL, 0.79 mmol, Sigma-Aldrich Corporation) in 1,2-dichloroethane (1.30 mL). Then, di-tert-butyl dicarbonate (0.086 g, 0.091 mL, 0.390 mmol, Sigma-Aldrich Corporation) was added to the reaction mixture. The overall reaction mixture was stirred and heated at 70 °C for 2 h. The reaction mixture was quenched with sat. aq. $NaHCO_3$ and the mixture diluted with DCM. The layers were separated, and the aqueous layer was extracted with DCM (3x). The combined organic extracts were dried over $MgSO_4$, filtered and

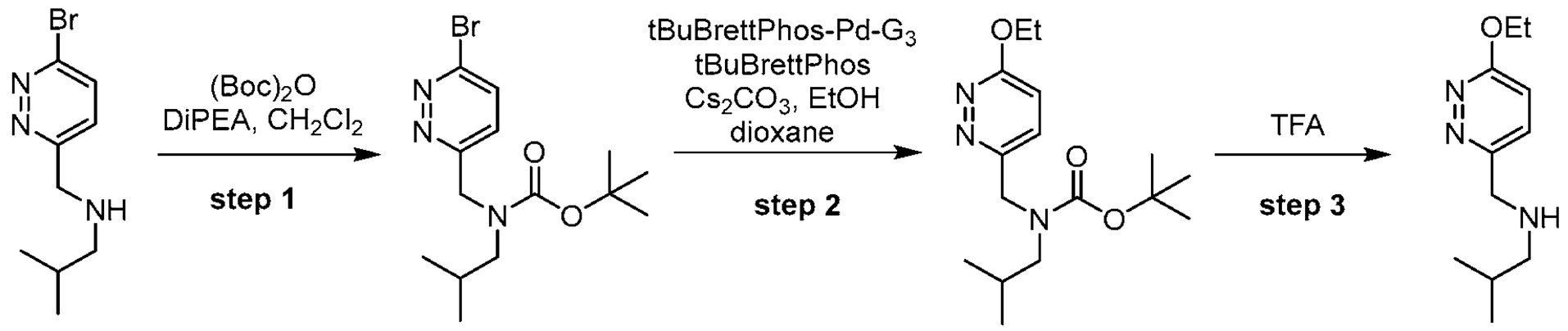
concentrated *in vacuo*. The crude material was absorbed onto a plug of silica gel and purified by chromatography through a Redi-Sep pre-packed silica gel column (12 g), eluting with a gradient of 0-30% 3:1 EtOAc:EtOH in heptane, to provide racemic tert-butyl ((6-bromopyridazin-3-yl)methyl)(1-cyclopropyl-2-methoxyethyl)carbamate (0.085 g, 0.220 mmol, 84 % yield) as tan solid. *m/z* (ESI): 386.0 $(M+H)^+$.

[0173] Step 2. The racemic sample was purified via preparative SFC using a Chiral Technologies IG column (250 X 21 mm, 5mm) with a mobile phase of 90% Liquid CO_2 and 10% iPrOH with 0.2% TEA using a flowrate of 80 mL/min to generate 390 mg of peak 1 with an *ee* of 98% and 380 mg of peak 2 with an ee of 98%. Absolute stereochemistry was assigned arbitrarily for these isomers and the more potent peak 2 was taken forward below as the (S)-isomer.

[0174] Step 3. Tert-butyl (*S*)-((6-bromopyridazin-3-yl)methyl)(1-cyclopropyl-2-methoxyethyl)carbamate (peak 2, 170 mg, 0.440 mmol), RuPhos (51.0 mg, 0.110 mmol, Aldrich), RuPhos PreCat G1 (90.0 mg, 0.110 mmol, Strem), cesium carbonate (470 mg, 1.40 mmol, Aldrich) and morpholine (0.077 mL, 0.88 mmol, Spectrum) were combined in degassed THF (2.9 mL) and heated at 85 °C for two hours to completion. The reaction was then cooled and diluted with EtOAc and filtered over a pad of diatomaceous earth. The filtrate was then concentrated and the residue was purified by medium pressure chromatography (silica, 0 to 100% EtOAc:Heptanes to 30 to 100% (3:1 EtOAc:EtOH:Heptanes) to give impure tert-butyl (S)-(1-cyclopropyl-2-methoxyethyl)((6-morpholinopyridazin-3-yl)methyl)carbamate.

[0175] Step 4. This material was dissolved in TFA (10 mL) and stirred for 10 minutes. The reaction mixture was then concentrated and the residue was then eluted through an SCX column eluting with 0 to 2M ammonia in MeOH and cocentrated to give (*S*)-1-cyclopropyl-2-methoxy-N-((6-morpholinopyridazin-3-yl)methyl)ethan-1-amine (110 mg, 0.37 mmol, 83% yield). *m/z* (ESI): 293.1 $(M+H)^+$.

[0176] Intermediate 201: N-((6-ethoxypyridazin-3-yl)methyl)-2-methylpropan-1-amine



17 201

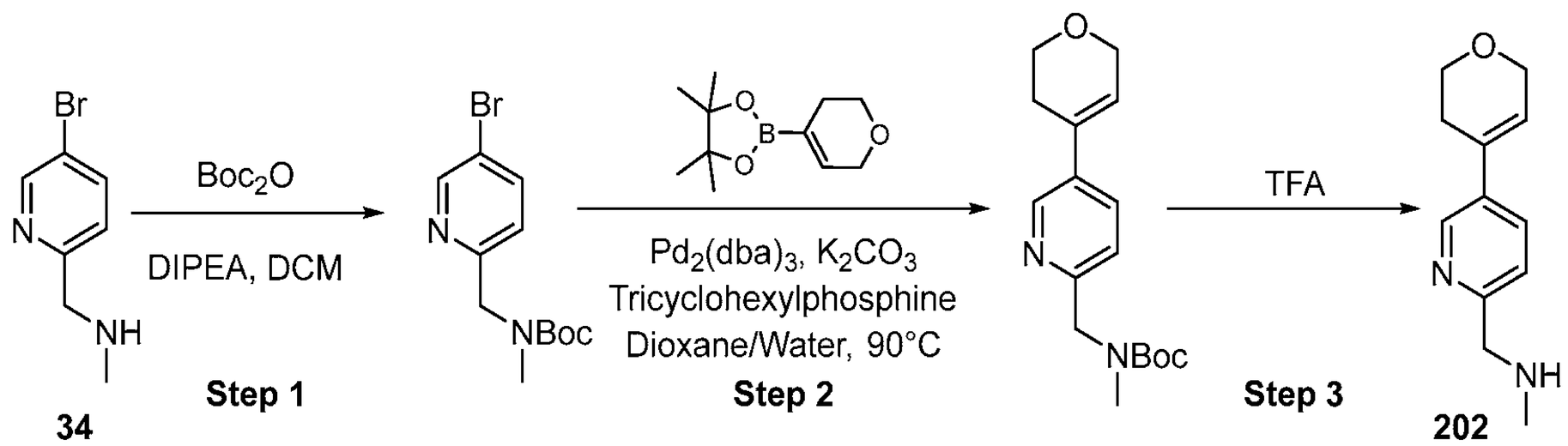
[0177] Step 1. N-((6-bromopyridazin-3-yl)methyl)-2-methylpropan-1-amine (**17,** 0.950 g, 3.89 mmol) and DIPEA (1.01 g, 1.36 mL, 7.78 mmol, Aldrich) were stirred in dichloromethane (19.5 mL) and then di-tert-butyl dicarbonate (1.36 g, 1.45 mL, 6.23 mmol, Oakwood Products, Inc.) was added. The reaction

was then stirred at room temperature overnight. The mixture was then partitioned between 200 mL of DCM and water. The layers were separated. The organic layer was dried over $MgSO_4$ and concentrated to give crude tert-butyl ((6-bromopyridazin-3-yl)methyl)(isobutyl)carbamate (1.89 g, 5.49 mmol, 141 % yield) that was ~30% contaminated with Boc anhydride side-product. This material was used directly in the next reaction. *m/z* (ESI): 344, 346 $(M+H)^+$

[0178] Step 2. A re-sealable screw-cap test tube (Tube A) was charged with tBuBrettPhos (170 mg, 0.350 mmol, 0.150 equiv), cesium carbonate (1.10 g, 3.30 mmol, 1.40 equiv), and tert-butyl ((6-bromopyridazin-3-yl)methyl)(isobutyl)carbamate (800 mg, 2.3 mmol, 1.0 equiv). Tube A was evacuated and backfilled with argon (3x), and ethanol (1000 µL, 17.0 mmol, 7.50 equiv) was then added into tube A via syringe. Simultaneously, a re-sealable screw-cap test tube equipped with a Teflon-coated magnetic stir bar (Tube B) was charged with tBuBrettPhos Pd G3 (300 mg, 0.350 mmol, 0.150 equiv). Tube B was then evacuated and backfilled with argon (3x), and 1,4-dioxane (12.0 mL) was added into tube B via syringe. The reaction mixture in tube B was stirred at room temperature for ~1 min to form a homogeneous solution. The pre-catalyst solution from tube B was transferred into tube A via syringe. The resulting reaction mixture in tube A was stirred at room temperature for 20 h. The crude product was diluted with ethyl acetate and concentrated in vacuo with the aid of a rotary evaporator. The crude product residue was purified by flash column chromatography by medium pressure chromatography (silica, 0 to 100% EtOAc:Heptanes) to afford ((6-ethoxypyridazin-3-yl)methyl)(isobutyl)carbamate. *m/z* (ESI): 310.1 $(M+H)^+$

[0179] Step 3. This material was then dissolved in TFA (10 mL) and stirred for 15 minutes to completion. The reaction mixture was then concentrated under reduced pressure and the residue was free based by dissolving in MeOH, eluting through an SCX column eluting with 0 to 2M ammonia in MeOH, and concentrating to give N-((6-ethoxypyridazin-3-yl)methyl)-2-methylpropan-1-amine with about 80% purity that was used successfully in the next reaction. 100 mg was obtained on first pass though SCX column with a trace of TFA present. *m/z* (ESI): 210.1 $(M+H)^+$ ^1H NMR (400 MHz, CHLOROFORM-d) δ ppm 7.41 - 7.52 (m, 1 H), 6.92 (d, J=9.0 Hz, 1 H), 4.57 (q, J=7.1 Hz, 2 H), 4.00 (s, 2 H), 2.43 - 2.51 (m, 2 H), 1.74 - 1.89 (m, 2 H), 1.45 (t, J=7.1 Hz, 3 H), 0.93 (d, J=6.5 Hz, 6 H)

[0180] Intermediate 202: 1-(5-(3,6-dihydro-2H-pyran-4-yl)pyridin-2-yl)-N-methylmethanamine

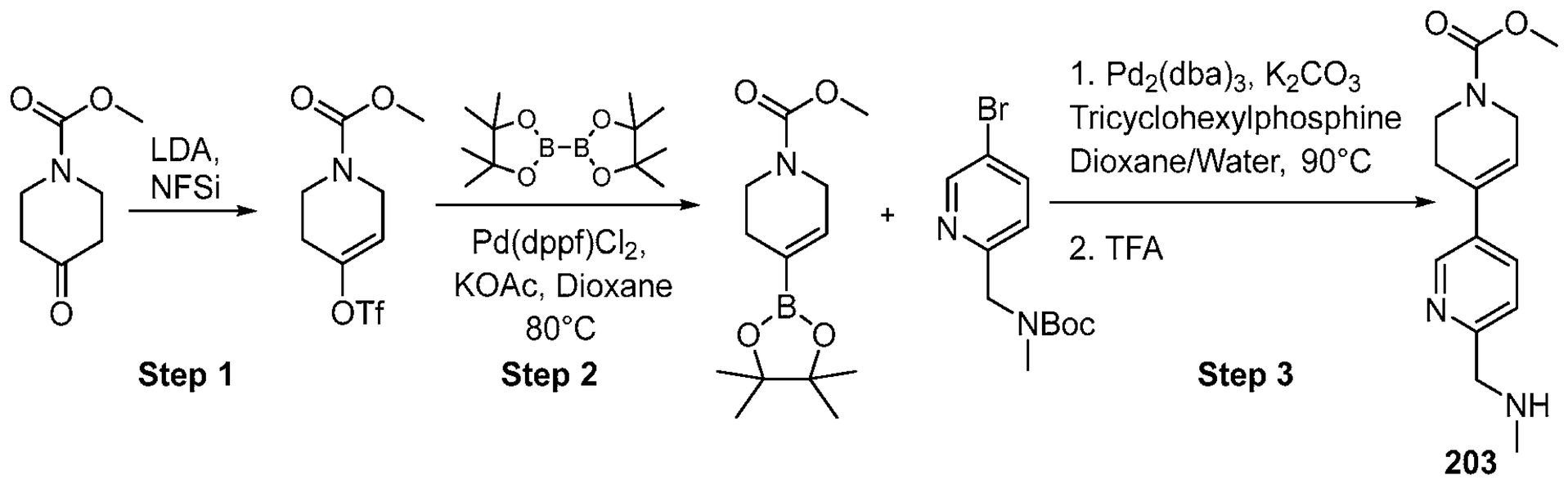


[0181] Step 1. 1-(5-Bromopyridin-2-yl)-N-methylmethanamine (0.950 g, 4.72 mmol, **34**) and DIPEA (1.22 g, 1.65 mL, 9.45 mmol, Aldrich) were stirred in dichloromethane (23.6 mL) and the di-tert-butyl dicarbonate (1.65 g, 1.76 mL, 7.56 mmol, Oakwood Products, Inc.) was added. The reaction was then stirred at room temp. overnight to completion. The mixture was then partitioned between 200 mL of DCM and 50 mL of water. The layers were separated. The organic layer was dried over $MgSO_4$ and concentrated to give crude tert-butyl ((5-bromopyridin-2-yl)methyl)(methyl)carbamate (1.42 g, 4.71 mmol, 100 % yield). *m/z* (ESI): 301.2, 303.1 $(M+H)^+$.

[0182] Steps 2. The 2-(3,6-dihydro-2H-pyran-4-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (837 mg, 3.98 mmol, Combi-Blocks), tricyclohexylphosphine (112 mg, 0.398 mmol, Strem), tert-butyl ((5-bromopyridin-2-yl)methyl)(methyl)carbamate (0.600 g, 1.99 mmol, From Step 1) and $Pd_2(dba)_3$ (182 mg, 0.199 mmol, Acros) were slurried in dioxane (7.00 mL) and then sparged with argon. The potassium carbonate (1.30 M solution) (4.14 mL, 5.38 mmol, Aldrich) was then added and the reaction mixture was heated to 90 °C for one hour. The reaction was cooled and then concentrated to a reduced volume. This residue was then taken up in water (30 mL) and extracted with dichloromethane (2 x 80 mL). The combined organic layers were dried over magnesium sulfate and concentrated. The crude product was purified by medium pressure chromatography (silica, 0 to 100% EtOAc:Heptanes) to give tert-butyl ((5-(3,6-dihydro-2H-pyran-4-yl)pyridin-2-yl)methyl)(methyl)carbamate (372 mg, 1.22 mmol, 61.3 % yield).

[0183] Step 3. This material was then dissolved in 7 mL of TFA and stirred for 10 minutes resulting in complete deprotection. The reaction mixture was then concentrated and the resulting TFA salt was free based by dissolving in MeOH, eluting through an SCX column using 0 to 2M ammonia in MeOH, and concentrating to give 1-(5-(3,6-dihydro-2H-pyran-4-yl)pyridin-2-yl)-N-methylmethanamine (90.0 mg, 440 mmol, 22.1% yield). *m/z* (ESI): 205.2 $(M+H)^+$.

[0184] Intermediate 203: 6-((methylamino)methyl)-3',6'-dihydro-[3,4'-bipyridine]-1'(2'H)-carboxylate



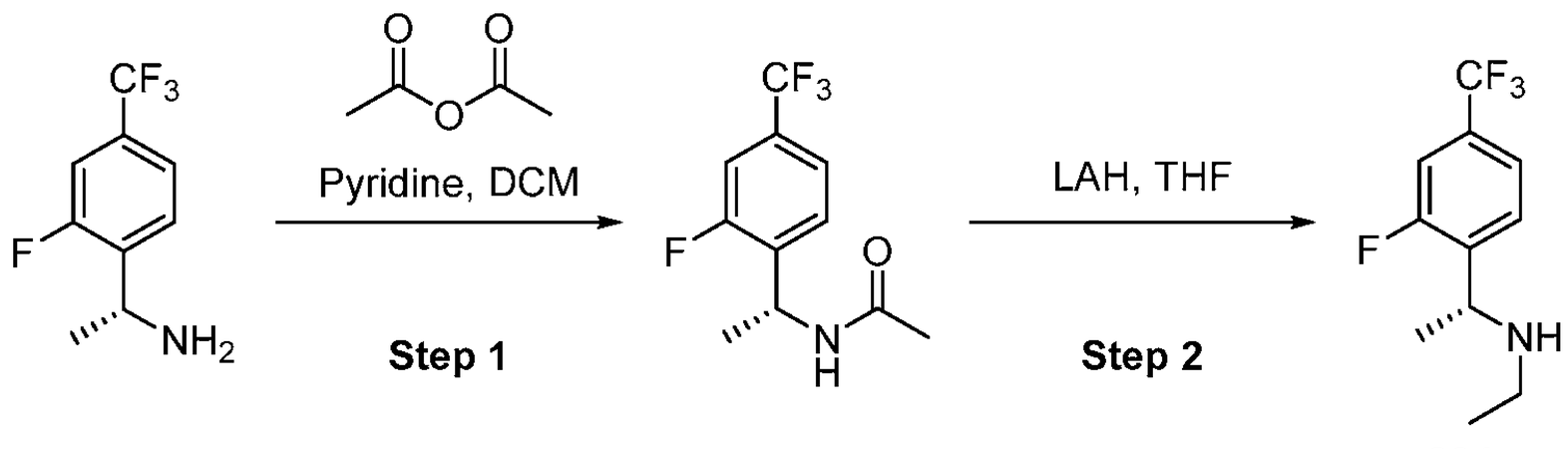
[0185] Step 1. Diisopropylamine (185 mg, 0.261 mL, 1.83 mmol, Aldrich) was dissolved in THF (7.00 mL) and cooled to -78 °C. Then, n-butyllithium (2.50 M in hexanes) (0.732 mL, 1.83 mmol, Aldrich) was added dropwise at -78 °C and stirred for 25 minutes. The mixture was raised out of the dry ice bath for 15 minutes then resubmerged. Methyl 4-oxopiperidine-1-carboxylate (250 mg, 1.59 mmol, Combi-Blocks) was then dissolved in THF (4.00 mL) and added slowly to the LDA solution at -78 °C and stirred for 45 minutes. N-phenyl-bis(trifluoromethanesulfonimide) (625 mg, 1.75 mmol, Combi-Blocks) dissolved in THF (5.00 mL) was added slowly and the reaction mixture was allowed to stir overnight while warming to room temperature. The reaction mixture was quenched with water (20 mL) and the mixture was extracted with hexanes (3 x 50 mL). The combined organic layers were washed with brine and dried over magnesium sulfate. The crude product was purified by medium pressure chromatography (silica, 0 to 40% ethyl acetate:hexanes) to give methyl 4-(((trifluoromethyl)sulfonyl)oxy)-3,6-dihydropyridine-1(2H)-carboxylate (249 mg, 0.861 mmol, 54.1% yield). *m/z* (ESI): 290.1 $(M+H)^+$.

[0186] Step 2. The methyl 4-(((trifluoromethyl)sulfonyl)oxy)-3,6-dihydropyridine-1(2H)-carboxylate (230 mg, 0.795 mmol), bis(pinacolato)diboron (242 mg, 0.954 mmol, Aldrich), 1,1'-bis(diphenylphosphino)ferrocene-palladium dichloride (64.9 mg, 0.080 mmol, Strem Chemicals, Inc.), and potassium acetate (312 mg, 3.18 mmol, Aldrich) were added to a flask with dioxane (2.65 mL). This mixture was heated at 80 °C overnight. The reaction mixture was cooled, filtered, and washed with ethyl acetate. The filtrate was concentrated and purified by medium pressure chromatography (silica, 0 to 60% EtOAc : heptanes) to give methyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,6-dihydropyridine-1(2H)-carboxylate (130 mg, 0.487 mmol, 61.2% yield) *m/z* (ESI): 268.2 $(M+H)^+$.

[0187] Step 3. Methyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,6-dihydropyridine-1(2H)-carboxylate (133 mg, 0.498 mmol, From Step 2), tricyclohexylphosphine (27.9 mg, 0.100 mmol, Strem), tert-butyl ((5-bromopyridin-2-yl)methyl)(methyl)carbamate (0.150 g, 0.498 mmol, Boc-**34**, see Step 1 for intermediate 202) and $Pd_2(dba)_3$ (45.6 mg, 0.050 mmol, Acros) were slurried in dioxane (1.74 mL) and sparged with argon. Potassium carbonate (1.30 M soln.) (1.03 mL, 1.35 mmol, Aldrich) was added and the reaction mixture was heated to 90°C for one hour. The reaction was cooled and concentrated to a

reduced volume. This residue was taken up in water (15 mL) and extracted with dichloromethane (2 x 40 mL). The combined organic layers were dried over magnesium sulfate and concentrated. The crude product was purified by medium pressure chromatography (silica, 0 to 100% EtOAc:Heptanes) to give methyl 6-(((tert-butoxycarbonyl)(methyl)amino)methyl)-3',6'-dihydro-[3,4'-bipyridine]-1'(2'H)-carboxylate (93.0 mg, 0.257 mmol, 51.7 % yield). The material was dissolved in TFA and stirred for 10 minutes to Boc-deprotect. The mixture was concentrated to give the TFA salt of the desired product. The salt was then free based by eluting through an SCX column eluting with 0 to 2M ammonia in methanol and concentrating to give methyl 6-((methylamino)methyl)-3',6'-dihydro-[3,4'-bipyridine]-1'(2'H)-carboxylate (63.0 mg, 0.241 mmol, 48.4 % yield) *m/z* (ESI): 262.2 $(M+H)^+$.

[0188] Intermediate 204: (R)-N-ethyl-1-(2-fluoro-4-(trifluoromethyl)phenyl)ethan-1-amine`



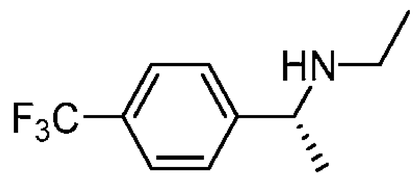
204

[0189] Step 1. To a 100-mL 2-neck round-bottomed flask was added (R)-1-(2-fluoro-4-(trifluoromethyl)phenyl)ethan-1-amine (0.50 g, 2.41 mmol, AP Bioscience) and pyridine (0.27 g, 0.27 mL, 3.38 mmol, Sigma-Aldrich Corporation) in dichloromethane (12 mL). The reaction mixture was cooled to -78 °C, then acetic anhydride (0.30 g, 0.27 mL, 2.90 mmol, Sigma-Aldrich Corporation) was added dropwise to the reaction mixture over 2 min, while under an inert (N2) atmosphere. The ice bath was removed, and the reaction mixture was stirred at rt for 2 h. The reaction mixture was cooled to 0°C, then the reaction mixture was quenched with 1 N HCl (2.4 mL). This mixture was diluted with heptane (20 mL), washed with 1N HCl (6 mL x 2), then sat. aq. $NaHCO_3$ (12 mL) and brine (12 mL). The organics were collected, then dried over $MgSO_4$, filtered and concentrated in vacuo, to provide (R)-N-(1-(2-fluoro-4-(trifluoromethyl)phenyl)ethyl)acetamide (0.43 g, 1.73 mmol, 72% yield) as white solid. ^1H NMR (400 MHz, DMSO-d_6) δ ppm 8.48 (br d, *J*=7.3 Hz, 1 H), 7.53 - 7.66 (m, 3 H), 5.13 (quin, *J*=7.2 Hz, 1 H), 1.86 (s, 3 H), 1.35 (d, *J*=7.1 Hz, 3 H). *m/z* (ESI): 250.0 $(M+H)^+$.

[0190] Step 2. To a 150-mL round-bottomed flask was added (R)-N-(1-(2-fluoro-4-(trifluoromethyl)phenyl)ethyl)acetamide (0.42 g, 1.69 mmol) in tetrahydrofuran (9 mL). Then lithium aluminum hydride solution, 2.0 M in tetrahydrofuran (2.1 mL, 4.21 mmol, Sigma-Aldrich Corporation) was added slowly to the reaction mixture over 2 min. The resulting reaction mixture was stirred at rt for 1 h, then the mixture was stirred and heated at 55 °C for 5 h. The reaction mixture was diluted with heptane

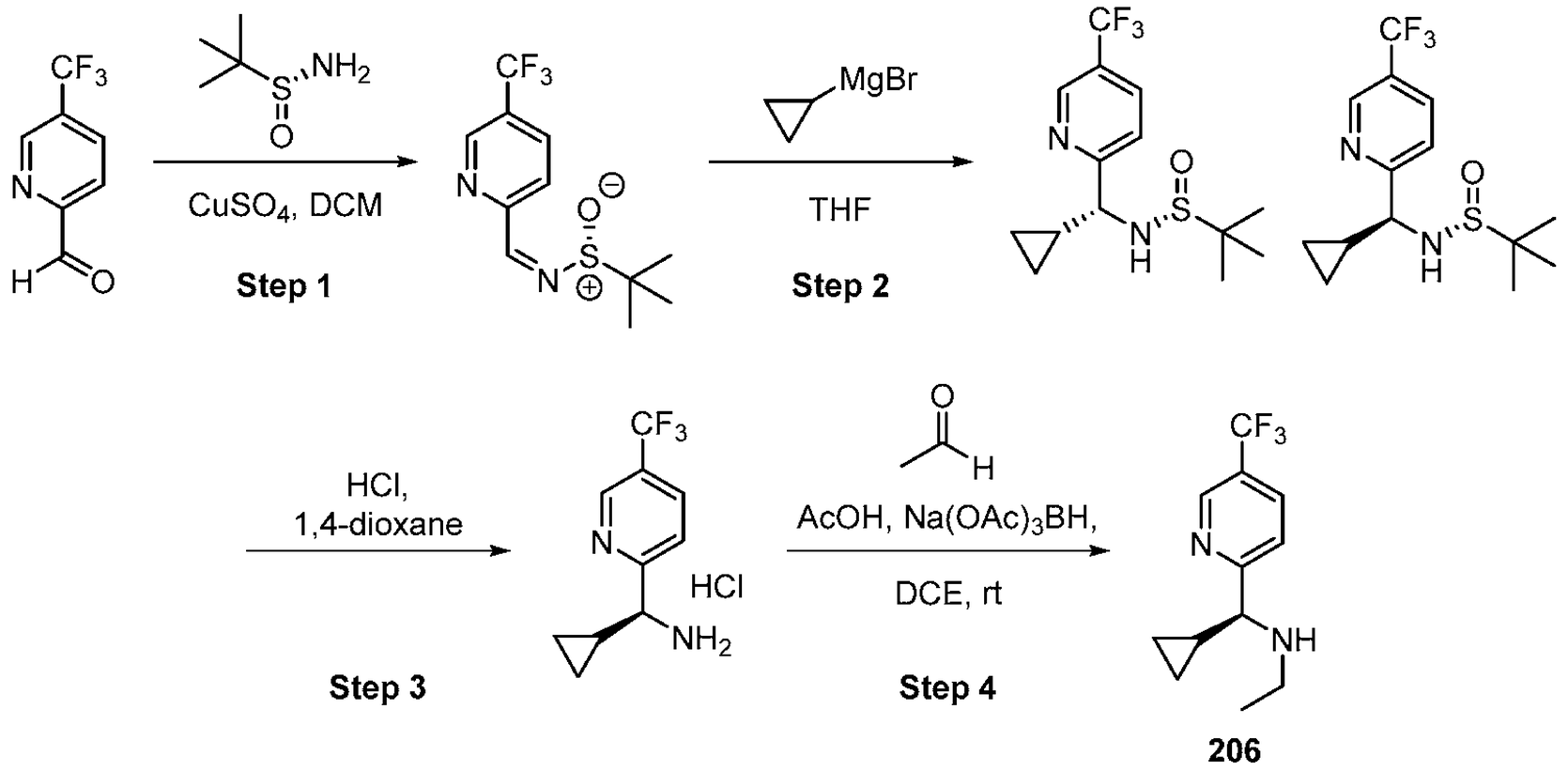
(15 mL) and cooled to 0°C. Then water (0.4 mL) was added to the mixture and stirred 1 min. Then aq. 15% NaOH (0.4 mL) was added to the mixture and stirred 1 min. Then, water (3 x 1.2 mL) was added to the mixture and the resulting mixture was warmed to rt over 15 min. $MgSO_4$ was added to the mixture and stirred an additional 15 min. The overall reaction mixture was filtered through a pad of Celite, then the filtrate was collected and concentrated in *vacuo*. The crude material was absorbed onto a plug of silica gel and purified by chromatography through a Redi-Sep pre-packed silica gel column (40 g), eluting with a gradient of 0-60% EtOAc:EtOH (3:1) in heptane, to provide (R)-N-ethyl-1-(2-fluoro-4-(trifluoromethyl)phenyl)ethan-1-amine (0.081 g, 0.344 mmol, 20.43 % yield) as light-yellow oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.76 (t, *J*=7.7 Hz, 1 H), 7.53 - 7.61 (m, 2 H), 4.07 (q, *J*=6.6 Hz, 1 H), 2.26 - 2.40 (m, 2 H), 2.08 - 2.17 (m, 1 H), 1.26 (d, *J*=6.7 Hz, 3 H), 0.98 (t, *J*=7.1 Hz, 3 H). *m/z* (ESI): 236.1 $(M+H)^+$.

[0191] Intermediate 205: (R)-N-ethyl-1-(4-(trifluoromethyl)phenyl)ethan-1-amine



[0192] Intermediate 205 was prepared in a manner similar to that described for Intermediate 204. *m/z* (ESI): 218.1 $(M+H)^+$

[0193] Intermediate 206: Preparation of (S)-N-(cyclopropyl(5-(trifluoromethyl)pyridin-2-yl)methyl)ethanamine



206

[0194] Step 1. To an oven-dried 100-mL round-bottomed flask was added (R)-(+)-2-methyl-2-propanesulfinamide (0.50 g, 4.13 mmol, AK Scientific, Inc.) in dichloromethane (8.25 mL). To this mixture was added copper (ii) sulfate (1.32 g, 8.25 mmol, Sigma-Aldrich Corporation) followed by 5-(trifluoromethyl)picolinaldehyde (0.75 g, 4.13 mmol, J&W Pharmlab). The resulting reaction mixture was

stirred at rt for 24 h. The reaction mixture was filtered through a pad of Celite and the filter cake was washed well with DCM. The filtrate was collected and concentrated *in vacuo*. The crude was purified by flash chromatography (silica, 0-20% EtOAc:EtOH (3:1) in heptane), to provide (R,E)-2-methyl-N-((5-(trifluoromethyl)pyridin-2-yl)methylene)propane-2-sulfinamide (1.105 g, 3.97 mmol, 96 % yield) as off-white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 9.15 - 9.19 (m, 1 H), 8.56 (s, 1 H), 8.42 (dd, *J*=8.2, 2.3 Hz, 1 H), 8.28 (d, *J*=8.2 Hz, 1 H), 1.23 (s, 9 H). *m/z* (ESI): 279.0 $(M+H)^+$.

[0195] Step 2. To an oven-dried 100-mL 2-neck round-bottomed flask was added (R,E)-2-methyl-N-((5-(trifluoromethyl)pyridin-2-yl)methylene)propane-2-sulfinamide (0.40 g, 1.44 mmol) in tetrahydrofuran (7.19 mL). The reaction mixture was cooled to -78 °C, then cyclopropylmagnesium bromide solution, 0.5 M in THF (5.17 mL, 2.59 mmol, Sigma-Aldrich Corporation) was added dropwise to the reaction mixture. After 10 min, the reaction was quenched with the addition of sat. aq. NH_4Cl (5.8 mL) and extracted with EtOAc (3 x 25 mL). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated in vacuo. The crude was purified by flash chromatography (silica, 0-60% EtOAc:DCM), to provide both diastereomers with peak 1 being assigned as the (R)-Sulfinamine (0.176 g, 0.55 mmol, 38% yield), a light-yellow oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.91 (s, 1 H), 8.24 (dd, *J*=8.4, 2.3 Hz, 1 H), 7.79 (d, *J*=8.4 Hz, 1 H), 5.82 (d, *J*=7.5 Hz, 1 H), 3.81 (t, *J*=8.0 Hz, 1 H), 1.12 - 1.24 (m, 10 H), 0.36 - 0.62 (m, 4 H). *m/z* (ESI): 321.1 $(M+H)^+$. Peak 2 was assigned as the (S)-Sulfinamine (0.099 g, 0.309 mmol, 22 % yield), awhite solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.89 (s, 1 H), 8.24 (dd, *J*=8.4, 2.3 Hz, 1 H), 7.75 (d, *J*=8.4 Hz, 1 H), 5.64 (d, *J*=6.3 Hz, 1 H), 3.74 (dd, *J*=9.0, 6.5 Hz, 1 H), 1.25 - 1.32 (m, 1 H), 1.10 (s, 9 H), 0.59 - 0.64 (m, 1 H), 0.42 - 0.51 (m, 3 H). *m/z* (ESI): 321.1 $(M+H)^+$. Absolute stereochemistry was assigned to sulfinimine intermediates based on analogy to literature examples (Tetrahedron Letters, S. D. Kuduk et al, 45 (2004) 6641–6643) and to purchased enantiopure amines.

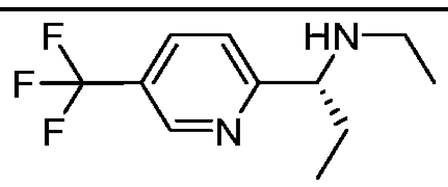
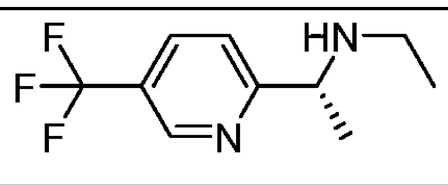
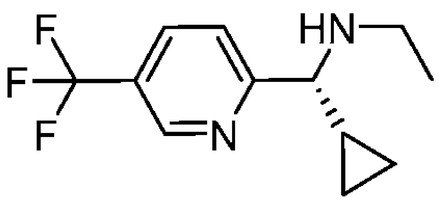
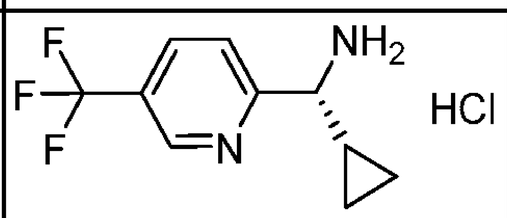
[0196] Step 3. To a 50-mL round-bottomed flask was added (S)-Sulfinamide (0.16 g, 0.48 mmol, Peak 2) and hydrogen chloride solution, 4.0 M in dioxane (0.15 mL, 0.61 mmol, Sigma-Aldrich Corporation) in 1,4-dioxane (2.42 mL). The resulting reaction mixture was stirred at rt for 10 min. The reaction mixture was concentrated in vacuo and the crude was carried to the next step of the synthesis, without further purification. *m/z* (ESI): 217.0 $(M+H)^+$.

[0197] Step 4. To a 50-mL round-bottomed flask was added (S)-cyclopropyl(5-(trifluoromethyl)pyridin-2-yl)methanamine hydrochloride (0.12 g, 0.48 mmol) and acetaldehyde (0.03 g, 0.03 mL, 0.61 mmol, Sigma-Aldrich Corporation) in dichloromethane (2.4 mL). Then titanium (IV) isopropoxide (0.17 g, 0.18 mL, 0.60 mmol, Aldrich) was added to the reaction mixture and stirred at rt for 16 h. The mixture was cooled to 0 °C, then methanol (0.16 g, 0.2 mL, 4.83 mmol, Sigma-Aldrich Corporation) was added to the mixture, followed by sodium borohydride (0.02 g, 0.48 mmol, Aldrich) and the resulting reaction mixture was stirred 2 h. The reaction mixture was concentrated in vacuo. The crude was purified by flash

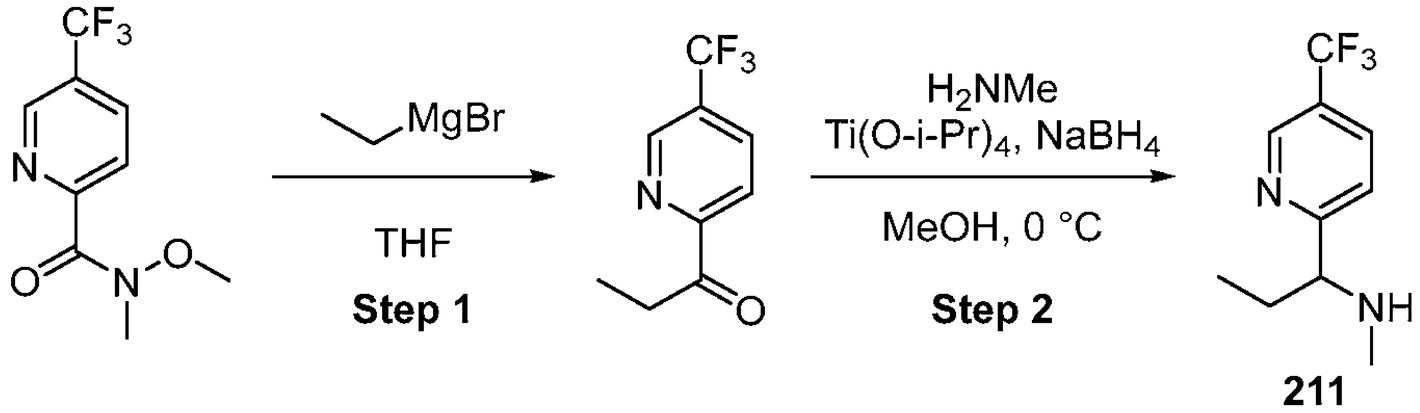
chromatography (silica, 0-35% MeOH:DCM), to provide (S)-N-(cyclopropyl(5-(trifluoromethyl)pyridin-2-yl)methyl)ethanamine (0.040 g, 0.164 mmol, 33.9 % yield) as tan solid. *m/z* (ESI): 245.1 $(M+H)^+$.

[0198] Primary and Secondary Amines in Table 13 were prepared in a manner similar to that described for Intermediate 206.

Table 13

Int. #	Chemical Structure	Name	*m/z* (ESI): $(M+H)^+$
207		(R)-N-ethyl-1-(5-(trifluoromethyl)pyridin-2-yl)propan-1-amine	233.1
208		(R)-N-ethyl-1-(5-(trifluoromethyl)pyridin-2-yl)ethan-1-amine	219.1
209		(R)-N-(cyclopropyl(5-(trifluoromethyl)pyridin-2-yl)methyl)ethanamine	245.1
210		(R)-cyclopropyl(5-(trifluoromethyl)pyridin-2-yl)methanamine	217.0

[0199] Intermediate 211: N-methyl-1-(5-(trifluoromethyl)pyridin-2-yl)propan-1-amine



211

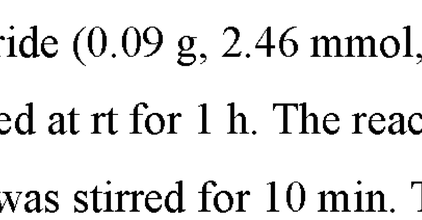
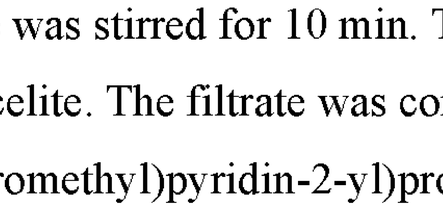
[0200] Step 1. To an oven-dried 2-neck 100-mL round-bottomed flask was added N-methoxy-N-methyl-5-(trifluoromethyl)picolinamide (0.29 g, 1.21 mmol, J&W Pharmlab) in tetrahydrofuran (6.1 mL). The reaction mixture was chilled to -78 °C, then ethylmagnesium chloride solution, 2.0 M in THF (1.83 mL, 3.65 mmol, Sigma-Aldrich Corporation) was added dropwise to the reaction mixture. The resulting reaction mixture was stirred for 15 min at -78 °C, then the mixture was quenched with sat. aq. NH_4Cl (6 mL). The mixture was warmed to rt. Then the reaction mixture was diluted with EtOAc (30 mL) and the aqueous layer was extracted with EtOAc (3x). The combined organic extracts were dried over $MgSO_4$,

filtered and concentrated in vacuo. The crude was used without further purification. *m/z* (ESI): 204.0 $(M+H)^+$.

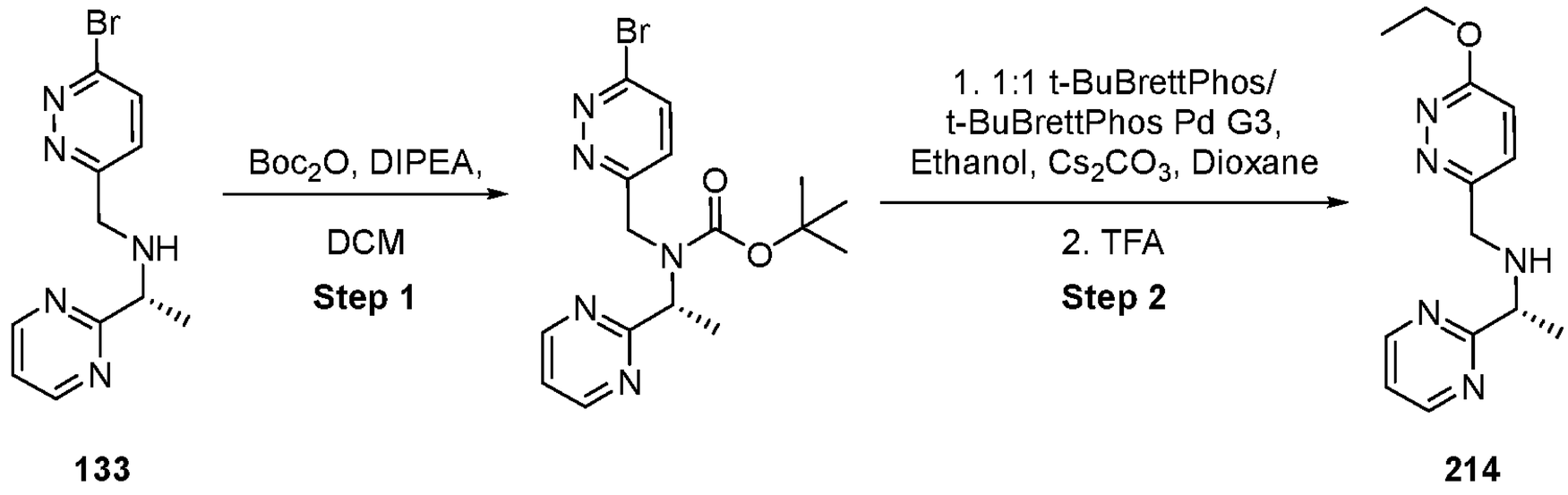
[0201] Step 2. To a 50-mL round-bottomed flask was added 1-(5-(trifluoromethyl)pyridin-2-yl)propan-1-one (0.10 g, 0.49 mmol) and methylamine solution, 2.0 M in tetrahydrofuran (0.37 mL, 0.74 mmol, Sigma-Aldrich Corporation) in methanol (2.5 mL). Then titanium (IV) isopropoxide (0.18 g, 0.18 mL, 0.62 mmol, Sigma-Aldrich) was added to the reaction mixture. The resulting reaction mixture was stirred at rt for 30 min, while under an inert atmosphere. Then the mixture was cooled to 0 °C and sodium borohydride (0.09 g, 2.46 mmol, Sigma-Aldrich) was added slowly to the reaction mixture. The mixture was stirred at rt for 1 h. The reaction mixture was treated with sat.aq. $NaHCO_3$ (0.5 mL) and the resulting mixture was stirred for 10 min. Then the mixture was diluted with MeOH (2 mL) and filtered through a pad of celite. The filtrate was concentrated in vacuo. This afforded N-methyl-1-(5-(trifluoromethyl)pyridin-2-yl)propan-1-amine as light-yellow solid. The mixture was carried to the next step of the synthesis, without further purification. *m/z* (ESI): 219.1 $(M+H)^+$.

[0202] Secondary Amines in Table 14 were prepared in a manner similar to that described for Intermediate 211.

Table 14

Int. #	Chemical Structure	Name	*m/z* (ESI): $(M+H)^+$
212		1-cyclopropyl-N-methyl-1-(5-(trifluoromethyl)pyridin-2-yl)methanamine	231.1
213		N-methyl-1-(5-(trifluoromethyl)pyridin-2-yl)ethan-1-amine	205.1

[0203] Intermediate 214: (R)-N-((6-ethoxypyridazin-3-yl)methyl)-1-(pyrimidin-2-yl)ethan-1-amine

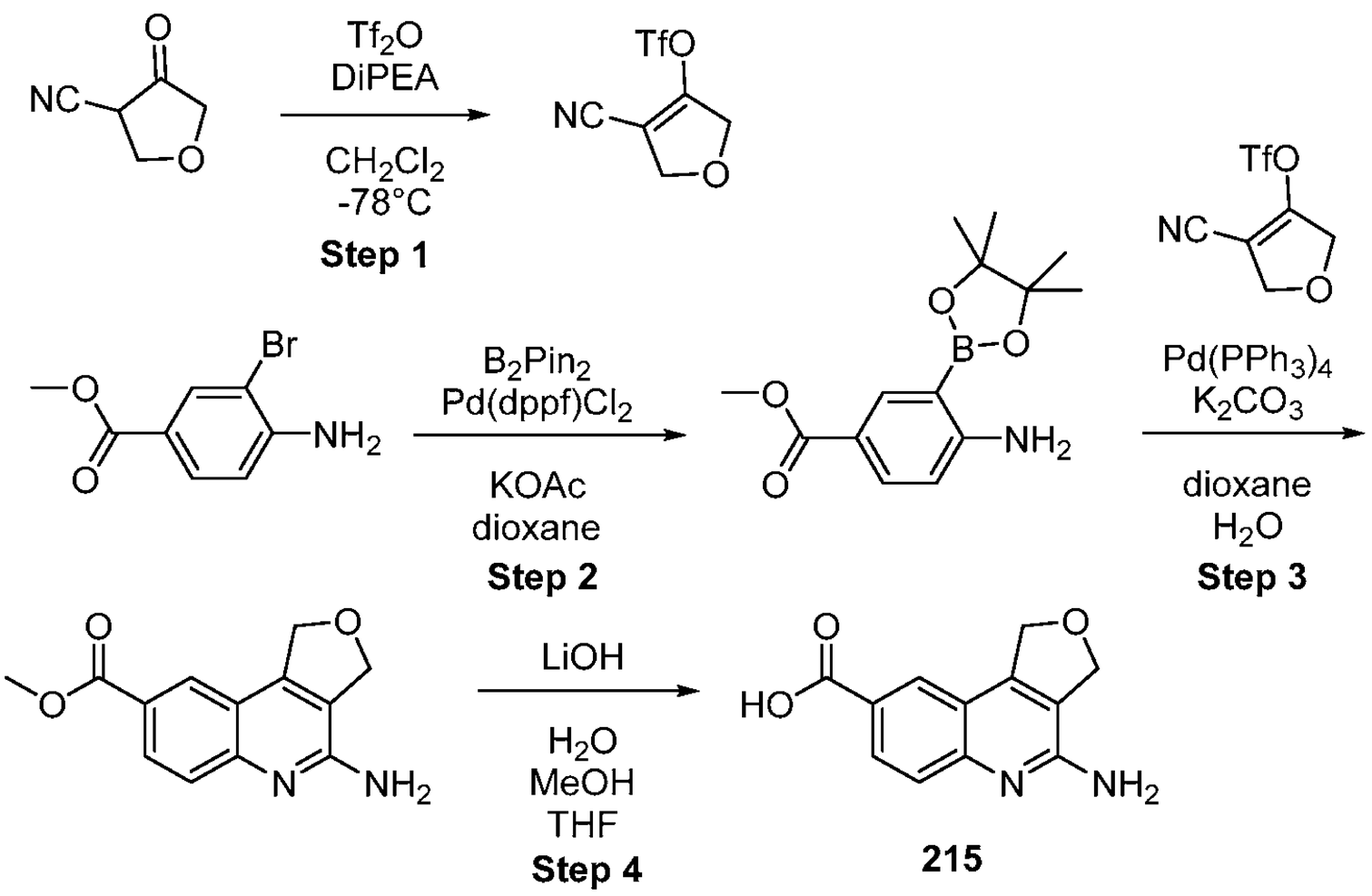


133 **214**

[0204] Step 1. (R)-N-((6-bromopyridazin-3-yl)methyl)-1-(pyrimidin-2-yl)ethan-1-amine (**133**, 0.840 g, 3.47 mmol) and DIPEA (0.897 g, 1.21 mL, 6.94 mmol, Aldrich) were stirred in dichloromethane (17.4 mL) and di-tert-butyl dicarbonate (1.21 g, 1.29 mL, 5.55 mmol, Oakwood Products, Inc.) was added. The reaction was then stirred at room temp overnight to completion. The mixture was partitioned between 200 mL of DCM and water. The layers were separated. The organic layer was dried over Na_2SO_4 and concentrated. The crude product was purified by medium pressure chromatography (silica, 0 to 100% EtOAc:Heptnes) to give tert-butyl (R)-((6-bromopyridazin-3-yl)methyl)(1-(pyrimidin-2-yl)ethyl)carbamate (1.61 g, 4.70 mmol, 136 % yield). *m/z* (ESI): 394.1, 396.1 $(M+H)^+$.

[0205] Step 2. t-butylBrettPhos (55.0 mg, 0.110 mmol, Aldrich) was mixed in dioxane (1.0 mL). In a separate flask t-butylBrettPhos Pd G3 (98.0 mg, 0.110 mmol, Aldrich), ethanol (0.300 mL, 5.70 mmol, Aldrich), (R)-((6-bromopyridazin-3-yl)methyl)(1-(pyrimidin-2-yl)ethyl)carbamate (300 mg, 0.76 mmol) and cesium carbonate (350 mg, 1.10 mmol, Aldrich) were slurried in dioxane (2.50 mL). The t-butylBrettPhos mixture was added to the second flask. This slurry was then stirred overnight to completion. The mixture was concentrated under reduced pressure and the residue was purified by medium pressure chromatography (silica, 0 to 100% EtOAc:Heptanes) to give tert-butyl (R)-((6-ethoxypyridazin-3-yl)methyl)(1-(pyrimidin-2-yl)ethyl)carbamate (231 mg, 0.643 mmol, 84.0 % yield). *m/z* (ESI): 360.0 $(M+H)^+$. This material was dissolved in TFA (10 mL) and stirred for 15 minutes to completion The reaction mixture was concentrated under reduced pressure and the residue was free based by dissolving in MeOH, eluting through an SCX column eluting with 0 to 2M ammonia in MeOH, and concentrating to give (R)-N-((6-ethoxypyridazin-3-yl)methyl)-1-(pyrimidin-2-yl)ethan-1-amine (**214**, 166 mg, 0.640 mmol, 84 % yield). *m/z* (ESI): 260.0 $(M+H)^+$.

[0206] Intermediate 215: 4-Amino-1,3-dihydrofuro[3,4-c]quinoline-8-carboxylic acid.



[0207] Step 1. To a stirred solution of 4-oxotetrahydrofuran-3-carbonitrile (0.500 g, 4.50 mmol) in dichloromethane (5.00 mL) was added DIPEA (0.943 mL, 5.40 mmol) and the reaction mixture was cooled to -78 °C. Then, triflic anhydride (0.760 mL, 4.50 mmol) was added dropwise at -78 °C for 1 min and the reaction mixture stirred at same temperature for 15 min. After completion of reaction, the reaction mixture was diluted with water, the organic layer was separated, washed with brine (2 x 10 mL), dried over sodium sulfate, and concentrated to give crude 4-cyano-2,5-dihydrofuran-3-yl trifluoromethanesulfonate (1.05 g, 4.32 mmol, 96 % yield), which was used in the next step without further purification.

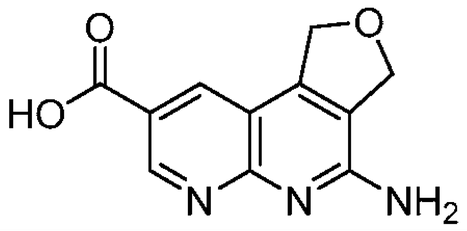
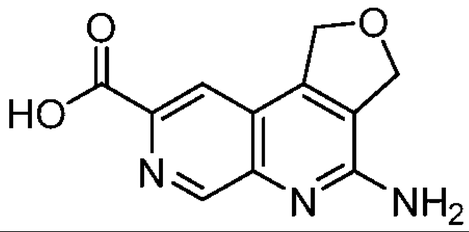
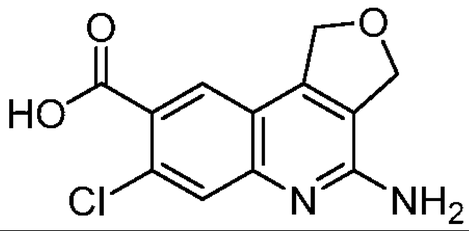
[0208] Step 2. To a 150-mL round-bottomed flask was added methyl 4-amino-3-bromobenzoate (4 g, 17.39 mmol, Combi-Blocks Inc.) and bis(pinacolato)diboron (8.83 g, 34.8 mmol, Frontier Scientific, Inc.) in 1,4-dioxane (58.0 mL). To the solution was then added potassium acetate (5.12 g, 52.2 mmol, Sigma-Aldrich Corporation) and the mixture was degassed by bubbling through with Argon for 5 minutes. Then, [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(ii), complex with dichloromethane (1.420 g, 1.739 mmol, Strem Chemicals, Inc.) was added. The reaction was stirred at 100°C. After 18 h the reaction was cooled down and the solid filtered under vacuum and the washed with DCM. The mother liquor was then concentrated to give a semisolid residue. DCM was added, and the solid formed collected by vacuum filtration. The mother liquor concentrated again, and this step was repeated. The desired methyl 4-amino-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (2.6 g, 9.38 mmol, 54.0 % yield) was isolated as a grey solid. m/z (ESI): 196.1 $(M+H)^+$ (boronic acid). ^{1}H NMR (400 MHz, CHLOROFORM-d) δ ppm 8.33 (d, J=2.1 Hz, 1 H), 7.90 (dd, J=8.6, 2.2 Hz, 1 H), 6.57 (d, J=8.5 Hz, 1 H), 5.20 (br s, 2 H), 3.87 (s, 3 H), 1.37 (s, 12 H).

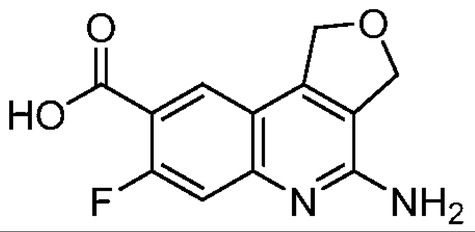
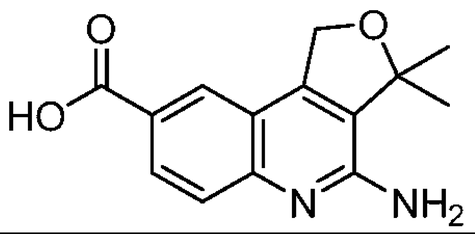
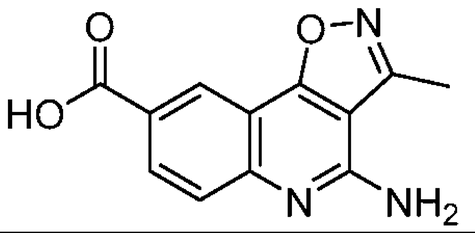
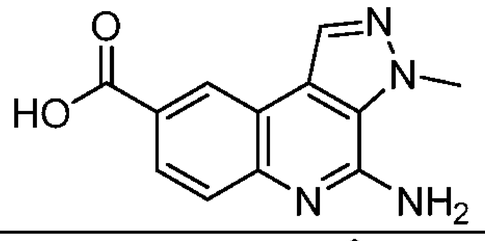
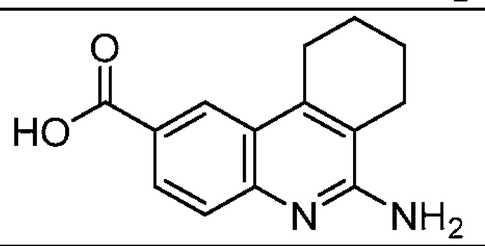
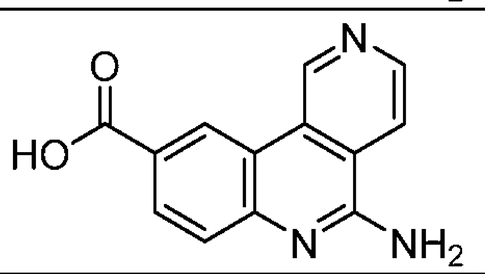
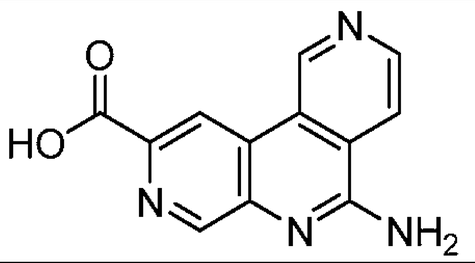
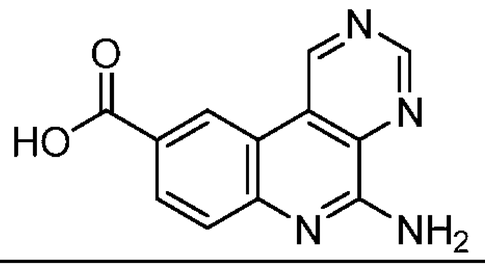
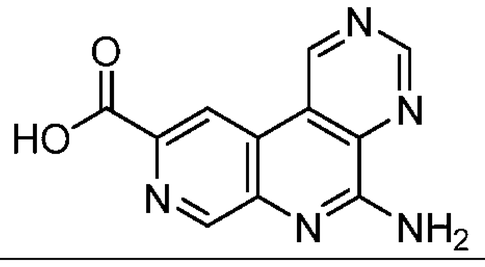
[0209] Step 3. To a stirred solution of 4-cyano-2,5-dihydrofuran-3-yl trifluoromethanesulfonate (10 g, 41.1 mmol) in 1,4-dioxane (200 mL) and water (20.00 mL) was added methyl 4-amino-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (9.12 g, 32.9 mmol), K_2CO_3 (17.05 g, 123 mmol), and $Pd(PPh_3)_4$ (4.75 g, 4.11 mmol) under nitrogen purging. Then, the reaction mixture heated at 80 °C for 16 h. The reaction mixture was concentrated, then diluted with ethyl acetate (50 mL) and water (50 mL) and stirred at room temperature for 30 min. Then, the solid formed was filtered and washed with ethyl acetate (50 mL) and 2% MeOH in DCM (50 mL), then dried under vacuum to give methyl 4-amino-1,3-dihydrofuro[3,4-c]quinoline-8-carboxylate (6.6 g, 27.0 mmol, 65.7 % yield) as gray solid. m/z (ESI): 245.3 $(M+H)^+$. ^1H NMR (400 MHz, TFA-d) δ ppm 8.59 – 8.67 (2H, m), 7.97 (1H, d, J=9.3 Hz), 5.94 (2H, t, J=3.5 Hz), 5.65 (2H, t, J=3.4 Hz), 4.24 (3H, s). Note: for some heterocycles $Pd(dppf)Cl_2$ was used in place of $Pd(PPh_3)_4$.

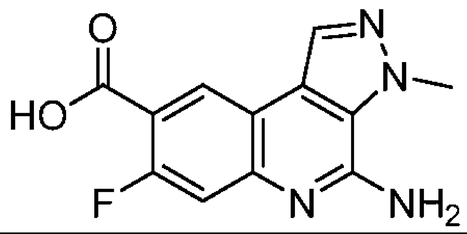
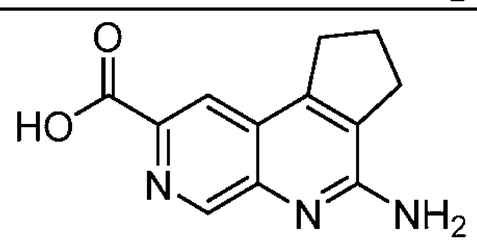
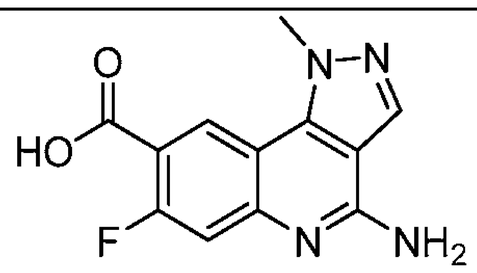
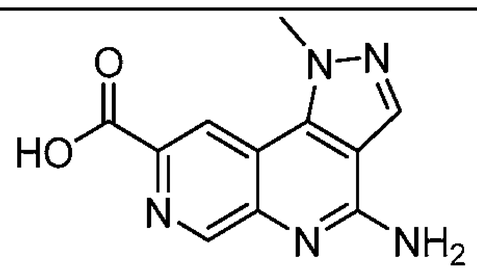
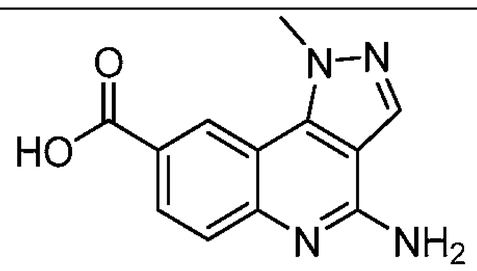
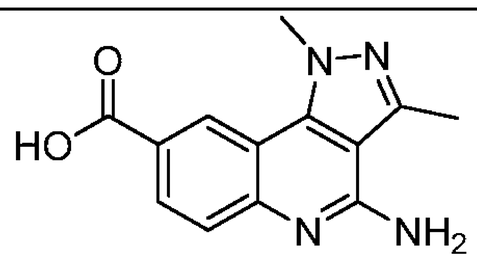
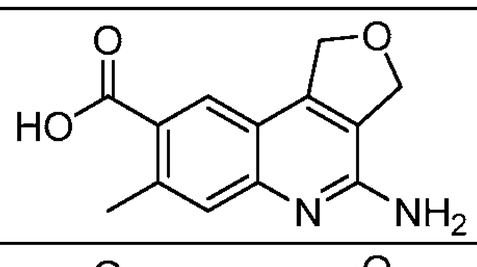
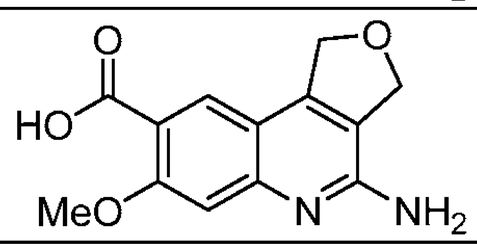
[0210] Step 4. To a stirred solution of methyl 4-amino-1,3-dihydrofuro[3,4-c]quinoline-8-carboxylate (30 g, 123 mmol) in water (300 mL):tetrahydrofuran (300 mL):methanol (300 mL) was added LiOH (11.77 g, 491 mmol) and the reaction mixture was heated at 75 °C for 3 h. The reaction mixture was concentrated and acidified with 1.5 N HCl up to pH 6.0. The solid obtained was filtered, washed with methanol (300 mL), and dried to give 4-amino-1,3-dihydrofuro[3,4-c]quinoline-8-carboxylic acid (28 g, 122 mmol, 99 % yield) as off-white solid. m/z (ESI): 231.2 $(M+H)^+$. ^1H NMR (400 MHz, DMSO-d) δ ppm 12.83 (1H, s), 7.88 – 8.30 (2H, m), 7.59 (1H, d, J=8.8 Hz), 7.02 (2H, s), 5.40 (2H, t, J=3.5 Hz), 5.03 (2H, t, J=3.6 Hz).

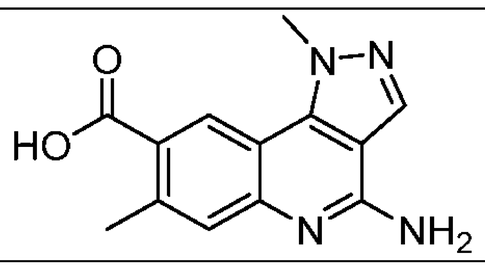
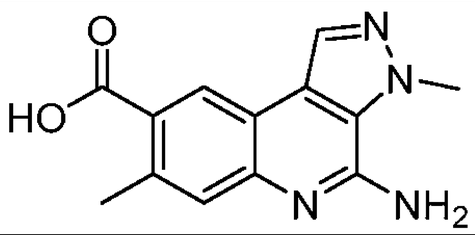
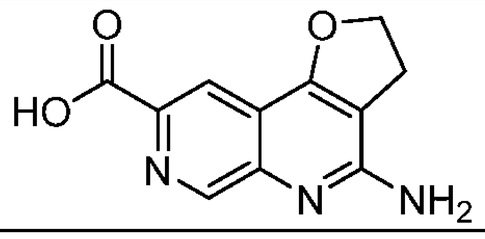
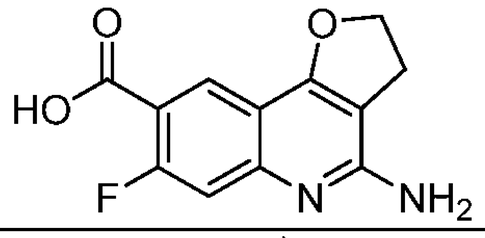
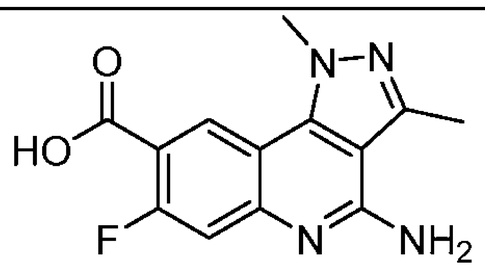
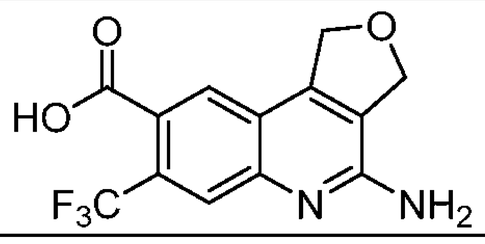
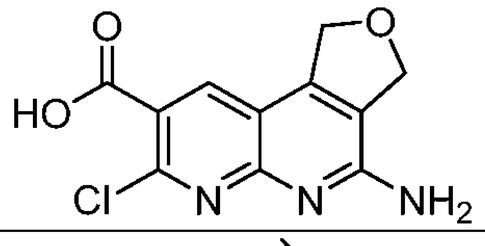
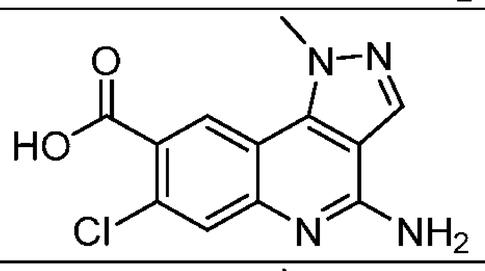
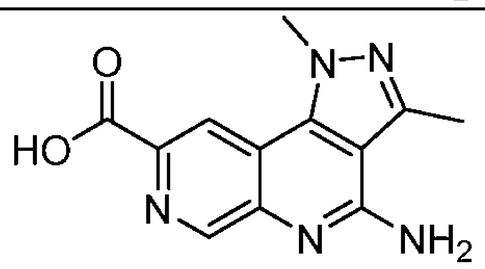
[0211] Acids in Table 15 were prepared in a manner similar to that described for Intermediate **215**.

Table 15

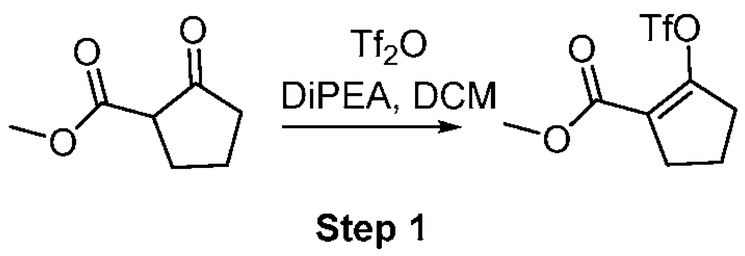
Int. #	Chemical Structure	Name	*m/z* (ESI): $(M+H)^+$
216		4-amino-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxylic acid	232.1
217		4-amino-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxylic acid	232.0
218		4-amino-7-chloro-1,3-dihydrofuro[3,4-c]quinoline-8-carboxylic acid	264.9

Int. #	Chemical Structure	Name	*m/z* (ESI): $(M+H)^+$
219		4-amino-7-fluoro-1,3-dihydrofuro[3,4-c]quinoline-8-carboxylic acid	249.0
220		4-amino-3,3-dimethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxylic acid	259.1
221		4-amino-3-methylisoxazolo[4,5-c]quinoline-8-carboxylic acid	244.0
222		4-amino-3-methyl-3H-pyrazolo[3,4-c]quinoline-8-carboxylic acid	243.1
223		6-amino-7,8,9,10-tetrahydrophenanthridine-2-carboxylic acid	243.2
224		5-aminobenzo[c][2,6]naphthyridine-9-carboxylic acid	240.1
225		5-aminopyrido[4,3-c][1,7]naphthyridine-9-carboxylic acid	241.1
226		5-aminopyrimido[4,5-c]quinoline-9-carboxylic acid	241.2
227		5-aminopyrimido[4,5-c][1,7]naphthyridine-9-carboxylic acid	241.1

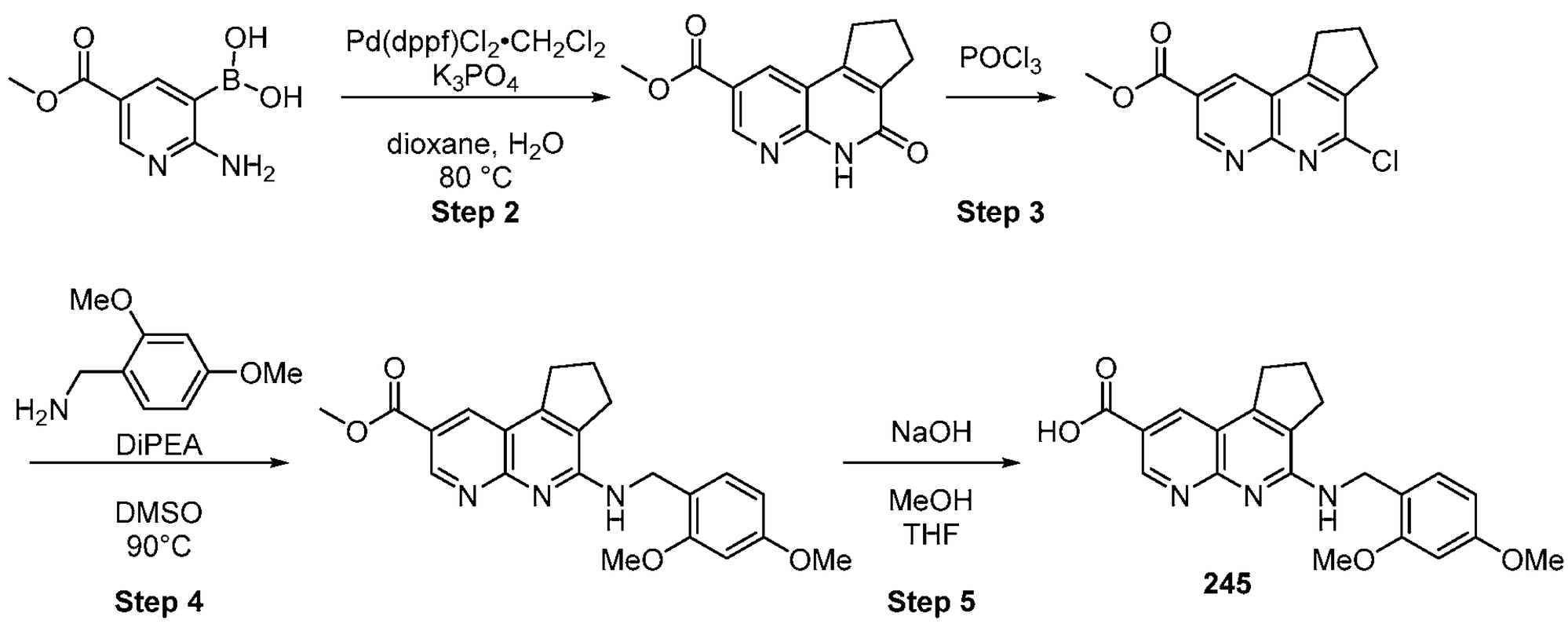
Int. #	Chemical Structure	Name	*m/z* (ESI): $(M+H)^+$
228		4-amino-7-fluoro-3-methyl-3H-pyrazolo[3,4-c]quinoline-8-carboxylic acid	261.1
229		6-amino-8,9-dihydro-7H-cyclopenta[c][1,7]naphthyridine-2-carboxylic acid	230.0
230		4-amino-7-fluoro-1-methyl-1H-pyrazolo[4,3-c]quinoline-8-carboxylic acid	261.0
231		4-amino-1-methyl-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxylic acid	244.0
232		4-amino-1-methyl-1H-pyrazolo[4,3-c]quinoline-8-carboxylic acid	243.0
233		4-amino-1,3-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxylic acid	257.0
234		4-amino-7-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxylic acid	245.2
235		4-amino-7-methoxy-1,3-dihydrofuro[3,4-c]quinoline-8-carboxylic acid	261.0

Int. #	Chemical Structure	Name	*m/z* (ESI): $(M+H)^+$
236		4-amino-1,7-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxylic acid	257.0
237		4-amino-3,7-dimethyl-3H-pyrazolo[3,4-c]quinoline-8-carboxylic acid	257.1
238		4-amino-2,3-dihydrofuro[3,2-c][1,7]naphthyridine-8-carboxylic acid	232.1
239		4-amino-7-fluoro-2,3-dihydrofuro[3,2-c]quinoline-8-carboxylic acid	249.1
240		4-amino-7-fluoro-1,3-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxylic acid	275.1
241		4-amino-7-(trifluoromethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxylic acid	298.9
242		4-amino-7-chloro-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxylic acid	265.9
243		4-amino-7-chloro-1-methyl-1H-pyrazolo[4,3-c]quinoline-8-carboxylic acid	277
244		4-amino-1,3-dimethyl-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxylic acid	258.1

[0212] Intermediate 245: 6-amino-8,9-dihydro-7H-cyclopenta[c][1,8]naphthyridine-2-carboxylic acid.



Step 1



[0213] Step 1. A mixture of methyl 2-oxocyclopentanecarboxylate (1.0 g, 0.877 mL, 7.03 mmol, Matrix Scientific) and 1,1'-dimethyltriethylamine (1.000 g, 1.352 mL, 7.74 mmol, Sigma-Aldrich Corporation) in DCM (15 mL) was cooled to -78°C and trifluoromethanesulfonic acid anhydride (7.03 mL, 7.03 mmol, Sigma-Aldrich Corporation) was added. After complete addition, the mixture was stirred at -78°C for 5 min, then the dry ice-bath was removed and stirred at rt. After 15 min, the mixture was concentrated to afford methyl 2-(((trifluoromethyl)sulfonyl)oxy)cyclopent-1-ene-1-carboxylate with quant. yield as a light-yellow solid to be used as is. m/z (ESI): 275 $(M+H)^+$.

[0214] Step 2. A mixture of methyl 2-(((trifluoromethyl)sulfonyl)oxy)cyclopent-1-ene-1-carboxylate (1.982 g, 7.23 mmol), (2-amino-5-(methoxycarbonyl)pyridin-3-yl)boronic acid (1.70 g, 8.67 mmol), potassium phosphate, tribasic (3.78 g, 21.69 mmol, Acros) and [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium (ii), complex with dichloromethane (0.177 g, 0.217 mmol, Strem Chemicals, Inc.) in 1,4-dioxane/water (10/0.60 mL) was heated at 80 °C for 1 h at which time it was brought to rt and diluted with EtOAc. A precipitate was formed which corresponded to the desired product. The precipitate was filtered and washed with EtOAc to yield methyl 6-oxo-6,7,8,9-tetrahydro-5H-cyclopenta[c][1,8]naphthyridine-2-carboxylate as a light gray solid with quant. yield. m/z (ESI): 245 $(M+H)^+$. ^{1}H NMR (400 MHz, DMSO-d6) δ ppm 11.93 - 12.58 (m, 1 H), 8.96 (d, J=2.1 Hz, 1 H), 8.33 (d, J=2.1 Hz, 1 H), 3.89 (s, 3 H), 3.13 (br t, J=7.6 Hz, 2 H), 2.78 (br t, J=7.3 Hz, 2 H), 2.08 - 2.18 (m, 2 H).

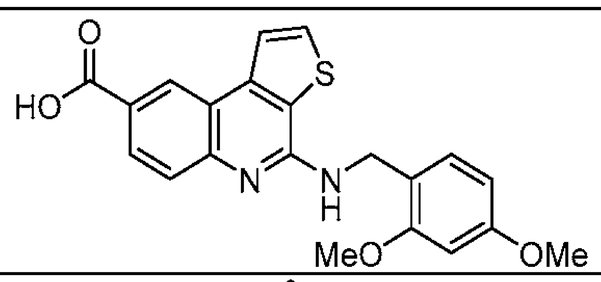
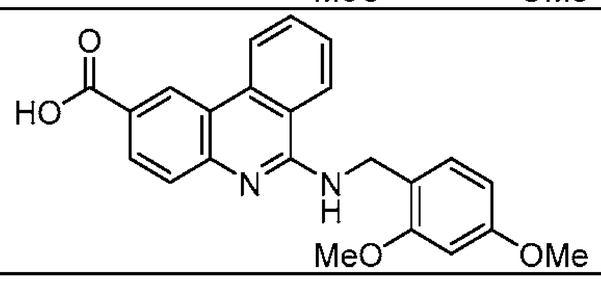
[0215] Step 3. A mixture of methyl 6-oxo-6,7,8,9-tetrahydro-5H-cyclopenta[c][1,8]naphthyridine-2-carboxylate (1.76 g, 7.21 mmol) in $POCl_3$ (24.68 g, 15 mL, 161 mmol, Aldrich) was heated to reflux for 30 min. The reaction went to completion and was carefully added to cold sat. $NaHCO_3$ to basify the reaction. After stirring for 15 min, the mixture was extracted with EtOAc and the combined organics were concentrated to afford methyl 6-chloro-8,9-dihydro-7H-cyclopenta[c][1,8]naphthyridine-2-carboxylate as a yellow solid with quant. yield. m/z (ESI): 263 $(M+H)^+$.

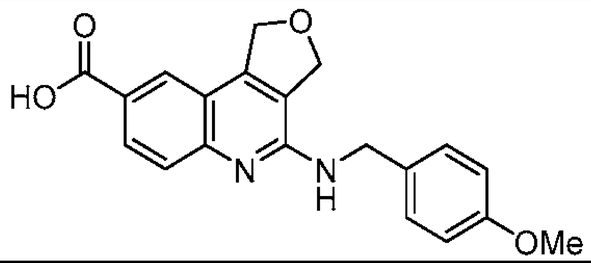
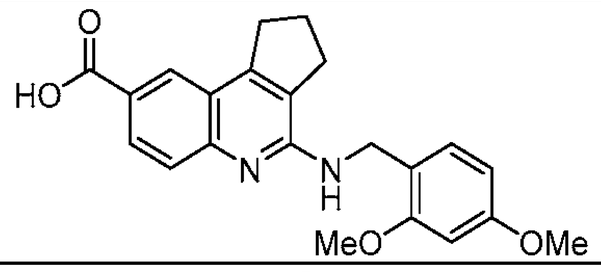
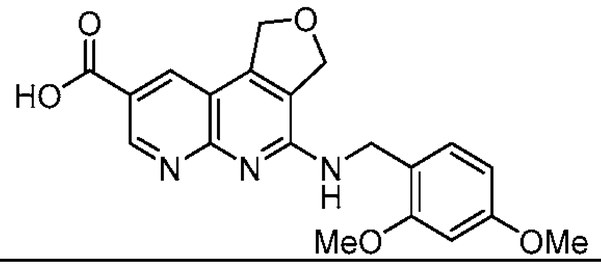
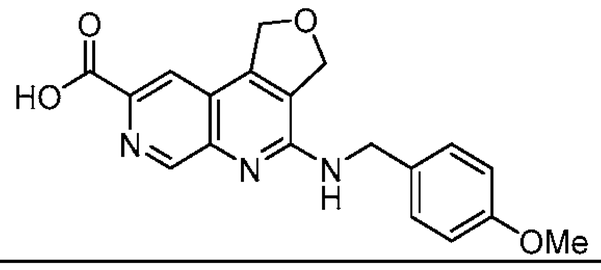
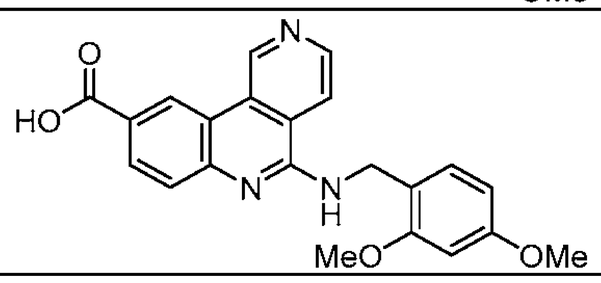
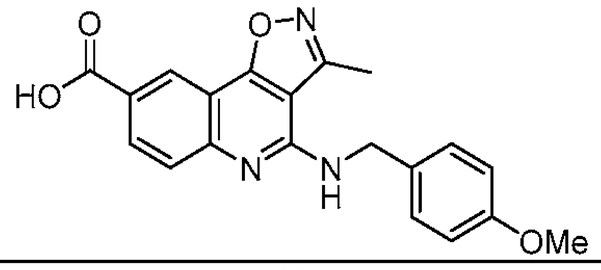
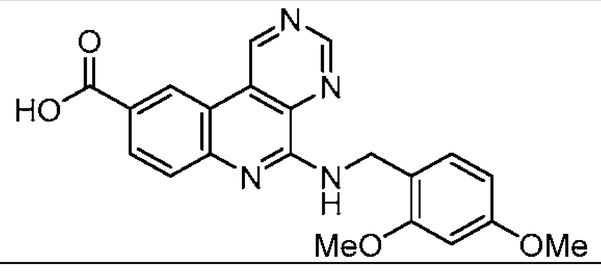
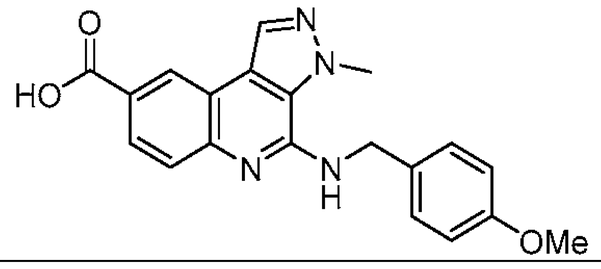
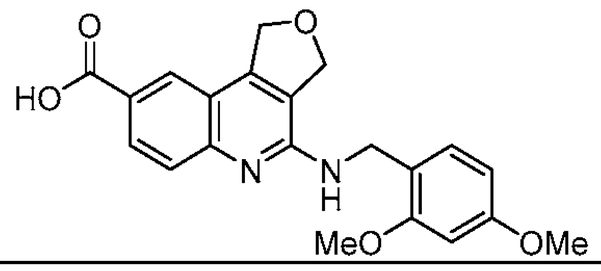
[0216] Step 4. To a suspension of methyl 6-chloro-8,9-dihydro-7H-cyclopenta[c][1,8]naphthyridine-2-carboxylate (1.89 g, 7.19 mmol) in DMSO (15 mL) was added DIPEA (2.79 g, 3.77 mL, 21.58 mmol, Aldrich) followed by the addition of (2,4-dimethoxyphenyl)methanamine (1.564 g, 1.405 mL, 9.35 mmol, Aldrich). The resulting mixture was heated at 90 °C overnight. Then, the reaction was cooled to rt, diluted with water, washed with sat. NH_4Cl and extracted with EtOAc. The combined organics were dried over Na_2SO_4, filtered and concentrated to afford methyl 6-((2,4-dimethoxybenzyl)amino)-8,9-dihydro-7H-cyclopenta[c][1,8]naphthyridine-2-carboxylate (2.18 g, 5.54 mmol, 77 % yield) as a yellow solid to be used as is. m/z (ESI): 394 $(M+H)^+$.

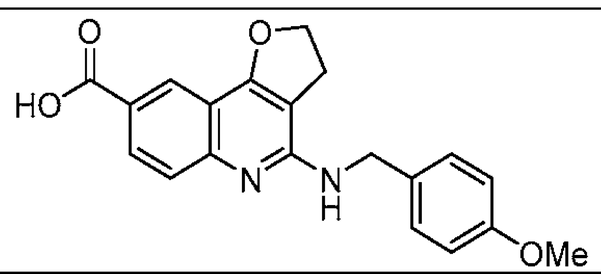
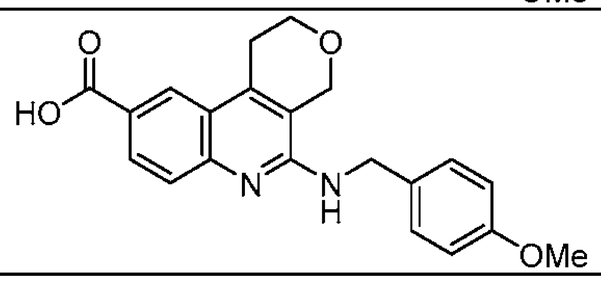
[0217] Step 5. To a solution of methyl 6-((2,4-dimethoxybenzyl)amino)-8,9-dihydro-7H-cyclopenta[c][1,8]naphthyridine-2-carboxylate (2.18 g, 5.54 mmol) in THF/MeOH (10/10 mL) was added NaOH (10 mL, 10.00 mmol) and the resulting solution was heated at 70 °C for 2 h at which time it was brought to rt and acidified with 10 mL 1M HCl. A light yellow precipitate was formed filtered off and azeotropically dried with toluene to afford 6-((2,4-dimethoxybenzyl)amino)-8,9-dihydro-7H-cyclopenta[c][1,8]naphthyridine-2-carboxylic acid hydrochloride (1.44 g, 3.46 mmol, 62.5% yield) as a yellow solid. m/z (ESI): 380.2 $(M+H)^+$.

[0218] Acids in Table 16 were prepared in a manner similar to that described for Intermediate **245**.

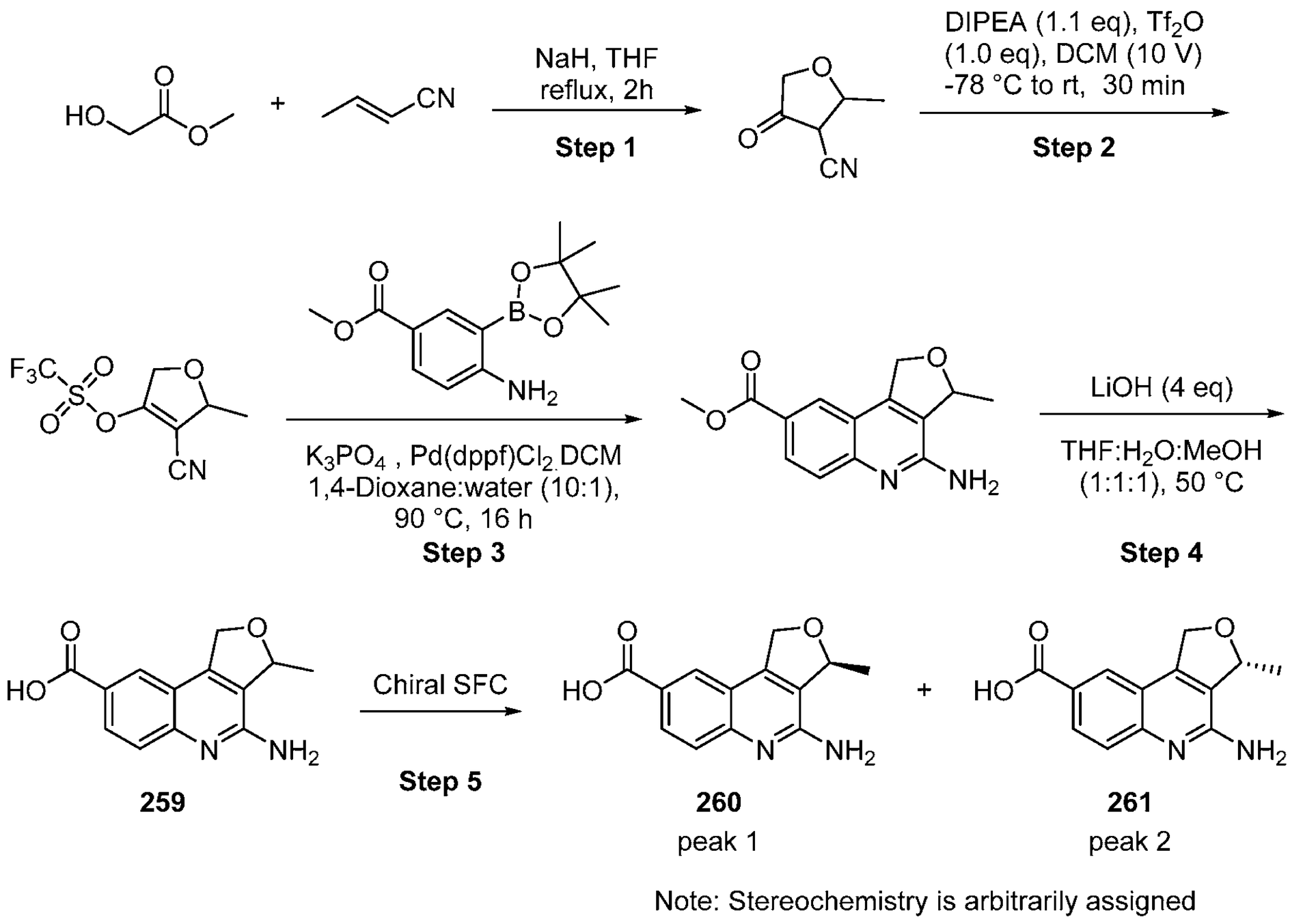
Table 16

Int. #	Chemical Structure	Name	*m/z* (ESI): $(M+H)^+$
246		4-aminothieno[2,3-c]quinoline-8-carboxylic acid	395.0
247		6-aminophenanthridine-2-carboxylic acid	389.2

Int. #	Chemical Structure	Name	*m/z* (ESI): $(M+H)^+$
248		4-((4-methoxybenzyl)amino)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxylic acid	351.0
249		4-((2,4-dimethoxybenzyl)amino)-2,3-dihydro-1H-cyclopenta[c]quinoline-8-carboxylic acid	379.2
250		4-((2,4-dimethoxybenzyl)amino)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxylic acid	382.2
251		4-((4-methoxybenzyl)amino)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxylic acid	352.2
252		5-((2,4-dimethoxybenzyl)amino)benzo[c][2,6]naphthyridine-9-carboxylic acid	390.2
253		4-((4-methoxybenzyl)amino)-3-methylisoxazolo[4,5-c]quinoline-8-carboxylic acid	364.1
254		5-((2,4-dimethoxybenzyl)amino)pyrimido[4,5-c]quinoline-9-carboxylic acid	391.2
255		4-((4-methoxybenzyl)amino)-3-methyl-3H-pyrazolo[3,4-c]quinoline-8-carboxylic acid	363.0
256		4-((2,4-dimethoxybenzyl)amino)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxylic acid	381.1

Int. #	Chemical Structure	Name	*m/z* (ESI): $(M+H)^+$
257		4-((4-methoxybenzyl)amino)-2,3-dihydrofuro[3,2-c]quinoline-8-carboxylic acid	351.2
258		5-((4-methoxybenzyl)amino)-1,4-dihydro-2H-pyrano[3,4-c]quinoline-9-carboxylic acid	365.1

[0219] Intermediate 259: 4-amino-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxylic acid



Note: Stereochemistry is arbitrarily assigned

[0220] Step 1. To a suspension of sodium hydride (11.10 g, 278 mmol 0.5 equiv., 60% in mineral oil) in anhydrous tetrahydrofuran (250 mL) was added methyl glycolate (42.4 mL, 555 mmol, 1.0 equiv) at room temperature under N_2 atmosphere. To the reaction mixture (E)-but-2-enenitrile (54.5 mL, 666 mmol, 1.2 equiv) was added slowly at 65 °C and stirred for 2h at same temperature. The reaction mixture was cooled and quenched with 2 N NaOH solution (250 mL) and extracted with diethyl ether (500 mL). The aqueous layer was acidified with conc. HCl to adjust the pH to ~1 and extracted with dichloromethane (2 x 500

mL). The combined organic layer was washed with brine (200 mL) and dried over sodium sulfate, filtered and concentrated under reduced pressure. The crude residue was purified by column chromatography over silica gel (230-400 mesh) using 10% ethyl acetate with hexanes as an eluent to 2-methyl-4-oxotetrahydrofuran-3-carbonitrile (22 g, 176 mmol, 32% yield) as a brown solid. *m/z* (ESI, Negative): 124.3 [M-1]. 1H NMR (400 MHz, Chloroform-d): δ ppm 4.40 – 4.27 (m, 2 H), 4.26 – 4.19 (m, 1 H), 3.24 – 2.99 (m, 1 H), 1.61 (dd, J=18.6, 6.2 Hz, 3 H).

[0221] Step 2. To a stirred solution of 2-methyl-4-oxotetrahydrofuran-3-carbonitrile (25.0 g, 200 mmol, 1.0 equiv) in dichloromethane (500 mL) was added DIPEA (69.8 mL, 400 mmol, 2.0 equiv) and triflic anhydride (47.1 mL, 280 mmol, 1.4 equiv) at -78 °C and stirred at same temperature for 15 min. The reaction mixture was quenched with slow addition of water (250 mL) and after attaining the room temperature, it was extracted with dichloromethane (2 x 500 mL). The combined organic layer was dried over sodium sulfate, filtered and concentrated under reduced pressure. The crude residue was stirred in diethyl ether and filtered. The mother liquor was concentrated under reduced pressure to give of 4-cyano-5-methyl-2,5-dihydrofuran-3-yl trifluoromethanesulfonate (35.0 g, crude) as a light brown adduct. The crude material was used for next step without further purification. *m/z*: 257.1 [Not ionized]

[0222] Step 3. To a stirred solution of of 4-cyano-5-methyl-2,5-dihydrofuran-3-yl trifluoromethanesulfonate (35 g, 136 mmol, 1.0 equiv) in 1,4-dioxane (1400 mL) and water (70.0 mL), was added methyl 4-amino-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (37.7 g, 136 mmol, 1.0 equiv) and potassium phosphate (87 g, 408 mmol, 3.0 equiv) under nitrogen atmosphere. The reaction mixture was degassed with nitrogen for 15 min and then $PdCl_2$(dppf)-DCM adduct (9.96 g, 13.61 mmol, 0.1 equiv) was added and the reaction mixture was heated at 90 °C for 16h. The reaction mass was concentrated under reduced pressure to get crude product. The crude residue was purified by column chromatography over silica gel (60-120 mesh) using 50% ethyl acetate with hexanes as an eluent to give methyl 4-amino-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxylate (25 g, 97 mmol, 71% yield) as a brown solid. *m/z*: 259.2 $(M+H)^+$ ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.11 (d, J = 2.0 Hz, 1H), 8.00 (dd, J = 8.8, 2.0 Hz, 1H), 7.58 (d, J = 8.8 Hz, 1H), 6.87 (s, 2H), 4.11 (q, J = 5.3 Hz, 1H), 3.87 (s, 2H), 3.17 (d, J = 5.3 Hz, 3H), 1.41 (d, J = 5.9 Hz, 3H).

[0223] Step 4. To a stirred solution of methyl 4-amino-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxylate (26.0 g, 101 mmol, 1.0 equiv) in tetrahydrofuran (130 mL), methanol (78 mL) and water (52 mL), was added lithium hydroxide (9.64 g, 403 mmol, 4.0 equiv) and stirred at 75°C for 4h. LCMS indicated completion of the reaction. The reaction mixture was concentrated under reduced pressure. The crude residue was dissolved in water (100 mL) and filtered to removed insoluble particles. The aqueous layer was acidified with con. HCl (pH 6 to 6.5). The precipitated solid was filtered, washed with water and dried under vacuum to get 4-amino-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxylic acid (17.5

g, 71.6 mmol, 71% yield) as an off-white solid. *m/z*: 245.1 $(M+H)^+$ ^1H NMR(TFA, 400 MHz): δ (ppm) 8.68 (t, *J*=6.2 Hz, 2H), 8.01 (dd, *J*=9.1, 4.2 Hz, 1H), 6.15 (s, 1H), 5.94 (m, 2H), 1.86 (t, *J*=5.4 Hz, 3H)

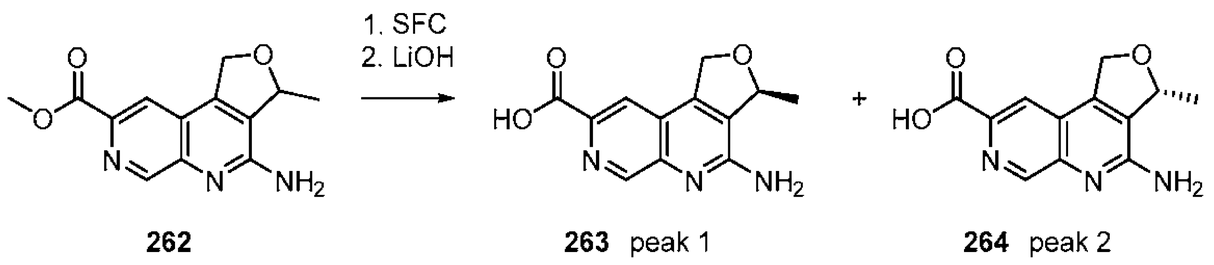
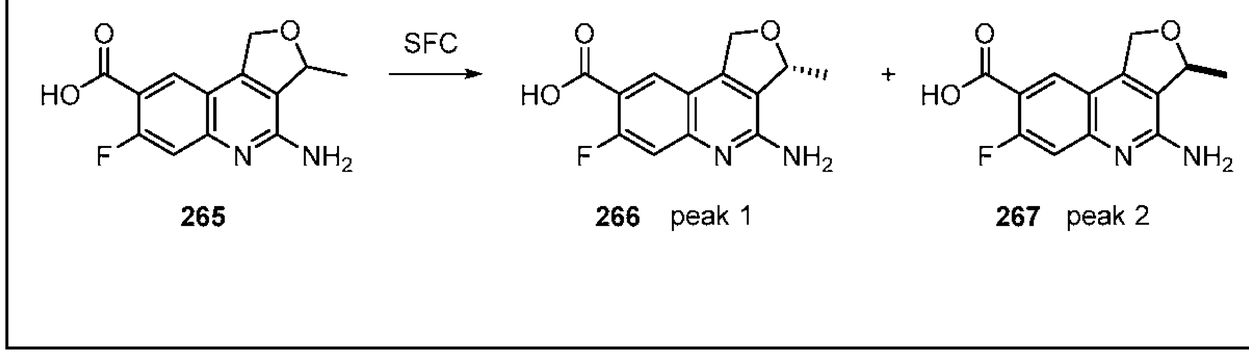
[0224] Step 5. Chiral SFC separation: 44.5 g of racemic 4-amino-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxylic acid was separated by chiral SFC to get 14 g of each isomer. Stereochemistry is assigned arbitrarily.

[0225] Separation Information:

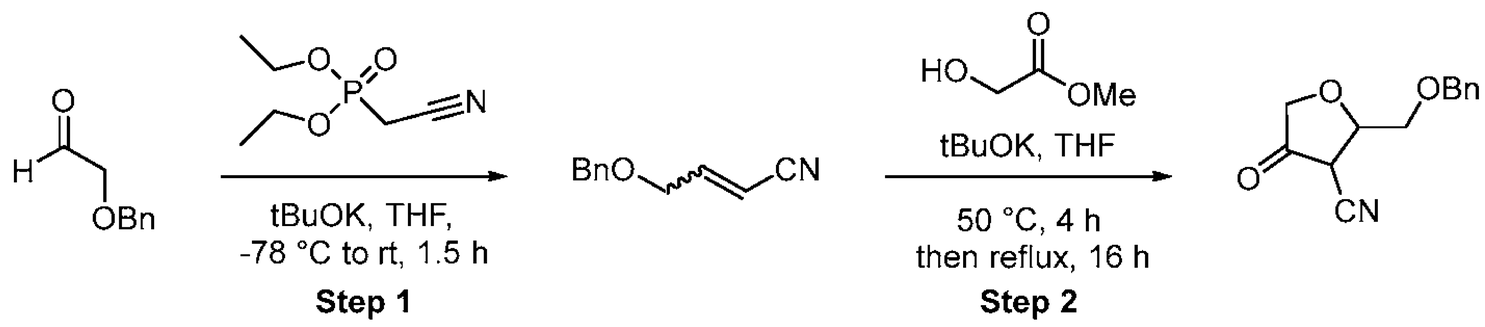
	Key	Value
1	Instrument	SFC 200
2	Column	ChiralPak- IC (250x30mm, 5μ)
3	Mobile Phase	Liquid CO_2: 0.5% DEA in Methanol (40:60)
4	Flow rate	100mL/ min
5	Pressure Drop	130bar
6	BPR	100 bar
7	UV Detector Wavelength	210 nm
8	Dissolution	14.0 g dissolved in 280mL of 2% of DEA in Methanol
9	Test Injections	2.5,1.5,1.8 mL
10	Processing	NA
11	Injection Volume	2.0 mL
12	Cycle time	4.14 min

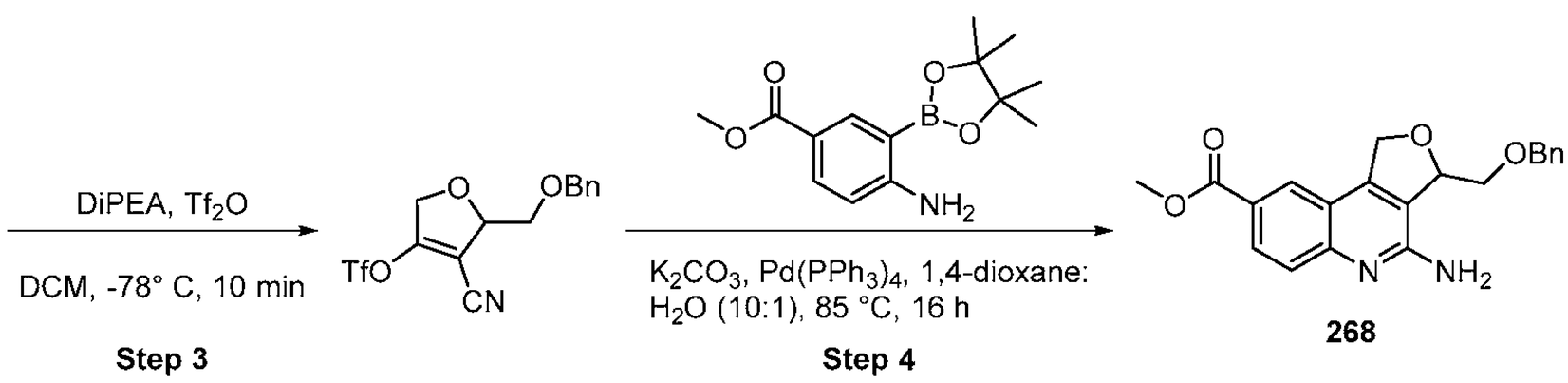
[0226] Racemic acids in Table 17 were prepared in a manner similar to that described for Intermediate **259**.

Table 17

Acids	**SFC Conditions**	*m/z* $(M+H)^+$
 **262** **263** peak 1 **264** peak 2	Chiralpak IG-3, 50×4.6mm I.D., 3um CO_2: MeOH (0.05% isopropylamine, v/v); 95:5 →1:1; 3 min gradient	246.0
 **265** **266** peak 1 **267** peak 2	1st peak, CHIRALPAK IG column (250 X 50mm, 10□m) with a mobile phase of 75% Liquid CO_2 and 25% MeOH with 0.3% NH_4OH using a flowrate of 200 mL/min	263.1

[0227] Intermediate 268: 4-amino-3-((benzyloxy)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxylic acid





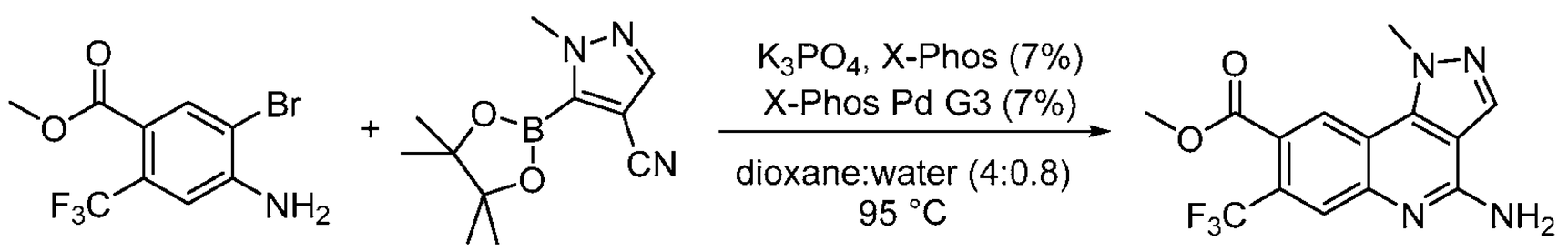
[0228] Step 1. To a stirred solution of diethyl (cyanomethyl)phosphonate (130 g, 732 mmol, 1.1 equiv) in tetrahydrofuran (2000 mL) was added potassium tert-butoxide (1 M solution in THF; 732 mL, 732 mmol, 1.1 equiv) at -78 °C and stirred for 30 min. To the reaction mixture, 2-(benzyloxy)acetaldehyde (100 g, 666 mmol, 1.0 equiv) was added at -78 °C and allowed to room temperature for 1 h. After completion, the reaction mixture was quenched with saturated NH_4Cl solution (1500 mL) and extracted with ethyl acetate (2 x 3000 mL). The combined organic layers were washed with brine solution (1000 mL) and dried over anhydrous Na_2SO_4, filtered and concentrated under vacuum. The crude residue was purified by column chromatography over silica gel (60-120 mesh) using 15% ethyl acetate with pet ether as eluent to give 4-(benzyloxy)but-2-enenitrile (100.6 g, 87% yield) as a colorless oil. *m/z*: 174.1 $(M+H)^+$. ^1H NMR (Chloroform-*d*, 400 MHz): δ (ppm) proton NMR showed mixture of isomers. 7.47 – 7.32 (m, 5H), 6.80-6.62 (m, 1H), 5.77-5.72 (m, 1H), 4.59 (d, *J* = 2.8 Hz, 2H), 4.18-4.16 (m, 2H).

[0229] Step 2. To a stirred solution of potassium tert-butoxide (1 M solution in THF; 289.0 mL, 289 mmol, 1.0 equiv) in tetrahydrofuran (260 mL) was added methyl 2-hydroxyacetate (22.03 mL, 289 mmol, 1.0 equiv) at RT and heated to 50°C under nitrogen atmosphere. To this, 4-(benzyloxy)but-2-enenitrile (50.0 g, 289 mmol, 1.0 equiv) was added and stirred at same temperature for 4 h. The reaction temperature was increased to 70°C and stirred for 16 h. After completion, reaction mixture was cooled to 0 °C and quenched with ice water (500 mL). The resultant solution was washed with diethyl ether (2 x 200 mL) and then acidified with conc. HCl (until pH of ~1-2) and then extracted with DCM (2 x 500 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under vacuum. The crude residue was purified by column chromatography over silica gel (60-120 mesh) using 26% ethyl acetate with pet ether as an eluent to give 2-((benzyloxy)methyl)-4-oxotetrahydrofuran-3-carbonitrile (9.2 g, 14% yield) as a colorless oil. LCMS (ESI, Positive) *m/z*: 232.0 $(M+H)^+$. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.41-7.28 (m, 5H), 4.83 – 4.60 (m, 2H), 4.52 (dd, *J* = 11.8, 6.6 Hz, 1H), 4.33 (dd, *J* = 17.0, 9.0 Hz, 1H), 4.11 – 3.89 (m, 2H), 3.82 – 3.68 (m, 2H).

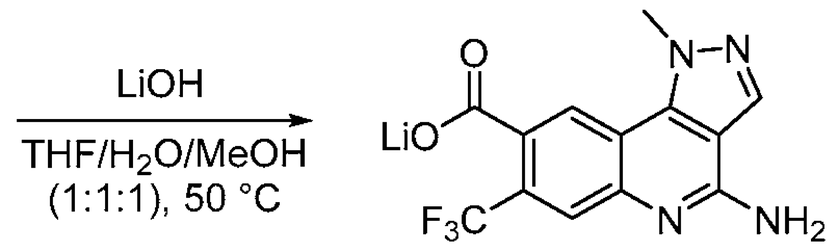
[0230] Step 3. To a stirred solution of 2-((benzyloxy)methyl)-4-oxotetrahydrofuran-3-carbonitrile (5.8 g, 25.08 mmol, 1.0 equiv) in dichloromethane (116 mL) were added triflic anhydride (6.75 mL, 40.1 mmol, 1.6 equiv) and DIPEA (8.76 mL, 50.2 mmol, 2.0 equiv) at -78 °C under N_2 atmosphere and stirred for 10 min. The reaction mixture was quenched with water (50 mL) and extracted with dichloromethane (2 x 200 mL). The combined organic layers were washed with brine solution (100 mL) and dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was washed with diethyl ether (200 mL) and filtered. The organic layer was concentrated under reduced pressure to give 5-((benzyloxy)methyl)-4-cyano-2,5-dihydrofuran-3-yl trifluoromethane sulfonate (7.65 g) as a light brown liquid, which was taken as such for next step.

[0231] Step 4. To a stirred solution of 5-((benzyloxy)methyl)-4-cyano-2,5-dihydrofuran-3-yl trifluoromethane sulfonate (7.65 g, 20.93 mmol, 1.0 equiv) in 1,4-dioxane (232 mL) and water (11.60 mL) were added methyl 4-amino-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (5.8 g, 20.93 mmol, 1.0 equiv), potassium carbonate (8.68 g, 62.8 mmol, 3.0 equiv) at room temperature. The reaction mixture was purged with N_2 gas for 15 min and then added $Pd(PPh_3)_4$ (1.209 g, 1.046 mmol, 0.05 equiv). Reaction mixture was heated at 80 °C for 16 h. After completion, the reaction mixture was concentrated under reduced pressure and the crude residue was purified by column chromatography over silica gel (60-120 mesh) using 80% ethyl acetate with pet ether as eluent to give 4-amino-3-((benzyloxy)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxylate (4.4 g, 58% yield) as an off white solid. *m/z*: 365.2 $(M+H)^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 8.12 (d, J = 2.0 Hz, 1H), 8.01 (dd, J = 8.9, 2.0 Hz, 1H), 7.59 (d, J = 8.8 Hz, 1H), 7.34 – 7.20 (m, 5H), 6.91 (br s, 2H), 5.49 (dq, J = 5.6, 3.6, 2.7 Hz, 1H), 5.44 – 5.32 (m, 2H), 4.56 – 4.44 (m, 2H), 3.90 – 3.73 (m, 5H). Ester 268 was treated with LiOH in THF and the lithium salt of 268 was used crude in amide coupling reactions.

[0232] Intermeidate 269: lithium 4-amino-1-methyl-7-(trifluoromethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxylate hydroxide



Step 1

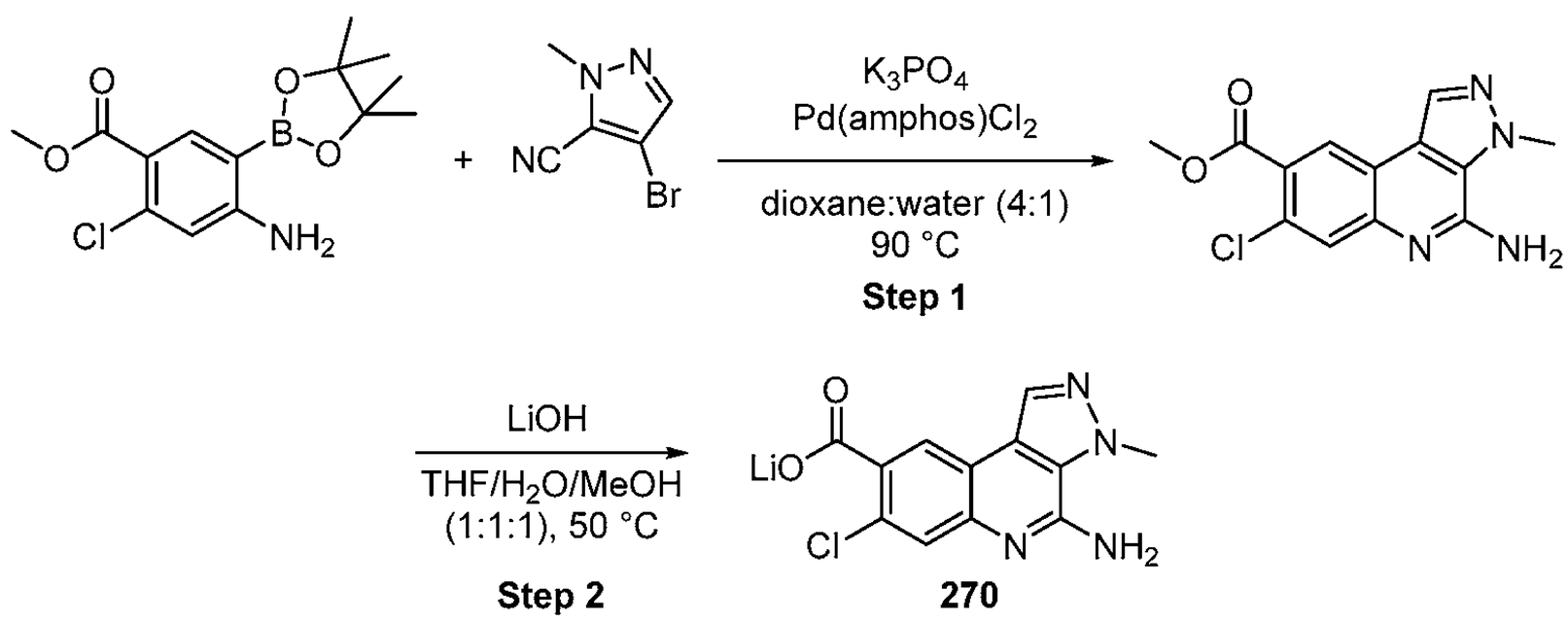


Step 2 **269**

[0233] Step 1. $K_3PO_4 \cdot H_2O$ (1.08 g, 4.70 mmol, Sigma-Aldrich Corporation), X-Phos (0.08 g, 0.16 mmol, Sigma-Aldrich Corporation), (2-dicyclohexylphosphino-2',4',6'-triisopropyl-1,1'-biphenyl)[2-(2'-amino-1,1'-biphenyl)]palladium (ii) methanesulfonate (0.14 mg, 0.16 mmol, Sigma-Aldrich Corporation), 1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1h-pyrazole-4-carbonitrile (1.10 g, 4.70 mmol, Enamine) and methyl 4-amino-5-bromo-2-(trifluoromethyl)benzoate (0.700 g, 2.349 mmol, Combi Blocks) were suspended in a degassed mixture of water (1.0 mL) and 1,4-dioxane (5.0 mL) and stirred at 60°C overnight and then at 90 °C for 18h. Volatiles were removed *in vacuo* and the crude product was purified via silica column chromatography (0 to 5% MeOH/DCM + 0.5% NH_3/MeOH) to yield methyl 4-amino-1-methyl-7-(trifluoromethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxylate (0.63 g, 1.94 mmol, 83 % yield) as an slight brownish solid. m/z (ESI): 324.8 $(M+H)^+$. ^1H NMR (400 MHz, DMSO-d6) δ ppm 8.71 - 8.76 (m, 1 H), 8.33 - 8.37 (m, 1 H), 7.87 - 7.92 (m, 1 H), 7.54 - 7.61 (m, 2 H), 4.41 - 4.46 (m, 3 H), 3.92 (s, 3 H). ^{19}F NMR (376 MHz, DMSO-d6) δ ppm -58.06.

[0234] Step 2. Methyl 4-amino-1-methyl-7-(trifluoromethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxylate (0.62 g, 1.90 mmol) and lithium hydroxide (0.91 g, 3.79 mmol, Sigma-Aldrich Corporation) were suspended in methanol (3.0 mL), H_2O (3.0 mL) and THF (3.0 mL) and stirrred at 50 °C for 2 hours. Volatiles of the crude mixture were removed in vacuo and the light brownish solid coevaporated with DCM twice, followed by coevaporation with toluene to give lithium 4-amino-1-methyl-7-(trifluoromethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxylate hydroxide (585 mg, 1.720 mmol, 91 % yield) that was used in subsequent steps without further purification. m/z (ESI): 310.9 $(M+H)^+$. ^1H NMR (400 MHz, DMSO-d6) δ ppm 8.33 (s, 1 H), 8.27 (s, 1 H), 7.68 (s, 1 H), 7.03 (br s, 2 H), 4.38 (s, 3 H). ^{19}F NMR (376 MHz, DMSO-d6) δ ppm -57.47.

[0235] Intermeidate 270: lithium 4-amino-7-chloro-3-methyl-3H-pyrazolo[3,4-c]quinoline-8-carboxylate hydroxide

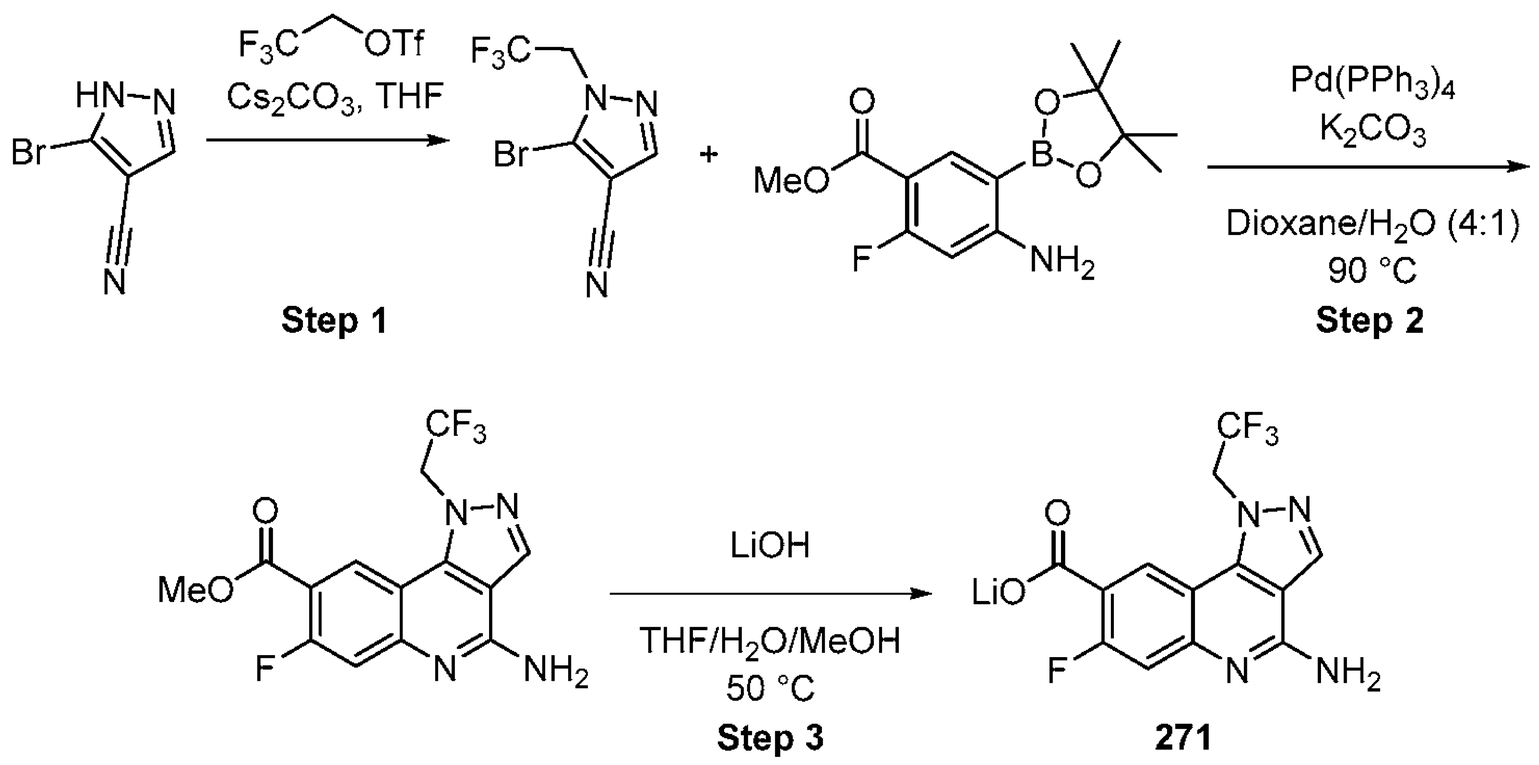


[0236] Step 1. 1H-pyrazole-5-carbonitrile, 4-bromo-1-methyl- (273 mg, 1.47 mmol), methyl 4-amino-2-chloro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (457 mg, 1.47 mmol), phosphoric acid,

tripotassium salt, monohydrate (1.35 g, 5.87 mmol, Sigma-Aldrich Corporation) and Pd(amphos)Cl_2 (72.7 mg, 0.10 mmol) were suspended in degassed water (1.0 mL) and 1,4-dioxane (4.00 mL) and stirred at 90 °C over night, whereas a yellow solid formed. Water (10 mL) was added after the mixture was cooled to rt and the precipitate filtered and washed with DCM, MeOH and acetone. 92 mg of a solid were dried and the organic wash was absorbed onto silica gel and purfied via column chromatography using 0 to 20 % MeOH + 0.5% NH_3 in MeOH/DCM) to yield methyl 4-amino-7-chloro-3-methyl-3H-pyrazolo[3,4-c]quinoline-8-carboxylate (164 mg, 0.564 mmol, 38.5% yield) as a orange solid. m/z (ESI): 291.000 $(M+H)^+$. 1H NMR (400 MHz, DMSO-d6) δ ppm 8.52 - 8.63 (m, 2 H), 7.60 (s, 1 H), 7.25 (s, 2 H), 4.35 (s, 3 H), 3.89 (s, 3 H).

[0237] Step 2. Methyl 4-amino-7-chloro-3-methyl-3H-pyrazolo[3,4-c]quinoline-8-carboxylate (164 mg, 0.56 mmol) was suspended in water (0.5 mL), methanol (0.5 mL) and tetrahydrofuran (0.5 mL) and then lithium hydroxide hydrate (47.3 mg, 1.13 mmol, Sigma-Aldrich Corporation) was added and the reaction was stirred at 50 °C for 90 minutes. Volatiles were removed in vacuo to yield lithium 4-amino-7-chloro-3-methyl-3H-pyrazolo[3,4-c]quinoline-8-carboxylate hydroxide (170 mg, 0.56 mmol, 98% yield) as a yellow solid. *m/z* (ESI): 277.0 $(M+H)^+$.

[0238] Intermediate 271: lithium 4-amino-7-fluoro-1-(2,2,2-trifluoroethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxylate

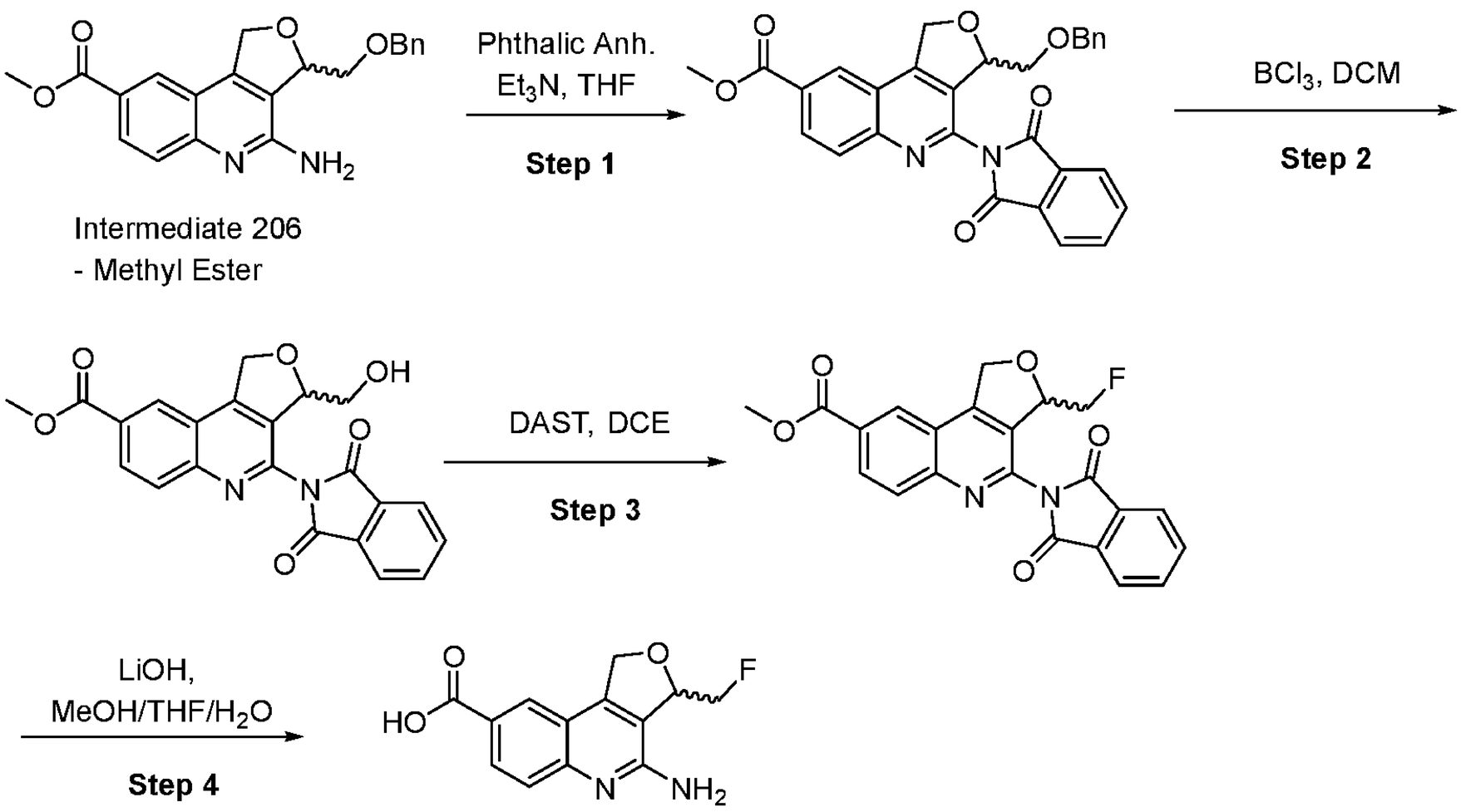


[0239] Step 1. To a 100-mL round-bottomed flask was added 5-bromo-1H-pyrazole-4-carbonitrile (1 g, 5.81 mmol, Enamine), cesium carbonate (3.79 g, 11.63 mmol, Sigma-Aldrich Corporation) and 2,2,2-trifluoroethyl triflate (1.687 g, 1.054 mL, 7.27 mmol, Combi-Blocks Inc.) in 1,4-dioxane (17.10 mL). The reaction mixture was stirred at 35 °C for 20 h. Upon completion as determined by LC-MS, the reaction was filtered and concentrated *in-vacuo* to afford the crude product. This was used as it is for the next step without further purification. *m/z* (ESI): 253.9 $(M+H)^+$

[0240] Step 2. To a 25-mL pressure vial was added methyl 4-amino-2-fluoro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (534 mg, 1.810 mmol), 5-bromo-1-(2,2,2-trifluoroethyl)-1H-pyrazole-4-carbonitrile (418 mg, 1.646 mmol), anhydrous potassium carbonate (1137 mg, 8.23 mmol, Acros Organics), and tetrakis(triphenylphosphine)palladium (190 mg, 0.165 mmol, Strem) in 1,4-dioxane (4388 µL) and water (1097 µL). The solution was degassed with N_2 for 10 mins and heated at 90 °C for 18 h. Upon completion as determined by LC-MS, the reaction mixture was cooled to room temperature and 5 ml of water was added. The product was filtered, and the precipitate was washed with 5 ml water twice and 5 ml of DCM thrice. The crude product was isolated as a solid and used as it is for the next step without further purification. *m/z* (ESI): 343.0 $(M+H)^+$

[0241] Step 3. To a 20 ml pressure vial was added methyl 4-amino-7-fluoro-1-(2,2,2-trifluoroethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxylate (544 mg, 1.589 mmol) and lithium hydroxide, monohydrate (133 mg, 3.18 mmol, Sigma-Aldrich Corporation) in tetrahydrofuran (1766 µL), methanol (1766 µL) and water (1766 µL) was stirred at 50 °C for 12 h. Upon completion via LCMS, the reaction mixture was cooled to room temperature and evaporated to dryness and used as it is for the next step. *m/z* (ESI): 329.1 $(M+H)^+$

[0242] Intermediate 272: 4-amino-3-(fluoromethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxylic acid hydrochloride



[0243] Step 1. Methyl 4-amino-3-((benzyloxy)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxylate (3.40 g, 9.33 mmol, 1.0 equiv, Intemediate 206-Methyl Ester) was dissolved in tetrahydrofuran (46.7 mL) and triethylamine (4.16 mL, 29.9 mmol, 3.2 equiv, Aldrich) and phthalic anhydride (2.76 g, 18.7 mmol,

2.0 equiv, Aldrich) were added. The reaction mixture was heated at reflux for four days. The reaction was then concentrated to dryness and then taken up in water (100 mL) and DCM (150 mL). The layers were separated and the aqueous layer was extracted with (1 x 200 mL) of DCM. The combined organic layers were dried over $MgSO_4$, filtered and the crude product was purified by medium pressure chromatography (silica, 0 to 100% EtOAc:Heptanes) to give methyl 3-((benzyloxy)methyl)-4-(1,3-dioxoisoindolin-2-yl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxylate (3.22 g, 6.51 mmol, 69.8% yield). *m/z* (ESI): 495.1 $(M+H)^+$.

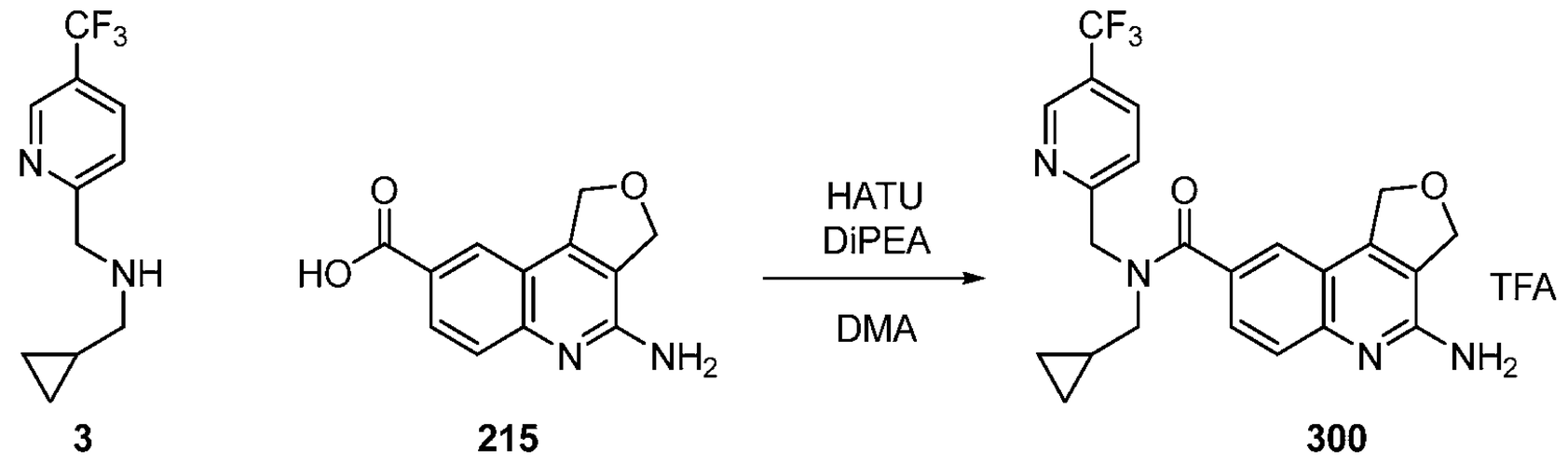
[0244] Step 2. Methyl 3-((benzyloxy)methyl)-4-(1,3-dioxoisoindolin-2-yl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxylate (4.22 g, 8.53 mmol, 1.0 equiv) was dissolved in dichloromethane (114 mL) and cooled to -78°C, then boron trichloride (1.0 M in DCM) (21.3 mL, 21.3 mmol, 2.5 equiv, Aldrich) was added and the resulting mixture was stirred in a dry ice bath for 1.5 hrs to completion. The slurry was recooled to -78°C and methanol (3.5 mL) was slowly added to quench the reaction mixture. The slurry was removed from the dry ice bath and allowed to slowly warm. The mixture was diluted with water (150 mL) and extracted with EtOAc (2 x 250 mL). The combined organic layers were combined and washed with brine (1 x 100 mL) and dried over $MgSO_4$. The filtrate was concentrated and then triturated with EtOAc/Hexanes to give the desired methyl 4-(1,3-dioxoisoindolin-2-yl)-3-(hydroxymethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxylate (2.83 g, 7.00 mmol, 82% yield). *m/z* (ESI): 405.1 $(M+H)^+$.

[0245] Step 3. Methyl 4-(1,3-dioxoisoindolin-2-yl)-3-(hydroxymethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxylate (998 mg, 2.47 mmol, 1.0 equiv) was dissolved in DCE (24.7 mL) and DAST (1.31 mL, 9.87 mmol, 4.0 equiv, Aldrich) was added slowly. The resulting mixture was stirred for 1.5 hours to completion. The reaction was quenched by slowly addition of the reaction mixture to 40 mL of satd. $NaHCO_3$ solution. This mixture was extracted with EtOAc (2 x 100 mL). The combined organic layers were washed with brine (1 x 45 ml) and dried over $MgSO_4$. The crude product was triturated with EtOAc and the precipitate was filtered and washed to give methyl 4-(1,3-dioxoisoindolin-2-yl)-3-(fluoromethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxylate (690 mg, 1.70 mmol, 68.8% yield). *m/z* (ESI): 406.9 $(M+H)^+$.

[0246] Step 4. Lithium hydroxide, monohydrate (273 mg, 6.50 mmol, 4.0 equiv, Sigma-Aldrich Corporation) was added to a suspension of methyl 4-(1,3-dioxoisoindolin-2-yl)-3-(fluoromethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxylate (660 mg, 1.62 mmol, 1.0 equiv) in MeOH (8.5 mL), THF (8.5 mL) and water (8.5 mL). The mixture was heated to 70 °C for 19 hours then cooled to room temperature. The organic solvent was removed *in vacuo* and the resulting aqueous solution was taken to pH 6 with 5N HCl solution. The resulting suspension was filtered and air dried to give 4-amino-3-(fluoromethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxylic acid hydrochloride (490 mg, 1.64 mmol, 101% yield). *m/z* (ESI): 263.1 $(M+H)^+$.

Examples

[0247] Example 300: 4-amino-N-(cyclopropylmethyl)-N-[[5-(trifluoromethyl)-2-pyridyl]methyl]-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide

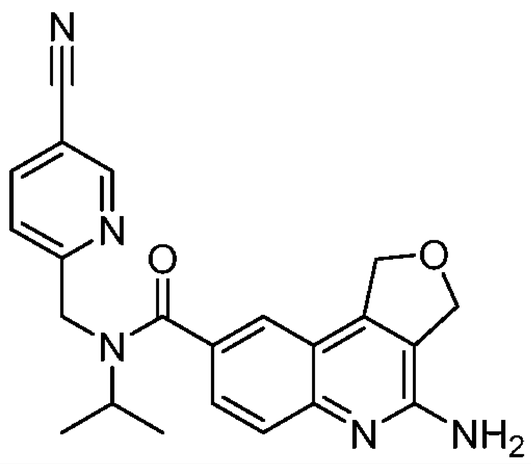
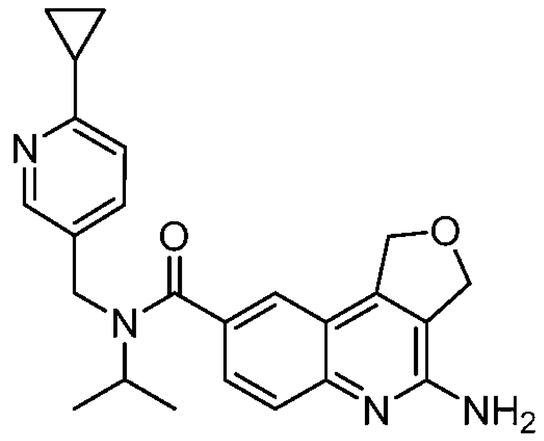
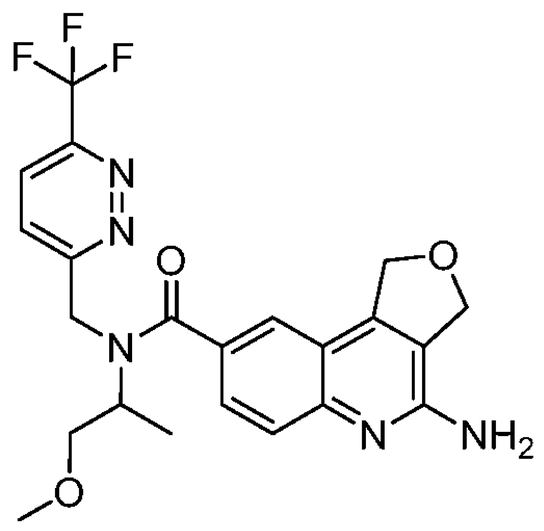
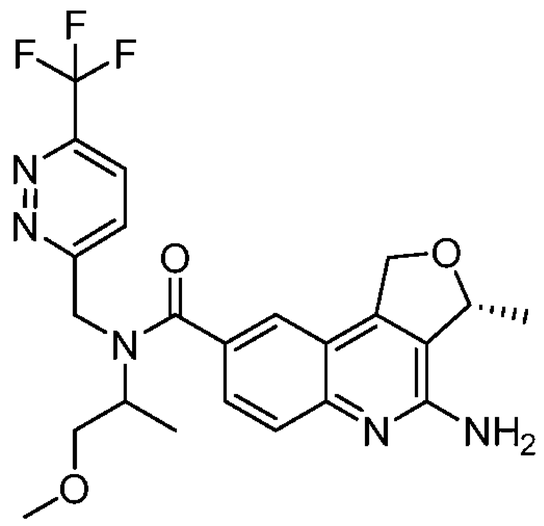


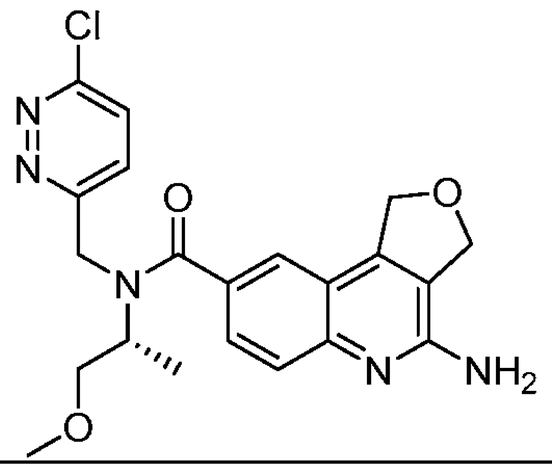
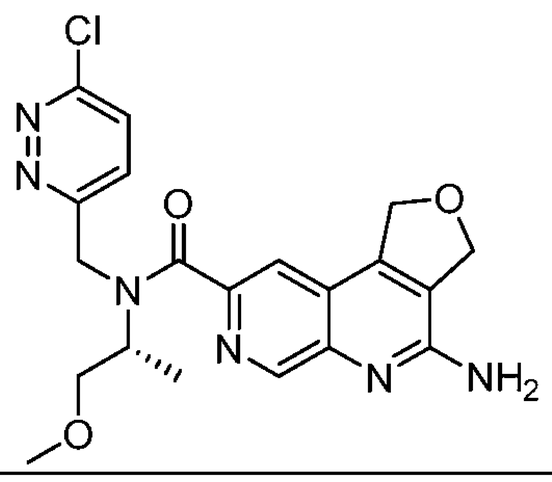
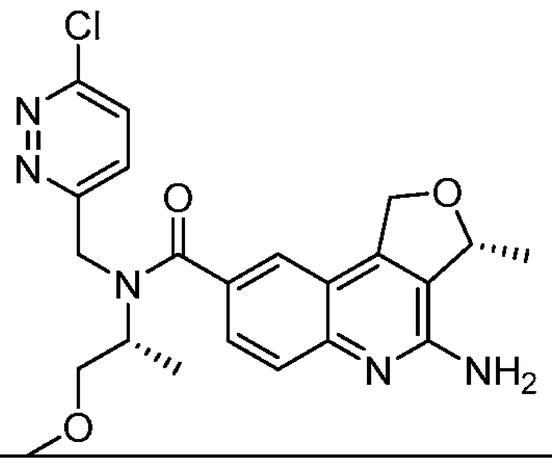
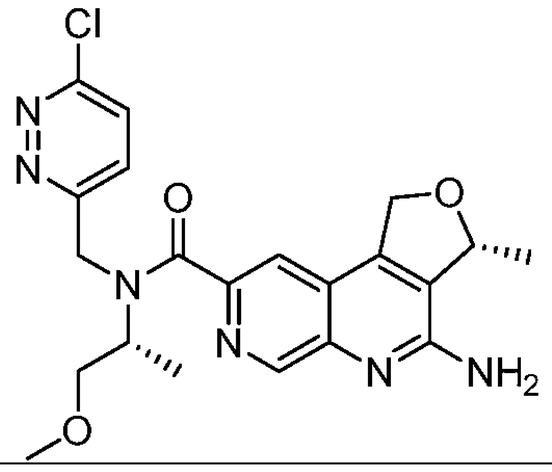
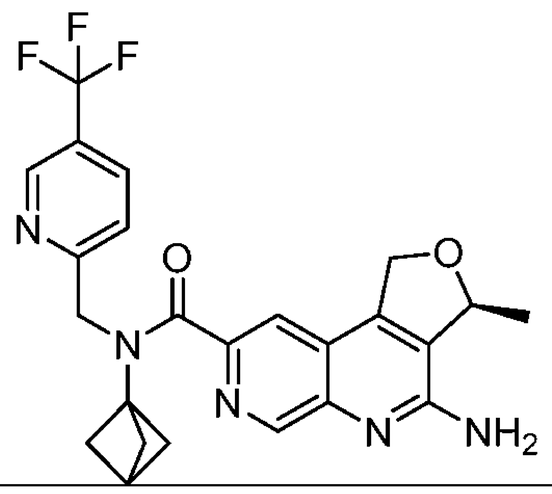
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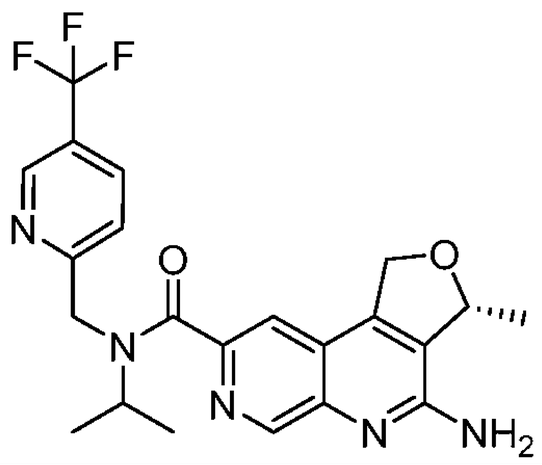
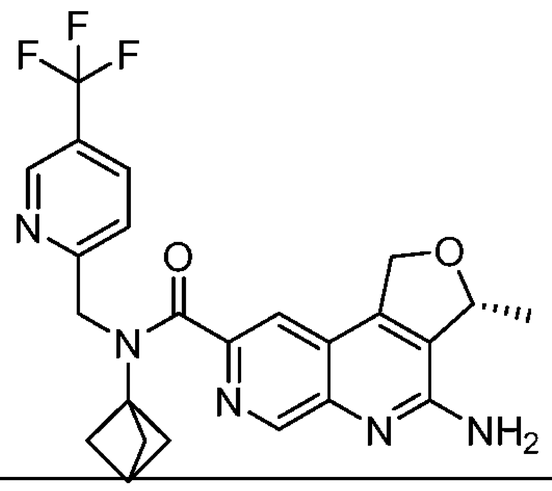
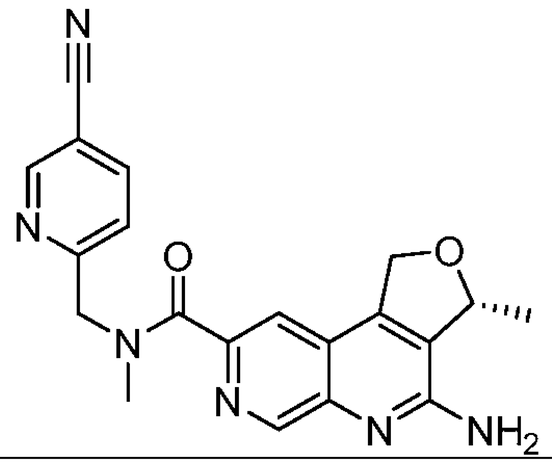
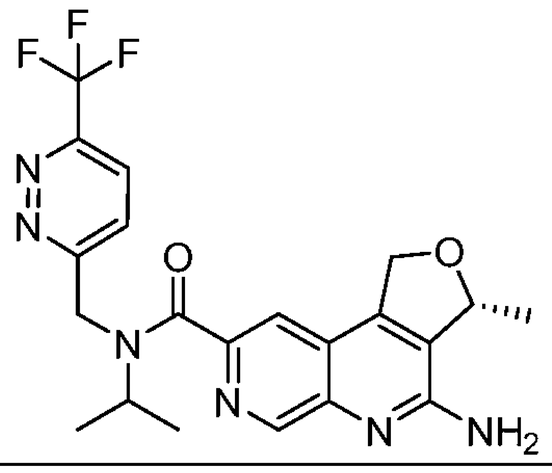
[0248] A mixture of 1-cyclopropyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)methanamine (**2**, 0.050 g, 0.217 mmol), 4-amino-1,3-dihydrofuro[3,4-c]quinoline-8-carboxylic acid (**165**, 0.057 g, 0.250 mmol), N, N-dimethylacetamide (2 mL), HATU (0.099 g, 0.261 mmol, Combi-Blocks) and diisopropylethylamine (0.112 g, 0.151 mL, 0.869 mmol, Aldrich) was stirred at rt overnight. The mixture was filtered and the crude material was purified by reverse phase prep HPLC (10-70% MeCN in water with 0.1% TFA) to give 4-amino-N-(cyclopropylmethyl)-N-[[5-(trifluoromethyl)-2-pyridyl]methyl]-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide 2,2,2-trifluoroacetate (105 mg, 0.189 mmol, 87% yield) as a white solid. m/z (ESI): 443 $(M+H)^+$. ^{1}H NMR (400 MHz, METHANOL-d4) δ ppm 8.88 (br s, 1 H), 8.04 - 8.16 (m, 1 H), 7.89 - 7.99 (m, 2 H), 7.46 - 7.88 (m, 2 H), 5.34 - 5.60 (m, 2 H), 4.86 - 5.25 (m, 4 H), 3.33 - 3.60 (m, 2 H), 0.93 - 1.18 (m, 1 H), 0.37 - 0.57 (m, 2 H), 0.00 - 0.31 (m, 2 H). ^{19}F NMR (377 MHz, METHANOL-d4) δ ppm -63.87 (s, 3 F), -77.15 (s, 3 F).

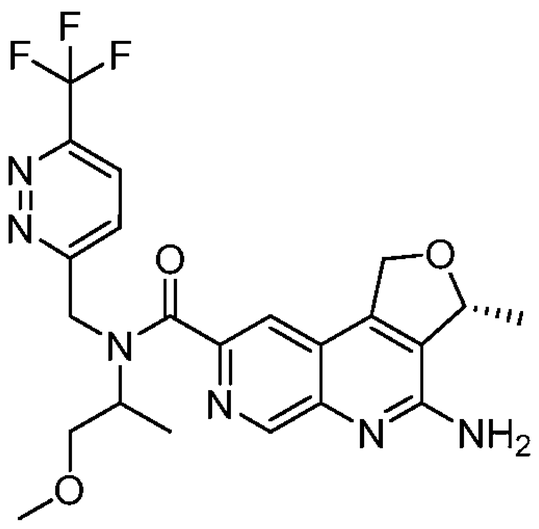
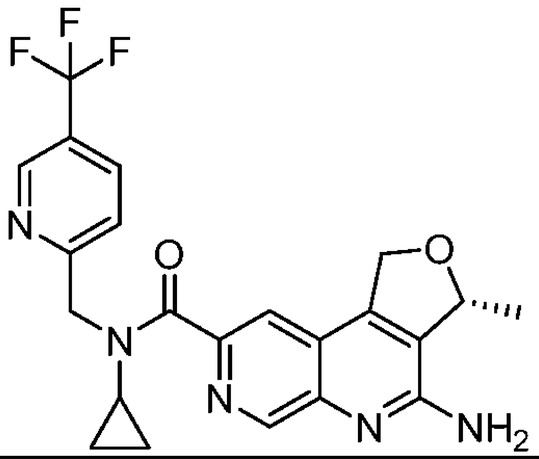
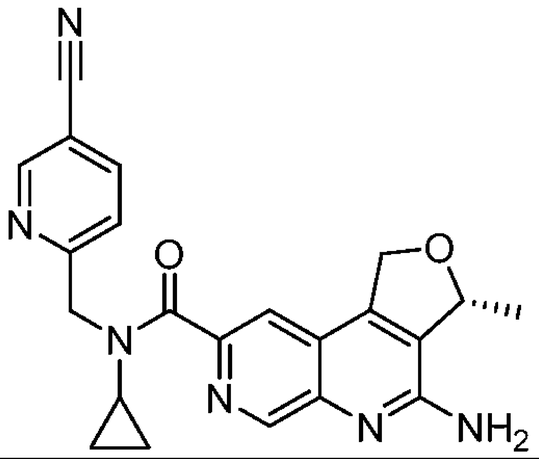
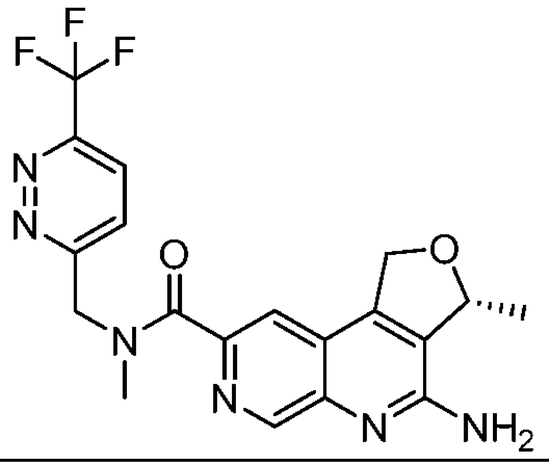
[0249] Compounds in Table 18 were prepared in a manner similar to that described above for example 300 using the indicated amide coupling reagent in the table.

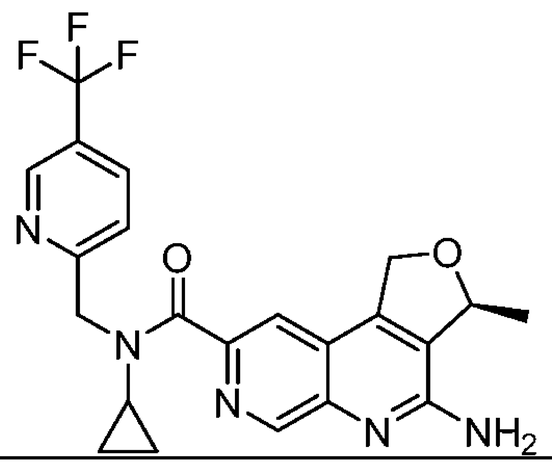
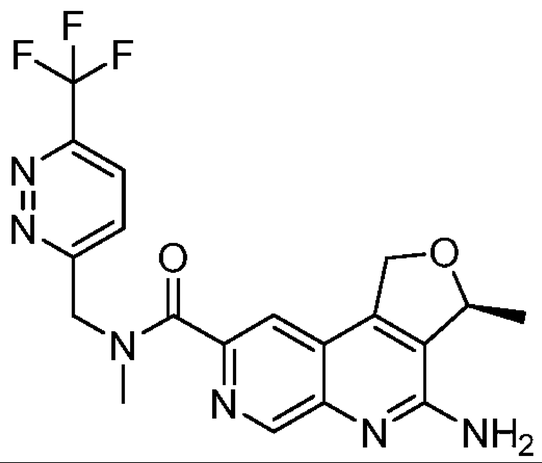
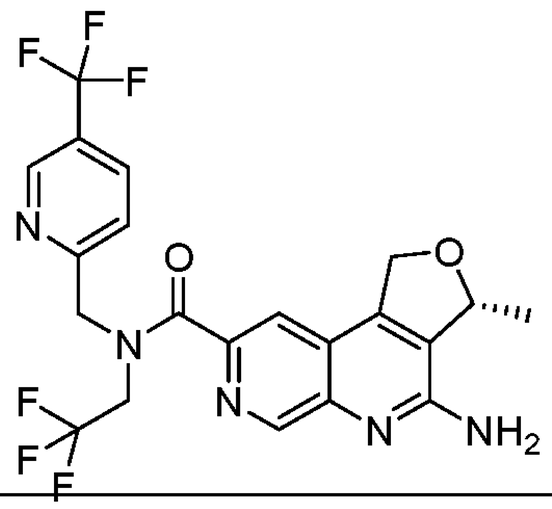
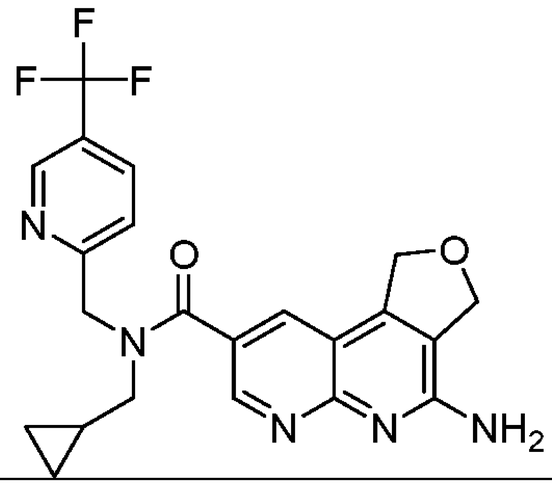
Table 18

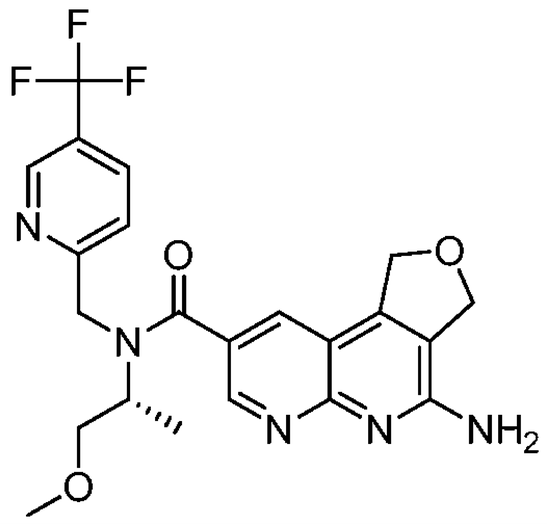
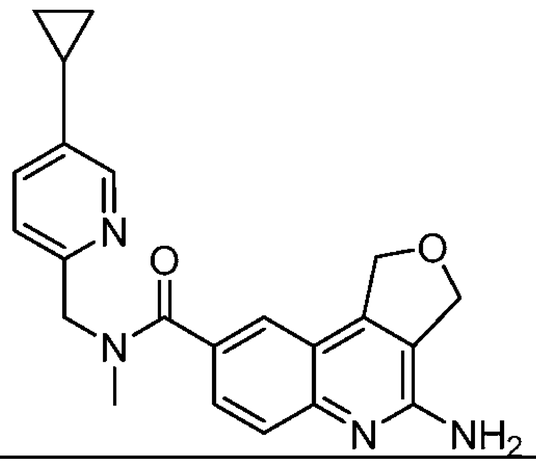
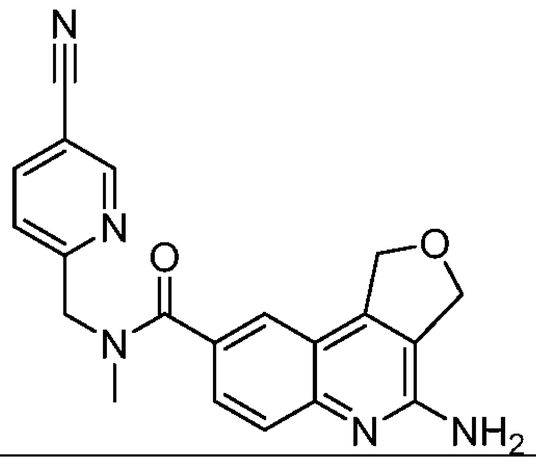
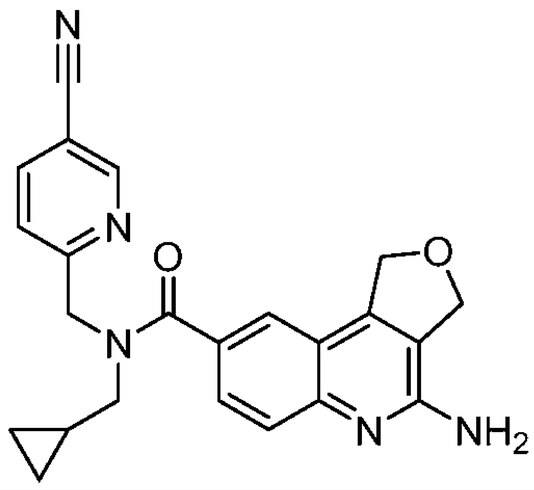
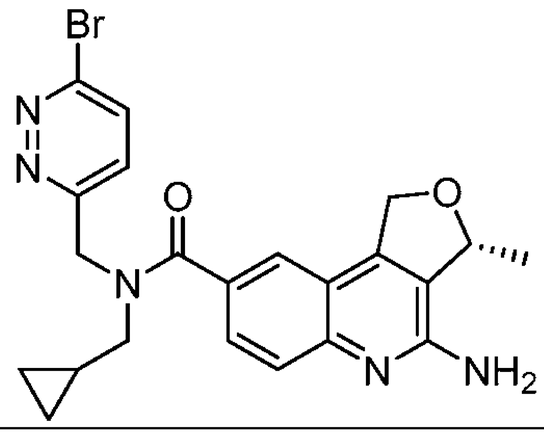
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
301		4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	CMPI	388.2
302		4-amino-N-((6-cyclopropyl-3-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	CMPI	403.2
303		4-amino-N-((2R)-1-methoxy-2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide and 4-amino-N-((2S)-1-methoxy-2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	CMPI	462.2
304		(3R)-4-amino-N-((2R)-1-methoxy-2-propanyl)-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide and (3R)-4-amino-N-((2S)-1-methoxy-2-propanyl)-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	CMPI	476.2

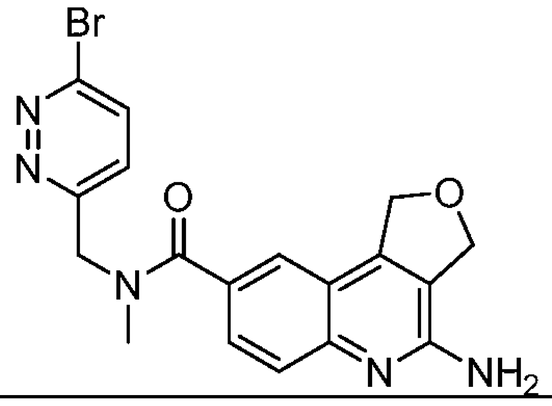
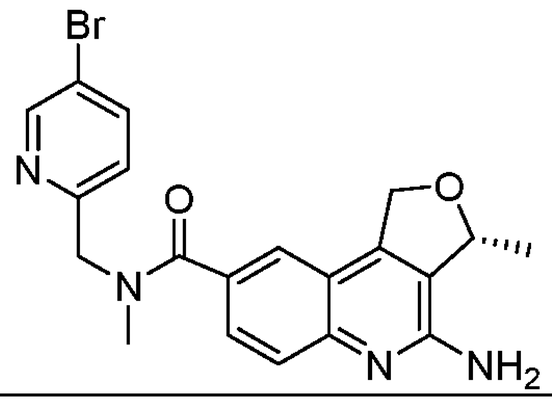
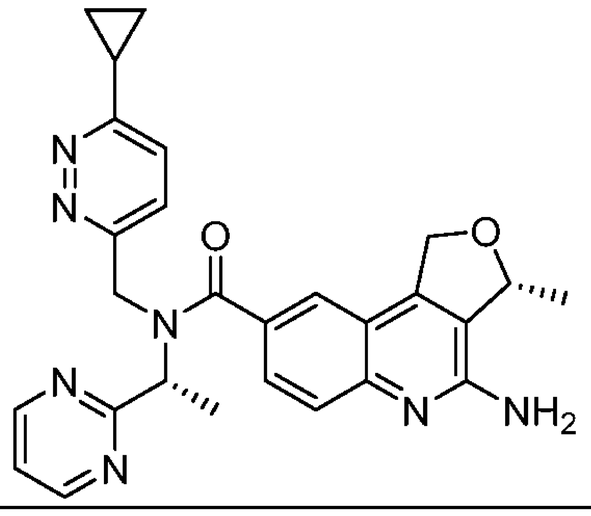
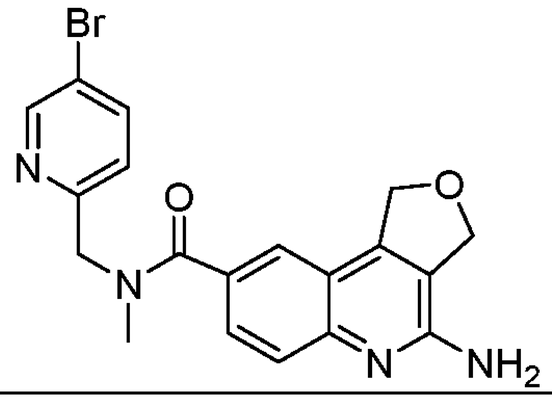
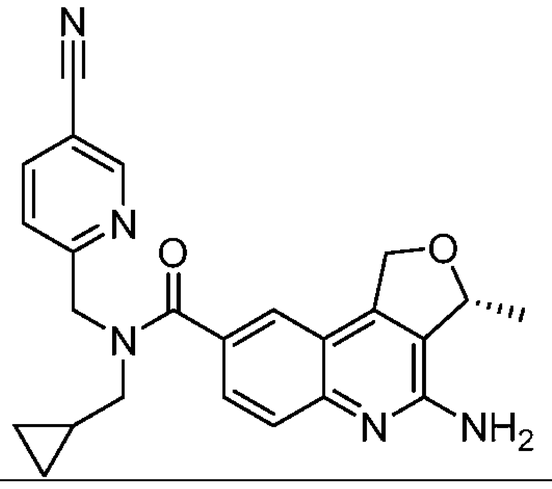
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
305		4-amino-N-((6-chloro-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	CMPI	428.2
306		4-amino-N-((6-chloro-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	CMPI	429.1
307		(3R)-4-amino-N-((6-chloro-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	CMPI	442.2
308		(3R)-4-amino-N-((6-chloro-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-3-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	CMPI	443.1
309		(3S)-4-amino-N-(bicyclo[1.1.1]pentan-1-yl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	CMPI	470.2

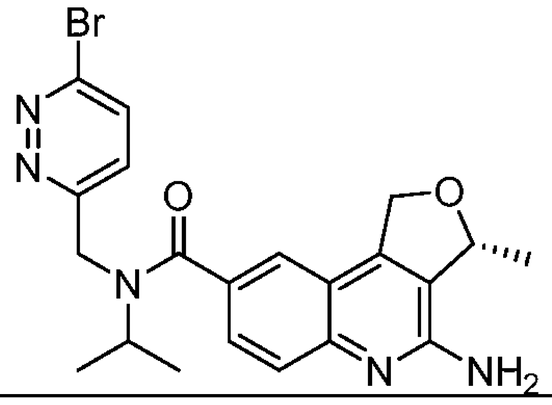
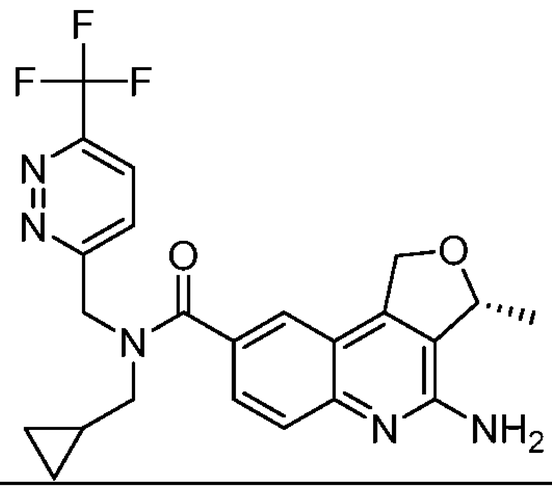
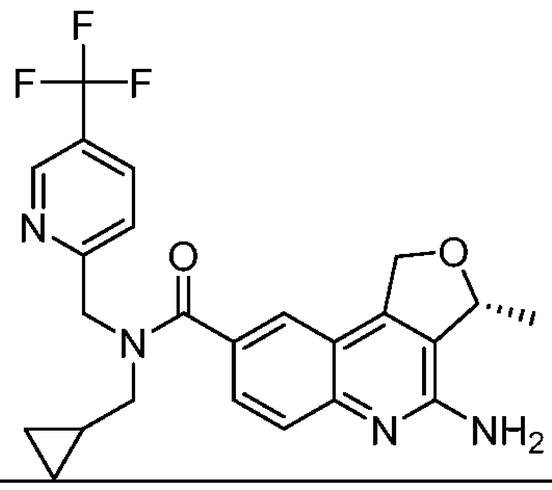
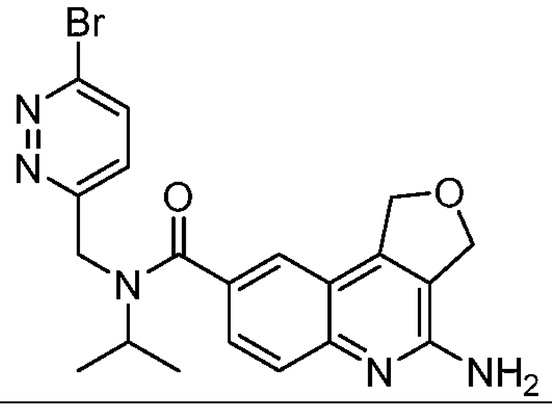
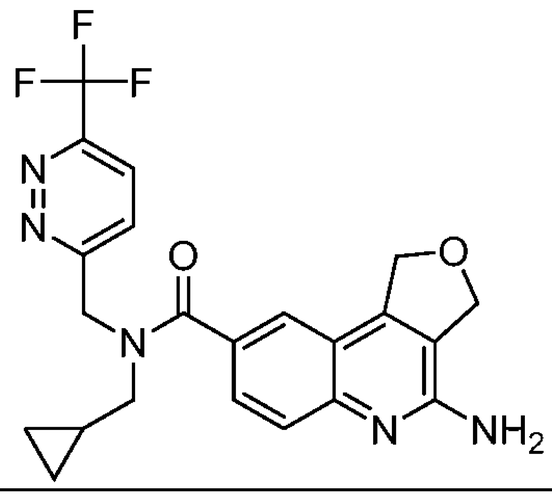
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
310		(3R)-4-amino-3-methyl-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	CMPI	446.2
311		(3R)-4-amino-N-(bicyclo[1.1.1]pentan-1-yl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	CMPI	470.2
312		(3R)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-N,3-dimethyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	CMPI	375.1
313		(3R)-4-amino-3-methyl-N-(2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	CMPI	447.2

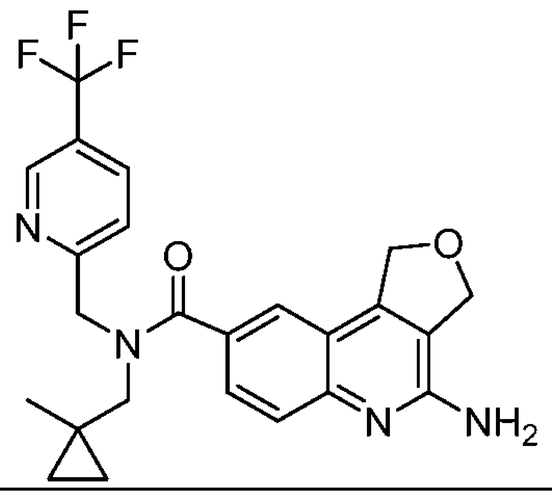
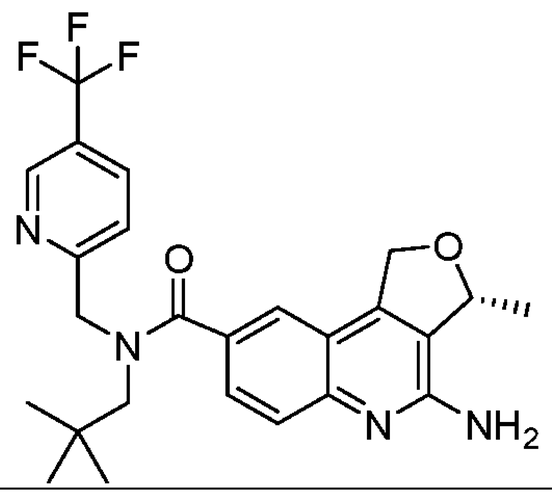
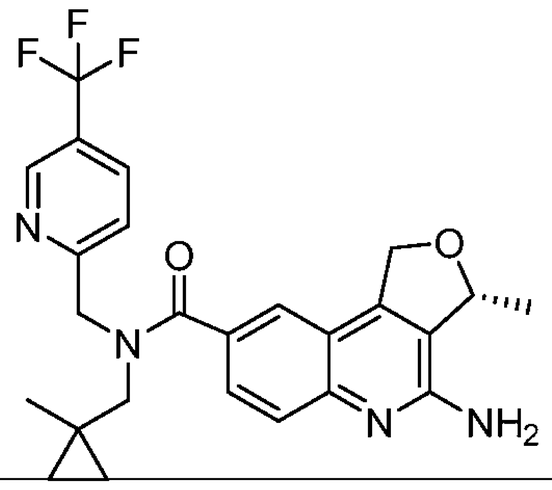
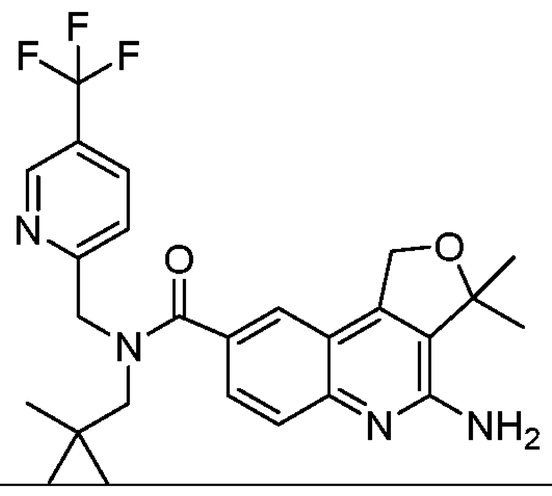
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
314		(3R)-4-amino-N-((2R)-1-methoxy-2-propanyl)-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide and (3R)-4-amino-N-((2S)-1-methoxy-2-propanyl)-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	CMPI	477.2
315		(3R)-4-amino-N-cyclopropyl-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	CMPI	444.2
316		(3R)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-cyclopropyl-3-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	CMPI	401.2
317		(3R)-4-amino-N,3-dimethyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	CMPI	419.1

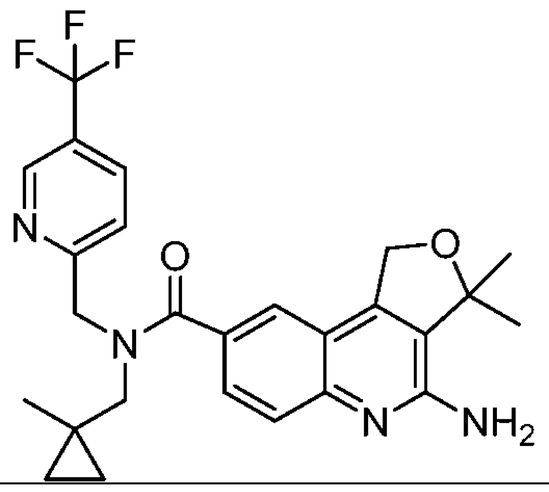
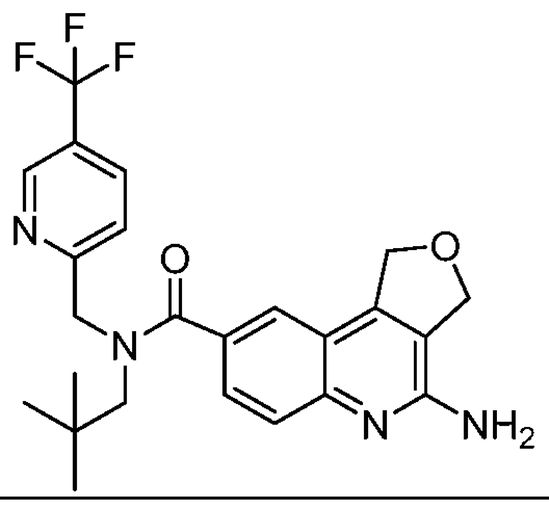
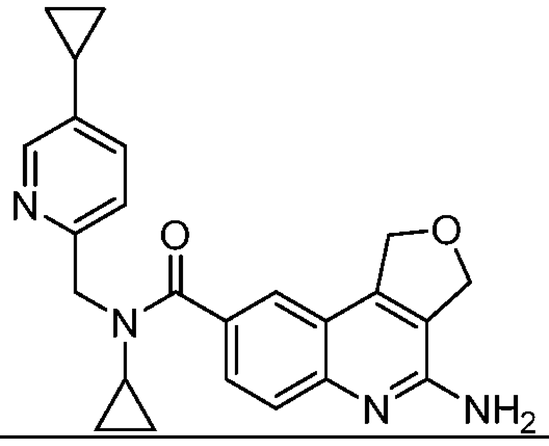
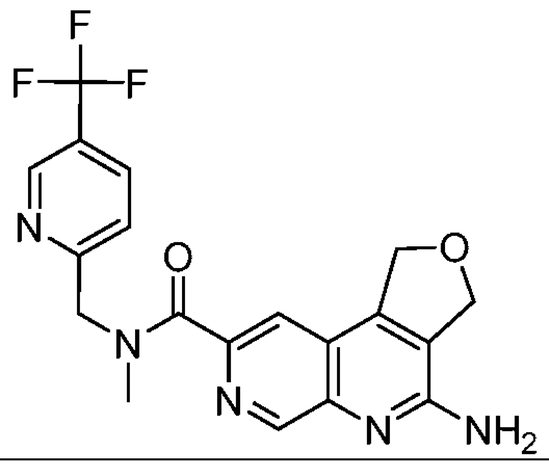
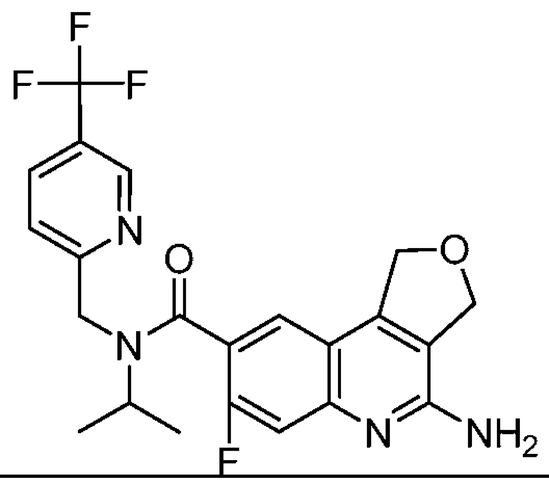
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
318		(3S)-4-amino-N-cyclopropyl-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	CMPI	444.2
319		(3S)-4-amino-N,3-dimethyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	CMPI	419.1
320		(3R)-4-amino-3-methyl-N-(2,2,2-trifluoroethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	CMPI	486.1
321		4-amino-N-(cyclopropylmethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide	DMB	444.2

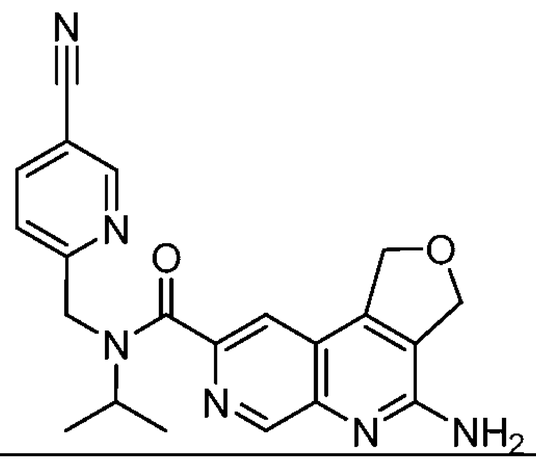
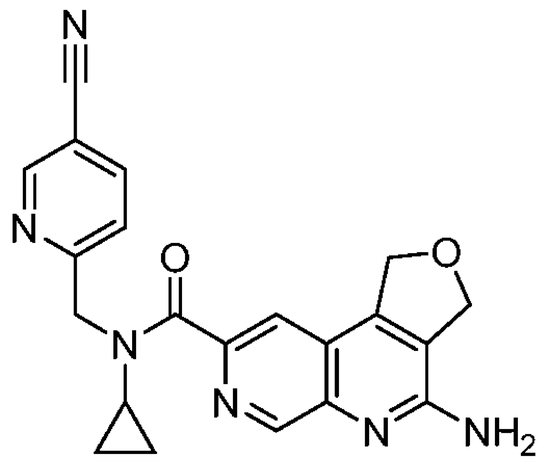
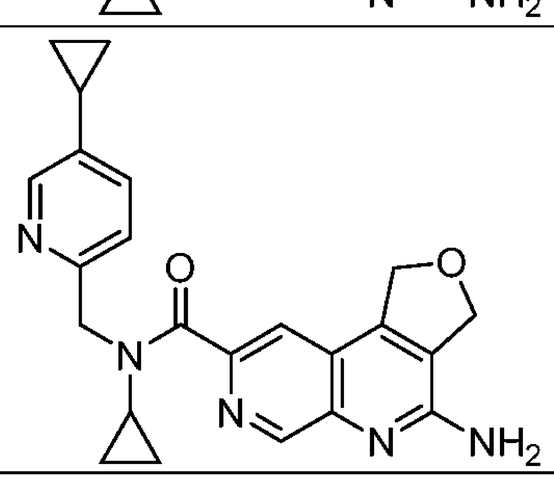
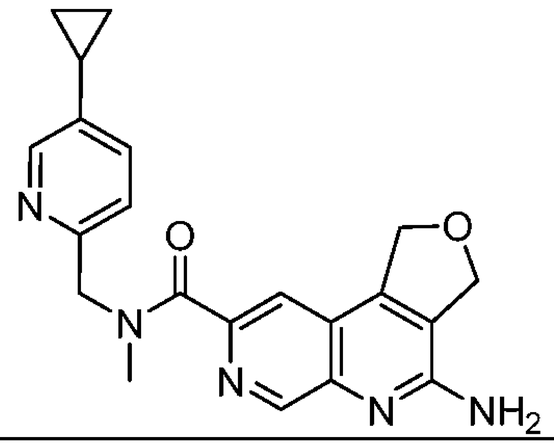
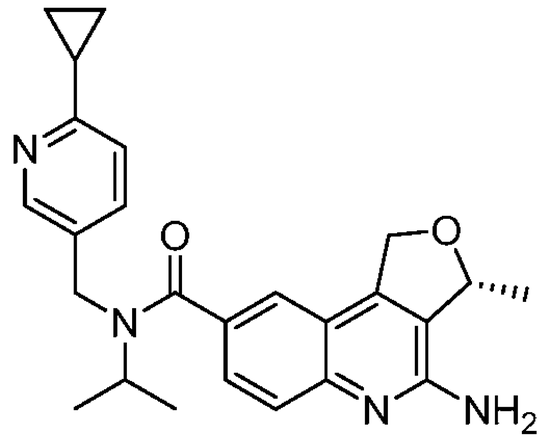
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
322		4-amino-N-((2R)-1-methoxy-2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide	DMB	462.2
323		4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	EDCI	375.2
324		4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	EDCI	360.2
325		4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-(cyclopropylmethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	400
326		(3R)-4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-(cyclopropylmethyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	468 and 470

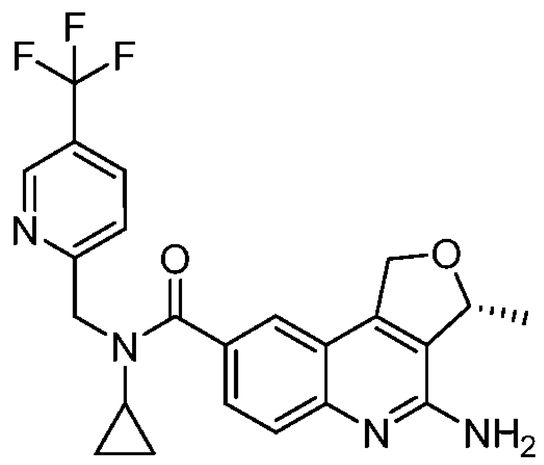
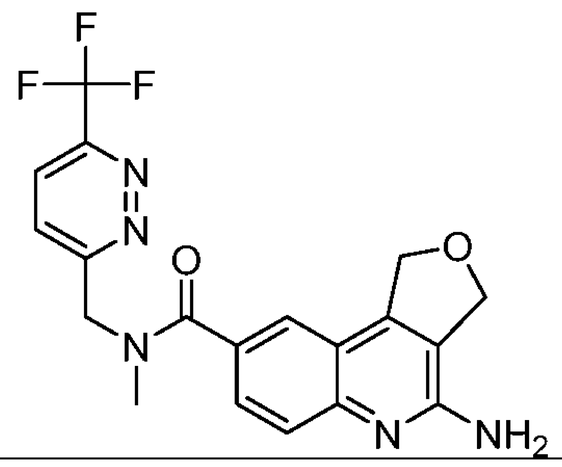
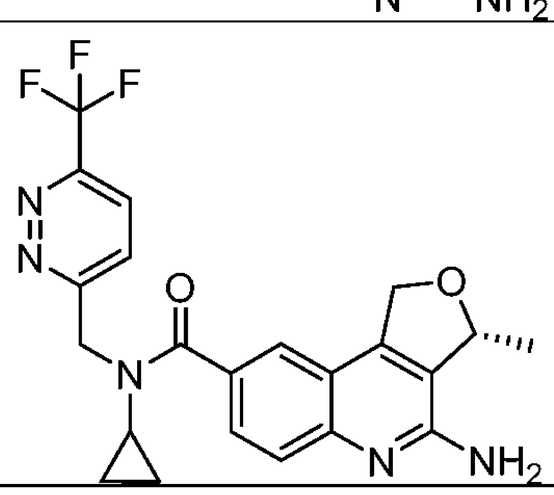
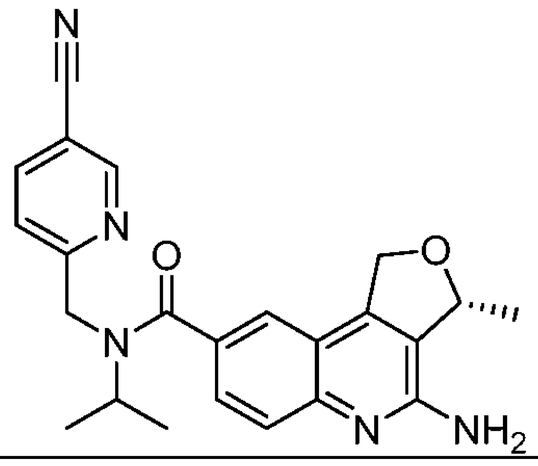
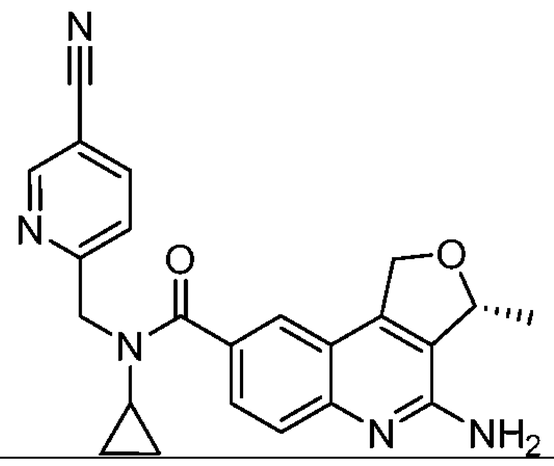
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
327		4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	414 and 416
328		(3R)-4-amino-N-((5-bromo-2-pyridinyl)methyl)-N,3-dimethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	427.0 and 429.0
329		(3R)-4-amino-N-((6-cyclopropyl-3-pyridazinyl)methyl)-3-methyl-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	482
330		4-amino-N-((5-bromo-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	413.0 and 415.0
331		(3R)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-(cyclopropylmethyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	414

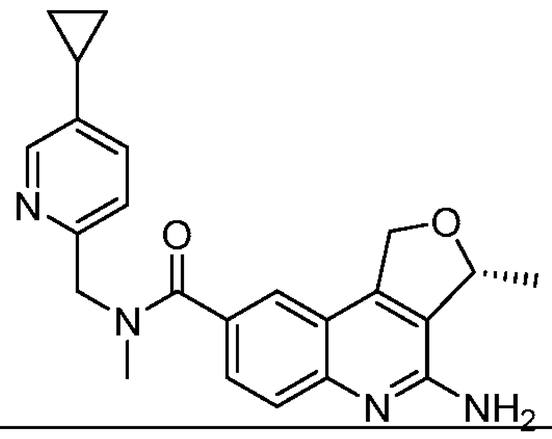
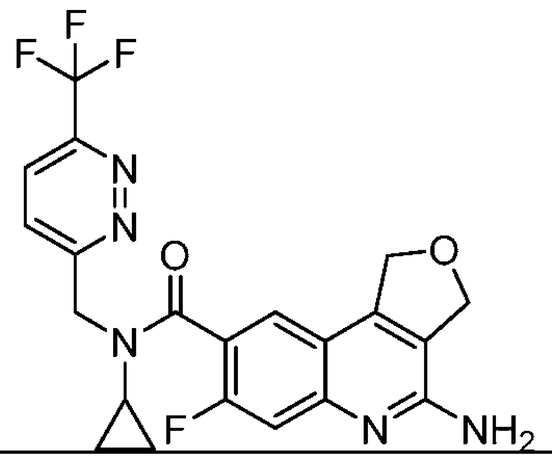
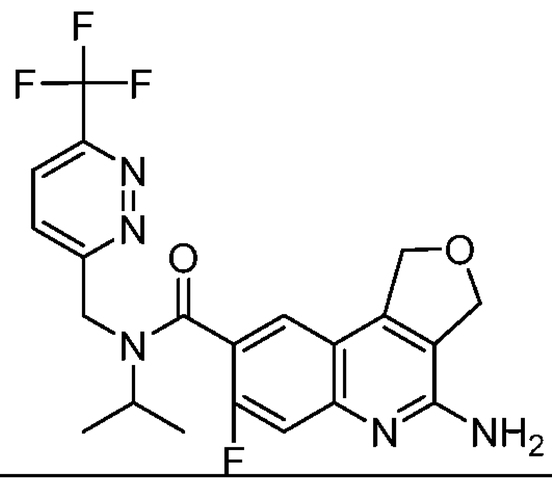
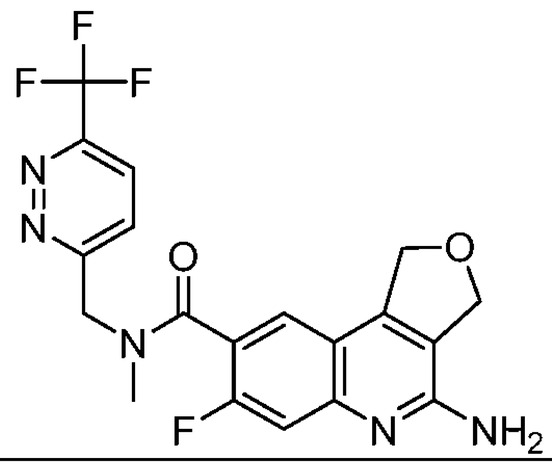
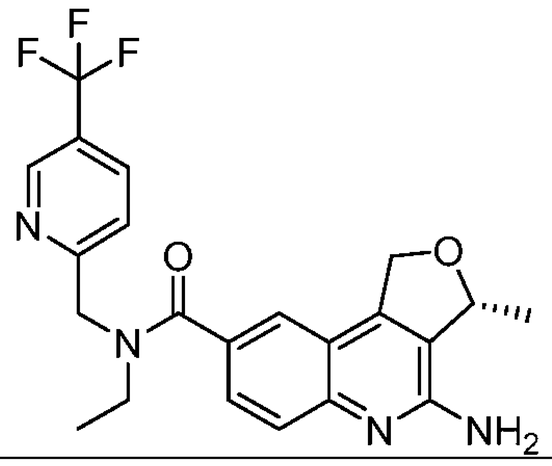
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
332		(3R)-4-amino-N-((6-bromo-3-pyridazinyl)methyl)-3-methyl-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	456 and 458
333		(3R)-4-amino-N-(cyclopropylmethyl)-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	458
334		(3R)-4-amino-N-(cyclopropylmethyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	457
335		4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	442 and 444
336		4-amino-N-(cyclopropylmethyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	444

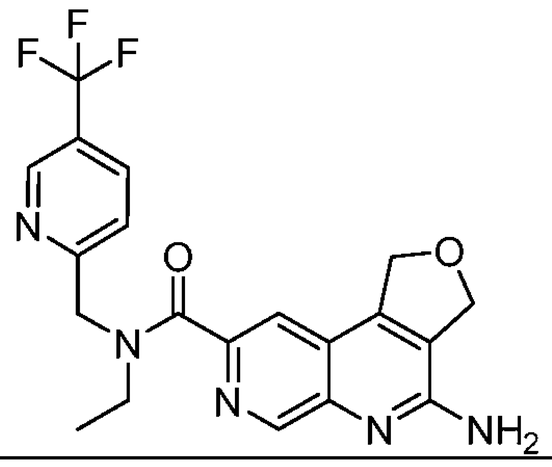
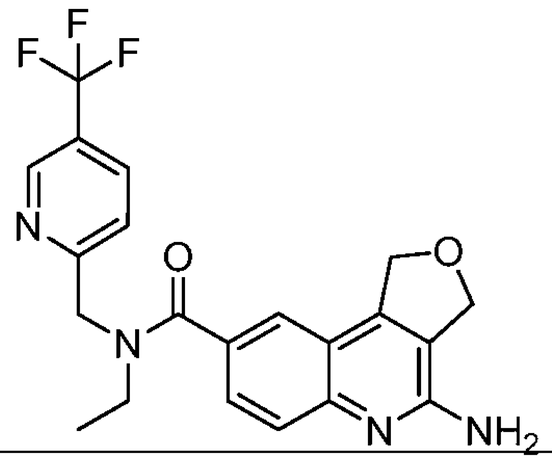
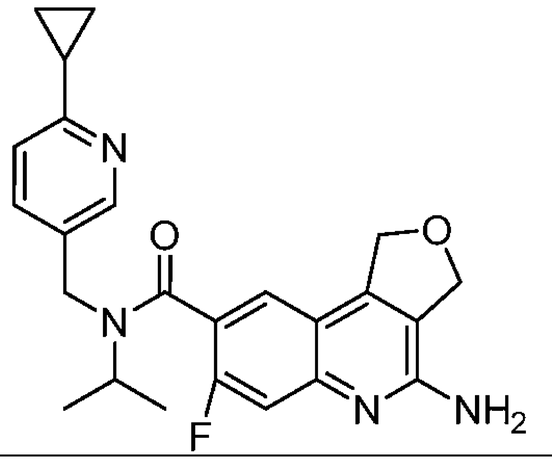
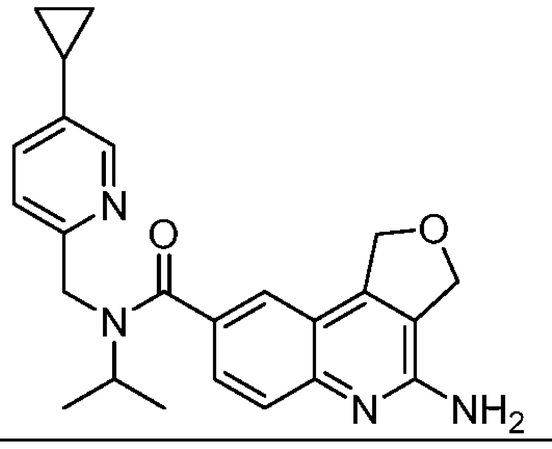
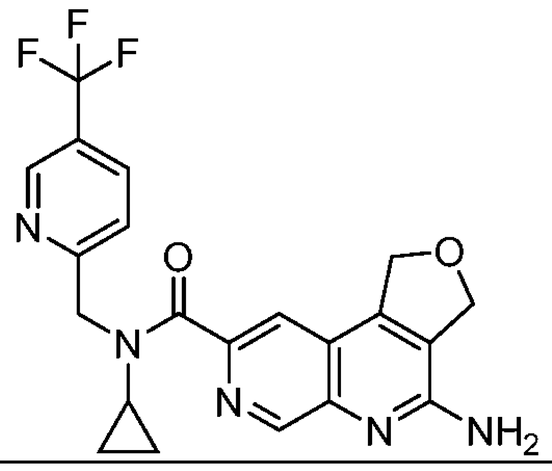
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
337		4-amino-N-((1-methylcyclopropyl)methyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	457.2
338		(3R)-4-amino-N-(2,2-dimethylpropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	473.2
339		(3R)-4-amino-3-methyl-N-((1-methylcyclopropyl)methyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	471.2
340		4-amino-N-(2,2-dimethylpropyl)-3,3-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	487.2

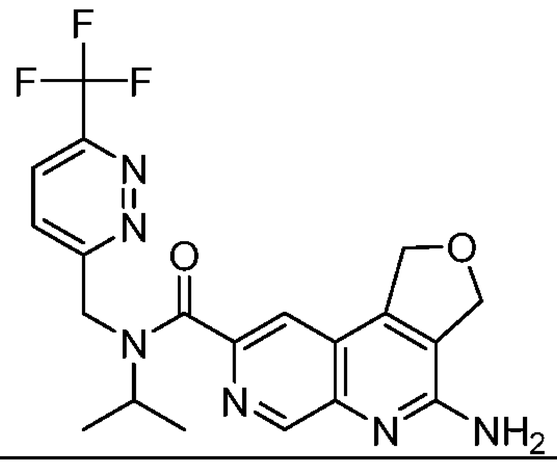
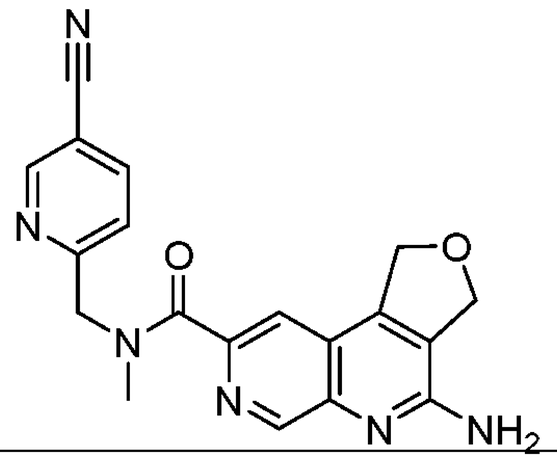
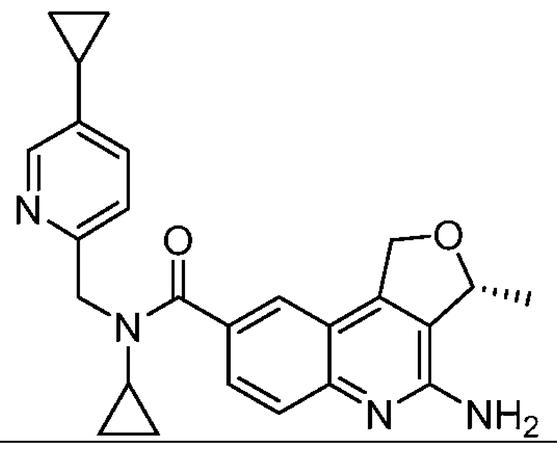
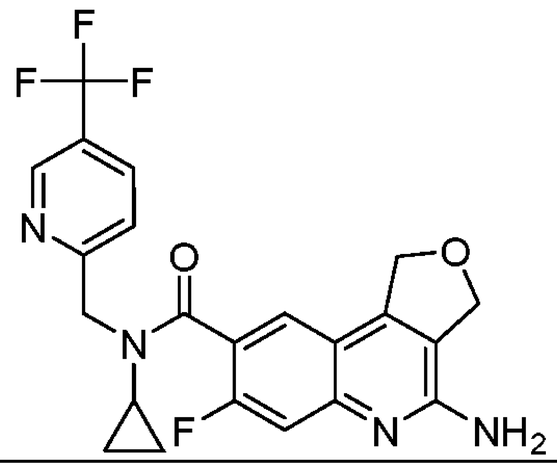
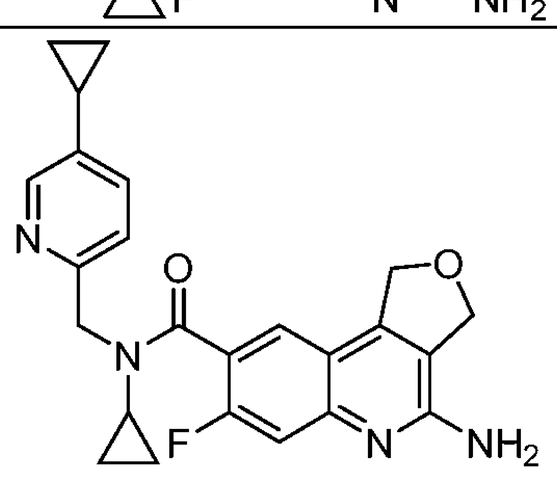
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
341		4-amino-3,3-dimethyl-N-((1-methylcyclopropyl)methyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	485.2
342		4-amino-N-(2,2-dimethylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	459.2
343		4-amino-N-cyclopropyl-N-((5-cyclopropyl-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	401.2
344		4-amino-N-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	404.1
345		4-amino-7-fluoro-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	449.2

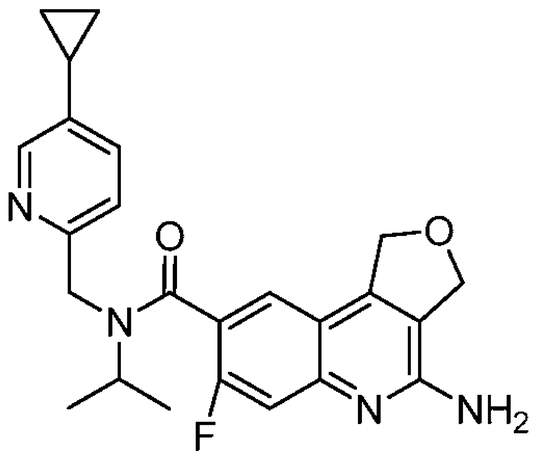
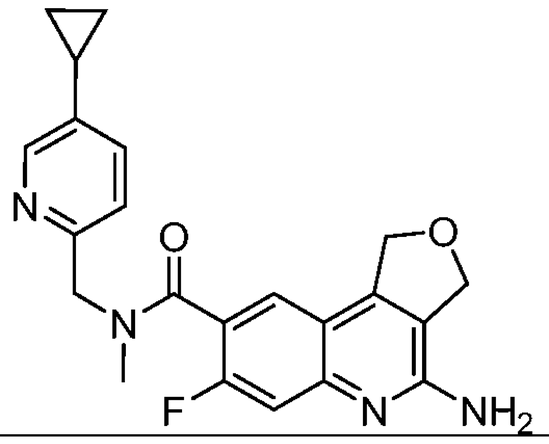
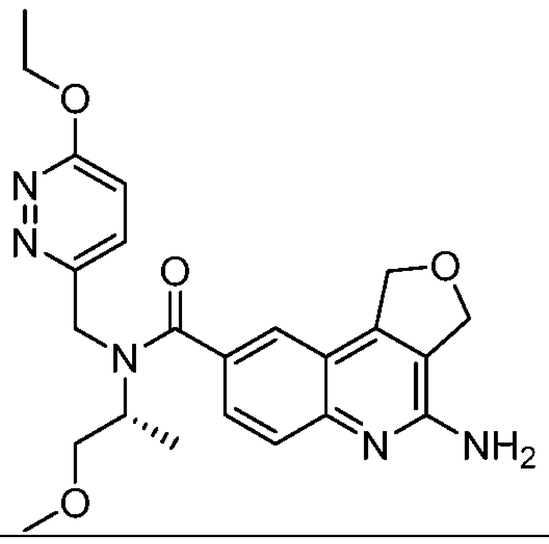
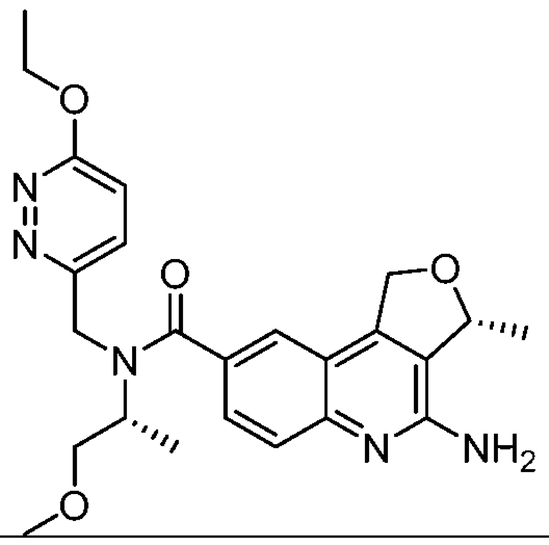
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
346		4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	389.2
347		4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-cyclopropyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	387.2
348		4-amino-N-cyclopropyl-N-((5-cyclopropyl-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	402.1
349		4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	376.1
350		(3R)-4-amino-N-((6-cyclopropyl-3-pyridinyl)methyl)-3-methyl-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	417.2

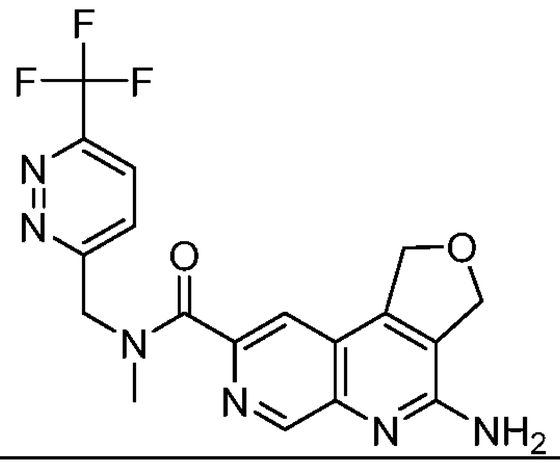
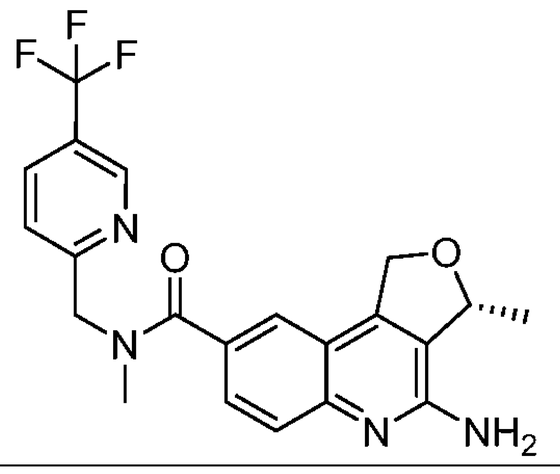
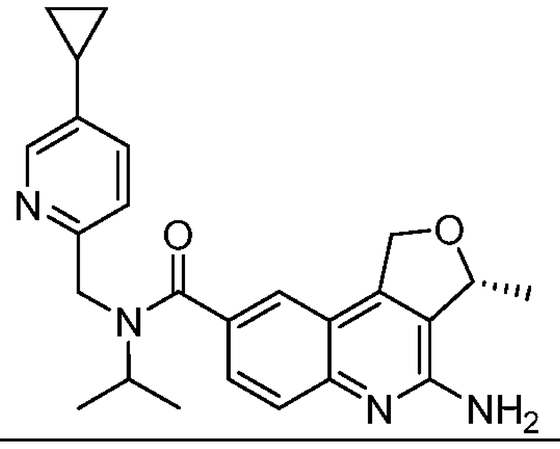
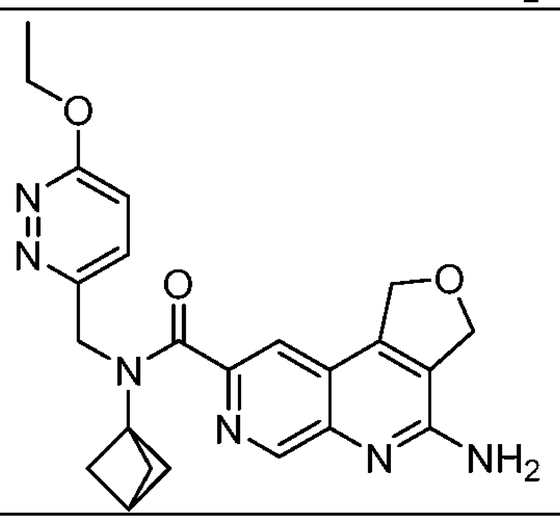
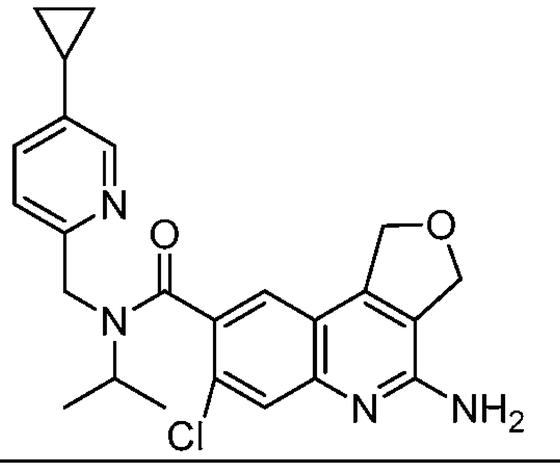
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
351		(3R)-4-amino-N-cyclopropyl-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	443.1
352		4-amino-N-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	404.1
353		(3R)-4-amino-N-cyclopropyl-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	444.2
354		(3R)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	402.2
355		(3R)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-cyclopropyl-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	400.2

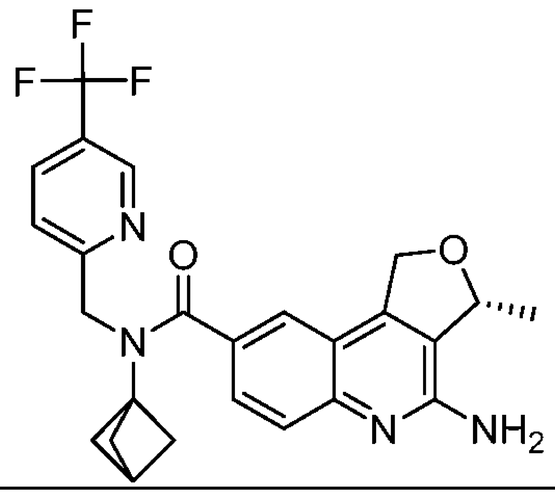
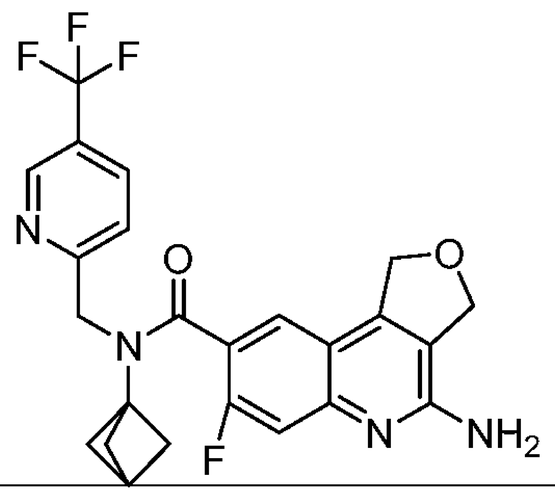
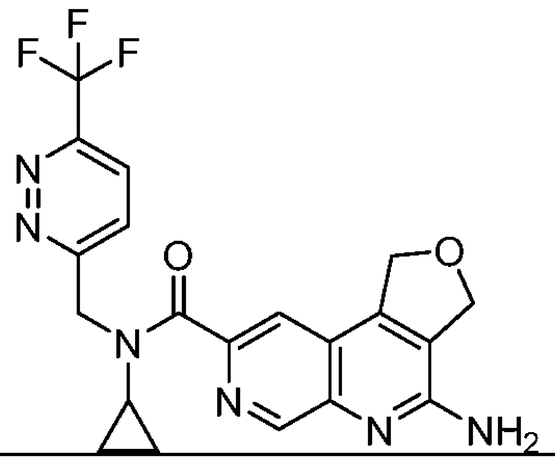
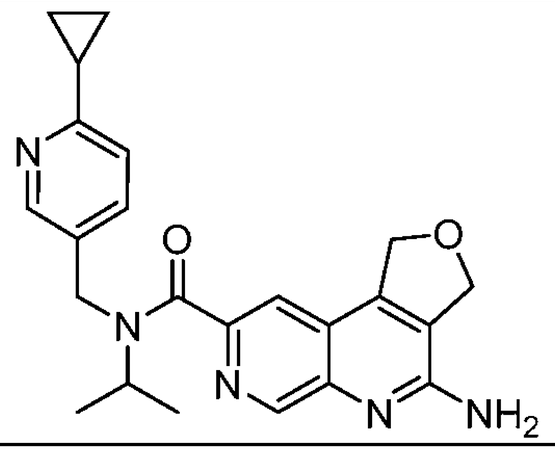
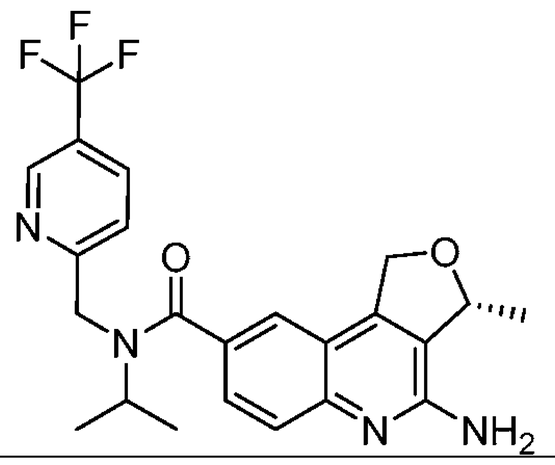
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
356		(3R)-4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-N,3-dimethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	389.2
357		4-amino-N-cyclopropyl-7-fluoro-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	448.1
358		4-amino-7-fluoro-N-(2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	450.1
359		4-amino-7-fluoro-N-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	422.1
360		(3R)-4-amino-N-ethyl-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	431.2

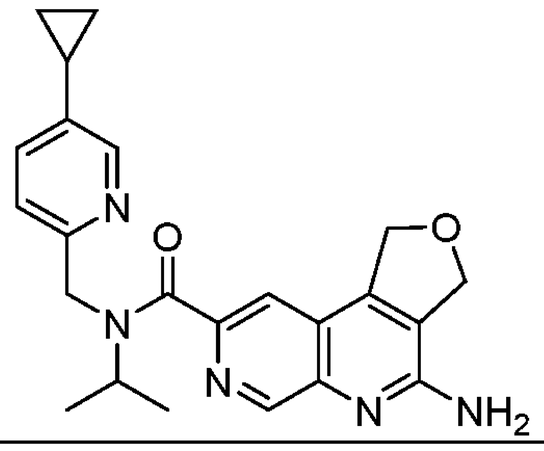
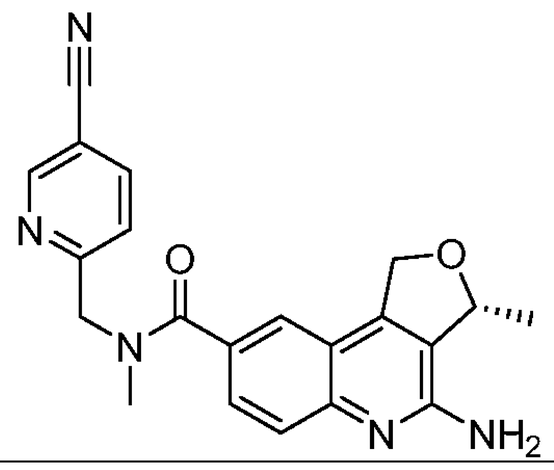
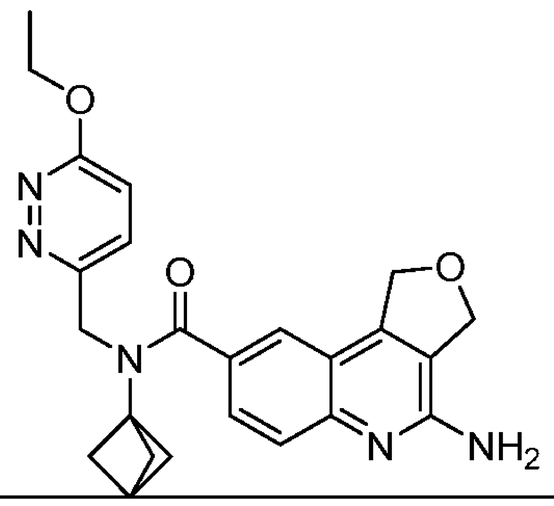
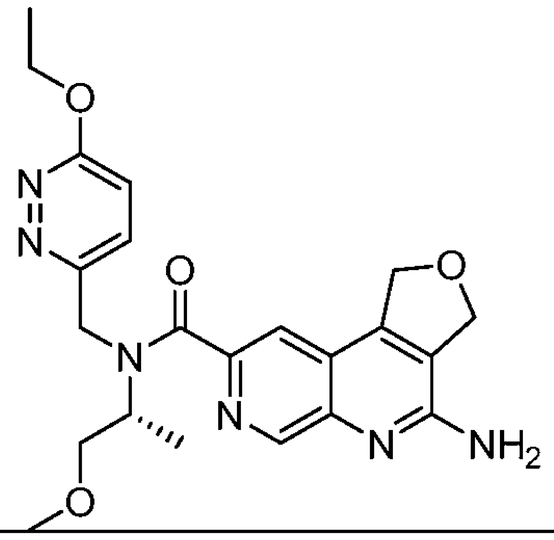
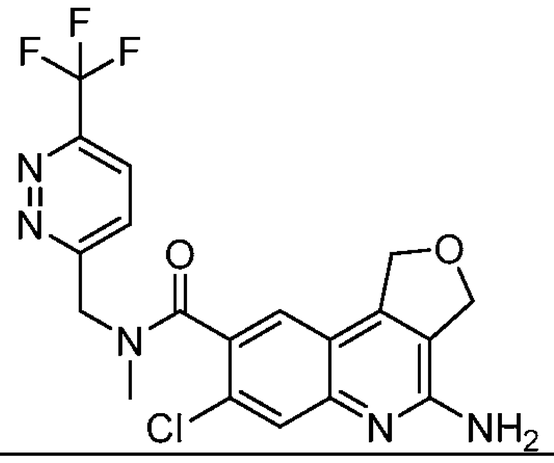
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
361		4-amino-N-ethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	418.2
362		4-amino-N-ethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	417.1
363		4-amino-N-((6-cyclopropyl-3-pyridinyl)methyl)-7-fluoro-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	421.2
364		4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	403.2
365		4-amino-N-cyclopropyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	430.1

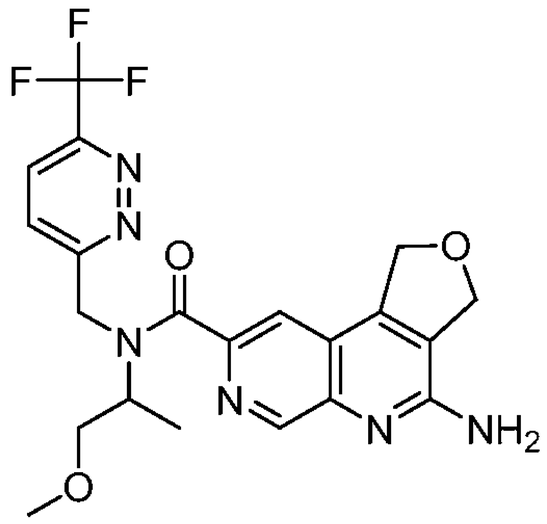
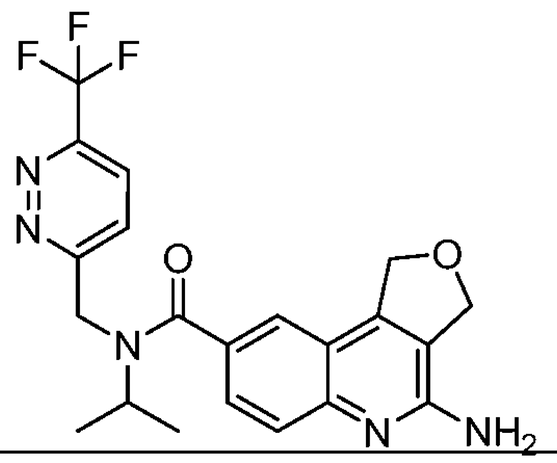
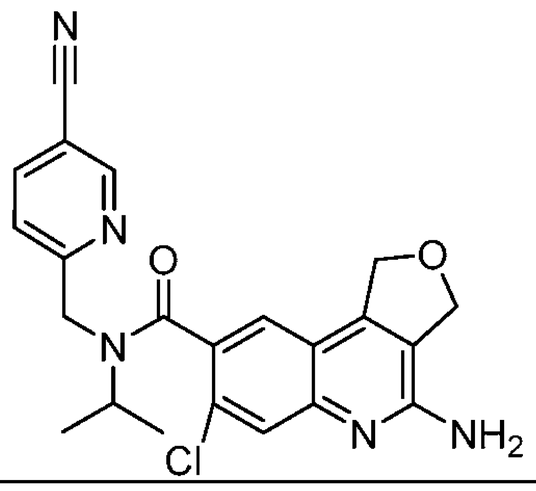
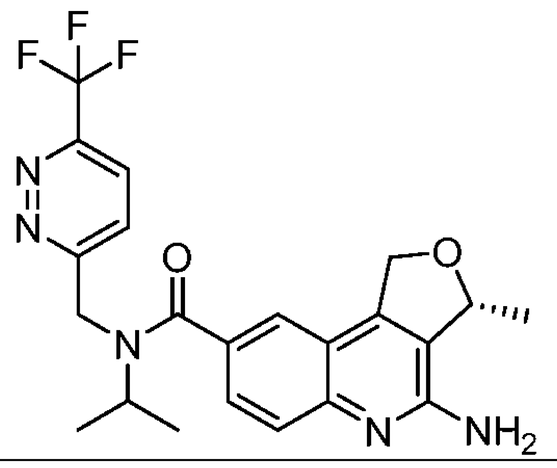
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
366		4-amino-N-(2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	433.2
367		4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	361.1
368		(3R)-4-amino-N-cyclopropyl-N-((5-cyclopropyl-2-pyridinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	415.2
369		4-amino-N-cyclopropyl-7-fluoro-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	447.1
370		4-amino-N-cyclopropyl-N-((5-cyclopropyl-2-pyridinyl)methyl)-7-fluoro-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	419.2

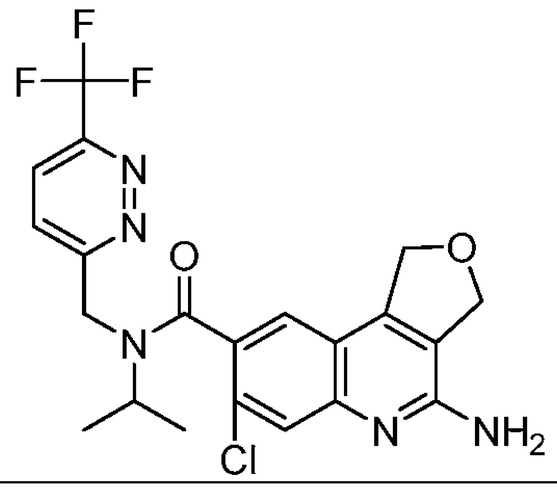
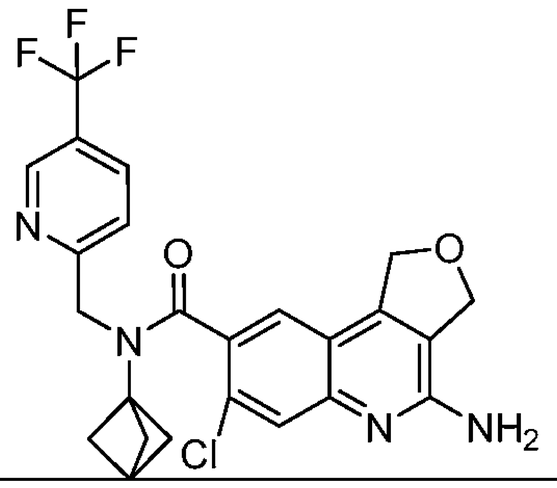
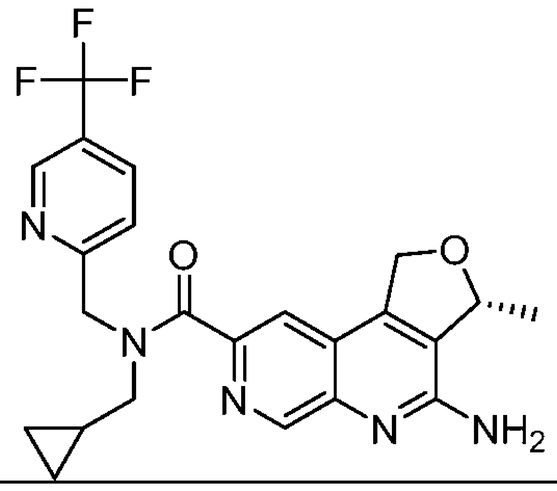
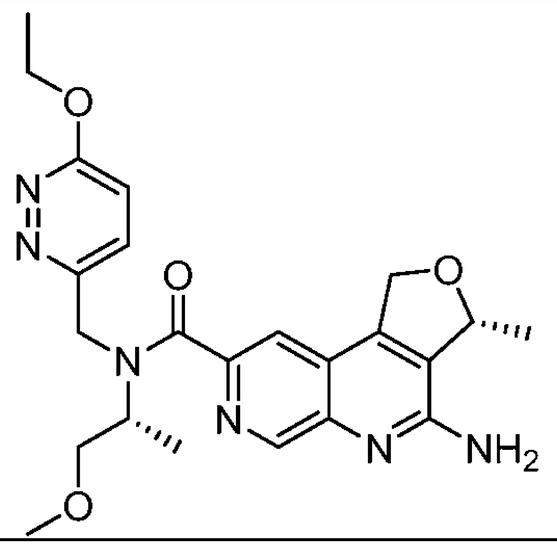
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
371		4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-7-fluoro-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	421.2
372		4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-7-fluoro-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	393.2
373		4-amino-N-((6-ethoxy-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	438.2
374		(3R)-4-amino-N-((6-ethoxy-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	452.3

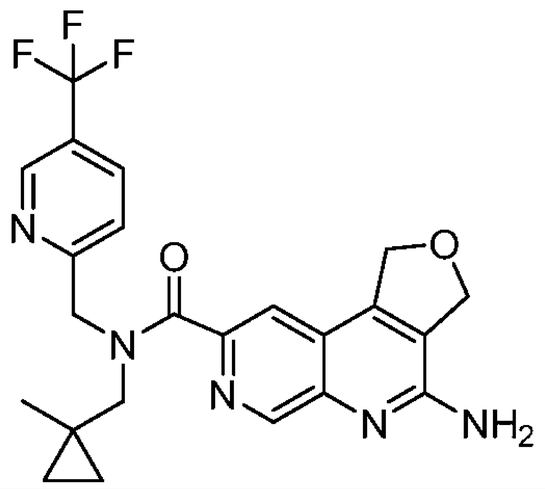
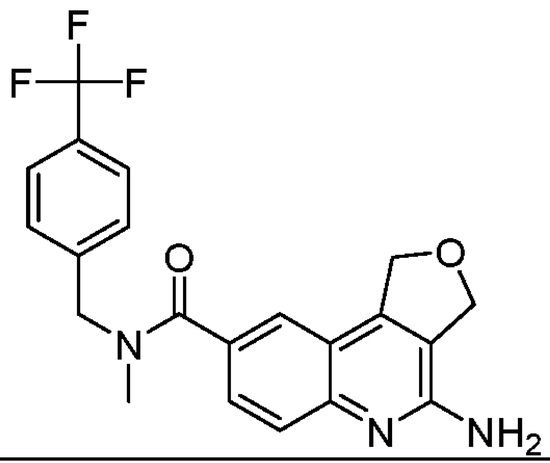
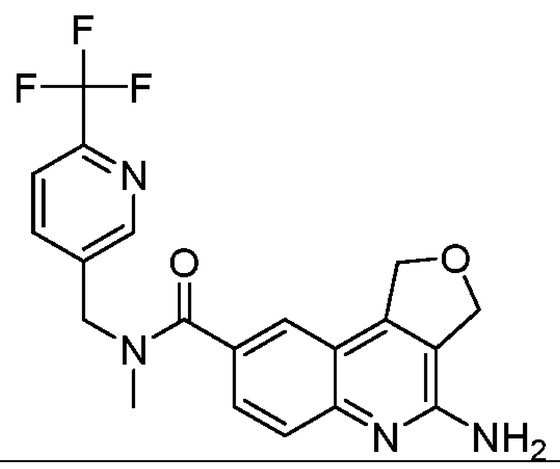
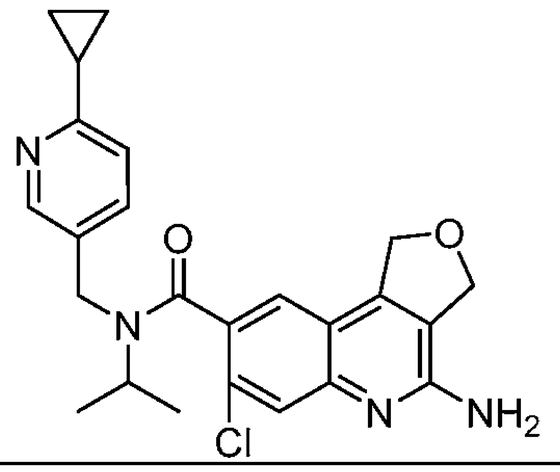
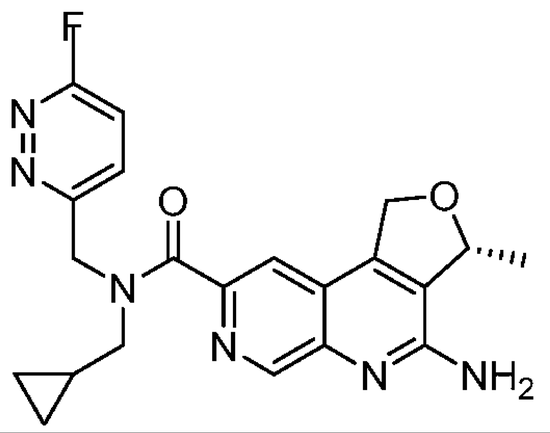
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
375		4-amino-N-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	405.1
376		(3R)-4-amino-N,3-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	417.1
377		(3R)-4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-3-methyl-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	417.2
378		4-amino-N-(bicyclo[1.1.1]pentan-1-yl)-N-((6-ethoxy-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	433.2
379		4-amino-7-chloro-N-((5-cyclopropyl-2-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	437.2

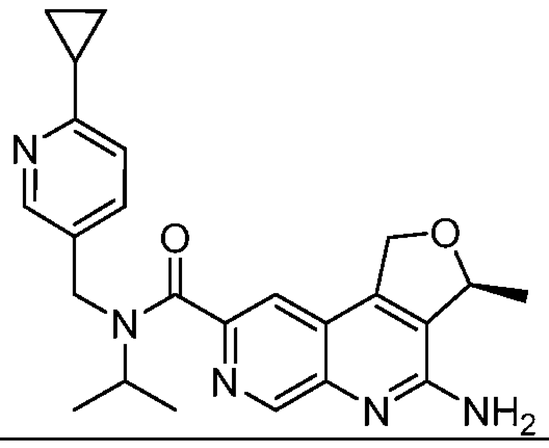
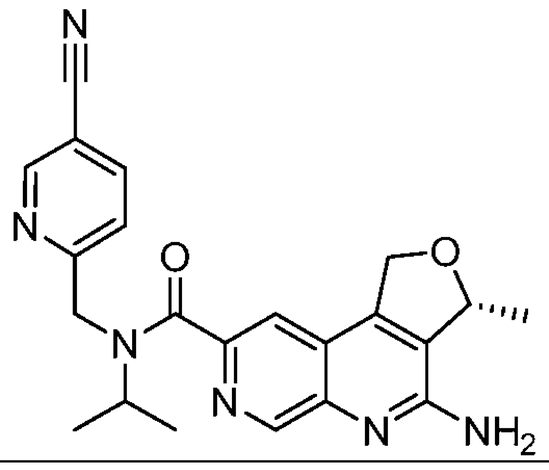
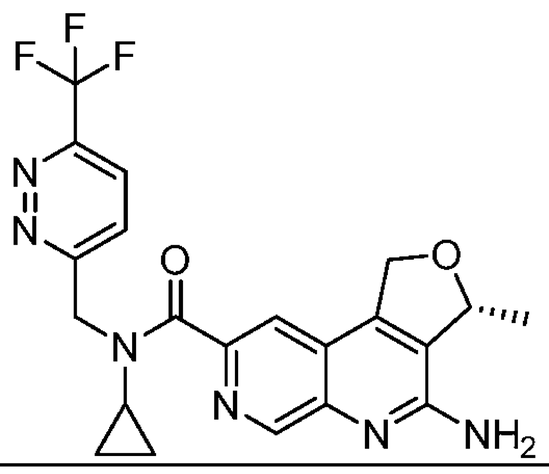
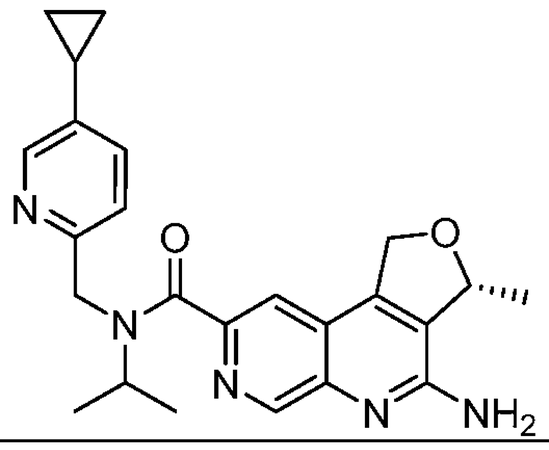
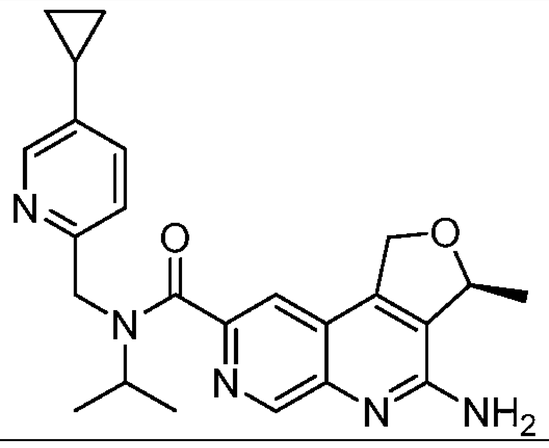
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
380		(3R)-4-amino-N-(bicyclo[1.1.1]pentan-1-yl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	469.2
381		4-amino-N-(bicyclo[1.1.1]pentan-1-yl)-7-fluoro-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	473.2
382		4-amino-N-cyclopropyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	431.1
383		4-amino-N-((6-cyclopropyl-3-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	404.2
384		(3R)-4-amino-3-methyl-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	445.2

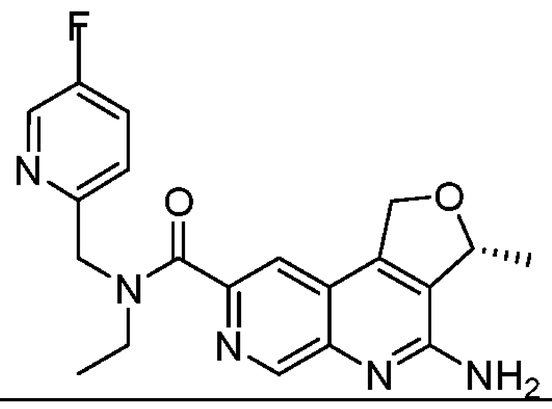
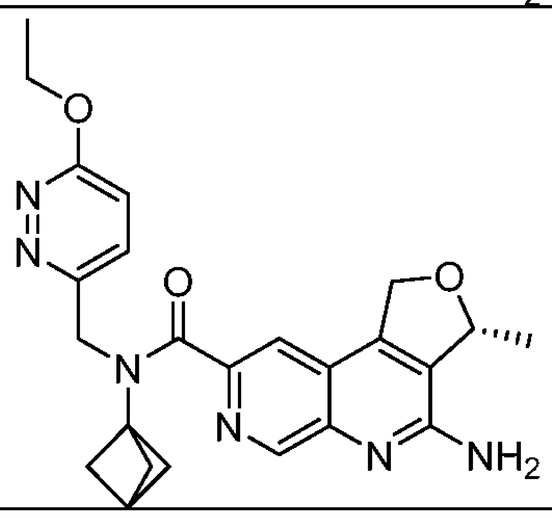
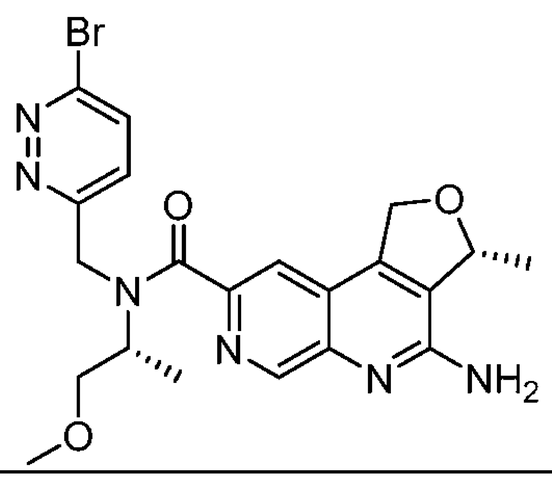
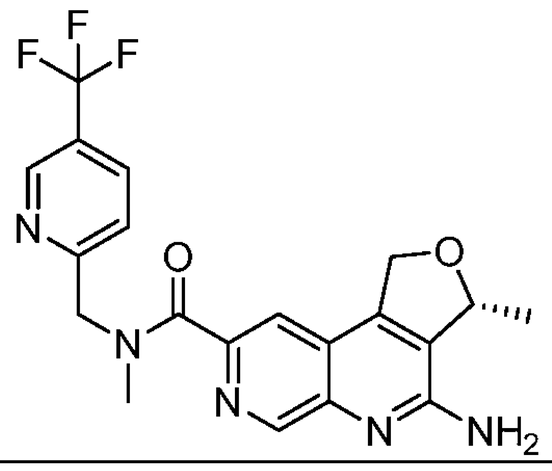
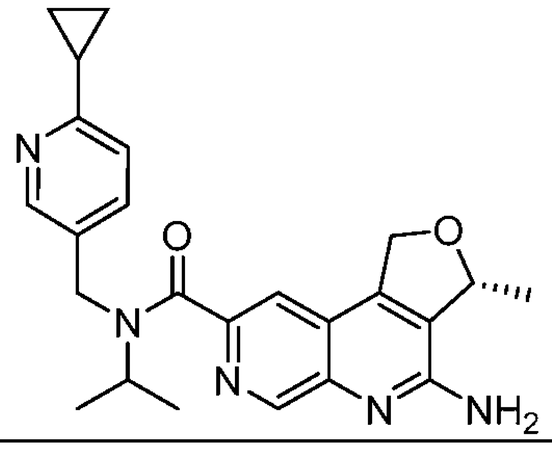
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
385		4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	404.2
386		(3R)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-N,3-dimethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	374.2
387		4-amino-N-(bicyclo[1.1.1]pentan-1-yl)-N-((6-ethoxy-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	432.2
388		4-amino-N-((6-ethoxy-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	439.2
389		4-amino-7-chloro-N-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	438.1

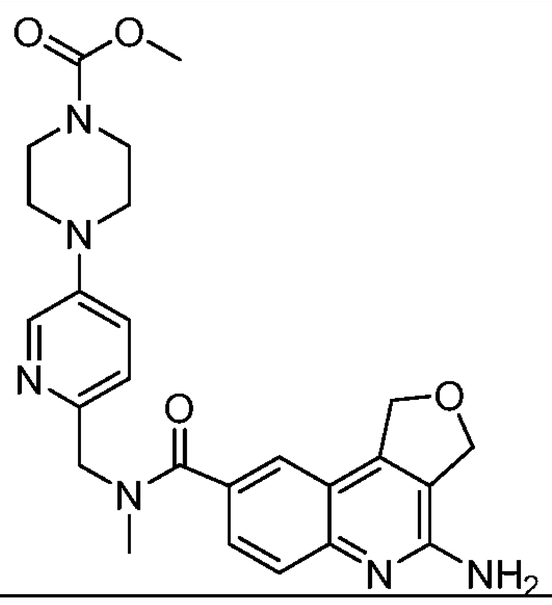
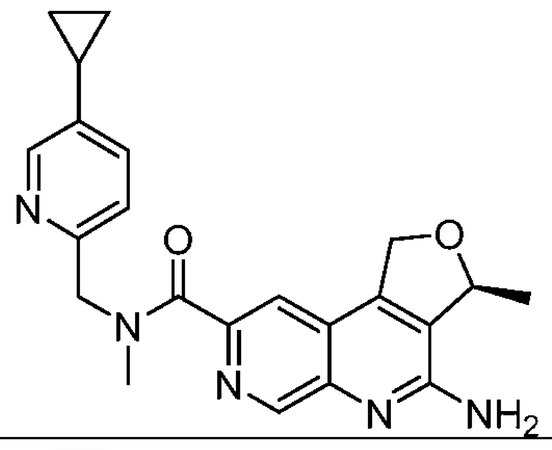
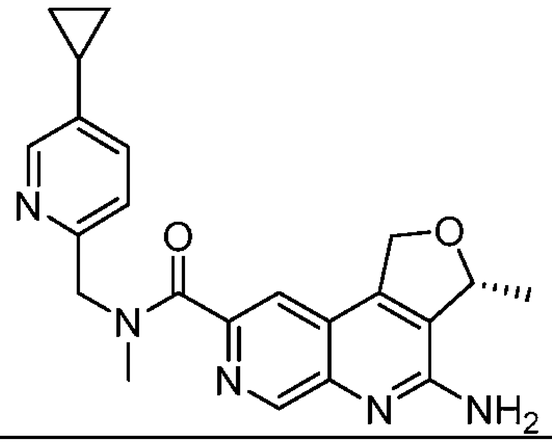
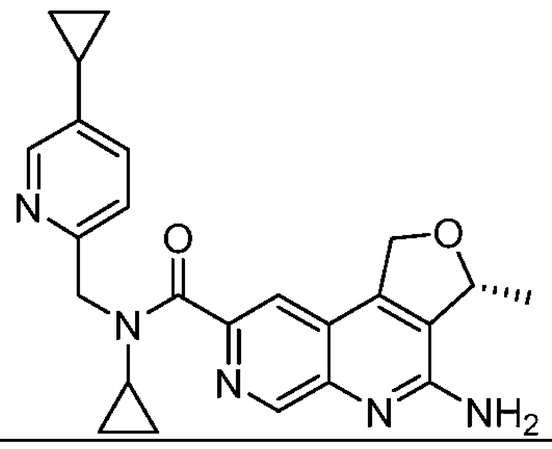
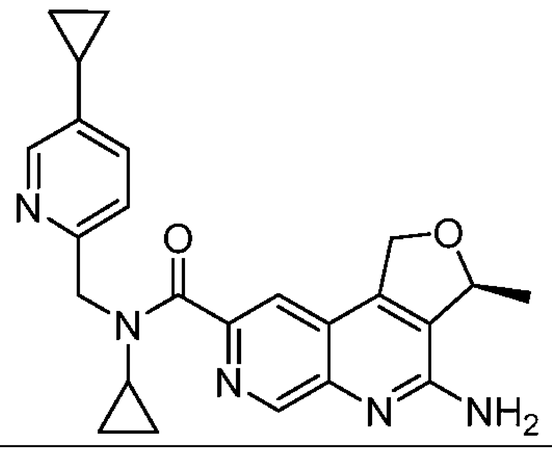
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
390		4-amino-N-((2R)-1-methoxy-2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide and 4-amino-N-((2S)-1-methoxy-2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	463.2
391		4-amino-N-(2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	432.1
392		4-amino-7-chloro-N-((5-cyano-2-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	422.1
393		(3R)-4-amino-3-methyl-N-(2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	446.2

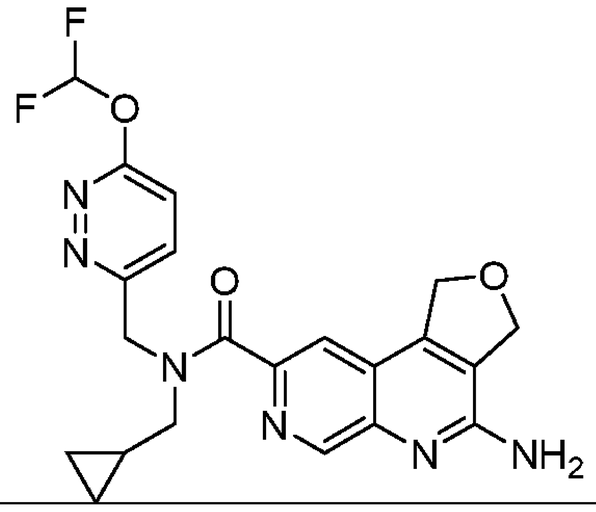
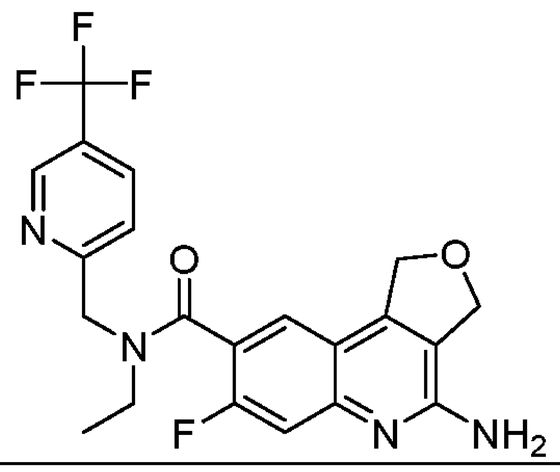
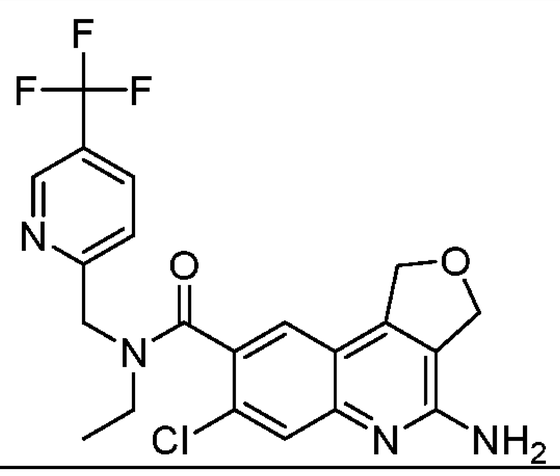
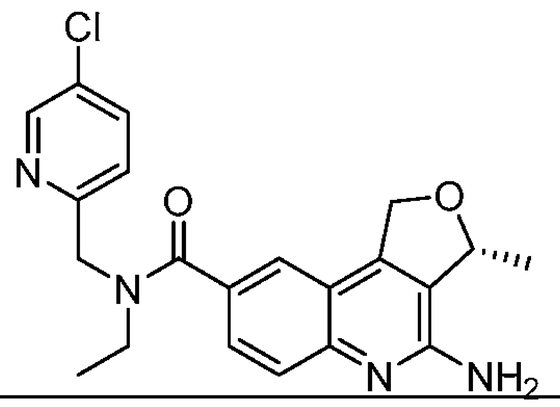
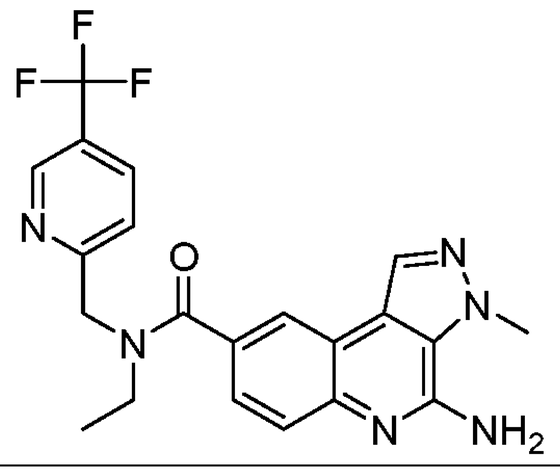
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
394		4-amino-7-chloro-N-(2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	466.1
395		4-amino-N-(bicyclo[1.1.1]pentan-1-yl)-7-chloro-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	489.1
396		(3R)-4-amino-N-(cyclopropylmethyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	458.2
397		(3R)-4-amino-N-((6-ethoxy-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-3-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	453.2

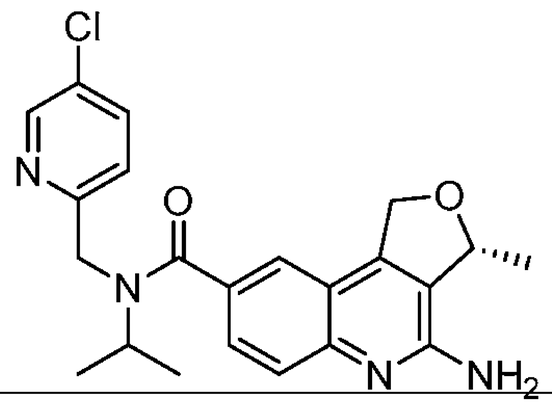
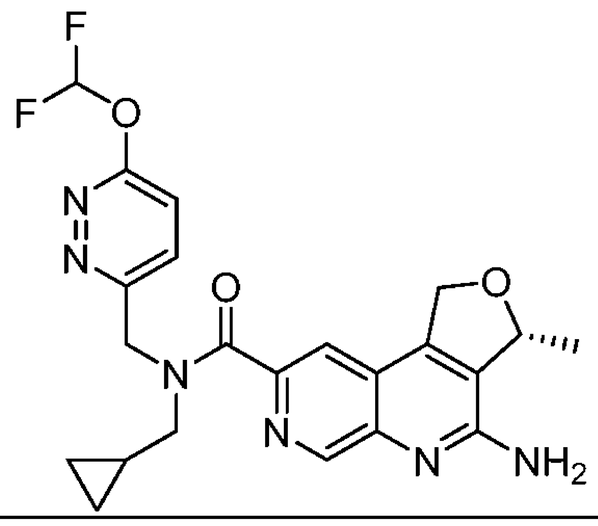
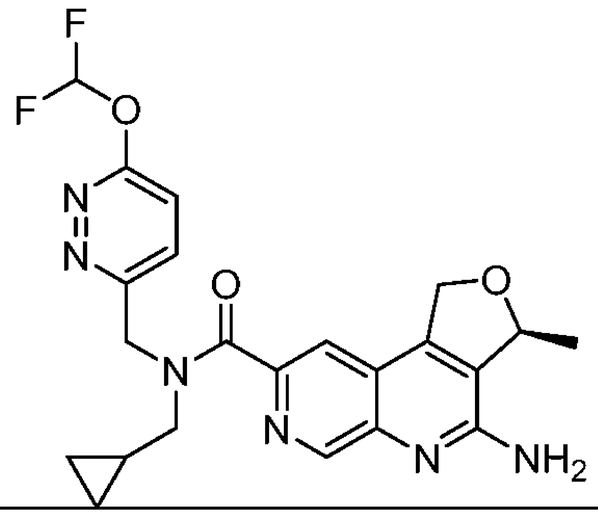
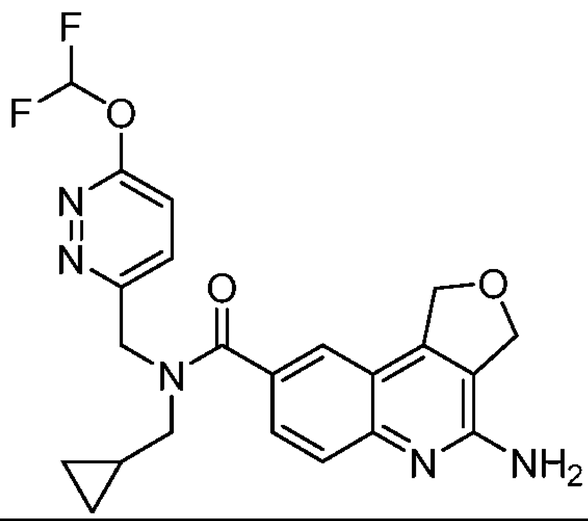
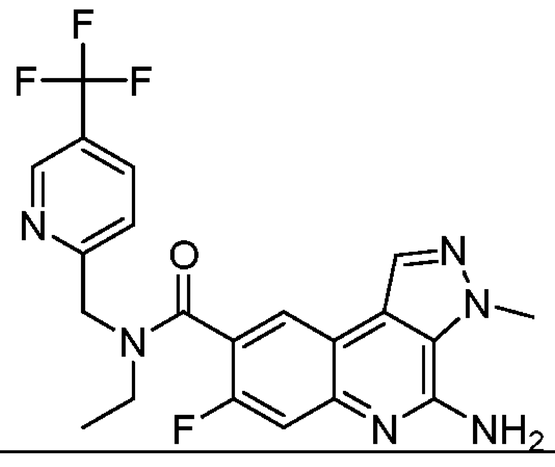
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
398		4-amino-N-((1-methylcyclopropyl)methyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	458.1
399		4-amino-N-methyl-N-(4-(trifluoromethyl)benzyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	402
400		4-amino-N-methyl-N-((6-(trifluoromethyl)-3-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	403
401		4-amino-7-chloro-N-((6-cyclopropyl-3-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	437.2
402		(3R)-4-amino-N-(cyclopropylmethyl)-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	495.2

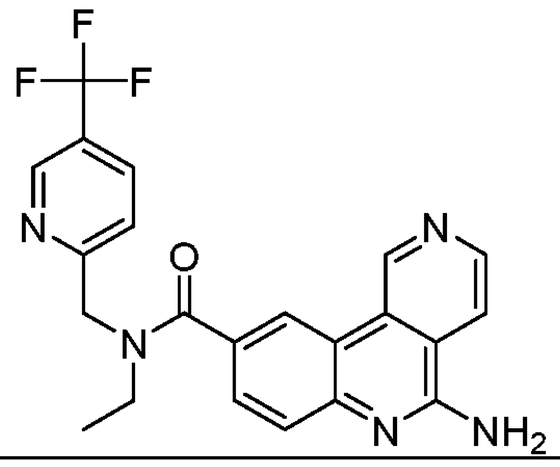
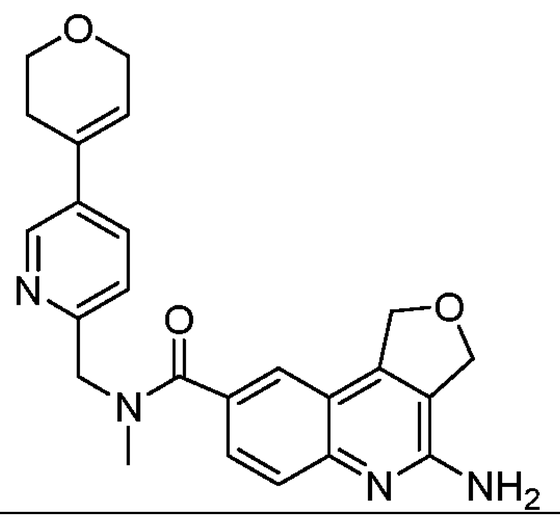
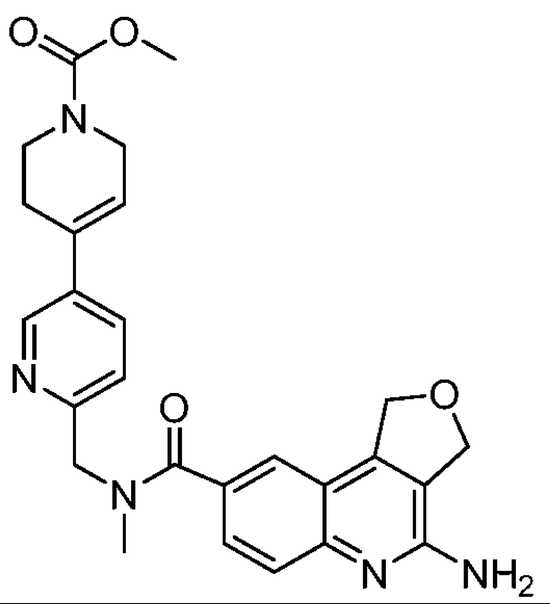
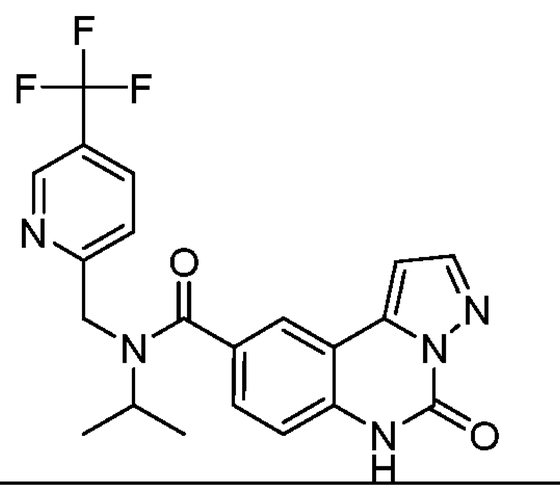
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
403		(3S)-4-amino-N-((6-cyclopropyl-3-pyridinyl)methyl)-3-methyl-N-(2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	418.1
404		(3R)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-N-(2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	403.2
405		(3R)-4-amino-N-cyclopropyl-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	445.1
406		(3R)-4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-3-methyl-N-(2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	418.1
407		(3S)-4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-3-methyl-N-(2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	418.1

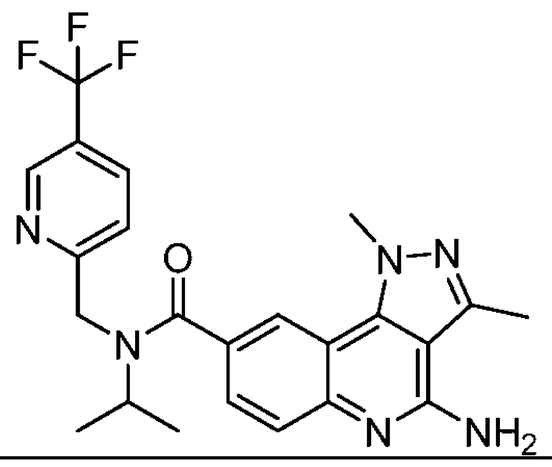
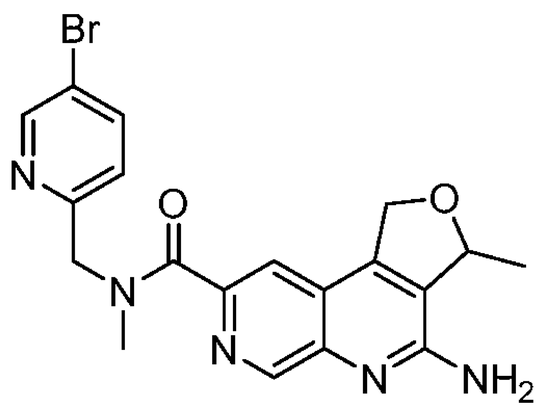
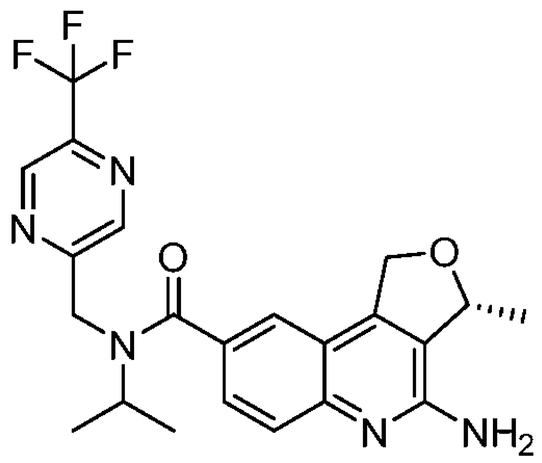
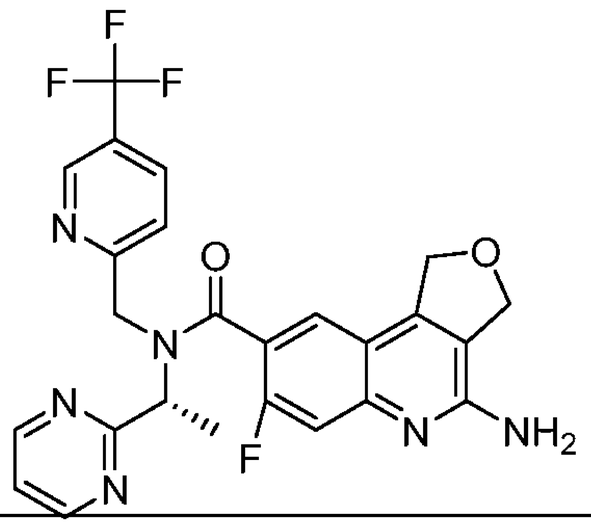
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
408		(3R)-4-amino-N-ethyl-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	432.2
409		(3R)-4-amino-N-(bicyclo[1.1.1]pentan-1-yl)-N-((6-ethoxy-3-pyridazinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	447.2
410		(3R)-4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-3-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	487.1
411		(3R)-4-amino-N,3-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	418.1
412		(3R)-4-amino-N-((6-cyclopropyl-3-pyridinyl)methyl)-3-methyl-N-(2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	

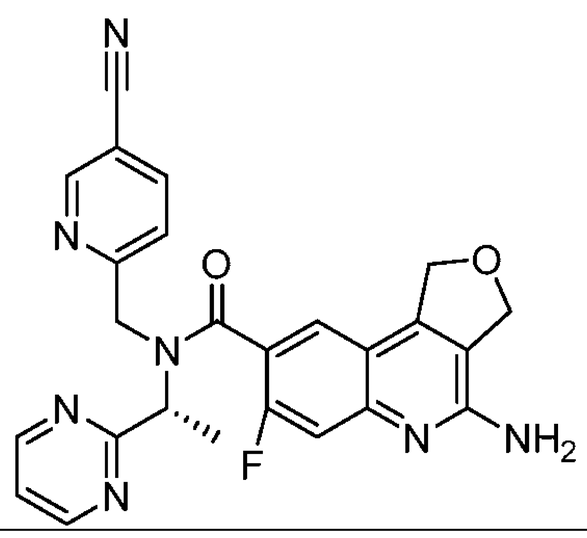
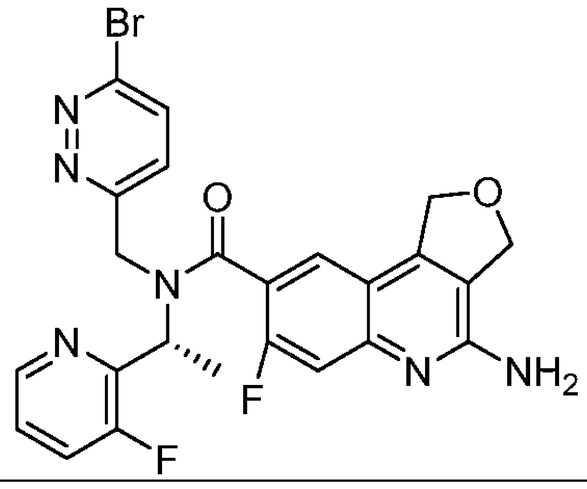
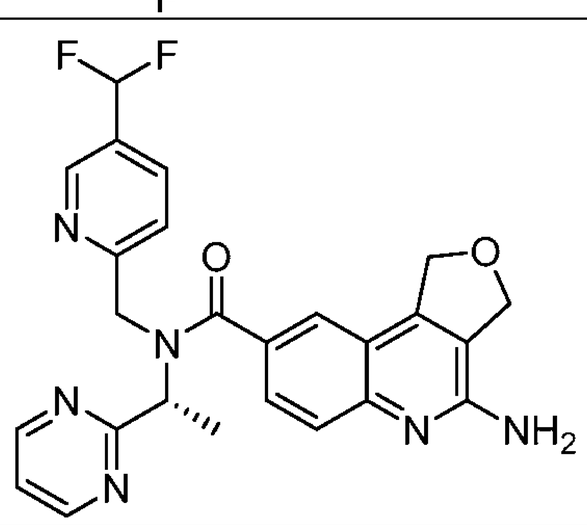
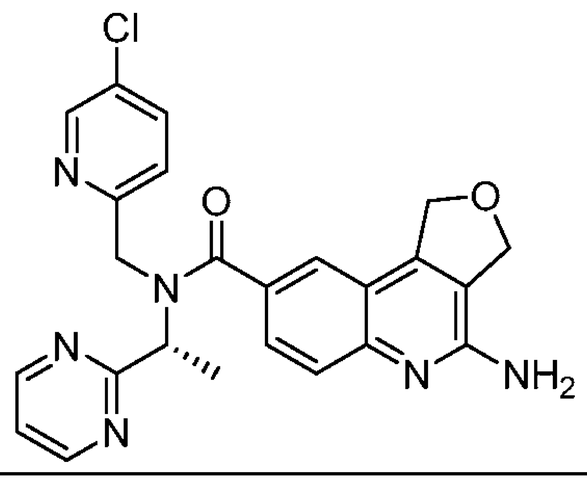
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
413		methyl 4-(6-((((4-amino-1,3-dihydrofuro[3,4-c]quinolin-8-yl)carbonyl)(methyl)amino)methyl)-3-pyridinyl)-1-piperazinecarboxylate	HATU	477.1
414		(3S)-4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-N,3-dimethyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	390.2
415		(3R)-4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-N,3-dimethyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	390.2
416		(3R)-4-amino-N-cyclopropyl-N-((5-cyclopropyl-2-pyridinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	416.1
417		(3S)-4-amino-N-cyclopropyl-N-((5-cyclopropyl-2-pyridinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	

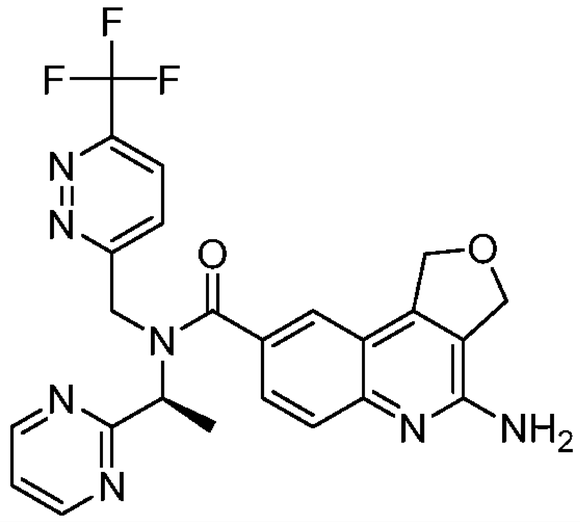
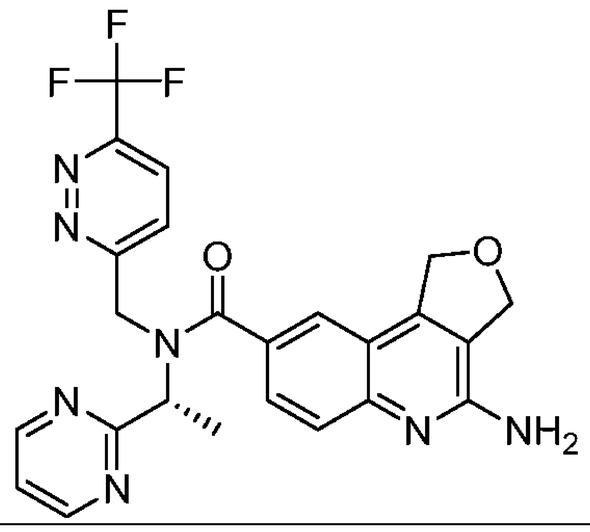
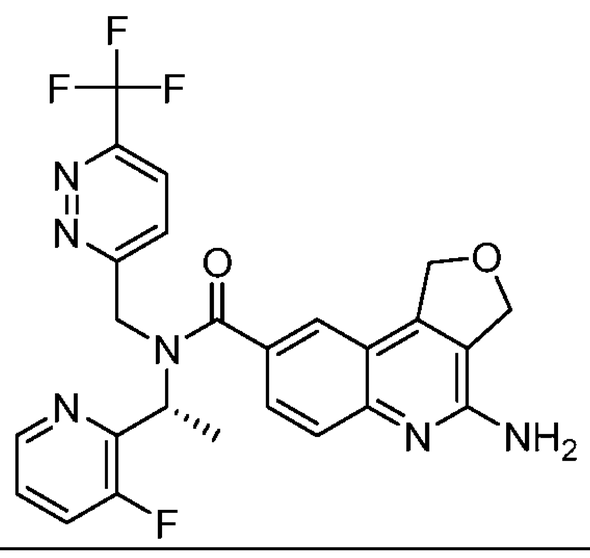
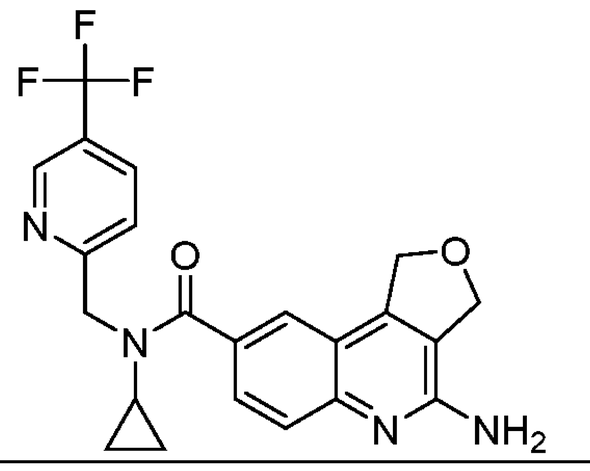
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
418		4-amino-N-(cyclopropylmethyl)-N-((6-(difluoromethoxy)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	443
419		4-amino-N-ethyl-7-fluoro-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	435
420		4-amino-7-chloro-N-ethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	451
421		(3R)-4-amino-N-((5-chloro-2-pyridinyl)methyl)-N-ethyl-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	397
422		4-amino-N-ethyl-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide	HATU	429

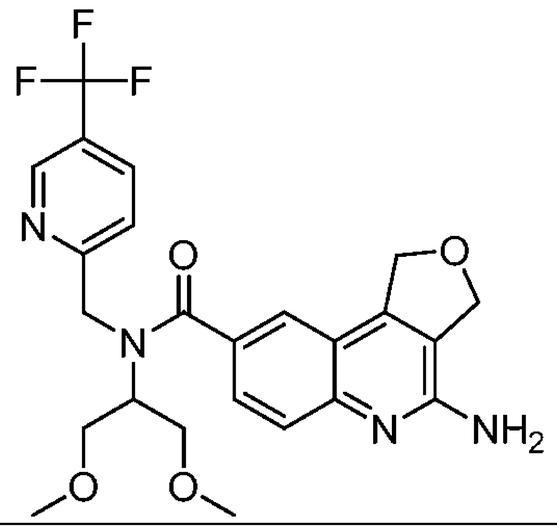
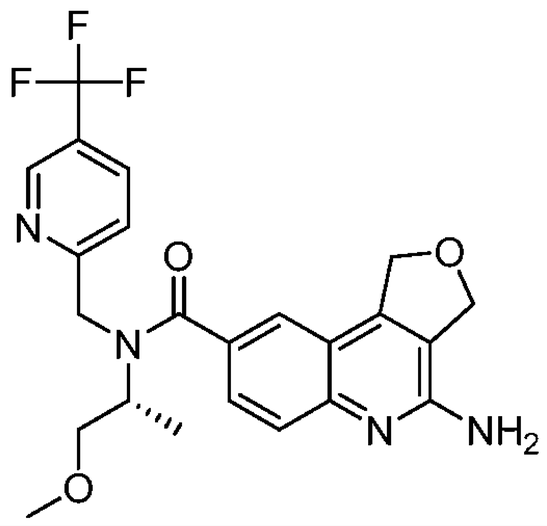
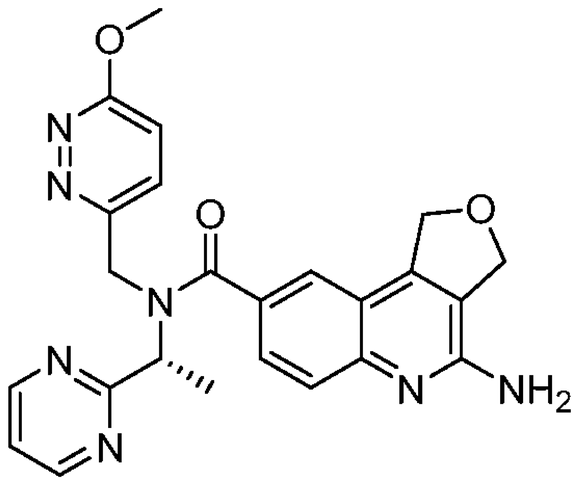
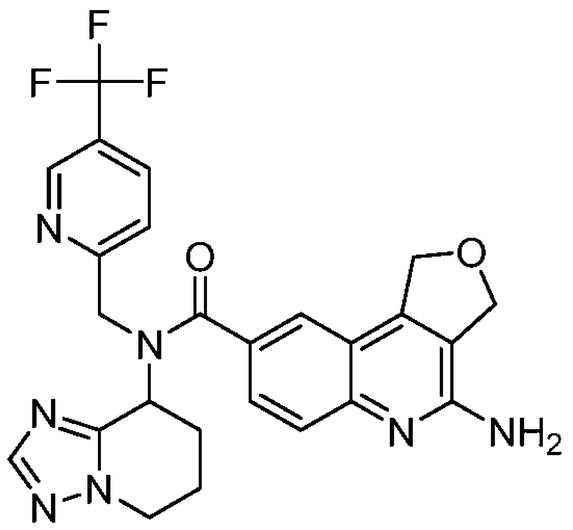
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
423		(3R)-4-amino-N-((5-chloro-2-pyridinyl)methyl)-3-methyl-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	411
424		(3R)-4-amino-N-(cyclopropylmethyl)-N-((6-(difluoromethoxy)-3-pyridazinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	457
425		(3S)-4-amino-N-(cyclopropylmethyl)-N-((6-(difluoromethoxy)-3-pyridazinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	457
426		4-amino-N-(cyclopropylmethyl)-N-((6-(difluoromethoxy)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	442
427		4-amino-N-ethyl-7-fluoro-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide	HATU	447

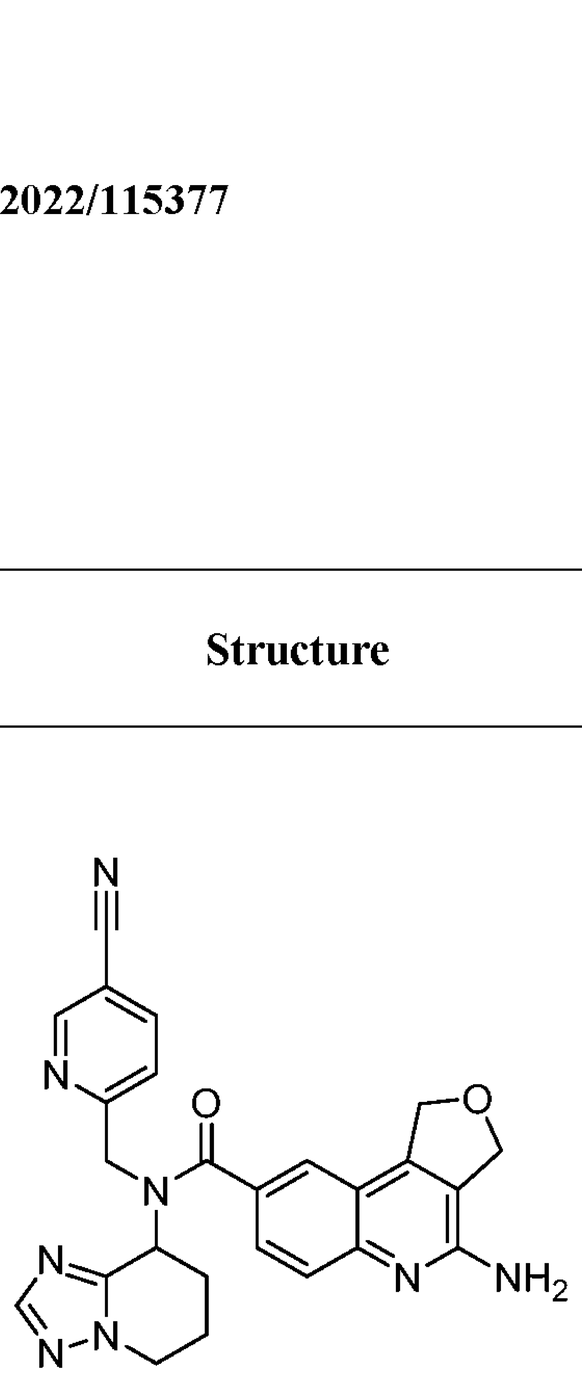
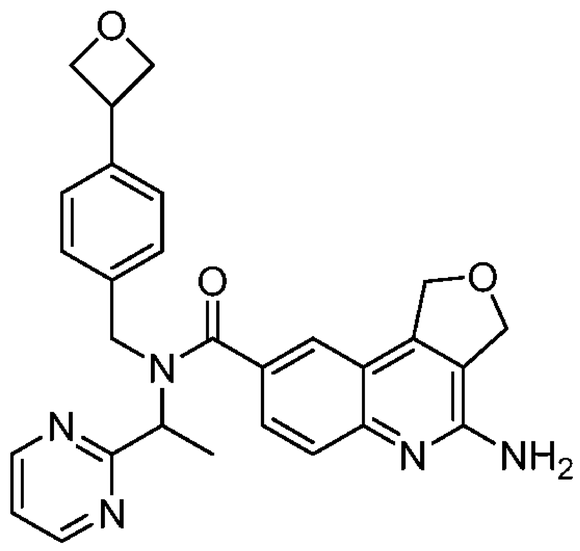
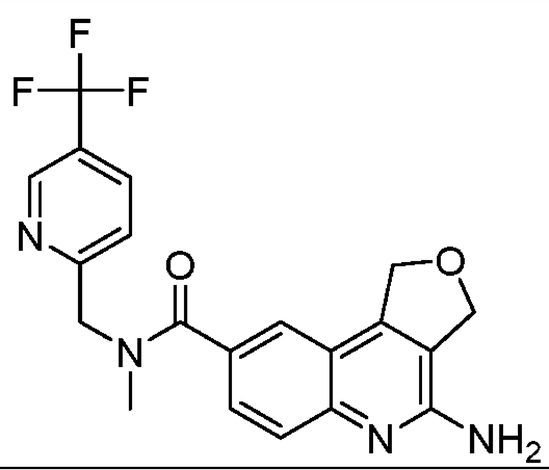
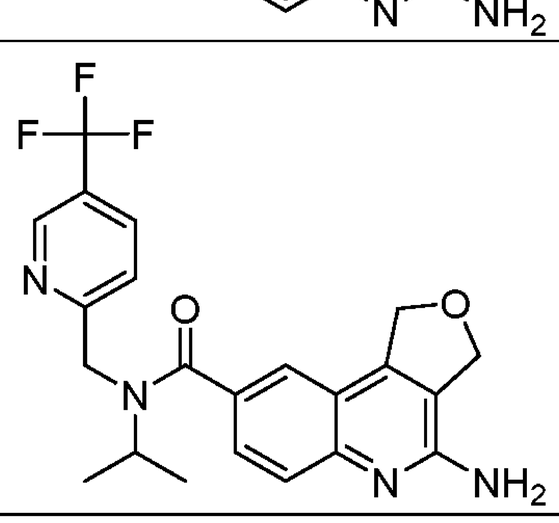
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
428		5-amino-N-ethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)benzo[c][2,6]naphthyridine-9-carboxamide	HATU	426
429		4-amino-N-((5-(3,6-dihydro-2H-pyran-4-yl)-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	417.1
430		methyl 6-((((4-amino-1,3-dihydrofuro[3,4-c]quinolin-8-yl)carbonyl)(methyl)amino)methyl)-3',6'-dihydro[3,4'-bipyridine]-1'(2'H)-carboxylate	HATU	474.1
431		5-oxo-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-5,6-dihydropyrazolo[1,5-c]quinazoline-9-carboxamide	HATU	430.2

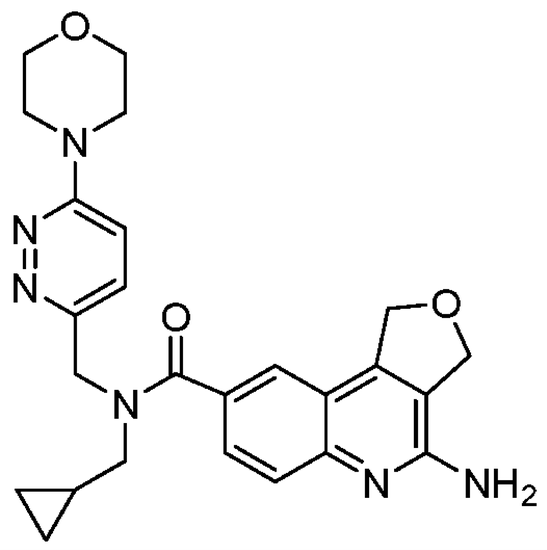
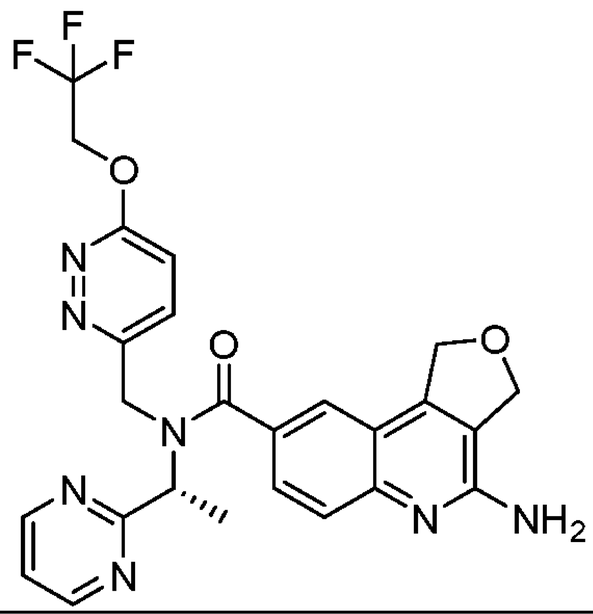
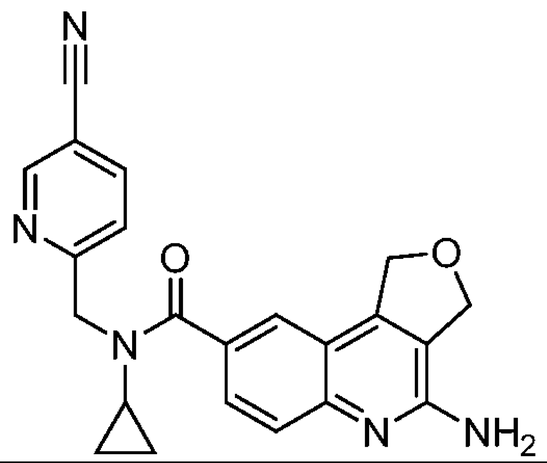
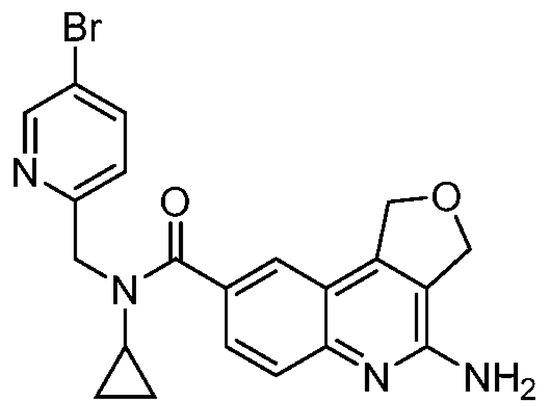
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
432		4-amino-1,3-dimethyl-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	HATU	457.2
433		(3R)-4-amino-N-((5-bromo-2-pyridinyl)methyl)-N,3-dimethyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide and (3S)-4-amino-N-((5-bromo-2-pyridinyl)methyl)-N,3-dimethyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	HATU	428 and 430
434		(3R)-4-amino-3-methyl-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyrazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HBTU	446.2
435		4-amino-7-fluoro-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	513.2

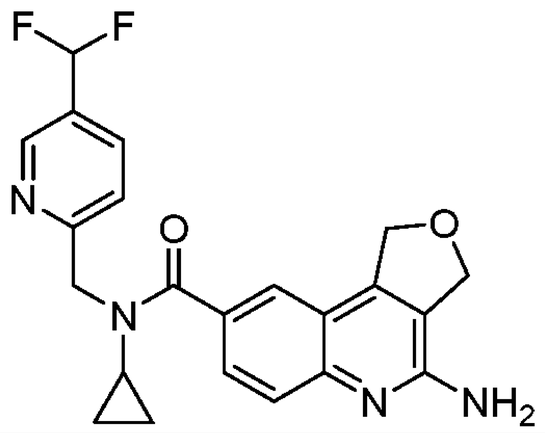
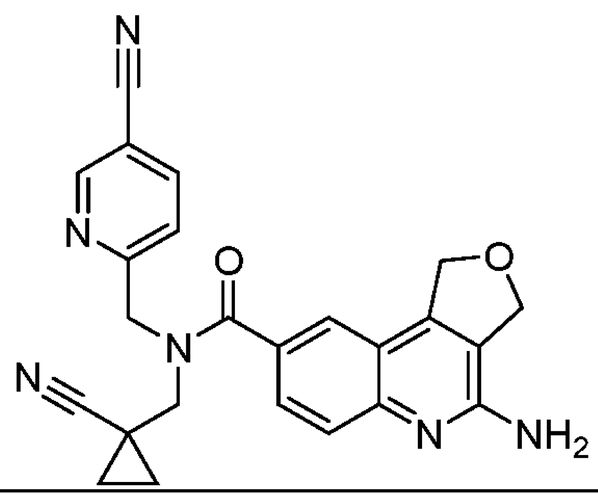
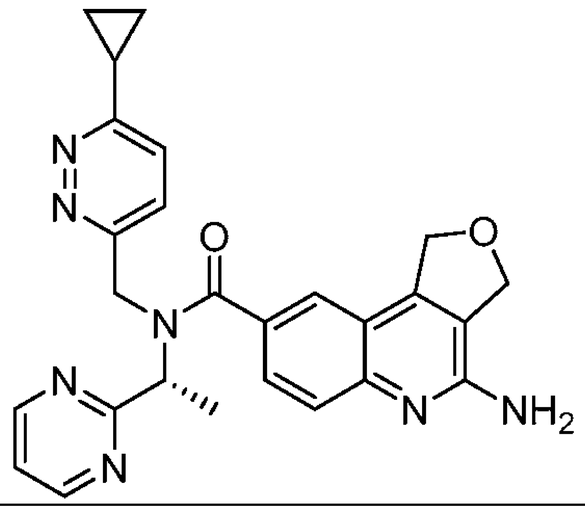
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
436		4-amino-N-((5-cyano-2-pyridinyl)methyl)-7-fluoro-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	470.2
437		4-amino-N-((6-bromo-3-pyridazinyl)methyl)-7-fluoro-N-((1R)-1-(3-fluoro-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	541 and 543
438		4-amino-N-((5-(difluoromethyl)-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	477.2
439		4-amino-N-((5-chloro-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	461.2

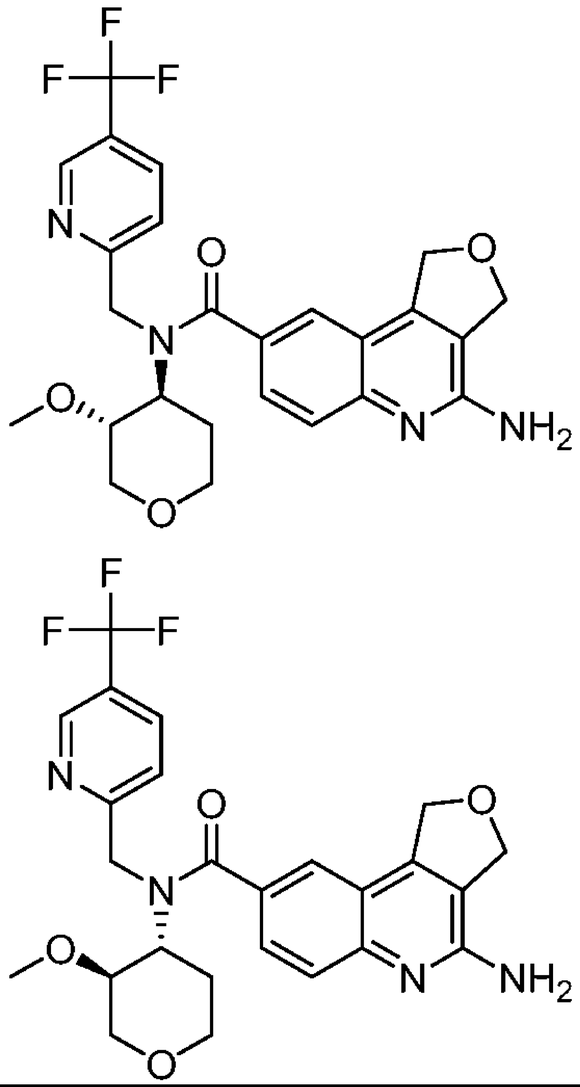
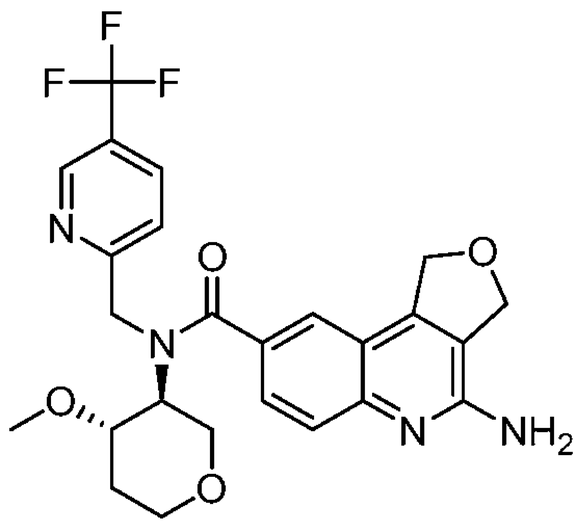
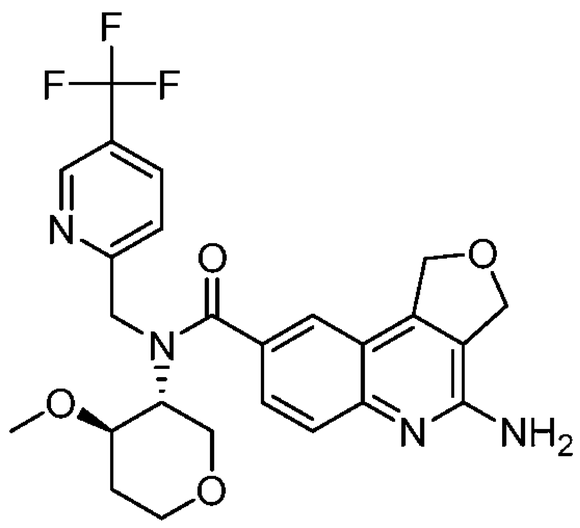
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
440		4-amino-N-((1S)-1-(2-pyrimidinyl)ethyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	496.2
441		4-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	496.2
442		4-amino-N-((1R)-1-(3-fluoro-2-pyridinyl)ethyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	513.2
443		4-amino-N-cyclopropyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	429.2

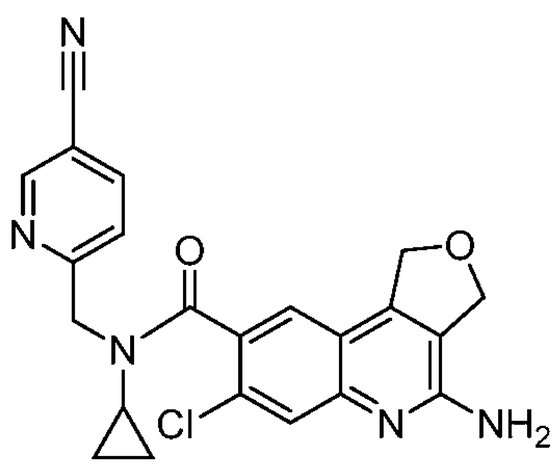
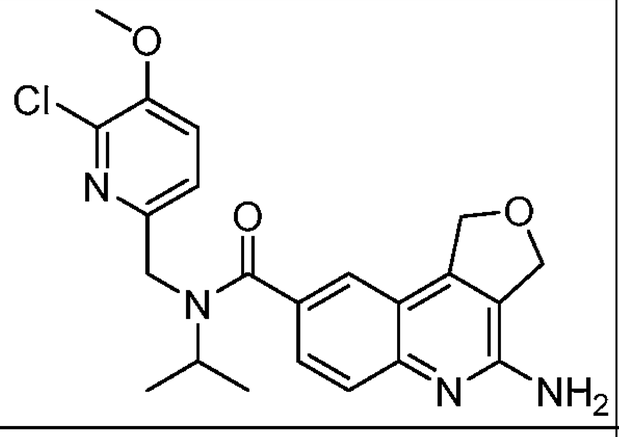
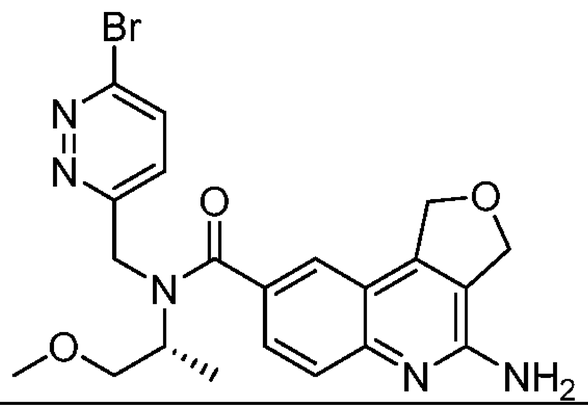
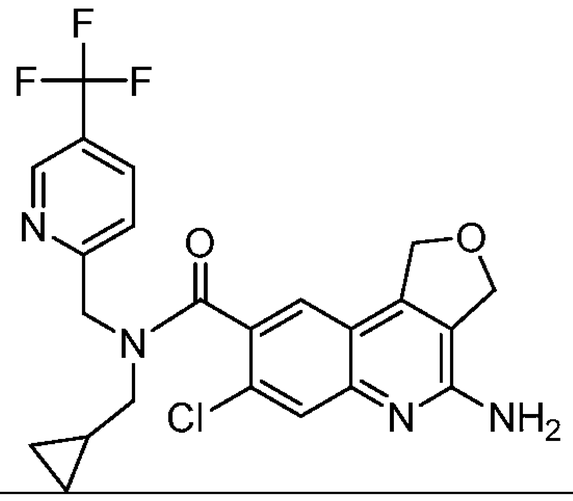
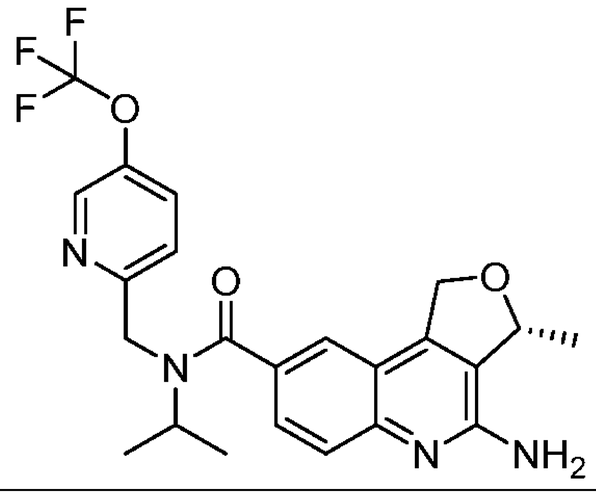
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
444		4-amino-N-(1,3-dimethoxy-2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	491.2
445		4-amino-N-((2R)-1-methoxy-2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	461.2
446		4-amino-N-((6-methoxy-3-pyridazinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	458.2
447		4-amino-N-((8R)-5,6,7,8-tetrahydro[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide and 4-amino-N-((8S)-5,6,7,8-tetrahydro[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	510.2

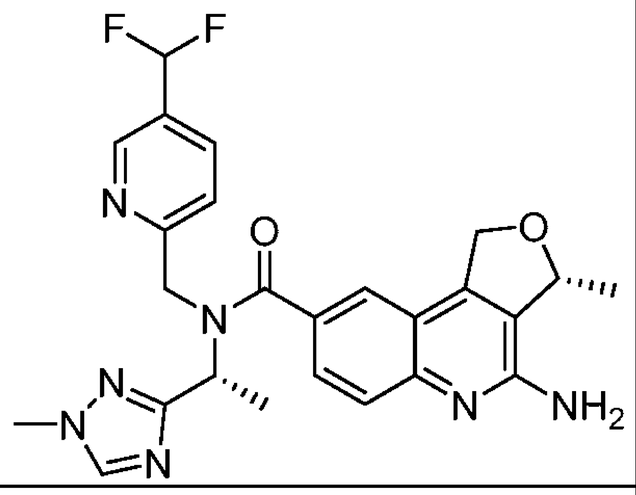
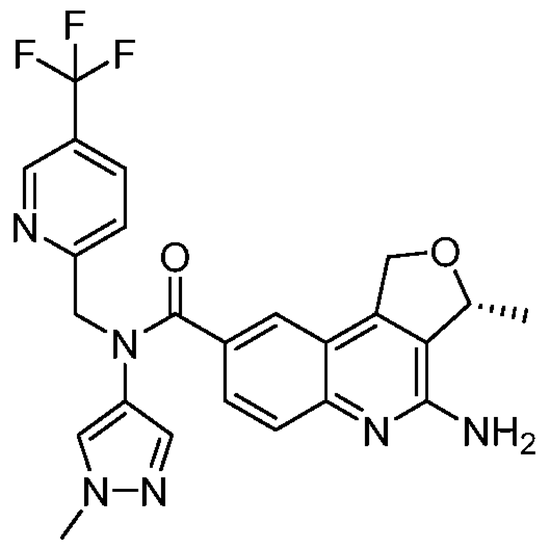
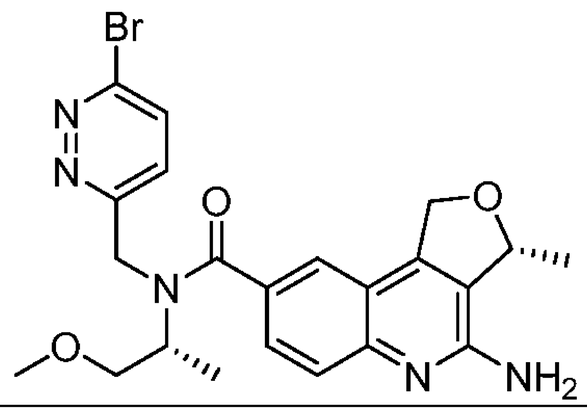
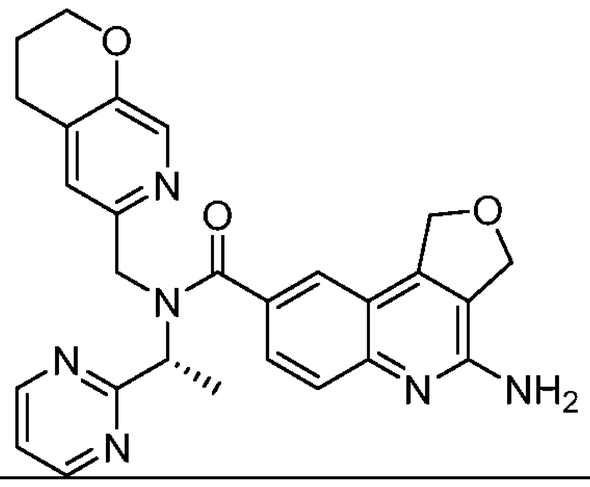
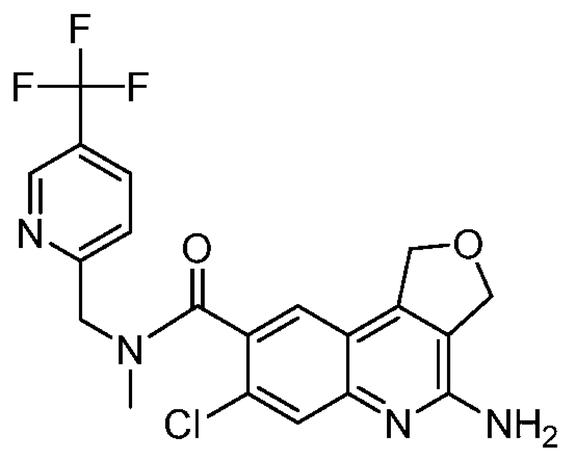
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
448		4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((8R)-5,6,7,8-tetrahydro[1,2,4]triazolo[1,5-a]pyridin-8-yl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide and 4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((8S)-5,6,7,8-tetrahydro[1,2,4]triazolo[1,5-a]pyridin-8-yl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	467.2
449		4-amino-N-(4-(3-oxetanyl)benzyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide and 4-amino-N-(4-(3-oxetanyl)benzyl)-N-((1S)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	481.6
450		4-amino-N-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	403.4
451		4-amino-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	431.4

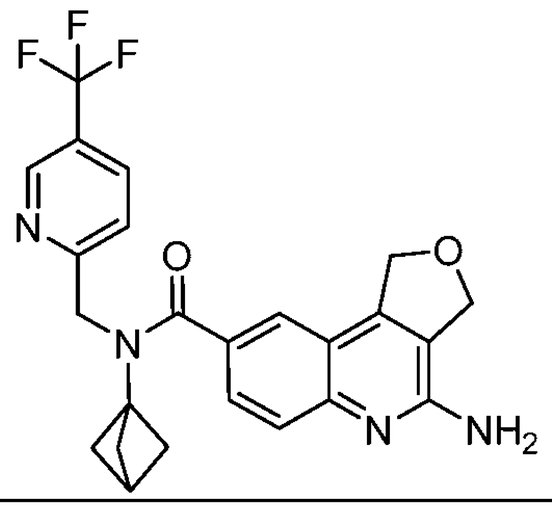
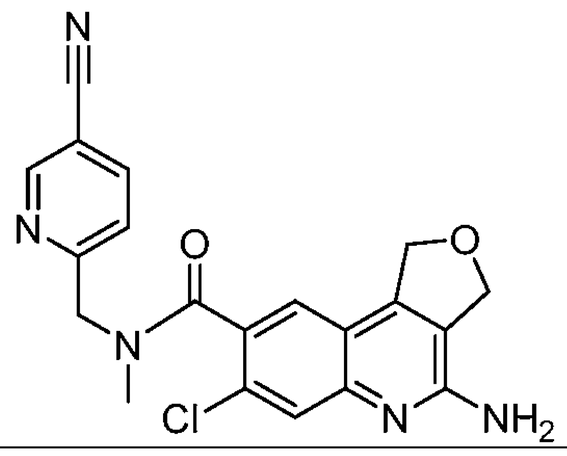
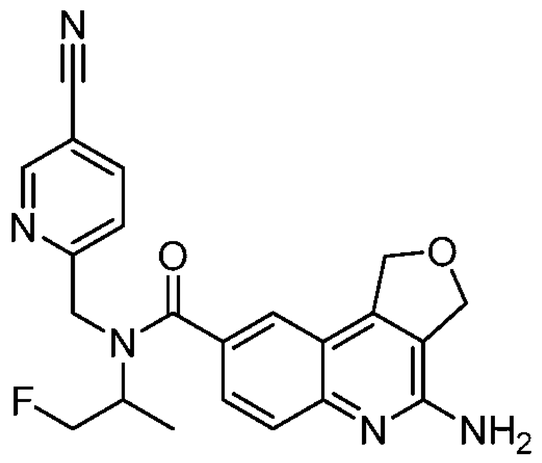
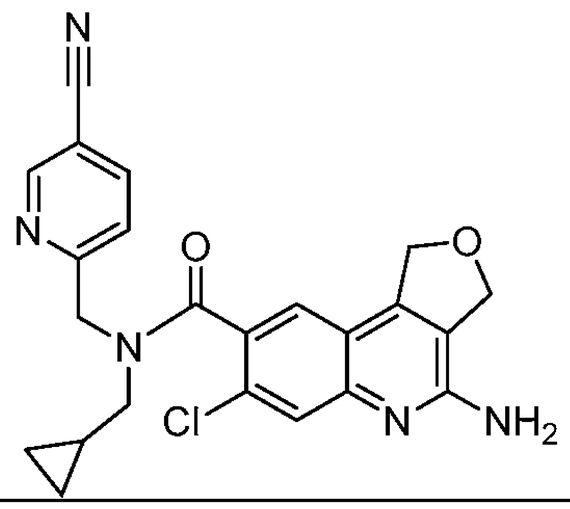
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
452		4-amino-N-(cyclopropylmethyl)-N-((6-(4-morpholinyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	461
453		4-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((6-(2,2,2-trifluoroethoxy)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	526.2
454		4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-cyclopropyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	386.1
455		4-amino-N-((5-bromo-2-pyridinyl)methyl)-N-cyclopropyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	439.0 and 441.0

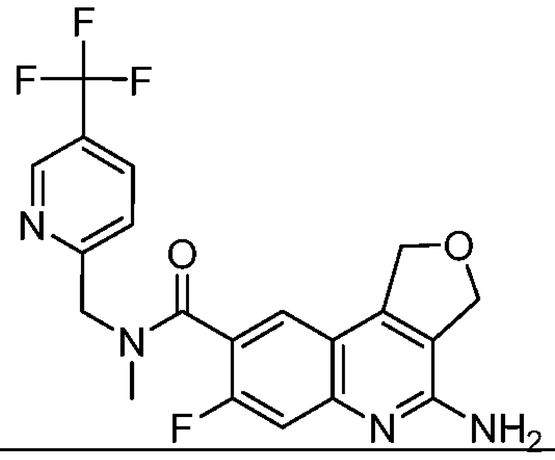
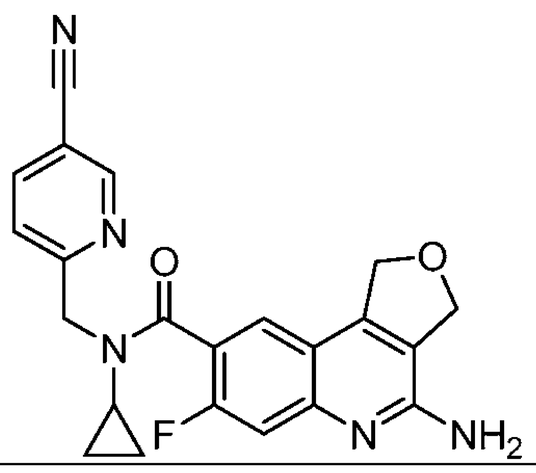
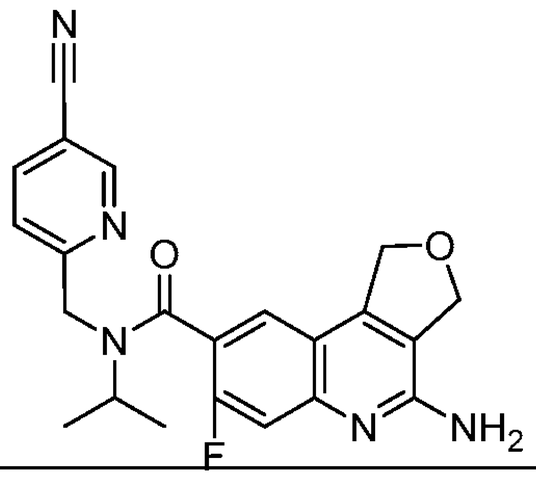
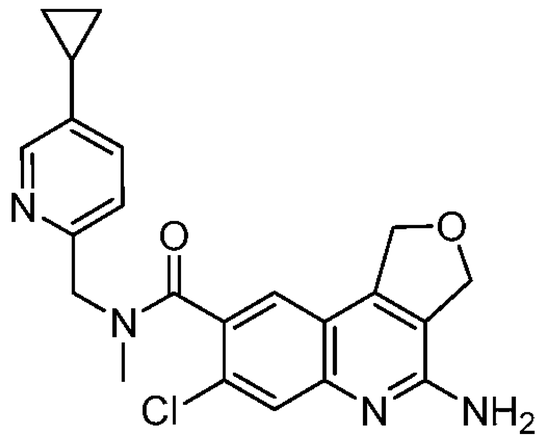
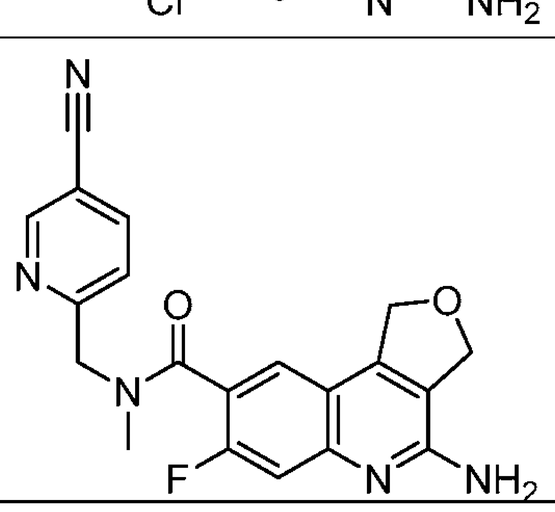
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
456		4-amino-N-cyclopropyl-N-((5-(difluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	411.2
457		4-amino-N-((1-cyanocyclopropyl)methyl)-N-((5-cyano-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	425
458		4-amino-N-((6-cyclopropyl-3-pyridazinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	468

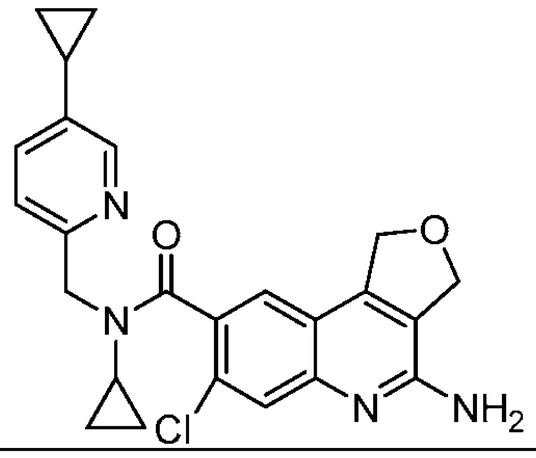
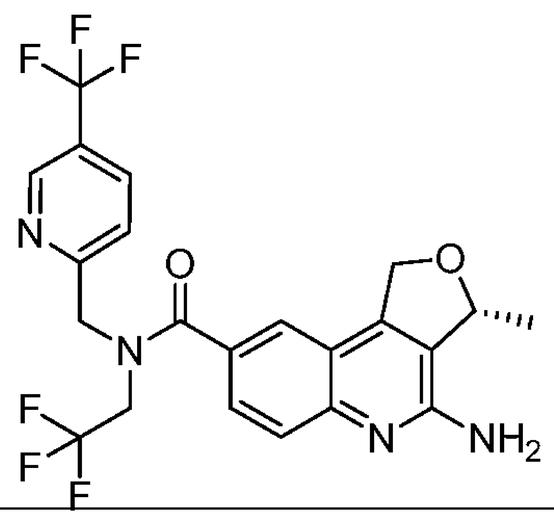
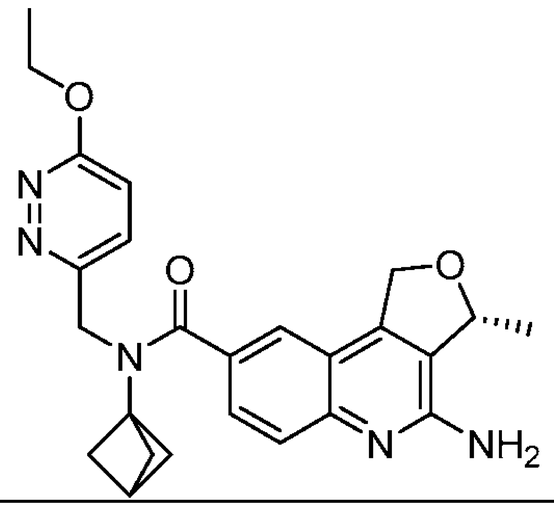
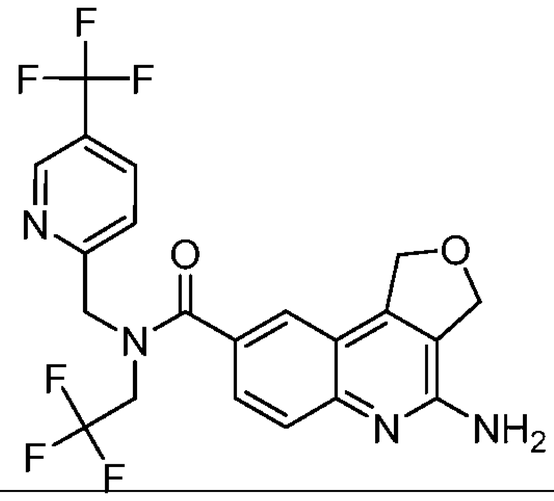
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
459		4-amino-N-((3R,4S)-3-methoxytetrahydro-2H-pyran-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide and 4-amino-N-((3S,4R)-3-methoxytetrahydro-2H-pyran-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	503.2
460	 	4-amino-N-((3R,4R)-4-methoxytetrahydro-2H-pyran-3-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide and 4-amino-N-((3S,4S)-4-methoxytetrahydro-2H-pyran-3-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	503.2

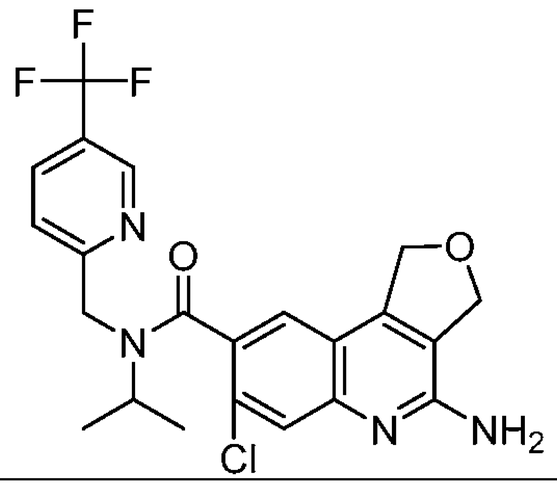
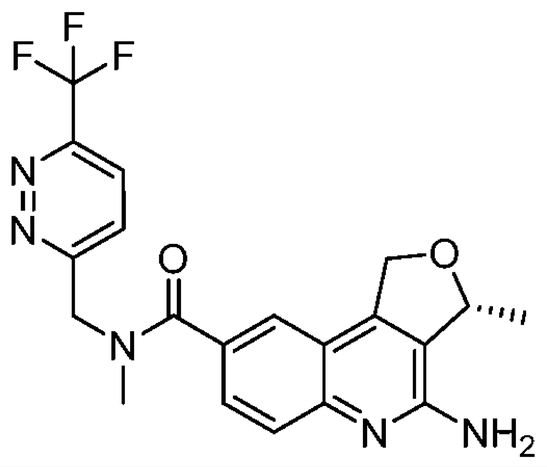
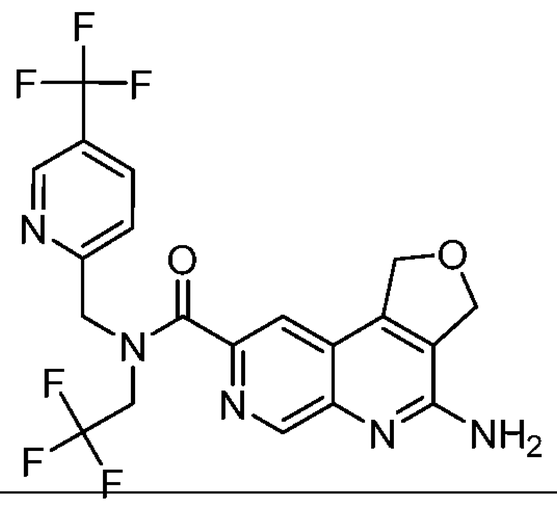
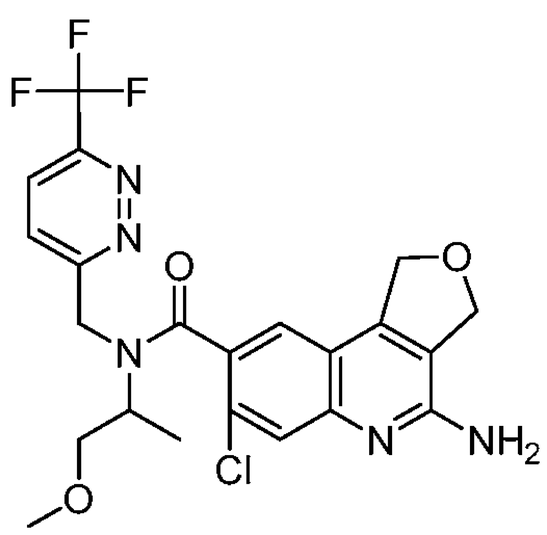
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
461		4-amino-7-chloro-N-((5-cyano-2-pyridinyl)methyl)-N-cyclopropyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	420.2
462		4-amino-N-((6-chloro-5-methoxy-2-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	427
463		4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	472.1 and 474.1
464		4-amino-7-chloro-N-(cyclopropylmethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	477.2
465		(3R)-4-amino-3-methyl-N-(2-propanyl)-N-((5-(trifluoromethoxy)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	461.2

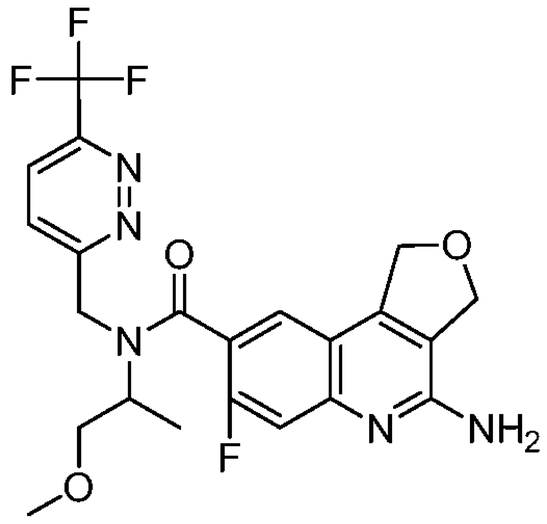
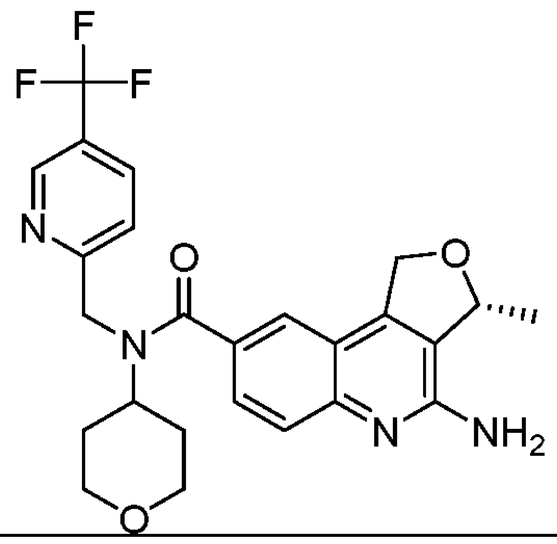
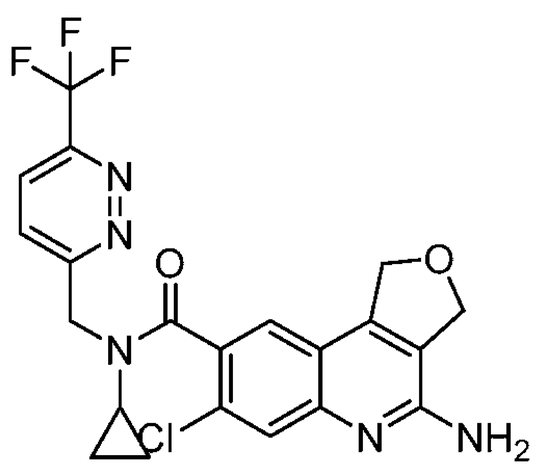
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
466		(3R)-4-amino-N-((5-(difluoromethyl)-2-pyridinyl)methyl)-3-methyl-N-((1R)-1-(1-methyl-1H-1,2,4-triazol-3-yl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	494
467		(3R)-4-amino-3-methyl-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	483.1
468		(3R)-4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	486.0 and 488.0
469		4-amino-N-(3,4-dihydro-2H-pyrano[2,3-c]pyridin-6-ylmethyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	483.2
470		4-amino-7-chloro-N-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	437.2

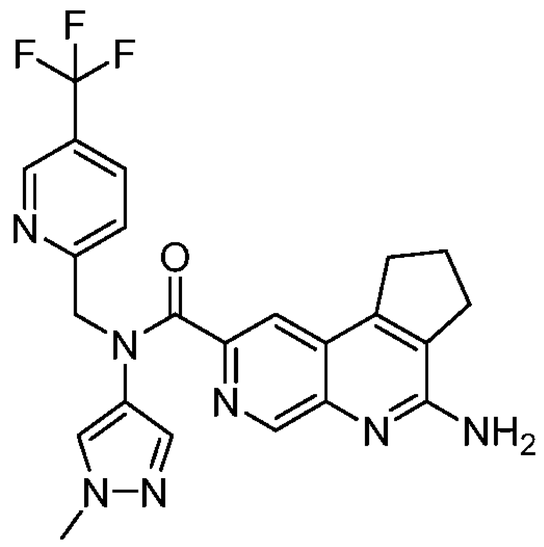
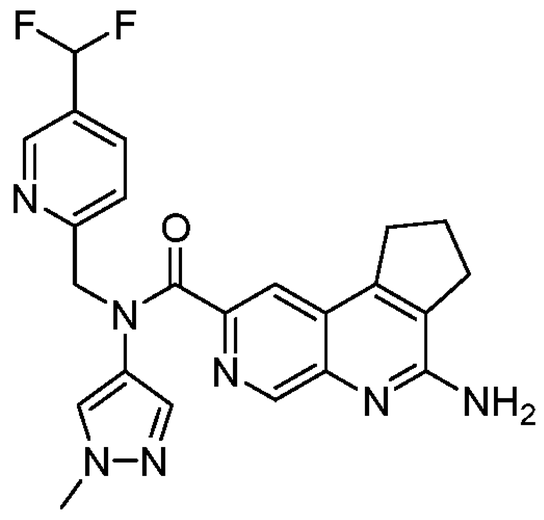
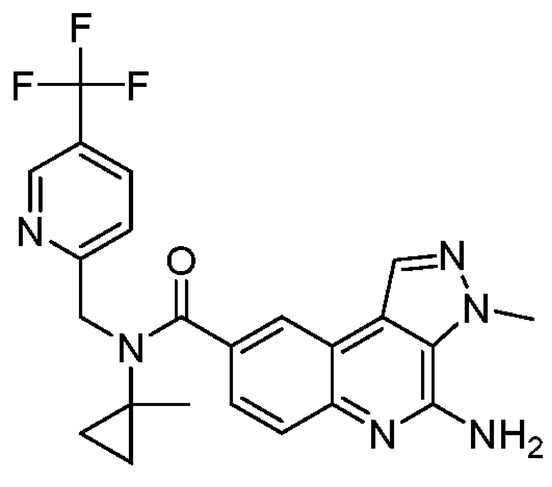
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
471		4-amino-N-(bicyclo[1.1.1]pentan-1-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	455.2
472		4-amino-7-chloro-N-((5-cyano-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	394
473		4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((2R)-1-fluoro-2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide and 4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((2S)-1-fluoro-2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	406.2
474		4-amino-7-chloro-N-((5-cyano-2-pyridinyl)methyl)-N-(cyclopropylmethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	434

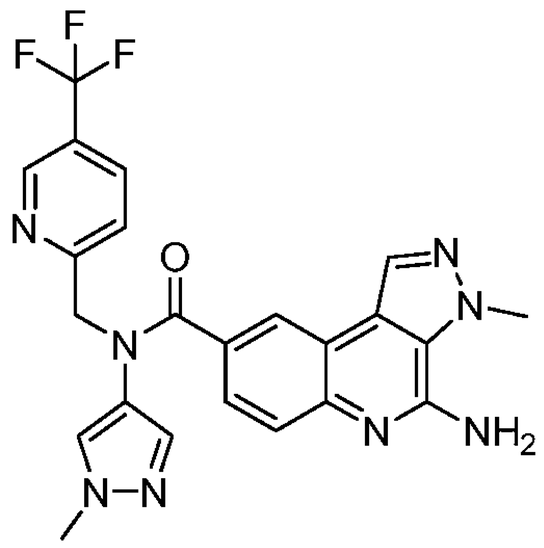
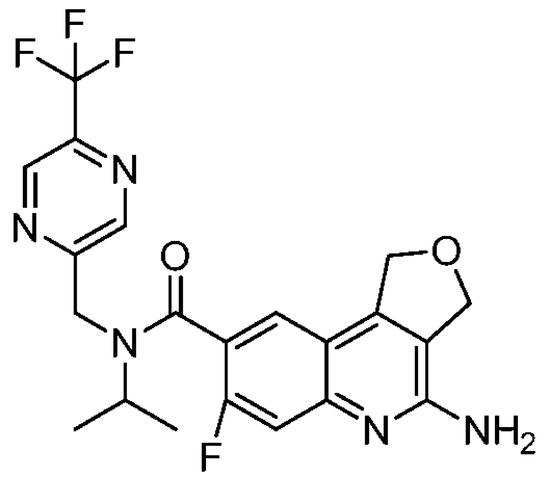
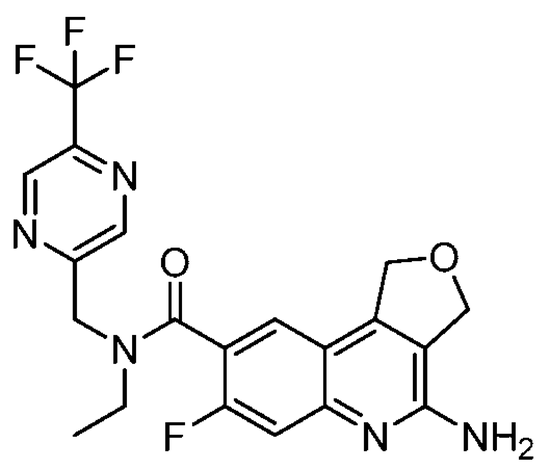
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
475		4-amino-7-fluoro-N-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	421.2
476		4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-cyclopropyl-7-fluoro-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	404.1
477		4-amino-N-((5-cyano-2-pyridinyl)methyl)-7-fluoro-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	406.2
478		4-amino-7-chloro-N-((5-cyclopropyl-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	409.1
479		4-amino-N-((5-cyano-2-pyridinyl)methyl)-7-fluoro-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	378.1

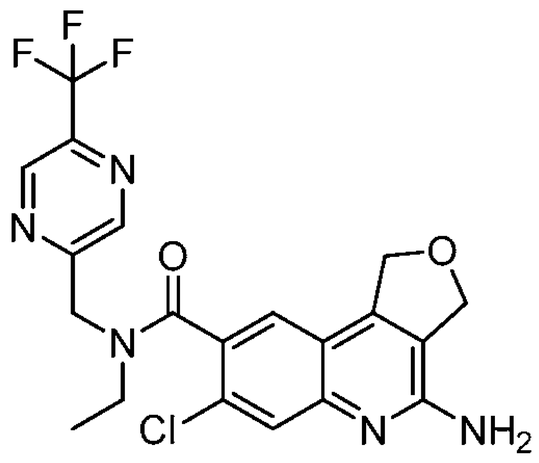
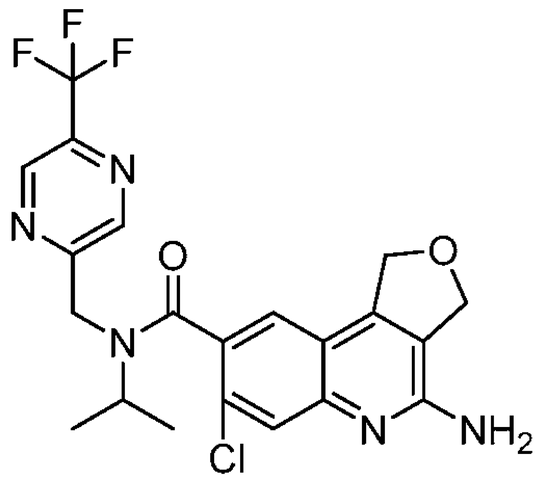
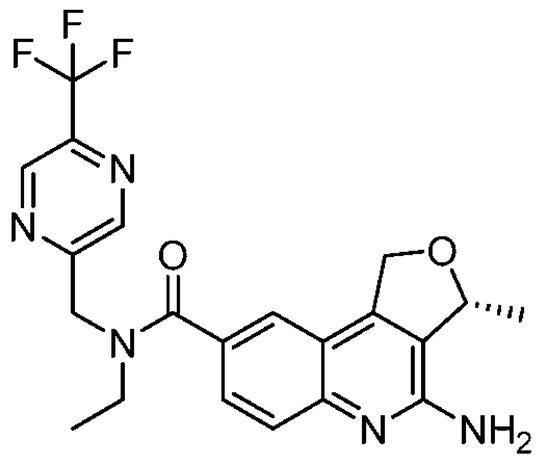
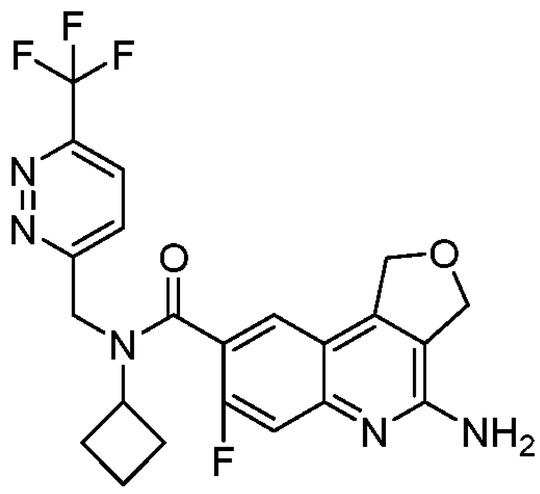
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
480		4-amino-7-chloro-N-cyclopropyl-N-((5-cyclopropyl-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	435.2
481		(3R)-4-amino-3-methyl-N-(2,2,2-trifluoroethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	485.2
482		(3R)-4-amino-N-(bicyclo[1.1.1]pentan-1-yl)-N-((6-ethoxy-3-pyridazinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	446.2
483		4-amino-N-(2,2,2-trifluoroethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	471.1

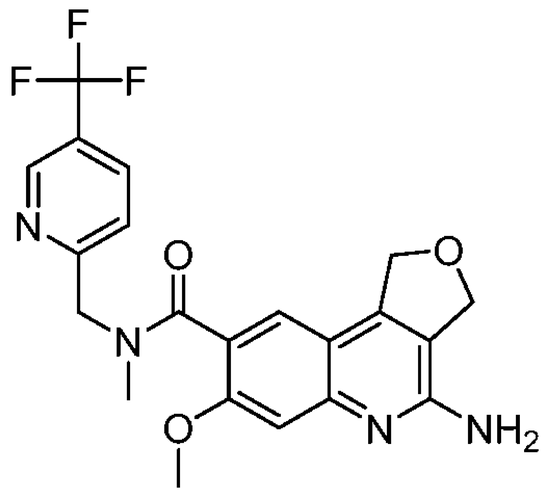
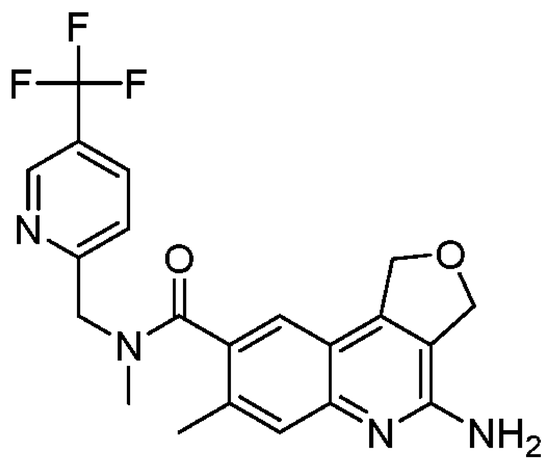
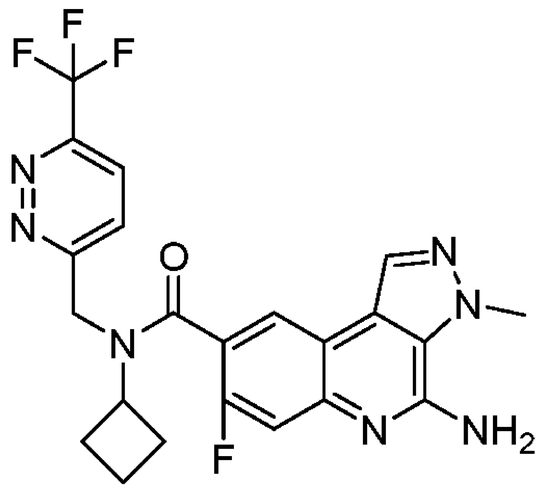
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
484		4-amino-7-chloro-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	465.1
485		(3R)-4-amino-N,3-dimethyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	418.1
486		4-amino-N-(2,2,2-trifluoroethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	PyBroP	472.1
487		4-amino-7-chloro-N-((2R)-1-methoxy-2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide and 4-amino-7-chloro-N-((2S)-1-methoxy-2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	496.1

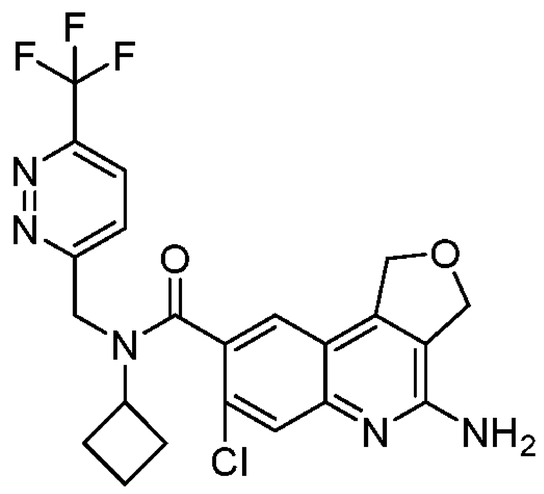
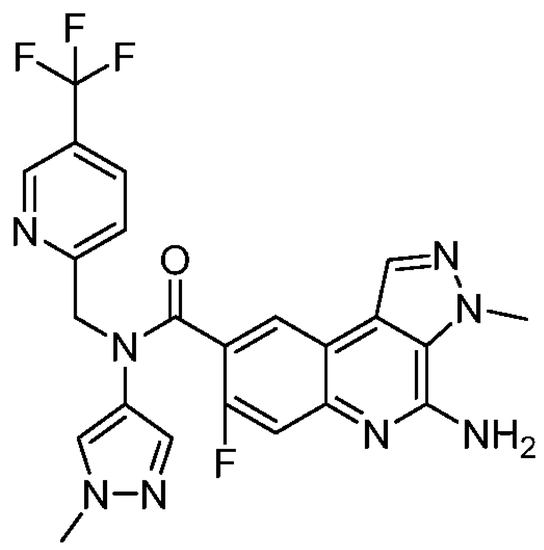
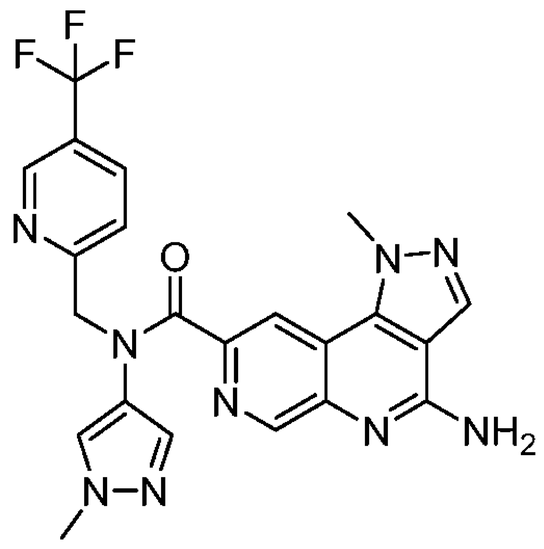
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
488		4-amino-7-fluoro-N-((2R)-1-methoxy-2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide and 4-amino-7-fluoro-N-((2S)-1-methoxy-2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	480.2
489		(3R)-4-amino-3-methyl-N-(tetrahydro-2H-pyran-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	487.2
490		4-amino-7-chloro-N-cyclopropyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	464.1

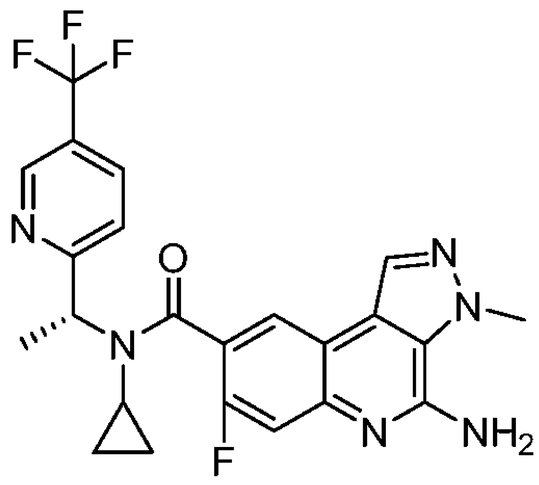
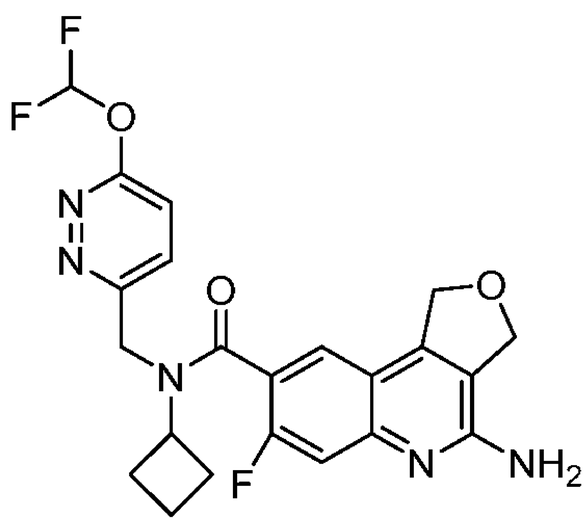
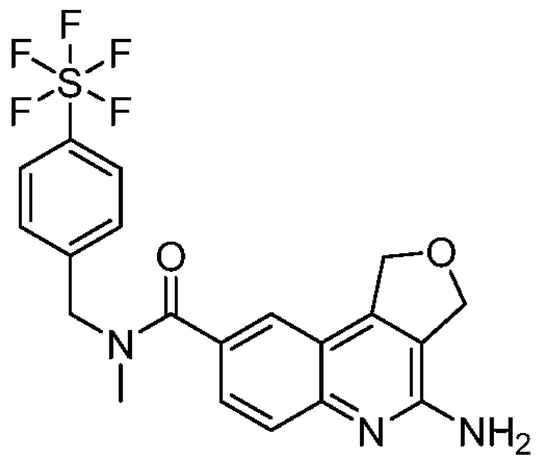
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
492		6-amino-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-8,9-dihydro-7H-cyclopenta[c][1,7]naphthyridine-2-carboxamide	PyBroP	468.2
493		6-amino-N-((5-(difluoromethyl)-2-pyridinyl)methyl)-N-(1-methyl-1H-pyrazol-4-yl)-8,9-dihydro-7H-cyclopenta[c][1,7]naphthyridine-2-carboxamide	PyBroP	450.2
494		4-amino-3-methyl-N-(1-methylcyclopropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide	PyBroP	455.2

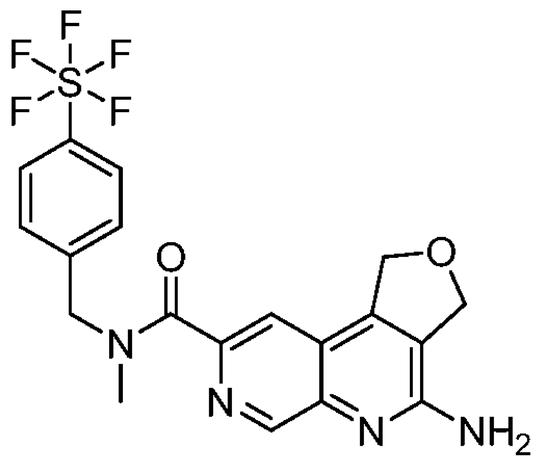
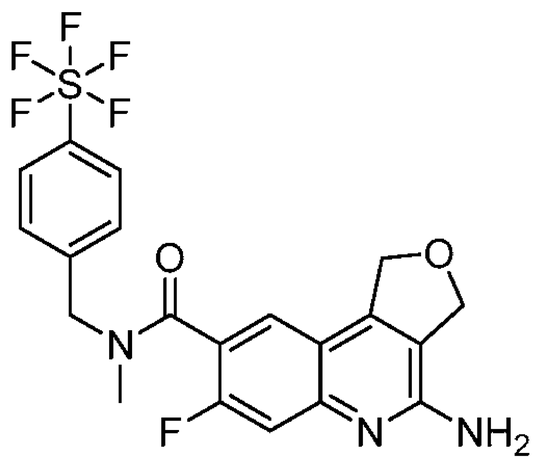
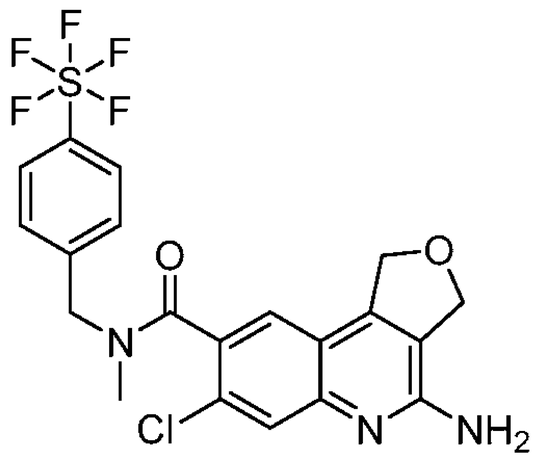
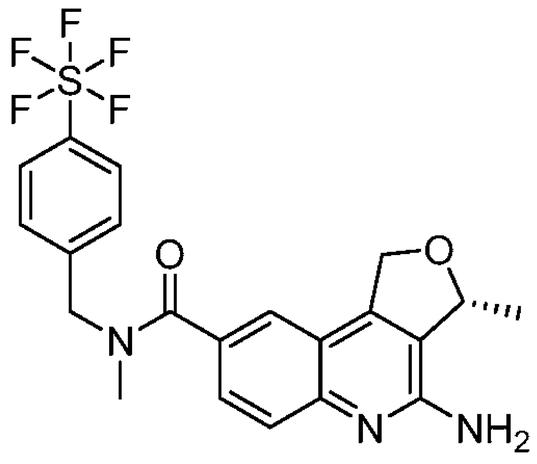
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
495		4-amino-3-methyl-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide	PyBroP	481.2
496		4-amino-7-fluoro-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyrazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	450.2
497		4-amino-N-ethyl-7-fluoro-N-((5-(trifluoromethyl)-2-pyrazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	436.15

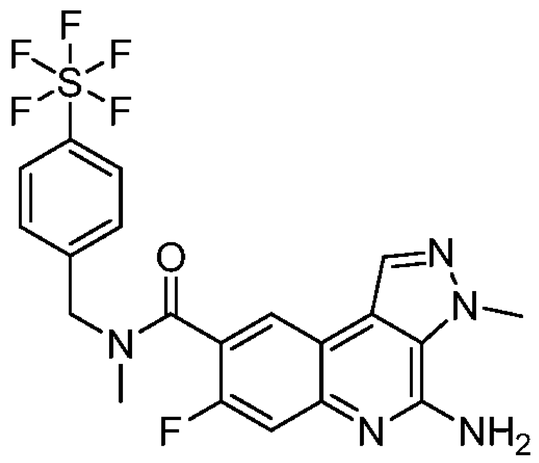
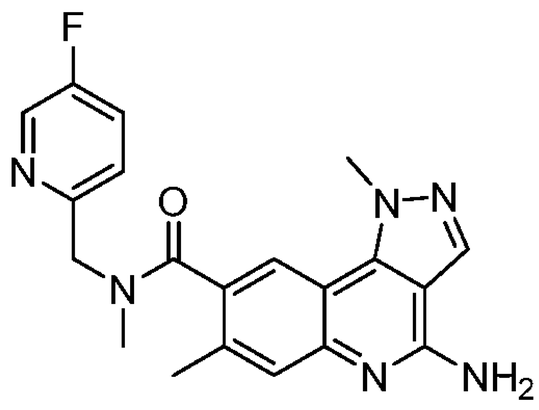
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
498		4-amino-7-chloro-N-ethyl-N-((5-(trifluoromethyl)-2-pyrazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	452.05
499		4-amino-7-chloro-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyrazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	466.2
500		(3R)-4-amino-N-ethyl-3-methyl-N-((5-(trifluoromethyl)-2-pyrazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	432.2
501		4-amino-N-cyclobutyl-7-fluoro-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	462.2

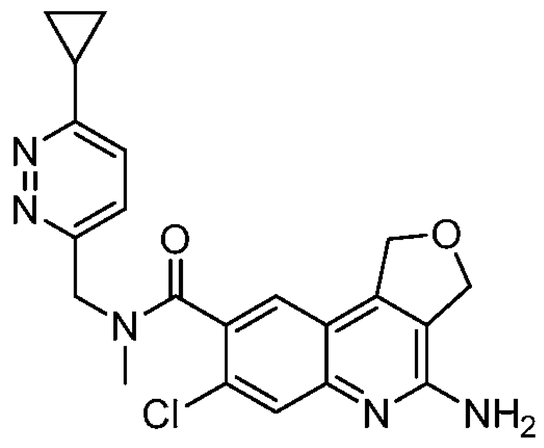
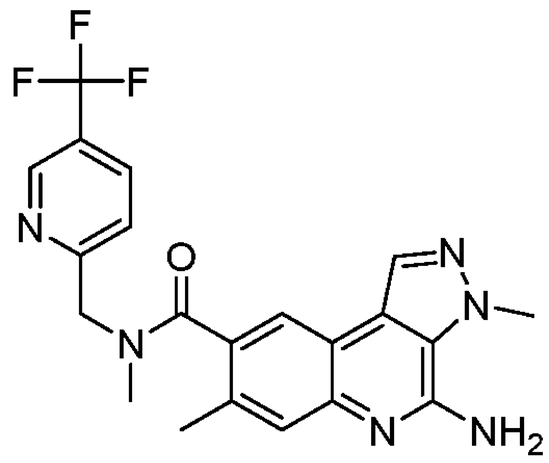
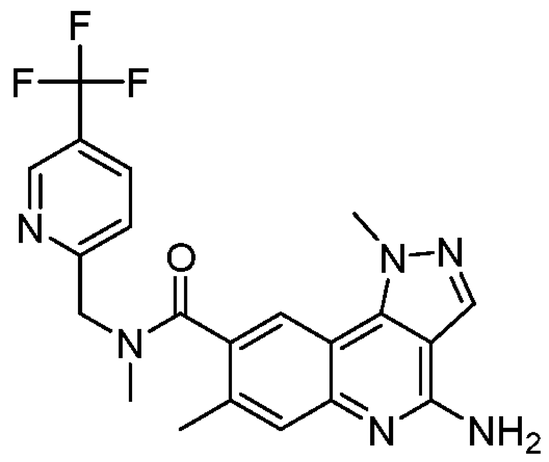
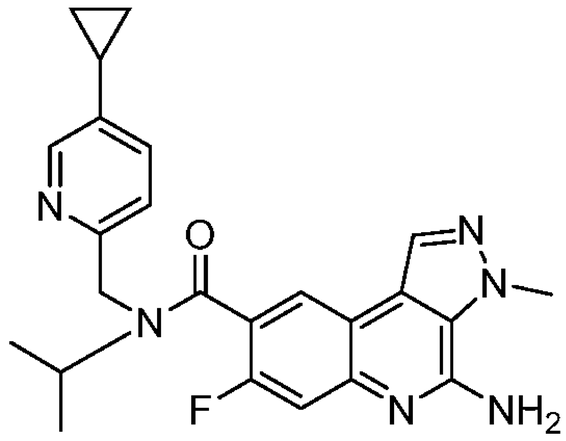
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
502		4-amino-7-methoxy-N-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	433.2
503		4-amino-N,7-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	417
504		4-amino-N-cyclobutyl-7-fluoro-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide	PyBroP	474.2

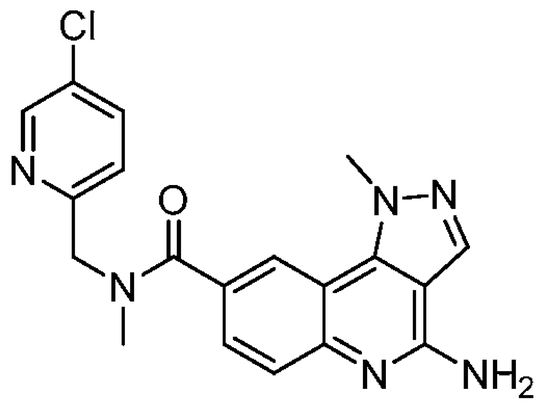
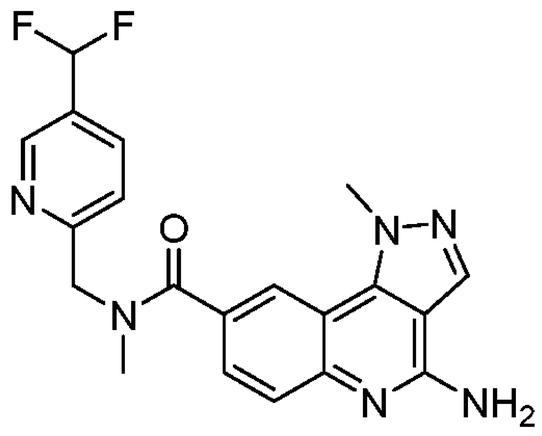
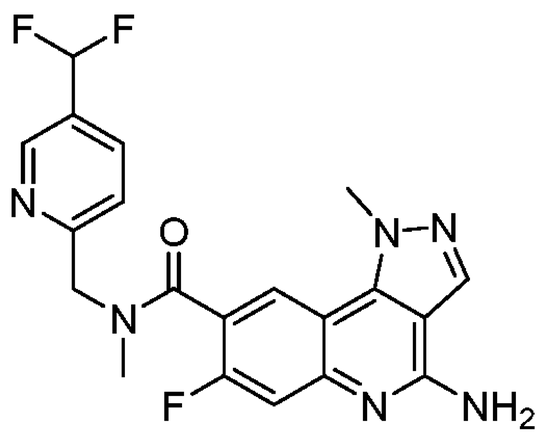
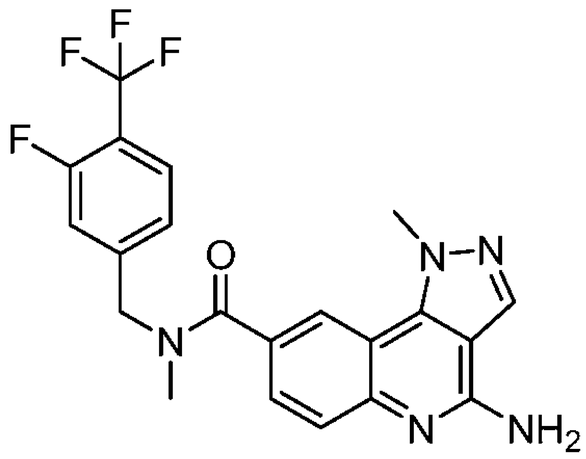
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
505		4-amino-7-chloro-N-cyclobutyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	PyBroP	478.2
506		4-amino-7-fluoro-3-methyl-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide	PyBroP	499.2
507		4-amino-1-methyl-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide	PyBroP	481.9

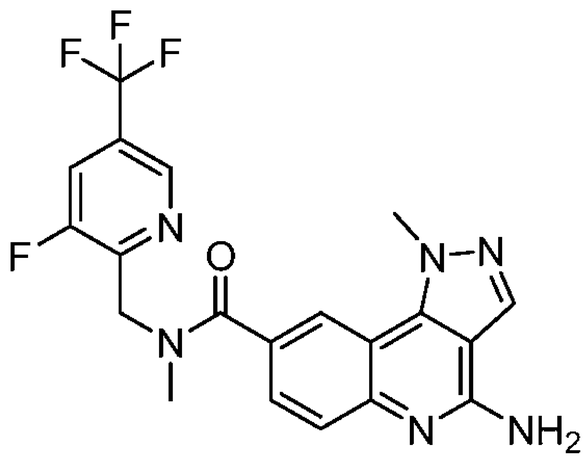
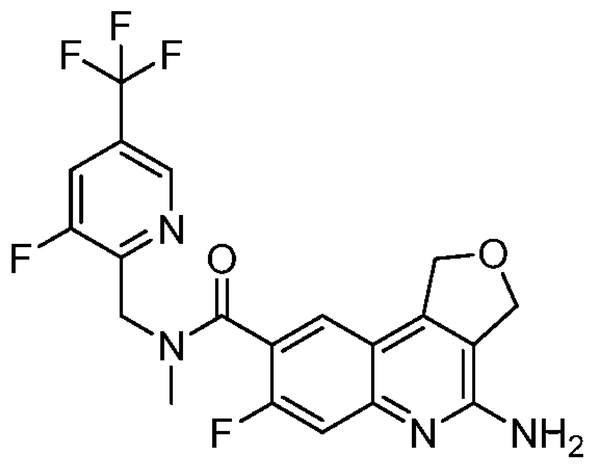
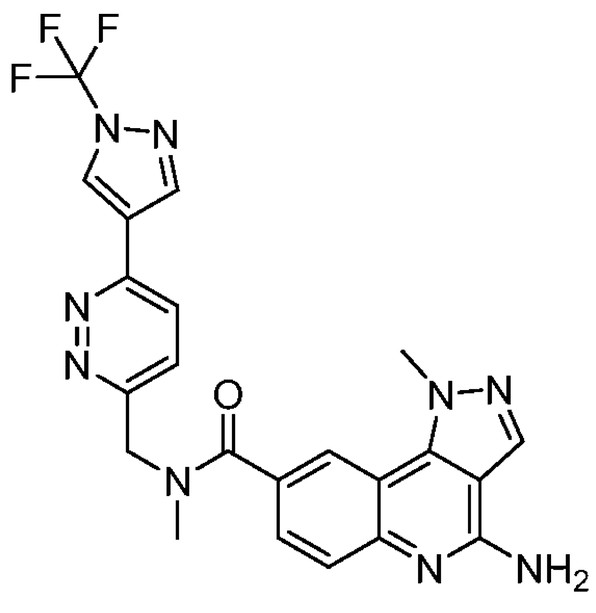
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
508		4-amino-N-cyclopropyl-7-fluoro-3-methyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide	PyBroP	473
509		4-amino-N-cyclobutyl-N-((6-(difluoromethoxy)-3-pyridazinyl)methyl)-7-fluoro-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	TBTU	460.15
510		4-amino-N-methyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	TBTU	460.9

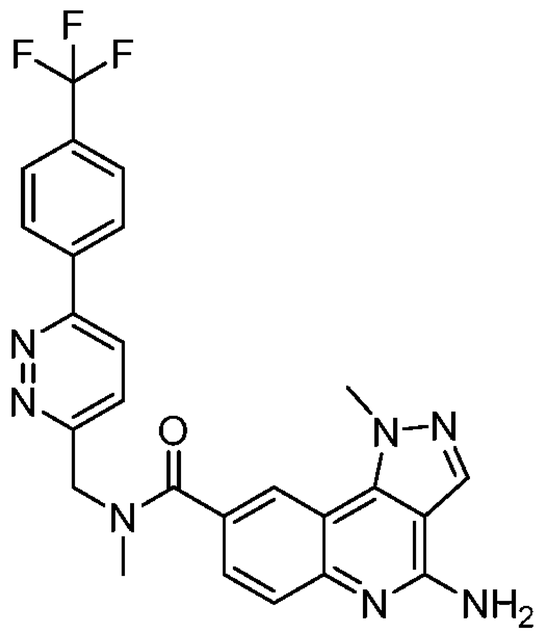
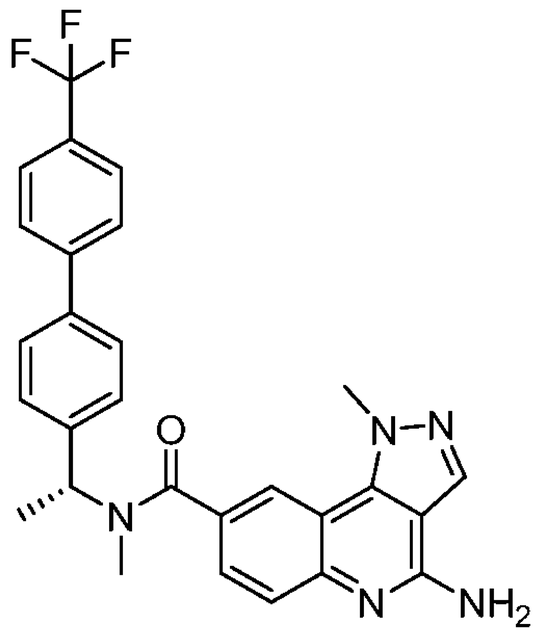
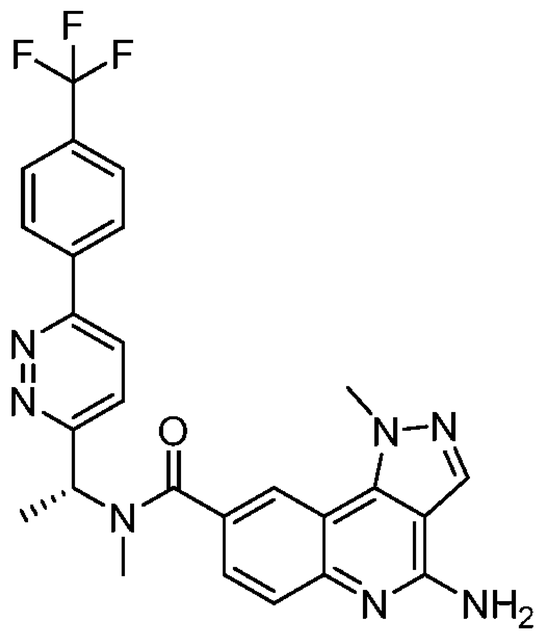
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
511		4-amino-N-methyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	TBTU	461.8
512		4-amino-7-fluoro-N-methyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	TBTU	478.7
513		4-amino-7-chloro-N-methyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	TBTU	494.8
514		(3R)-4-amino-N,3-dimethyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	TBTU	474.8

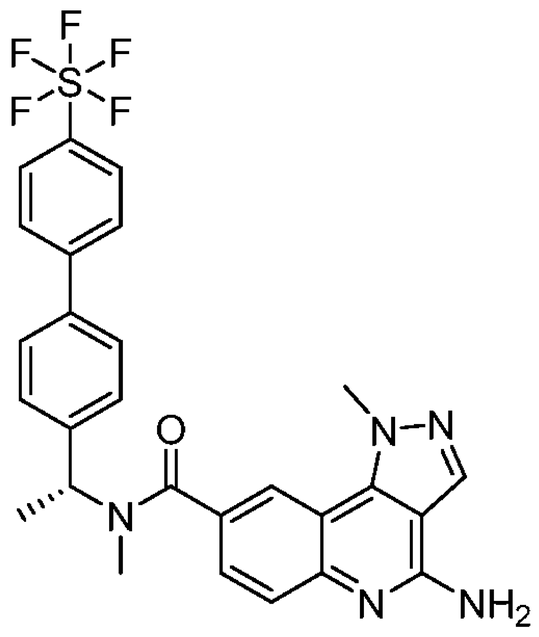
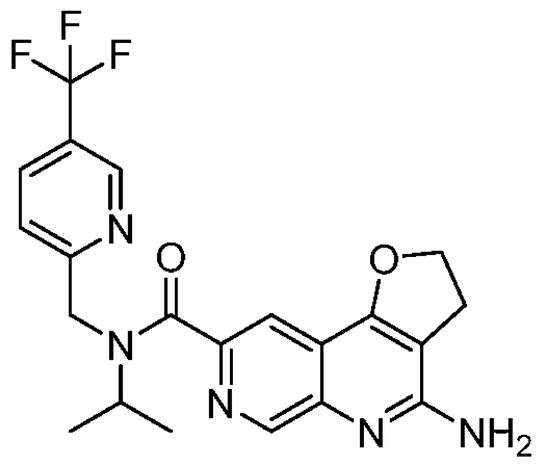
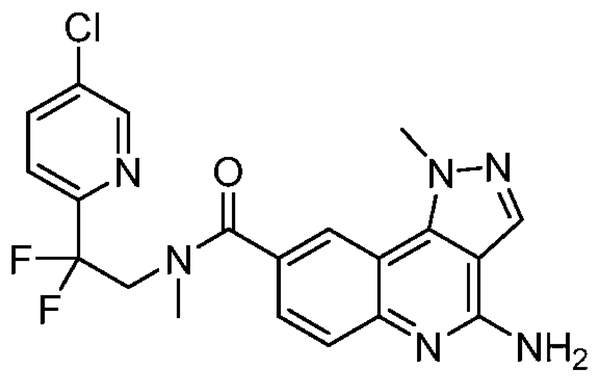
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
515		4-amino-7-fluoro-N,3-dimethyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide	TBTU	490.7
516		4-amino-N-((5-fluoro-2-pyridinyl)methyl)-N,1,7-trimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	TBTU	379.2
517		4-amino-N-((6-cyclopropyl-3-pyridazinyl)methyl)-7-fluoro-N,3-dimethyl-3H-pyrazolo[3,4-c]quinoline-8-carboxamide	TBTU	406.2
518		4-amino-N-((6-cyclopropyl-3-pyridazinyl)methyl)-7-fluoro-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	TBTU	406.2

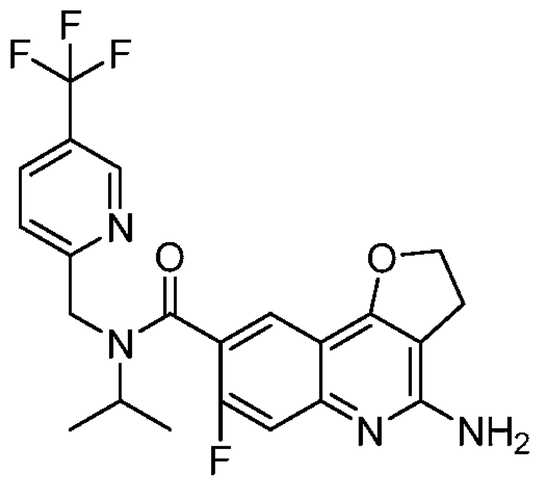
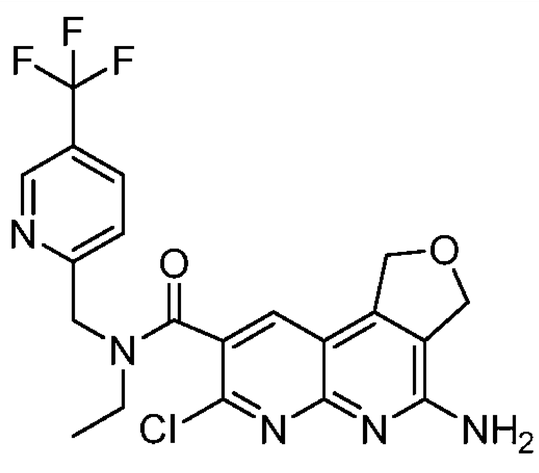
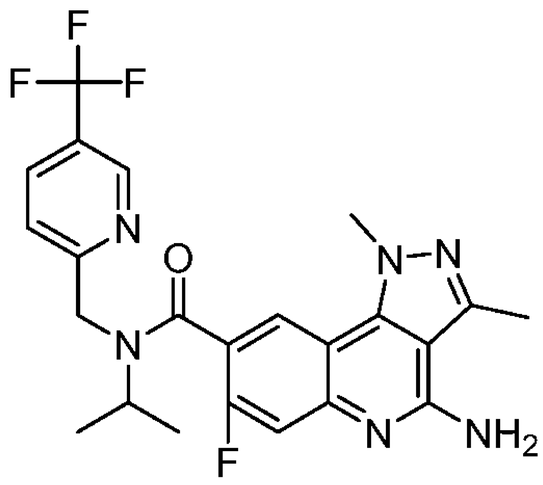
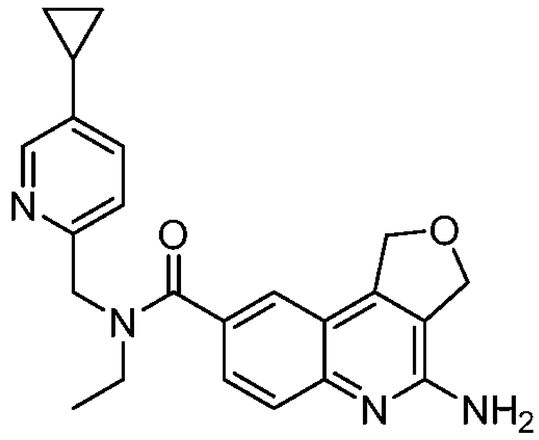
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
519		4-amino-7-chloro-N-((6-cyclopropyl-3-pyridazinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	TBTU	410.2
520		4-amino-N,3,7-trimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide	TBTU	429.2
521		4-amino-N,1,7-trimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	TBTU	429.2
522		4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-7-fluoro-3-methyl-N-(2-propanyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide	TBTU	433.0

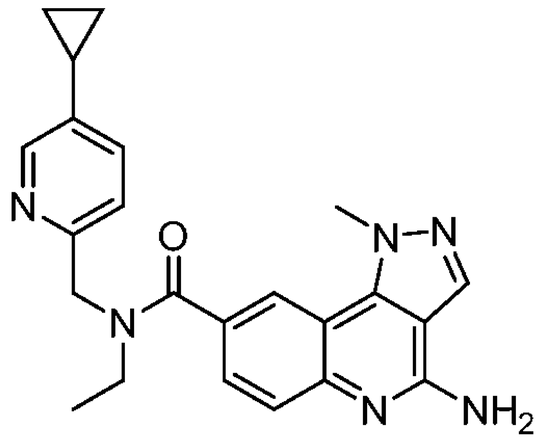
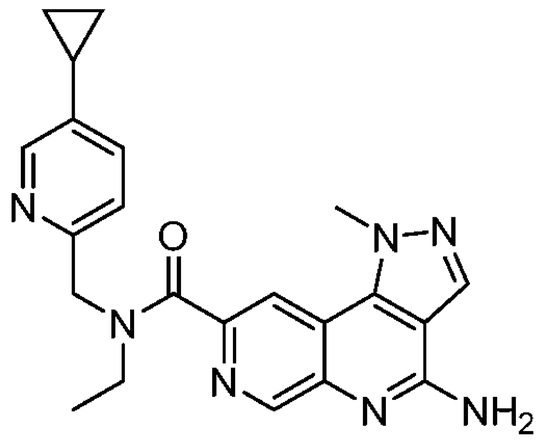
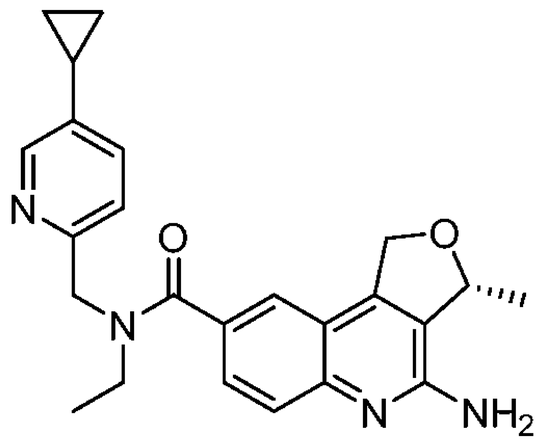
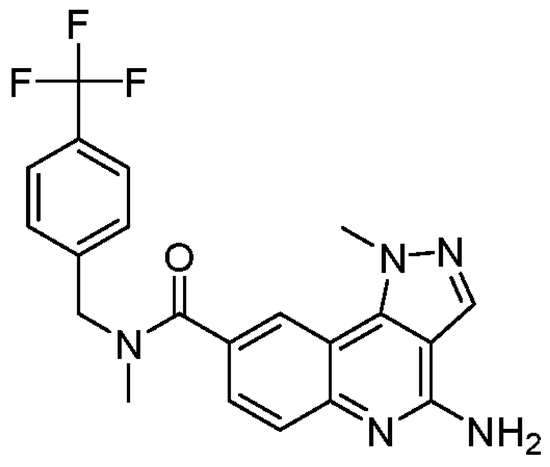
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
523		4-amino-N-((5-chloro-2-pyridinyl)methyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	TBTU	380.9
524		4-amino-N-((5-(difluoromethyl)-2-pyridinyl)methyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	TBTU	397.0
525		4-amino-N-((5-(difluoromethyl)-2-pyridinyl)methyl)-7-fluoro-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	TBTU	415.9
526		4-amino-N-(3-fluoro-4-(trifluoromethyl)benzyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	TBTU	432.1

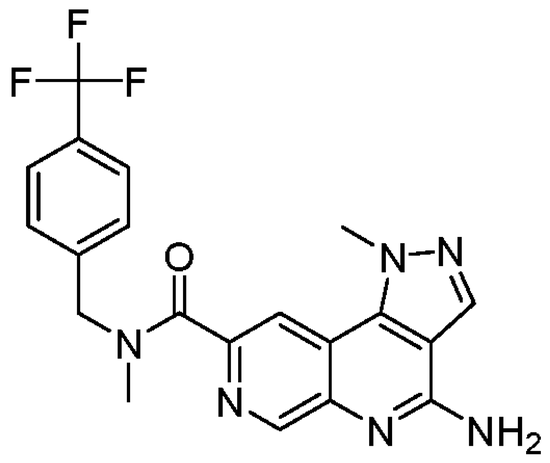
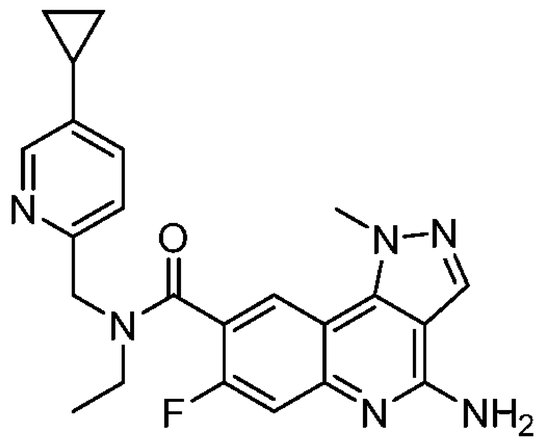
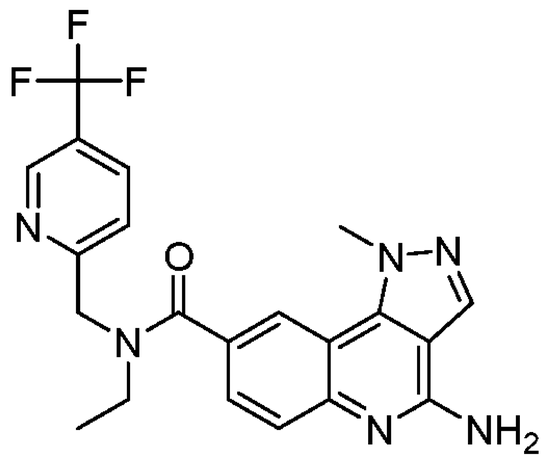
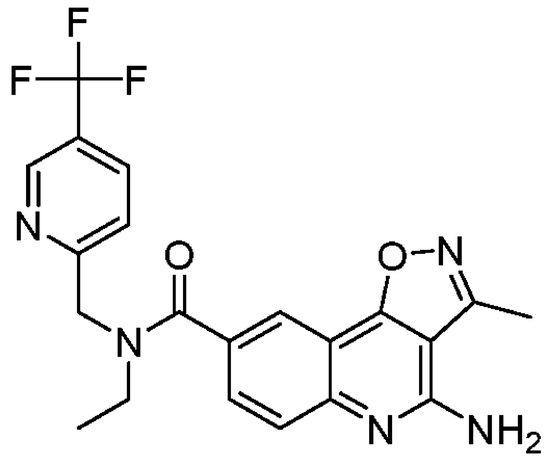
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
527		4-amino-N-((3-fluoro-5-(trifluoromethyl)-2-pyridinyl)methyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	TBTU	433.1
528		4-amino-7-fluoro-N-((3-fluoro-5-(trifluoromethyl)-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	TBTU	439.1
529		4-amino-N,1-dimethyl-N-((6-(1-(trifluoromethyl)-1H-pyrazol-4-yl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	TBTU	482.2

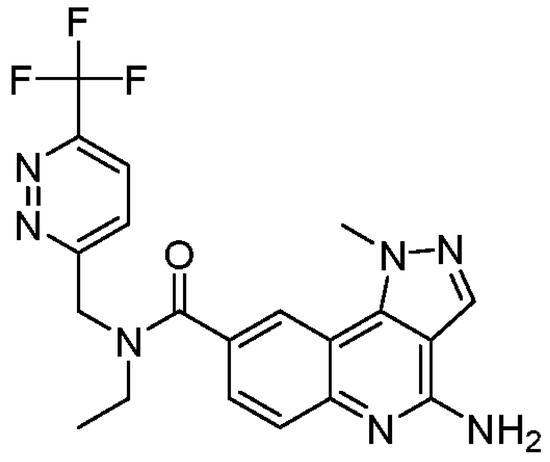
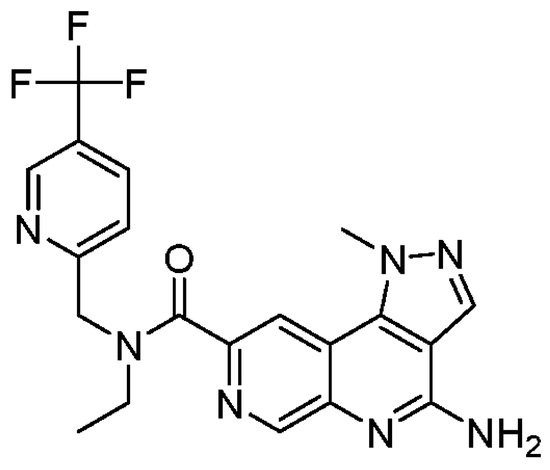
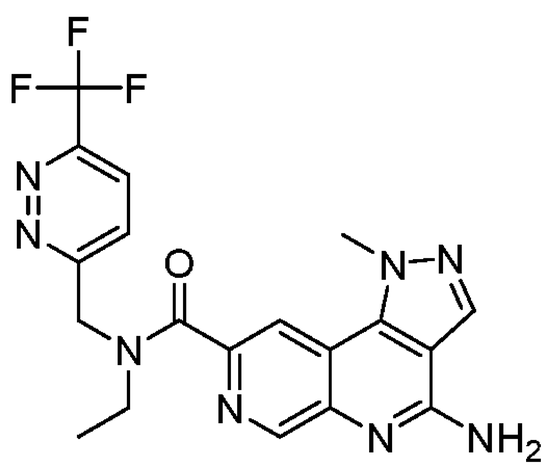
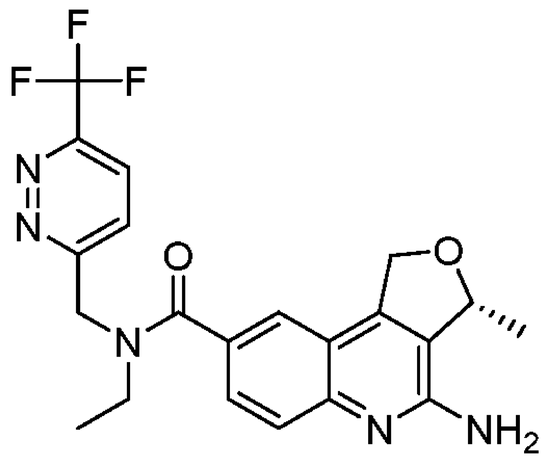
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
530		4-amino-N,1-dimethyl-N-((6-(4-(trifluoromethyl)phenyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	TBTU	492.1
531		4-amino-N,1-dimethyl-N-((1R)-1-(4'-(trifluoromethyl)[biphenyl]-4-yl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	TBTU	504.2
532		4-amino-N,1-dimethyl-N-((1R)-1-(6-(4-(trifluoromethyl)phenyl)-3-pyridazinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	TBTU	506.2

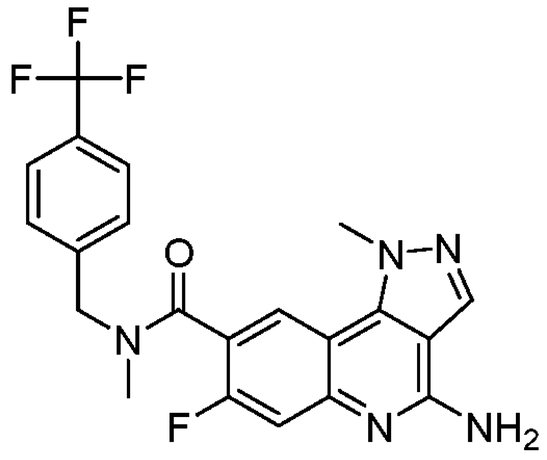
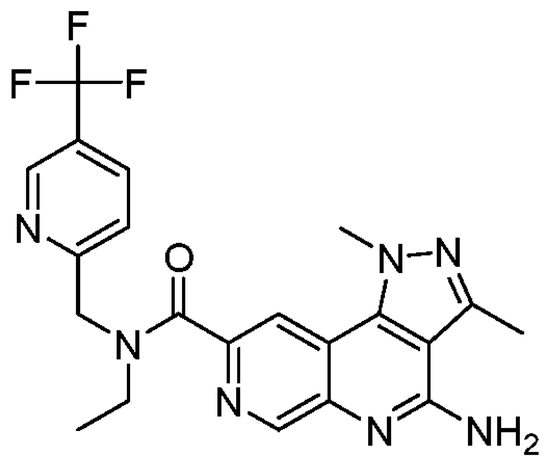
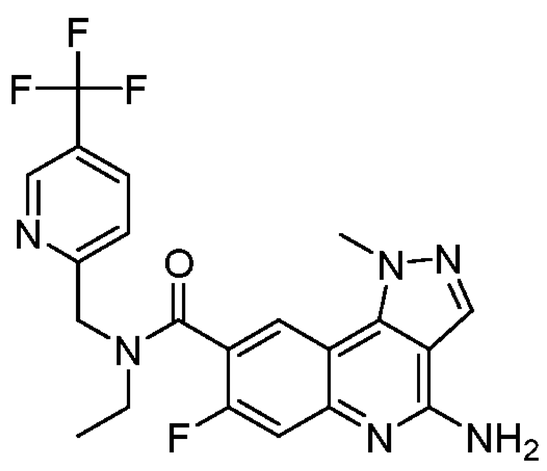
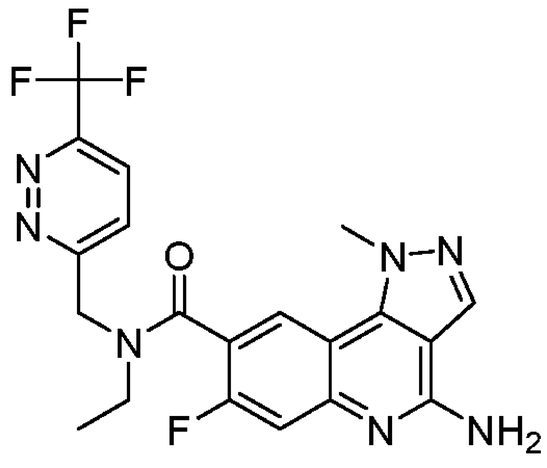
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
533		4-amino-N,1-dimethyl-N-((1R)-1-(4'-(pentafluoro-lambda~6~-sulfanyl)[biphenyl]-4-yl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	TBTU	563.2
534		4-amino-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-2,3-dihydrofuro[3,2-c][1,7]naphthyridine-8-carboxamide	HATU	432.1
535		4-amino-N-(2-(5-chloro-2-pyridinyl)-2,2-difluoroethyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	HATU	431.0

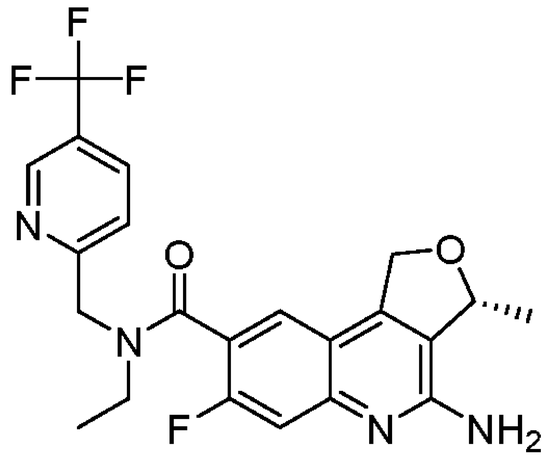
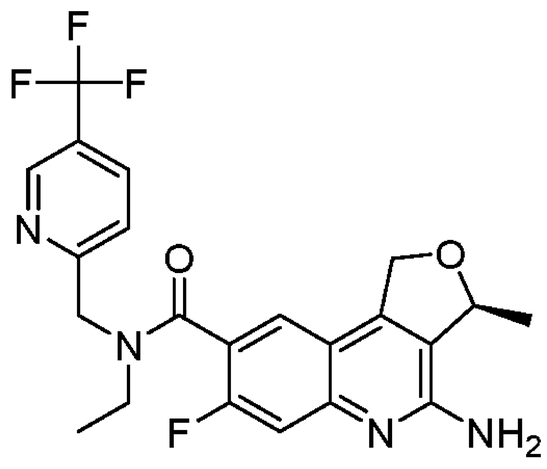
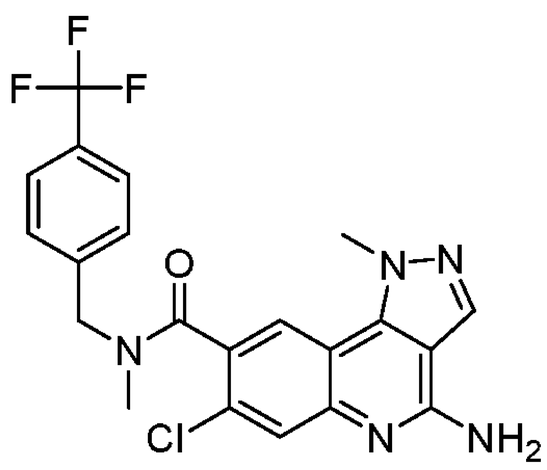
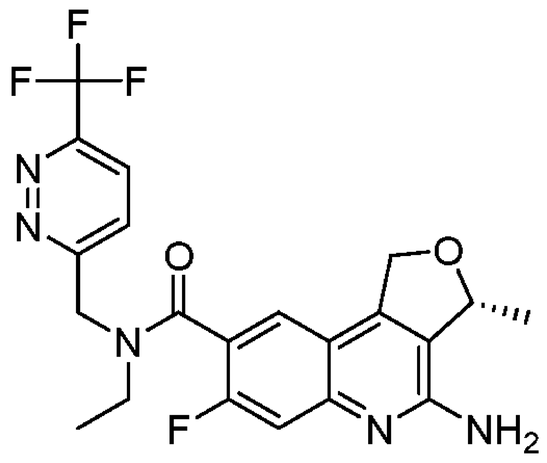
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
536		4-amino-7-fluoro-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-2,3-dihydrofuro[3,2-c]quinoline-8-carboxamide	HATU	449.0
537		4-amino-7-chloro-N-ethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide	HATU	451.9
538		4-amino-7-fluoro-1,3-dimethyl-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	HATU	475.1
539		4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	389.0

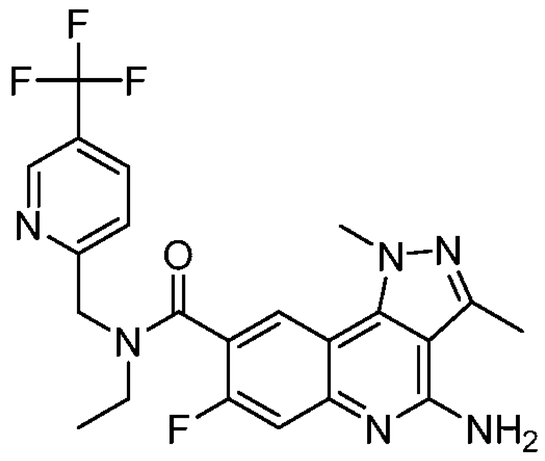
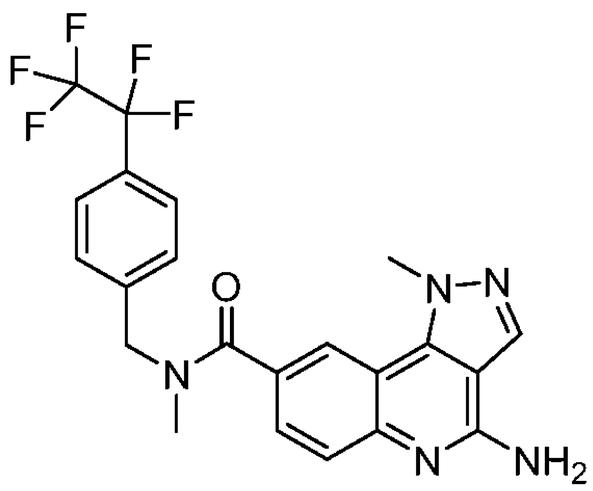
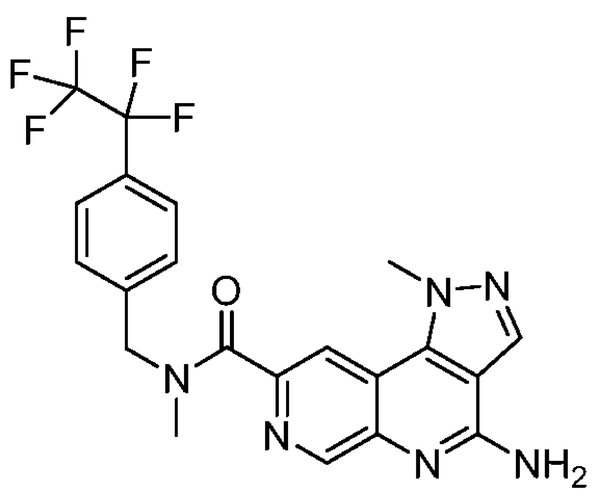
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
540		4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-N-ethyl-1-methyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	HATU	401.0
541		4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-N-ethyl-1-methyl-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide	HATU	402.0
542		(3R)-4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-N-ethyl-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	403.0
543		4-amino-N,1-dimethyl-N-(4-(trifluoromethyl)benzyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	HATU	414.0

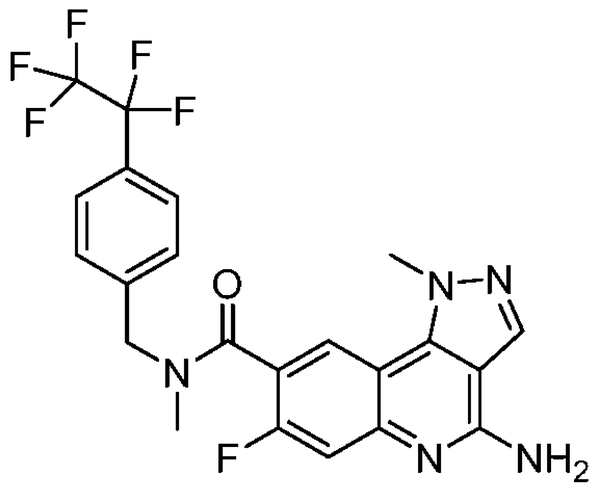
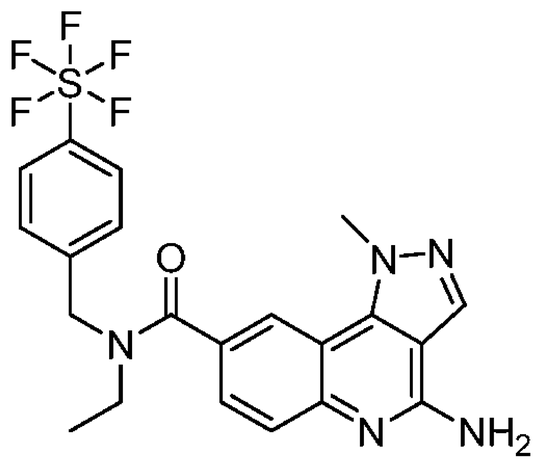
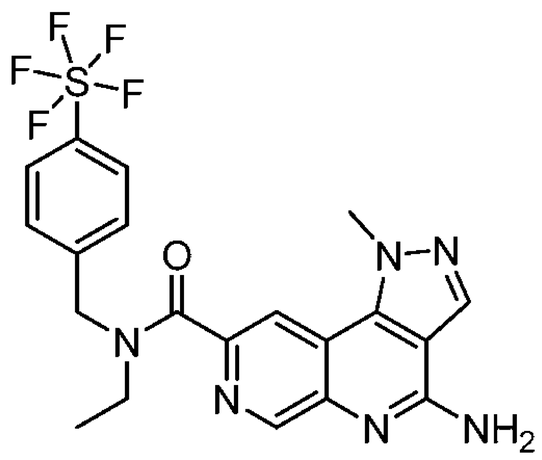
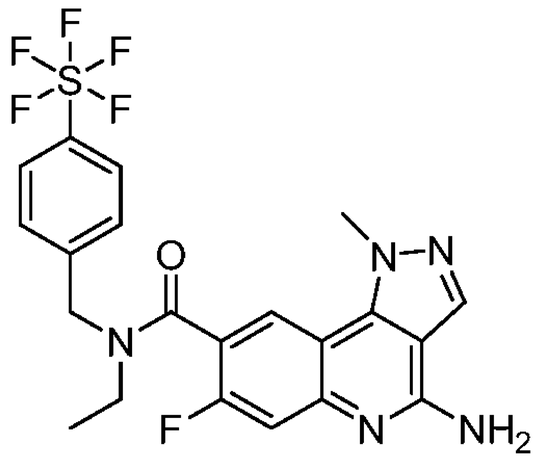
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
544		4-amino-N,1-dimethyl-N-(4-(trifluoromethyl)benzyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide	HATU	415.0
545		4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-N-ethyl-7-fluoro-1-methyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	HATU	419.0
546		4-amino-N-ethyl-1-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	HATU	429.0
547		4-amino-N-ethyl-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)[1,2]oxazolo[4,5-c]quinoline-8-carboxamide	HATU	430.0

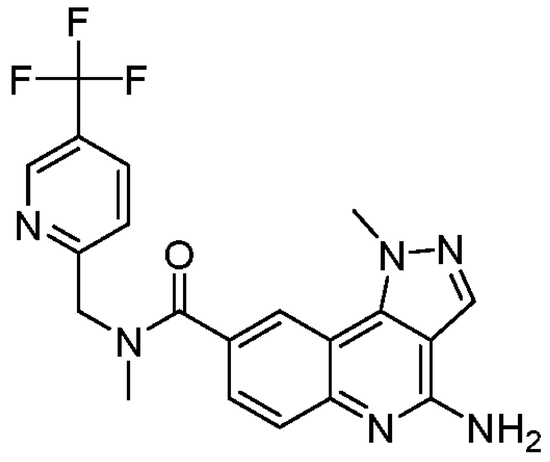
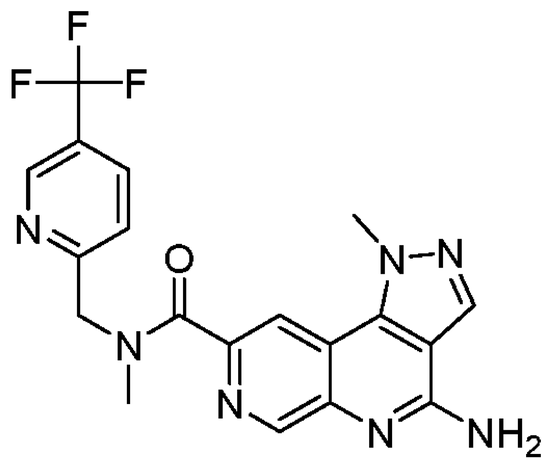
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
548		4-amino-N-ethyl-1-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	HATU	430.0
549		4-amino-N-ethyl-1-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide	HATU	430.0
550		4-amino-N-ethyl-1-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide	HATU	431.0
551		(3R)-4-amino-N-ethyl-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	432.0

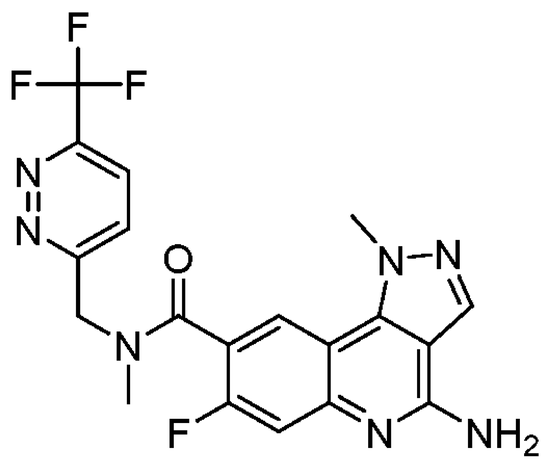
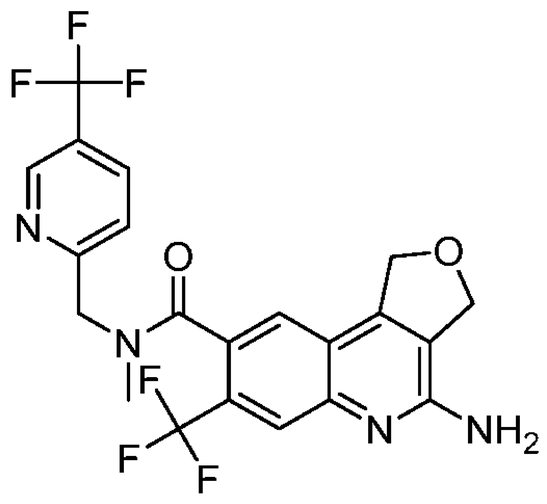
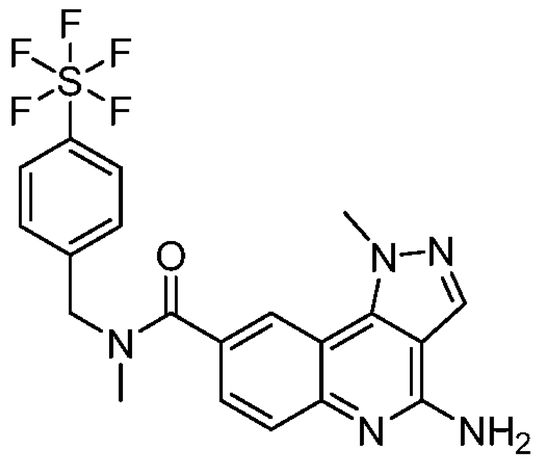
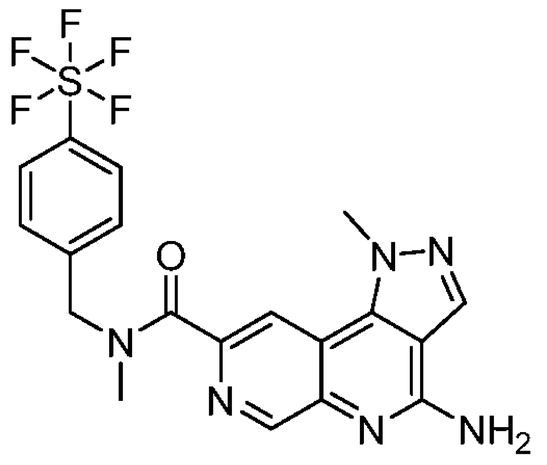
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
552		4-amino-7-fluoro-N,1-dimethyl-N-(4-(trifluoromethyl)benzyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	HATU	432.0
553		4-amino-N-ethyl-1,3-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide	HATU	444.0
554		4-amino-N-ethyl-7-fluoro-1-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	HATU	447.0
555		4-amino-N-ethyl-7-fluoro-1-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	HATU	448.0

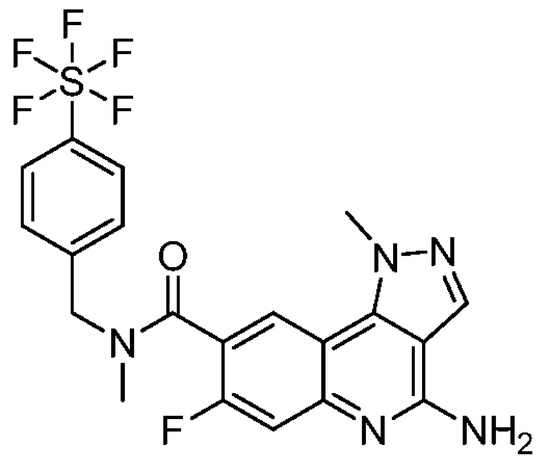
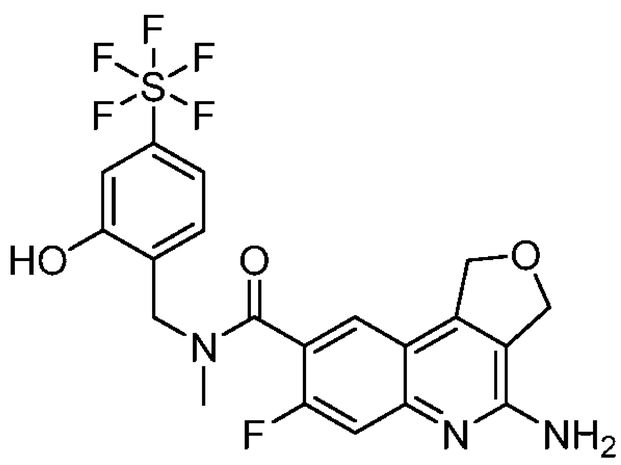
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
556		(3R)-4-amino-N-ethyl-7-fluoro-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	449.0
557		(3S)-4-amino-N-ethyl-7-fluoro-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	449.0
558		4-amino-7-chloro-N,1-dimethyl-N-(4-(trifluoromethyl)benzyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	HATU	448.0
559		(3R)-4-amino-N-ethyl-7-fluoro-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	HATU	450.1

Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
560		4-amino-N-ethyl-7-fluoro-1,3-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	HATU	461.0
561		4-amino-N,1-dimethyl-N-(4-(pentafluoroethyl)benzyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	HATU	464.0
562		4-amino-N,1-dimethyl-N-(4-(pentafluoroethyl)benzyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide	HATU	465.0

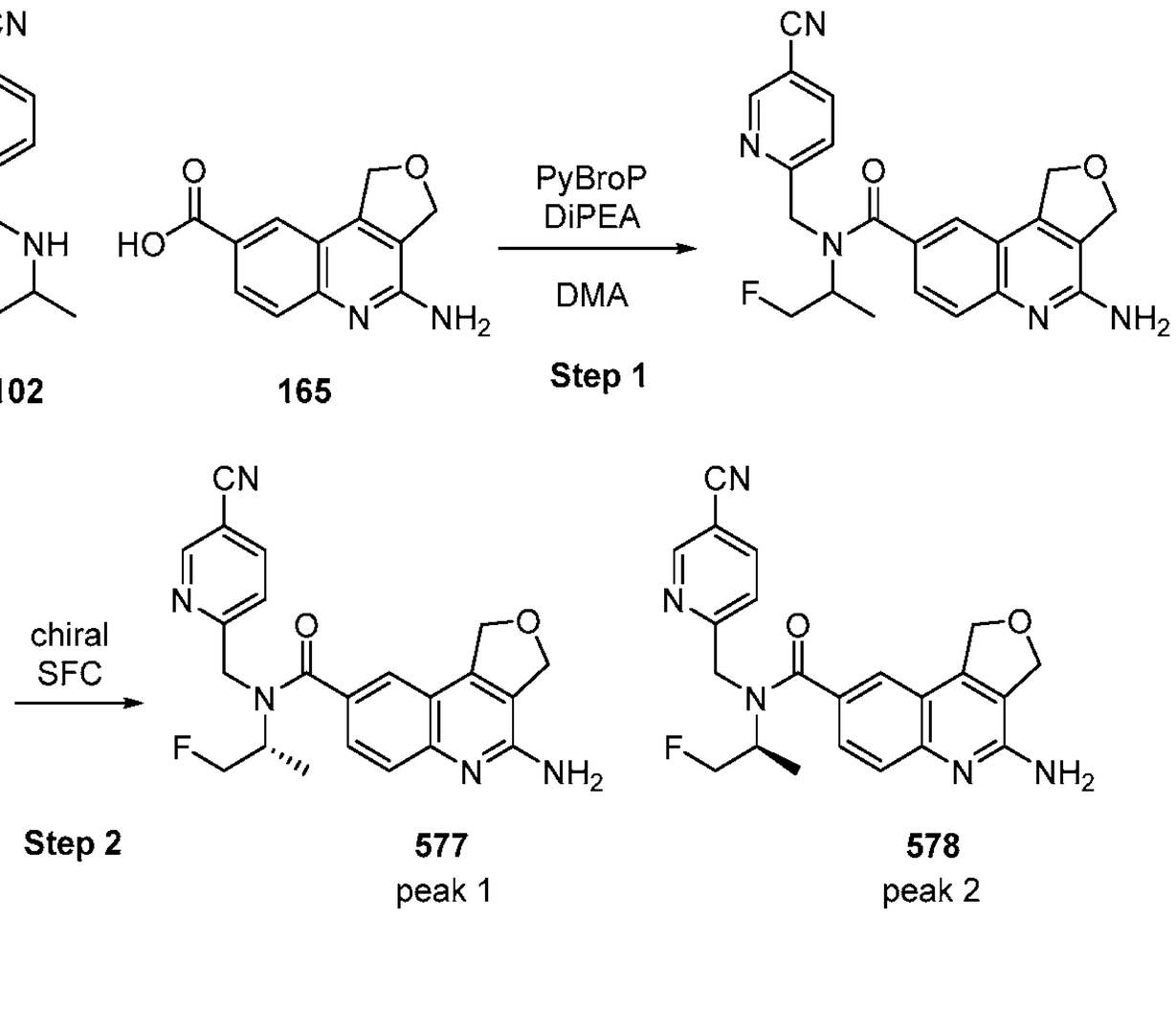
Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
563		4-amino-7-fluoro-N,1-dimethyl-N-(4-(pentafluoroethyl)benzyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	HATU	482.0
564		4-amino-N-ethyl-1-methyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	HATU	486.0
565		4-amino-N-ethyl-1-methyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide	HATU	487.0
566		4-amino-N-ethyl-7-fluoro-1-methyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	HATU	504.0

Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
567		4-amino-N,1-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	TBTU	415.0
568		4-amino-N,1-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide	TBTU	415.9
569		4-amino-N-cyclopropyl-1-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	TBTU	441.2
570		4-amino-N-cyclopropyl-7-fluoro-1-(2,2,2-trifluoroethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	TBTU	527.2

Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
571		4-amino-7-fluoro-N,1-dimethyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	TBTU	433.9
572		4-amino-N-methyl-7-(trifluoromethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	TBTU	471.1
573		4-amino-N,1-dimethyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	TBTU	472.9
574		4-amino-N,1-dimethyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide	TBTU	473.2

Ex.	Structure	Name	Coupling Reagent	m/z (ESI): $(M+H)^+$
575		4-amino-7-fluoro-N,1-dimethyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	TBTU	490.8
576		4-amino-7-fluoro-N-(2-hydroxy-4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	TBTU	494.8

[0250] Example 577 and 578: 4-amino-N-((5-cyanopyridin-2-yl)methyl)-N-(1-fluoropropan-2-yl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide

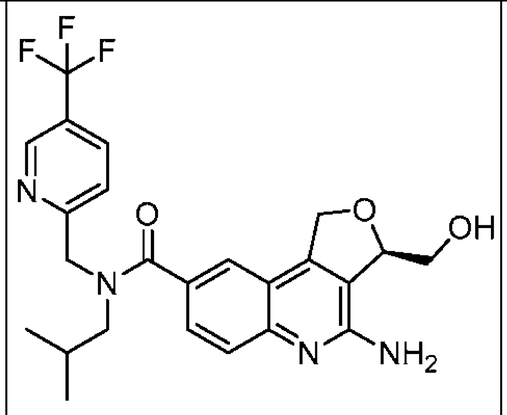
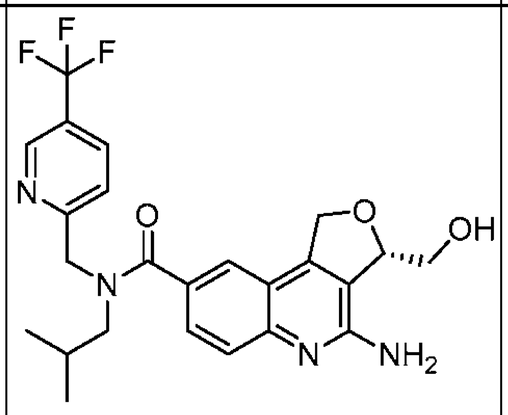
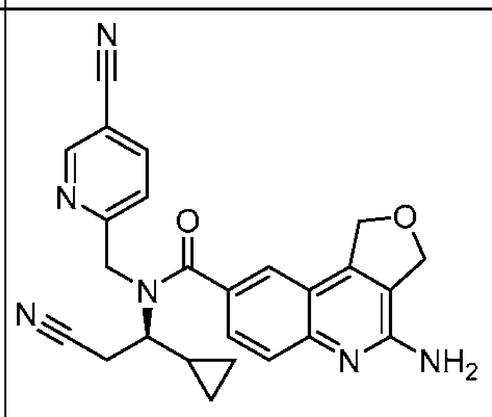
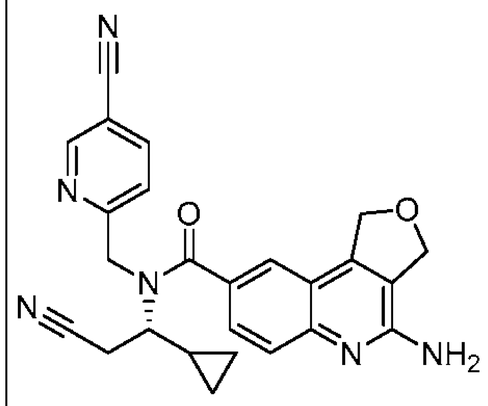


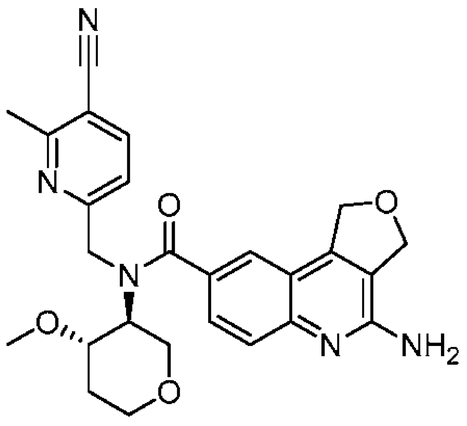
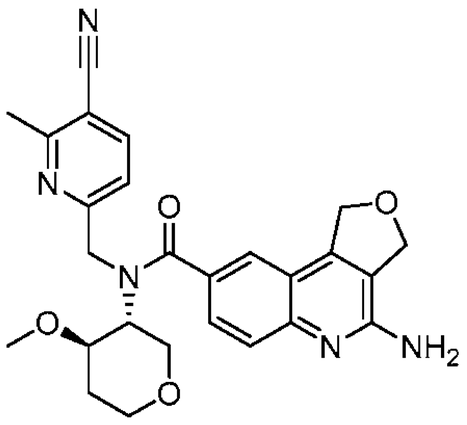
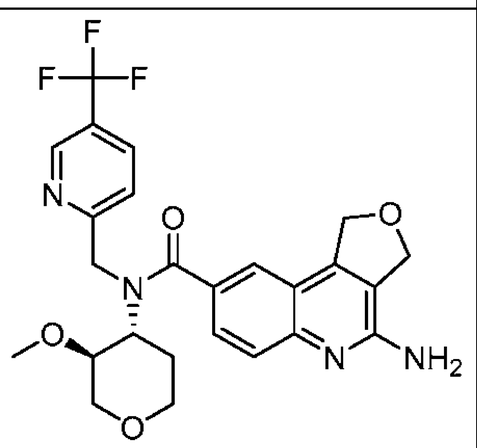
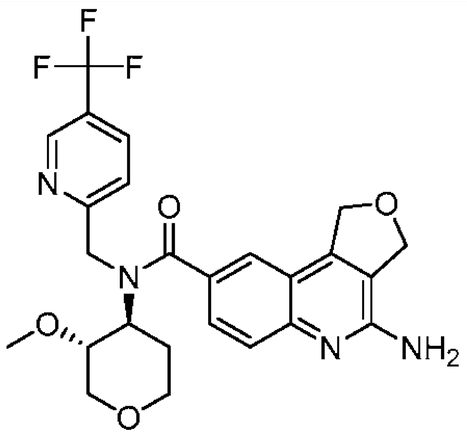
[0251] Step 1. To a stirred mixture of 4-amino-1,3-dihydrofuro[3,4-c]quinoline-8-carboxylic acid (**215,** 131 mg, 0.569 mmol), 6-(((1-fluoropropan-2-yl)amino)methyl)nicotinonitrile (**102,** 100 mg, 0.518 mmol) and bromotri(pyrrolidin-1-yl)phosphonium hexafluorophosphate(V) (483 mg, 1.035 mmol, Aldrich) in DMAC (1.5 mL) was added at rt N-ethyl-N-isopropylpropan-2-amine (201 mg, 0.271 mL, 1.553 mmol, Aldrich). The resulting mixture was briefly sonicated and the stirred at rt for 1 h. The crude mixture was directly loaded onto a silica gel precolumn (25 g) and subjected to combi-flash column chromatography on a 12-g ISCO gold column eluting with MeOH/DCM (15 min from 0% to 18%) (2 X) to give two portions of the desired product. The less pure portion was dissolved in DMSO/methanol/TFA and subjected to preparative reverse-phase HPLC (Gemini™ Prep C18 10 µm column; Phenomenex; gradient elution of 10 to 75% MeCN in water, where both solvents contain 0.1% TFA 15 min in a 24-min method) to give 140 mg of 4-amino-N-((5-cyanopyridin-2-yl)methyl)-N-(1-fluoropropan-2-yl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide 2,2,2-trifluoroacetate as a white solid. *m/z* (ESI): 406.2 $(M+H)^+$. ^{1}H NMR (METHANOL-d4, 400 MHz) δ 8.89 (s, 1H), 8.0-8.3 (m, 1H), 7.4-7.9 (m, 4H), 6.1-6.1 (m, 1H), 5.4-5.6 (m, 2H), 5.1-5.3 (m, 2H), 4.97 (s, 2H), 4.2-4.6 (m, 3H), 1.1-1.5 (m, 3H). ^{19}F NMR (METHANOL-d4, 376 MHz) δ -221.55 (br s, 1F).

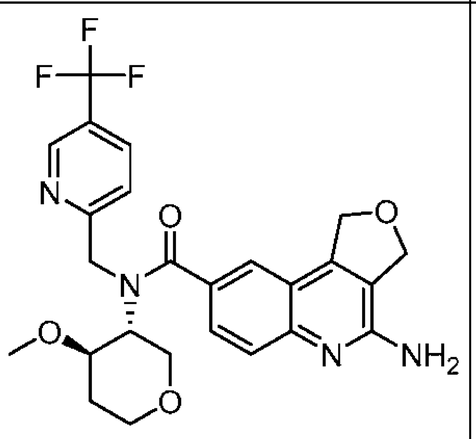
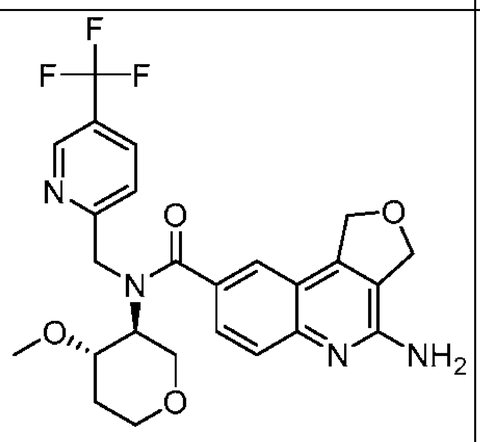
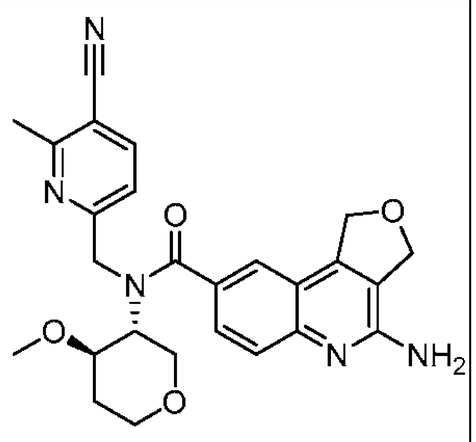
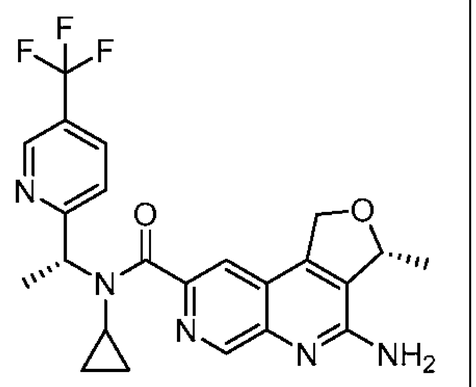
[0252] Step 2. The racemate was purified via preparative SFC using a Chiral Technologies OJ column (250 X 21 mm, 5mm) with a mobile phase of 75% Liquid CO_2 and 25% MeOH with 0.2% TEA using a flowrate of 80 mL/min. The more potent (measured by IC_{50} in HCT116 MTAP null cell viability assay) enantiomer was assigned as the *(R)*-; the less potent (measured by IC_{50} in HCT116 MTAP null cell viability assay) enantiomer was assigned as *(S)*-. The 1st eluting peak was (R)-4-amino-N-((5-cyanopyridin-2-yl)methyl)-N-(1-fluoropropan-2-yl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide (**577**, 54.0 mg, 0.133 mmol, 25.7 % yield). The 2nd eluting peak was (S)-4-amino-N-((5-cyanopyridin-2-yl)methyl)-N-(1-fluoropropan-2-yl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide (**578**, 56.1 mg, 0.138 mmol, 26.7% yield). *m/z* (ESI): 406.2 $(M+H)^+$. ^{1}H NMR (DMSO-d6, 500 MHz) δ 8.99 (d, 1H, J=1.8 Hz), 8.26 (br s, 1H), 7.56 (br s, 4H), 6.67 (br s, 2H), 5.34 (br s, 2H), 5.01 (br s, 2H), 4.7-4.9 (m, 2H), 4.2-4.7 (m, 3H), 3.1-3.3 (m, 1H), 1.15 (br s, 3H).

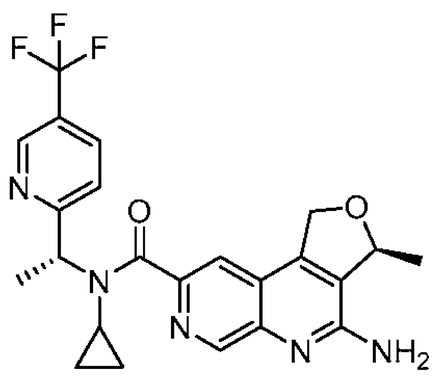
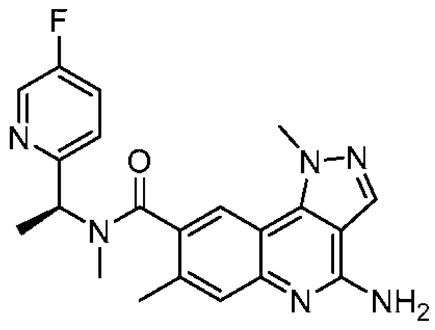
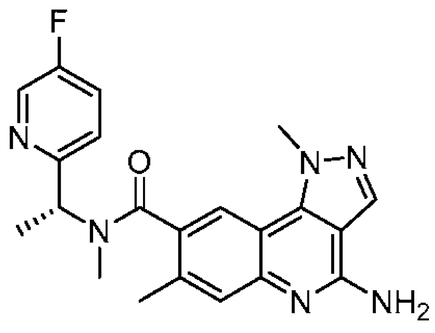
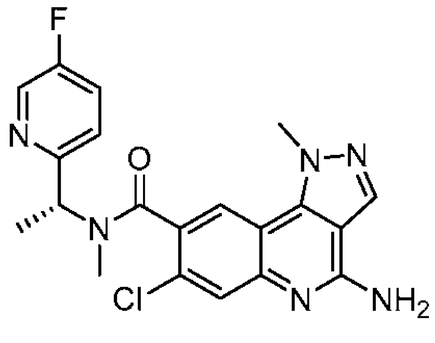
[0253] Compounds in Table 19 were prepared in a manner similar to that described for **577** and **578** utilizing the indicated coupling agent.

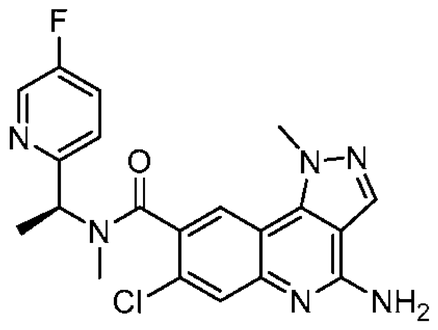
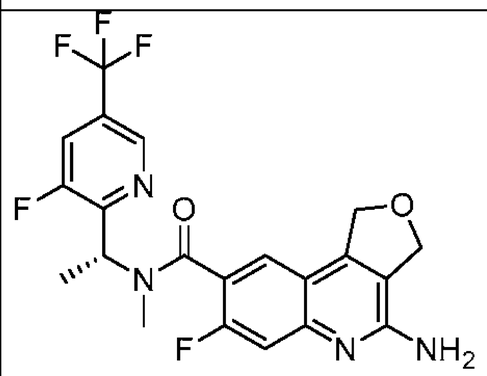
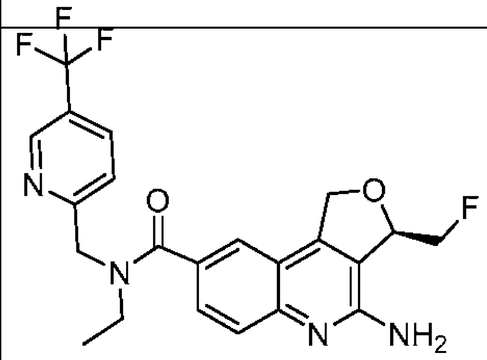
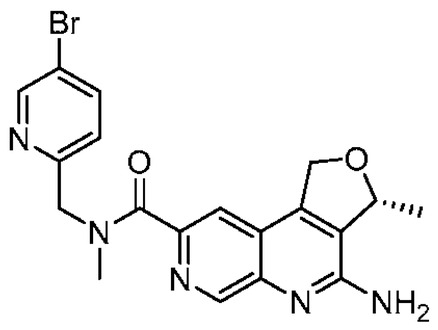
Table 19

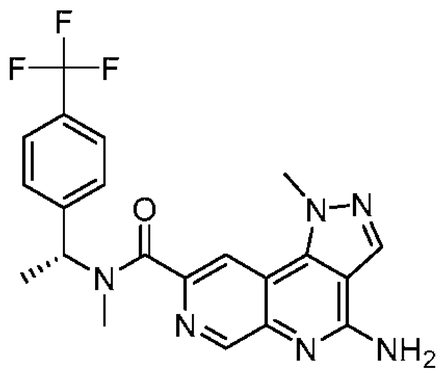
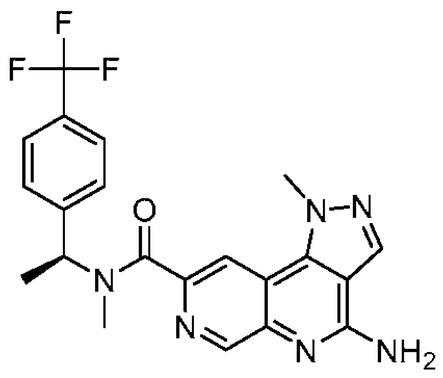
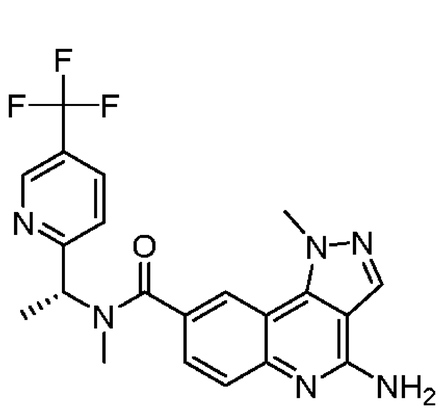
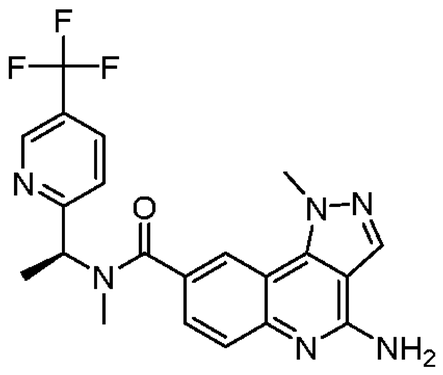
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$	Coupling Reagent	SFC
579		(3R)-4-amino-3-(hydroxymethyl)-N-(2-methylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	475.2	HATU	1st peak, Chiralpak IA column (250 x 21 mm, 5 μm) with a mobile phase of 70% Liquid CO_2 and 30% MeOH with 0.2% DEA using a flowrate of 80 mL/min
580		(3S)-4-amino-3-(hydroxymethyl)-N-(2-methylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	475.2	HATU	2nd peak, Chiralpak IA column (250 x 21 mm, 5 μm) with a mobile phase of 70% Liquid CO_2 and 30% MeOH with 0.2% DEA using a flowrate of 80 mL/min
581		4-amino-N-((1R)-2-cyano-1-cyclopropylethyl)-N-((5-cyano-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	439.1	PyBroP	1st peak, Chiral Tech AS Column (250x21 mm, 5mm) with a mobile phase of 85% liquid CO_2 & 15% MeOH with 0.2% TEA using a flowrate of 80 mL/min
582		4-amino-N-((1S)-2-cyano-1-cyclopropylethyl)-N-((5-cyano-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	439.1	PyBroP	2nd peak, Chiral Tech AS Column (250x21 mm, 5mm) with a mobile phase of 85% liquid CO_2 & 15% MeOH with 0.2% TEA using a flowrate of 80 mL/min

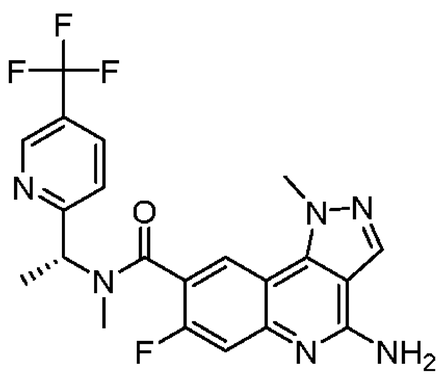
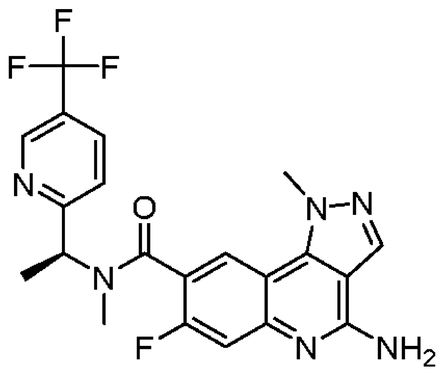
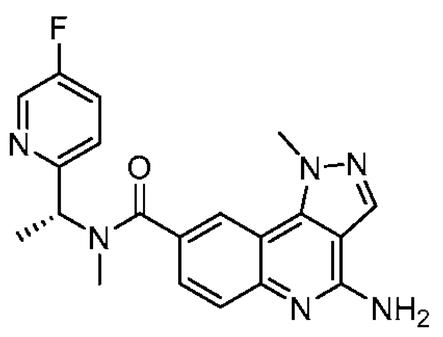
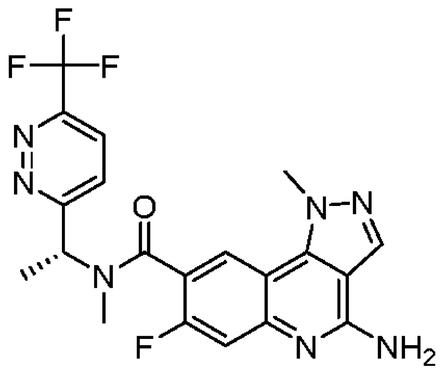
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$	Coupling Reagent	SFC
583	 	4-amino-N-((5-cyano-6-methyl-2-pyridinyl)methyl)-N-((3R,4R)-4-methoxytetrahydro-2H-pyran-3-yl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide and 4-amino-N-((5-cyano-6-methyl-2-pyridinyl)methyl)-N-((3S,4S)-4-methoxytetrahydro-2H-pyran-3-yl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	474.2	PyBroP	2nd peak, Chiral Technologies AS column (250 X 21 mm, 5mm) with a mobile phase of 80% Liquid CO_2 and 20% MeOH with 0.2% TEA using a flowrate of 80 mL/min
584		4-amino-N-((3S,4R)-3-methoxytetrahydro-2H-pyran-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	503.2	PyBroP	1st peak, Chiral Technologies AS column (250 X 21 mm, 5mm) with a mobile phase of 90% Liquid CO_2 and 10% MeOH with 0.2% TEA using a flowrate of 100 mL/min
585		4-amino-N-((3R,4S)-3-methoxytetrahydro-2H-pyran-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	503.2	PyBroP	2nd peak, Chiral Technologies AS column (250 X 21 mm, 5mm) with a mobile phase of 90% Liquid CO_2 and 10% MeOH with 0.2% TEA using a flowrate of 100 mL/min

Ex.	Structure	Name	m/z (ESI): $(M+H)^+$	Coupling Reagent	SFC
586		4-amino-N-((3R,4R)-4-methoxytetrahydro-2H-pyran-3-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	503.2	PyBroP	1st peak, Chiral Technologies AS column (250 X 21 mm, 5mm) with a mobile phase of 90% Liquid CO_2 and 10% MeOH with 0.2% TEA using a flowrate of 100 mL/min
587		4-amino-N-((3S,4S)-4-methoxytetrahydro-2H-pyran-3-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	503.2	PyBroP	2nd peak, Chiral Technologies AS column (250 X 21 mm, 5mm) with a mobile phase of 90% Liquid CO_2 and 10% MeOH with 0.2% TEA using a flowrate of 100 mL/min
588		4-amino-N-((5-cyano-6-methyl-2-pyridinyl)methyl)-N-((3R,4R)-4-methoxytetrahydro-2H-pyran-3-yl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	474.2	PyBroP	1st peak, Chiral Technologies AS column (250 X 21 mm, 5mm) with a mobile phase of 80% Liquid CO_2 and 20% MeOH with 0.2% TEA using a flowrate of 80 mL/min
589		(3R)-4-amino-N-cyclopropyl-3-methyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	458	PyBroP	1st peak, Chiralpak OD column (250 X 21 mm, 5um) with a mobile phase of 85% Liquid CO_2 and 15% MeOH+TEA using a flowrate of 70 mL/min

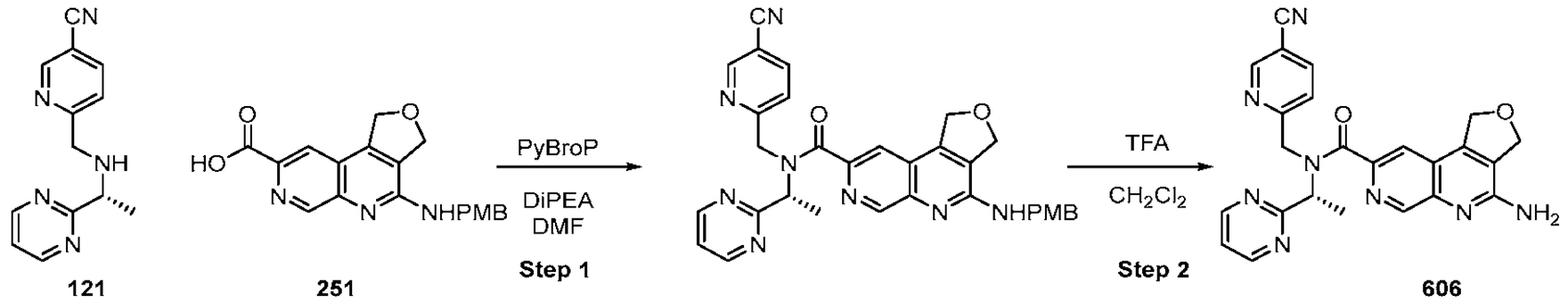
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$	Coupling Reagent	SFC
590		(3S)-4-amino-N-cyclopropyl-3-methyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	458	PyBroP	2nd peak, Chiralpak OD column (250 X 21 mm, 5um) with a mobile phase of 85% Liquid CO_2 and 15% MeOH+TEA using a flowrate of 70 mL/min
591		4-amino-N-((1S)-1-(5-fluoro-2-pyridinyl)ethyl)-N,1,7-trimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	393.2	TBTU	2nd peak, Chiralcel OD column (2 x 25 cm, 5 micron) with a mobile phase of 80% Liquid CO_2 and 20% methanol, using a flowrate of 70 mL/min
592		4-amino-N-((1R)-1-(5-fluoro-2-pyridinyl)ethyl)-N,1,7-trimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	393.2	TBTU	1st peak, Chiralcel OD column (2 x 25 cm, 5 micron) with a mobile phase of 80% Liquid CO_2 and 20% methanol, using a flowrate of 70 mL/min
593		4-amino-7-chloro-N-((1R)-1-(5-fluoro-2-pyridinyl)ethyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	413.9	TBTU	1st peak, Chiralpak AD (3 x 25 cm, 5 micron) with a mobile phase of 65% Liquid CO_2 and 35% isopropanol w/ 0.1% diethylamine, using a flowrate of 70 mL/min

Ex.	Structure	Name	m/z (ESI): $(M+H)^+$	Coupling Reagent	SFC
594		4-amino-7-chloro-N-((1S)-1-(5-fluoro-2-pyridinyl)ethyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	413.9	TBTU	2nd peak, Chiralpak AD (3 x 25 cm, 5 micron) with a mobile phase of 65% Liquid CO_2 and 35% isopropanol w/ 0.1% diethylamine, using a flowrate of 70 mL/min
595		4-amino-7-fluoro-N-((1R)-1-(3-fluoro-5-(trifluoromethyl)-2-pyridinyl)ethyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	453.2	TBTU	1st peak, Chiralpak AD column (2 x 15 cm, 5 micron) with a mobile phase of 60% Liquid CO_2 and 40% methanol, using a flowrate of 50 mL/min
596		(3R)-4-amino-N-ethyl-3-(fluoromethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	449.2	HATU	1st peak, Chiralcel OJ column (2 x 25 cm, 5 micron) with a mobile phase of 90% Liquid CO_2 and 10% methanol w/ 0.1% diethylamine using a flowrate of 60 mL/min
597		(3R)-4-amino-N-((5-bromo-2-pyridinyl)methyl)-N,3-dimethyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	428.0, 430.0	HATU	2nd peak, Chiral Technologies AS column (250 X 21 mm, 5mm) with a mobile phase of 80% Liquid CO_2 and 20% MeOH with 0.2% TEA using a flowrate of 80 mL/min.

Ex.	Structure	Name	m/z (ESI): $(M+H)^+$	Coupling Reagent	SFC
598		4-amino-N,1-dimethyl-N-((1R)-1-(4-(trifluoromethyl)phenyl)ethyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide	429.2	TBTU	1st peak, Chiralcel OD column (2 x 25 cm, 5 micron) with a mobile phase of 80% Liquid CO_2 and 20% methanol w/ 0.1% diethylamine using a flowrate of 50 mL/min
599		4-amino-N,1-dimethyl-N-((1S)-1-(4-(trifluoromethyl)phenyl)ethyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide	429.2	TBTU	2nd peak, Chiralcel OD column (2 x 25 cm, 5 micron) with a mobile phase of 80% Liquid CO_2 and 20% methanol w/ 0.1% diethylamine using a flowrate of 50 mL/min
600		4-amino-N,1-dimethyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	429. 2	TBTU	1st peak, (S,S) Whelk-O column (2 x 25 cm, 5 micron) with a mobile phase of 70% Liquid CO_2 and 30% methanol w/ 0.1% diethylamine using a flowrate of 60 mL/min
601		4-amino-N,1-dimethyl-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	429. 2	TBTU	2nd peak, (S,S) Whelk-O column (2 x 25 cm, 5 micron) with a mobile phase of 70% Liquid CO_2 and 30% methanol w/ 0.1% diethylamine using a flowrate of 60 mL/min

Ex.	Structure	Name	m/z (ESI): $(M+H)^+$	Coupling Reagent	SFC
602		4-amino-7-fluoro-N,1-dimethyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	447.2	TBTU	1st peak, (S,S) Whelk-O column (2 x 25 cm, 5 micron) with a mobile phase of 65% Liquid CO_2 and 35% methanol w/ 0.1% diethylamine using a flowrate of 60 mL/min
603		4-amino-7-fluoro-N,1-dimethyl-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	447.2	TBTU	2nd peak, (S,S) Whelk-O column (2 x 25 cm, 5 micron) with a mobile phase of 65% Liquid CO_2 and 35% methanol w/ 0.1% diethylamine using a flowrate of 60 mL/min
604		4-amino-N-((1R)-1-(5-fluoro-2-pyridinyl)ethyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	379.2	TBTU	1st peak, Chiralpak AS column (2 x 25 cm, 5 micron) with a mobile phase of 80% Liquid CO_2 and 20% isopropanol w/ 0.1% deithylamine using a flowrate of 60mL/min
605		4-amino-7-fluoro-N,1-dimethyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	447.9	TBTU	1st peak, Regis (S,S) Whelk-01 column (250 X 21 mm, 5mm) with a mobile phase of 60% Liquid CO_2 and 40% MeOH with 0.2% TEA using a flowrate of 70 mL/min

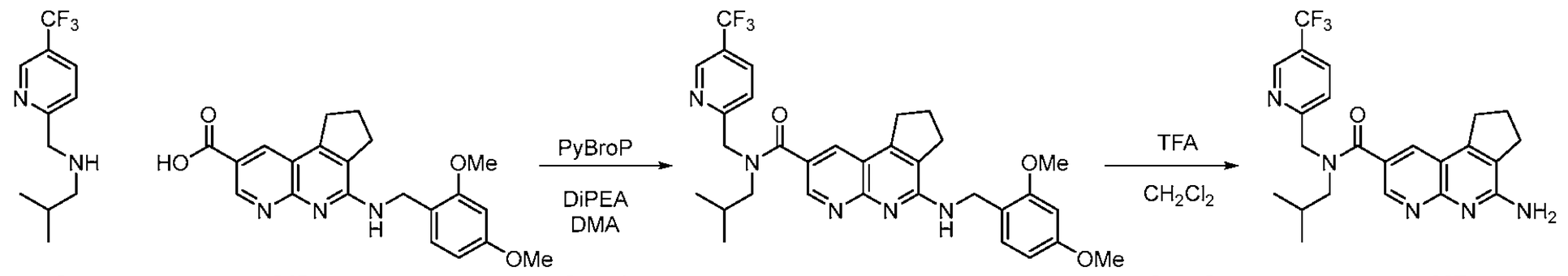
[0254] Example 606: (R)-4-amino-N-((5-cyanopyridin-2-yl)methyl)-N-(1-(pyrimidin-2-yl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide.



[0255] Step 1. To a solution of (R)-6-(((1-(pyrimidin-2-yl)ethyl)amino)methyl)nicotinonitrile (**121,** 0.118 g, 0.495 mmol), 4-((4-methoxybenzyl)amino)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxylic acid hydrochloride (**251,** 0.160 g, 0.413 mmol) and 1,1'-dimethyltriethylamine (0.533 g, 0.721 mL, 4.13 mmol, Sigma-Aldrich Corporation) in DMF (5 mL) was added bromotripyrrolidinophosphonium hexafluorophosphate (0.192 g, 0.413 mmol, Sigma-Aldrich Corporation) and the resulting mixture was heated at 50°C for 1 h. The reaction was brought to rt, diluted with water and sat.$NaHCO_3$, and extracted with EtOAc (3x). The combined organics were dried over Na_2SO_4, filtered and concentrated. The crude residue was diluted in toluene (3 mL) and concentrated (3x). The residue was then chromatographed on silica gel using 0-50% 3:1 EtOAc/EtOH in heptane to afford (R)-N-((5-cyanopyridin-2-yl)methyl)-4-((4-methoxybenzyl)amino)-N-(1-(pyrimidin-2-yl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide (0.112 g, 0.196 mmol, 47.4% yield) as a pale yellow solid. *m/z* (ESI): 573.2 $(M+H)^+$.

[0256] Step 2. To a solution of (R)-N-((5-cyanopyridin-2-yl)methyl)-4-((4-methoxybenzyl)amino)-N-(1-(pyrimidin-2-yl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide (0.112 g, 0.196 mmol, 47.4 % yield) in DCM (2 mL) was added TFA (22.20 g, 15 mL, 195 mmol, Aldrich) and the resulting mixture was stirred at 70°C for 24 h. The reaction was washed with 10% Na_2CO_3 and extracted with DCM. The combined organics were concentrated and chromatographed on silica gel using 0-50% 3:1 EtOAc/EtOH in heptane and repurified by HPLC to afford (R)-4-amino-N-((5-cyanopyridin-2-yl)methyl)-N-(1-(pyrimidin-2-yl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide as an off-white solid (**606,** 0.070 g, 0.155 mmol, 78.9% yield). *m/z* (ESI): 453.2 $(M+H)^+$. 1H NMR (400 MHz, DMSO-d6) δ ppm 8.58 - 8.93 (m, 4 H), 8.24 (dd, J=8.3, 2.1 Hz, 1 H), 7.80 (s, 1 H), 7.31 - 7.54 (m, 2 H), 6.97 - 7.12 (m, 2 H), 5.78 - 5.88 (m, 1 H), 5.18 - 5.44 (m, 2 H), 4.96 - 5.09 (m, 3 H), 4.55 (d, J=17.2 Hz, 1 H), 1.54 - 1.72 (m, 3 H).

[0257] Example 607: 6-amino-N-isobutyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-8,9-dihydro-7H-cyclopenta[c][1,8]naphthyridine-2-carboxamide.



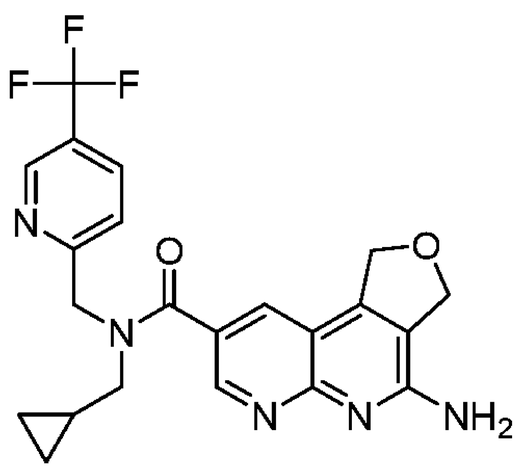
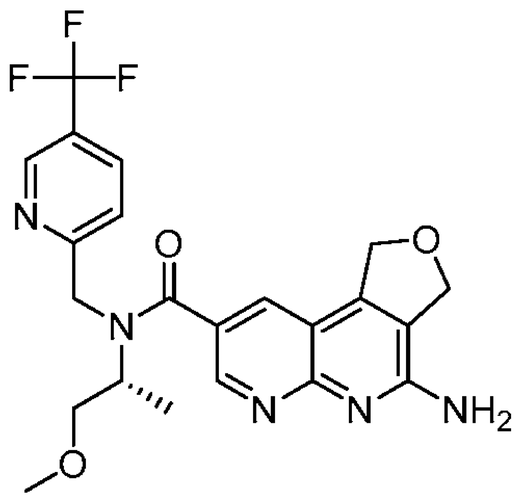
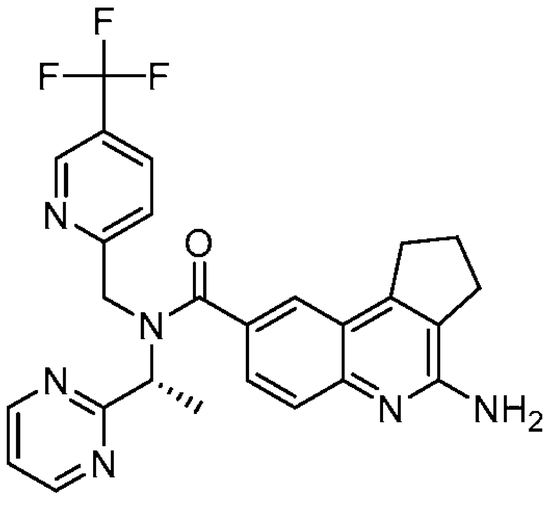
2 245 Step 1 Step 2 607

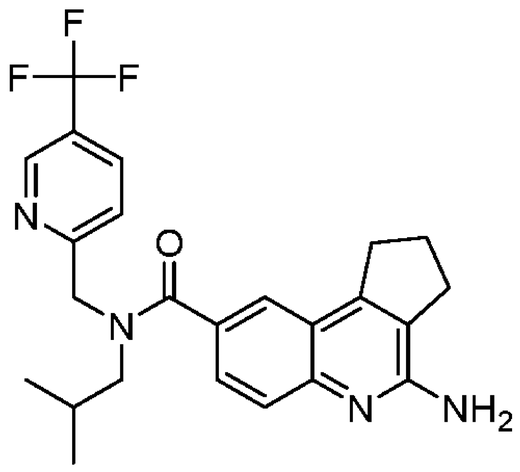
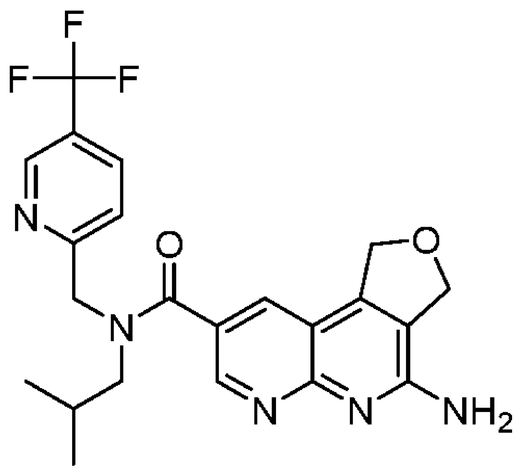
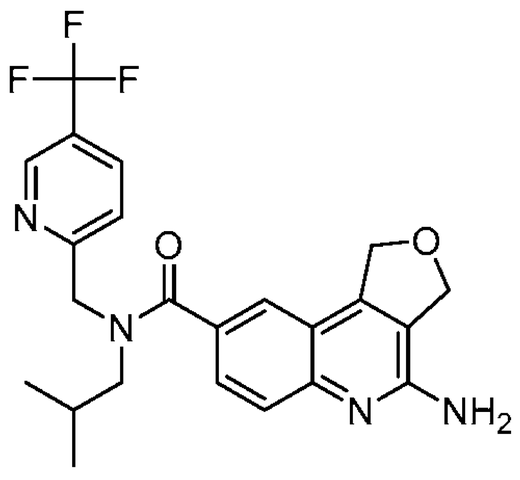
[0258] Step 1. To a solution of 2-methyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)propan-1-amine (**2,** 0.101 g, 0.435 mmol), 6-((2,4-dimethoxybenzyl)amino)-8,9-dihydro-7H-cyclopenta[c][1,8]naphthyridine-2-carboxylic acid hydrochloride (**245,** 0.217 g, 0.522 mmol) and 1,1'-dimethyltriethylamine (0.562 g, 0.760 mL, 4.35 mmol, Sigma-Aldrich Corporation) in DMA (4 mL) was added bromotripyrrolidinophosphonium hexafluorophosphate (0.203 g, 0.435 mmol, Sigma-Aldrich Corporation) and the resulting mixture was heated at 60°C for 1 h. The reaction was brought to rt, diluted with water, sat. $NaHCO_3$ and extracted with EtOAc (3x). The combined organics were dried over Na_2SO_4, filtered, and concentrated. The residue was then chromatographed on silica gel using 0-40% 3:1 EtOAc/EtOH in heptane to afford 6-((2,4-dimethoxybenzyl)amino)-N-isobutyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-8,9-dihydro-7H-cyclopenta[c][1,8]naphthyridine-2-carboxamide as a light yellow oil. *m/z* (ESI): 594.2 $(M+H)^+$.

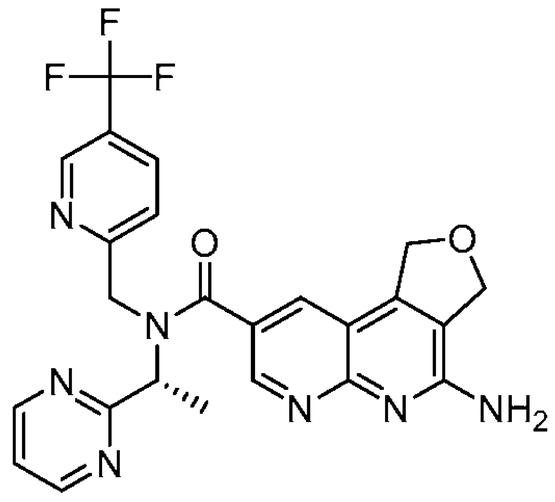
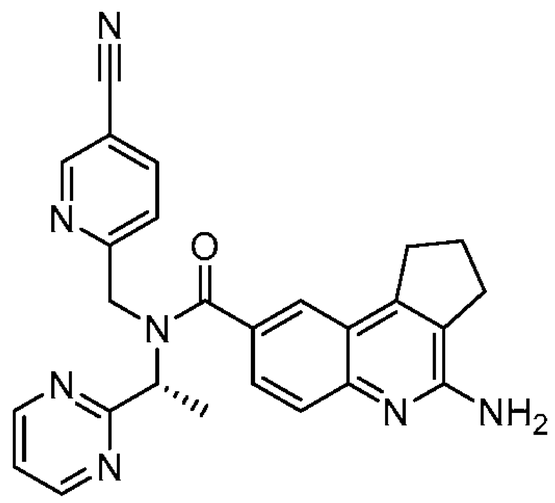
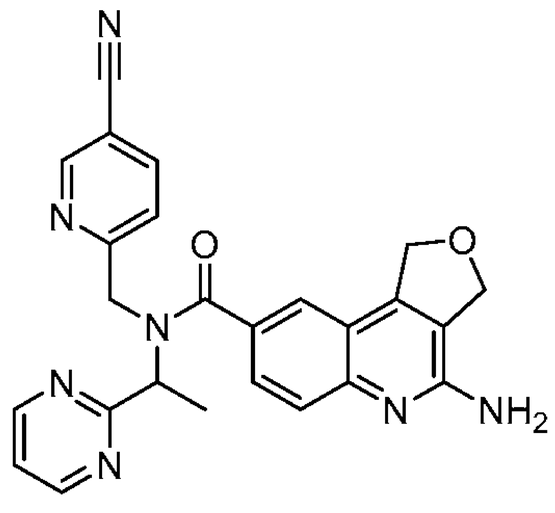
[0259] Step 2. To a solution of 6-((2,4-dimethoxybenzyl)amino)-N-isobutyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-8,9-dihydro-7H-cyclopenta[c][1,8]naphthyridine-2-carboxamide in DCM (2 mL) was added TFA (14.80 g, 10 mL, 130 mmol, Aldrich) and the resulting mixture was heated at 50°C for 1h. The reaction was concentrated, washed with 10% Na_2CO_3 and extracted with DCM. The combined organics were concentrated and chromatographed on silica gel using 0-60% 3:1 EtOAc/EtOH in heptane to afford 6-amino-N-isobutyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-8,9-dihydro-7H-cyclopenta[c][1,8]naphthyridine-2-carboxamide (**607,** 0.035 g, 0.079 mmol, 18.15 % yield) as a white solid. *m/z* (ESI): 444.2 $(M+H)^+$. ^1H NMR (400 MHz, DMSO-d6) δ ppm 8.98 (s, 1 H), 8.62 - 8.74 (m, 1 H), 8.13 - 8.27 (m, 1 H), 7.86 - 8.11 (m, 1 H), 7.48 (br s, 1 H), 6.58 - 7.06 (m, 2 H), 4.62 - 5.04 (m, 3 H), 2.90 - 3.23 (m, 2 H), 2.82 (br d, J=5.2 Hz, 2 H), 2.10 - 2.28 (m, 2 H), 1.83 - 2.12 (m, 1 H), 0.65 - 1.01 (m, 7 H).

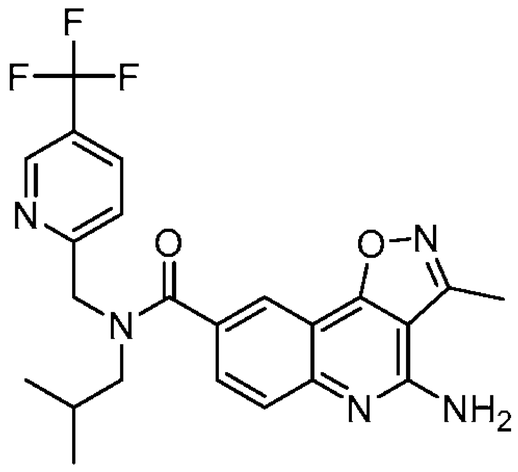
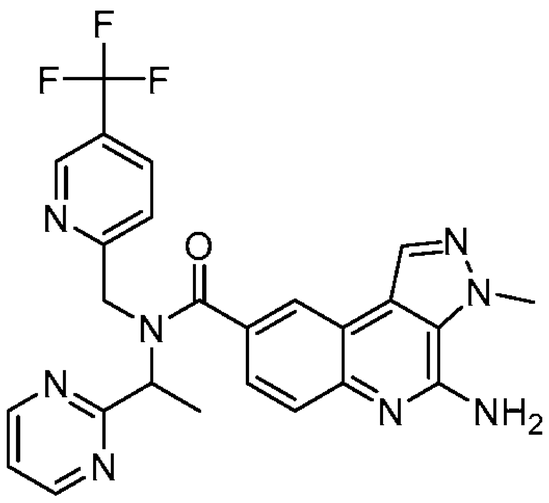
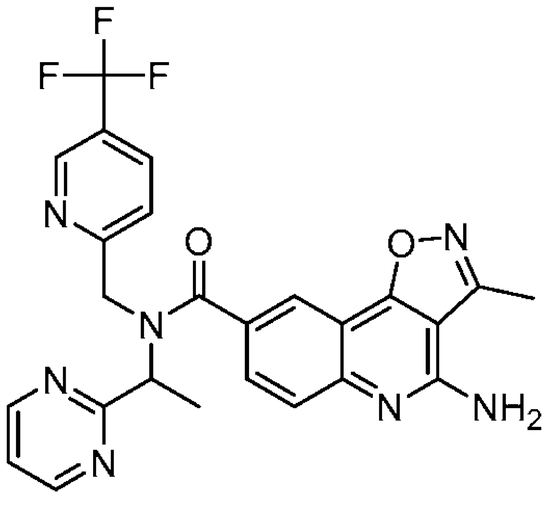
[0260] Compounds in Table 20 were prepared in a manner similar to that described above for examples 606 and 607.

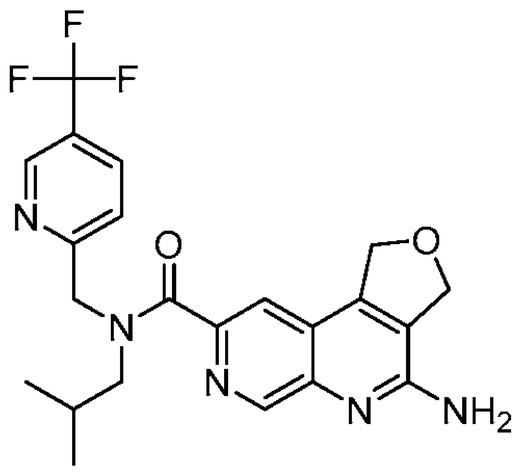
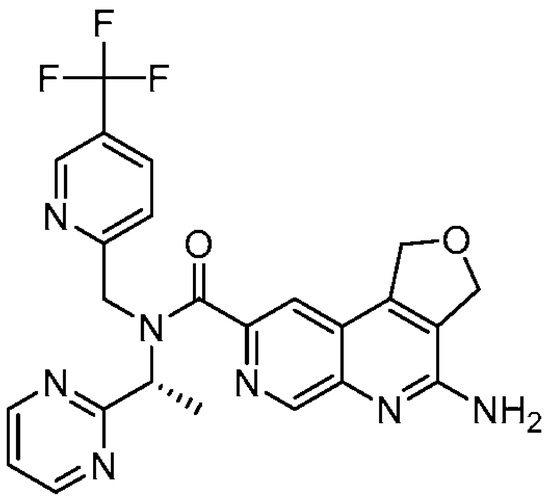
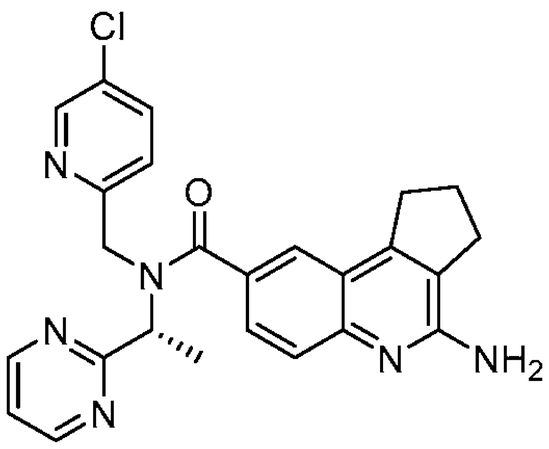
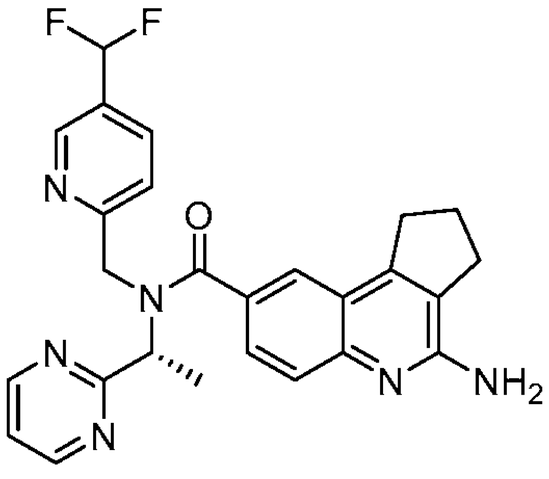
Table 20

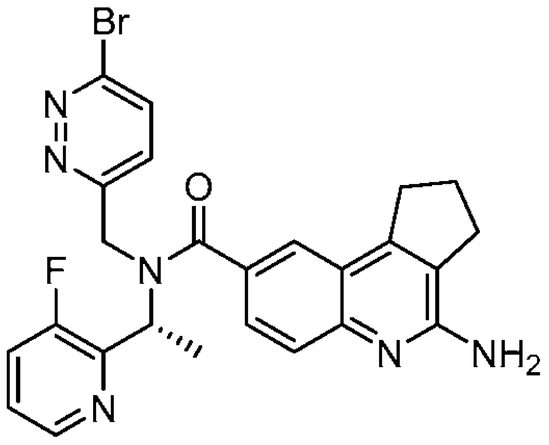
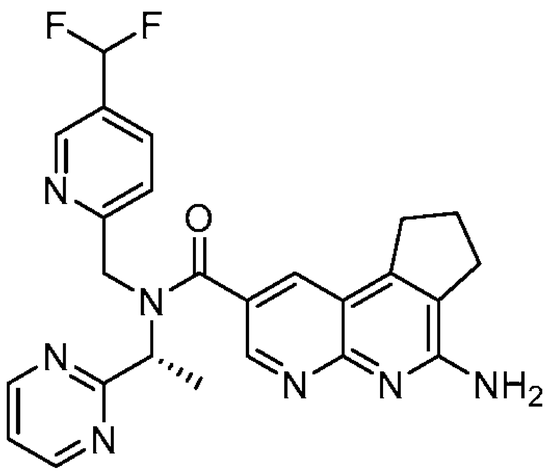
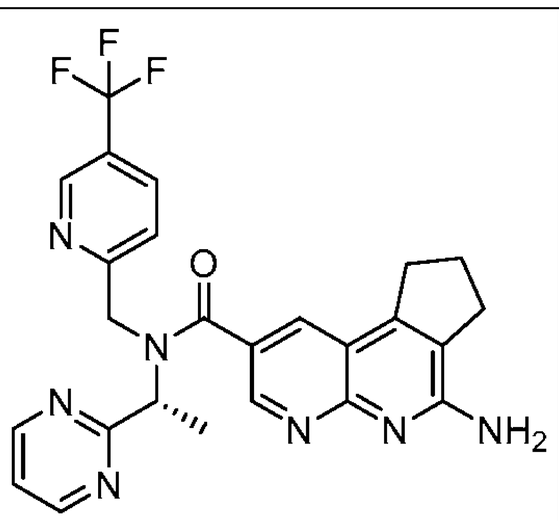
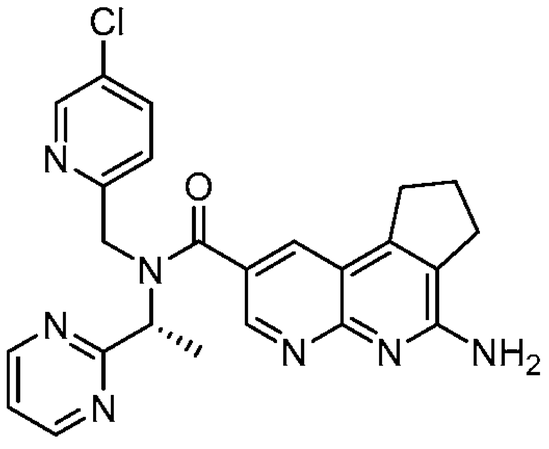
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
608		4-amino-N-(cyclopropylmethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide	444.2
609		4-amino-N-((2R)-1-methoxy-2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide	462.2
610		4-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-2,3-dihydro-1H-cyclopenta[c]quinoline-8-carboxamide	493.0

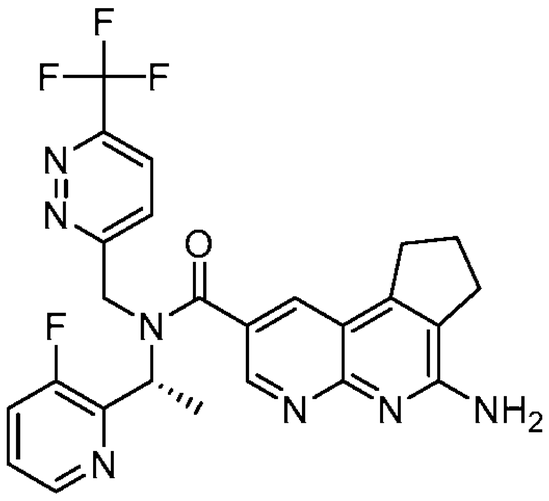
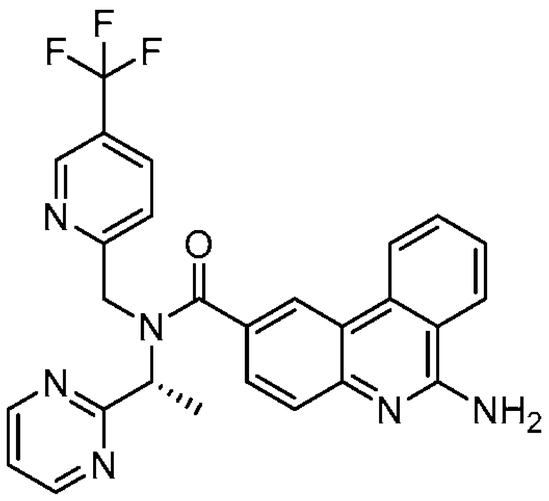
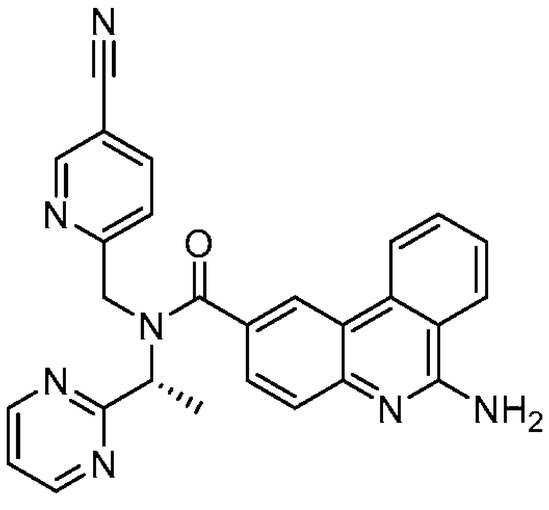
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
611		4-amino-N-(2-methylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-2,3-dihydro-1H-cyclopenta[c]quinoline-8-carboxamide	443.0
612		4-amino-N-(2-methylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide	446.0
613		4-amino-N-(2-methylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	445.3

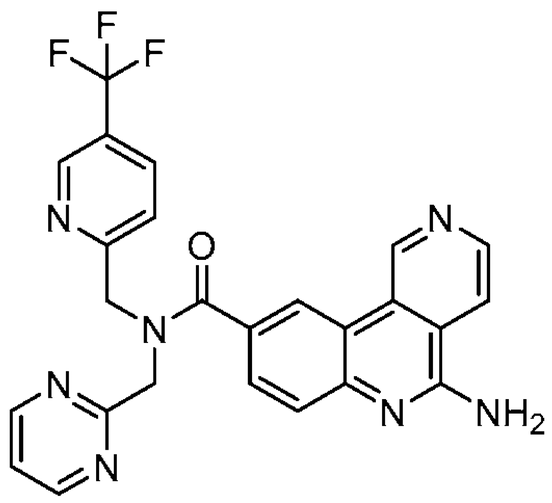
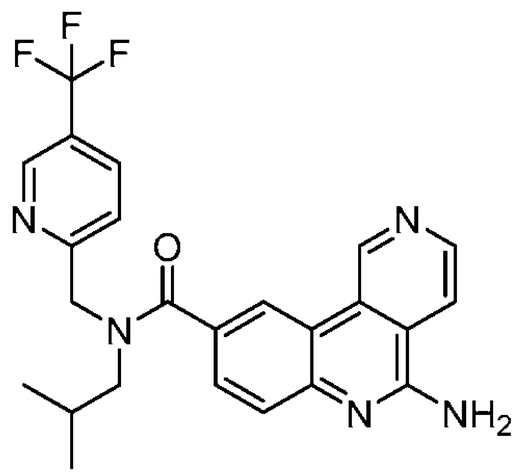
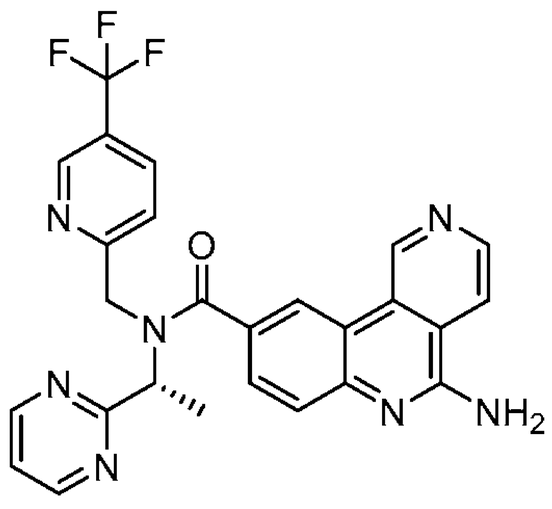
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
614		4-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide	496.0
615		4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-2,3-dihydro-1H-cyclopenta[c]quinoline-8-carboxamide	450.0
616		4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide and 4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((1S)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	452.2

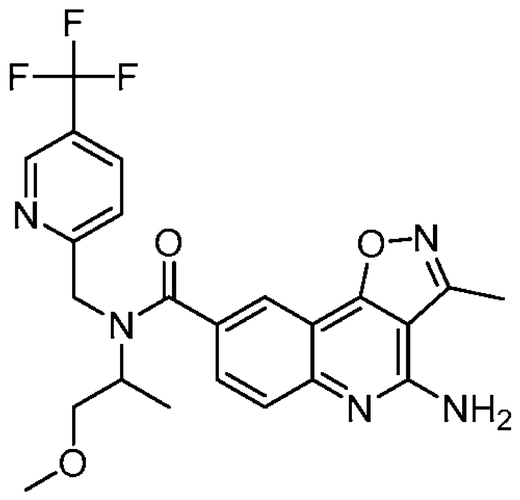
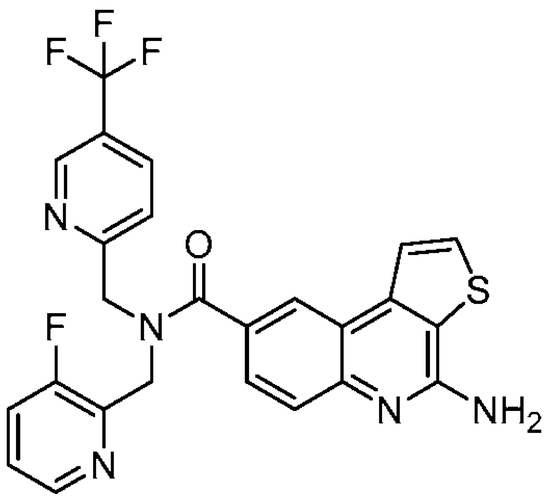
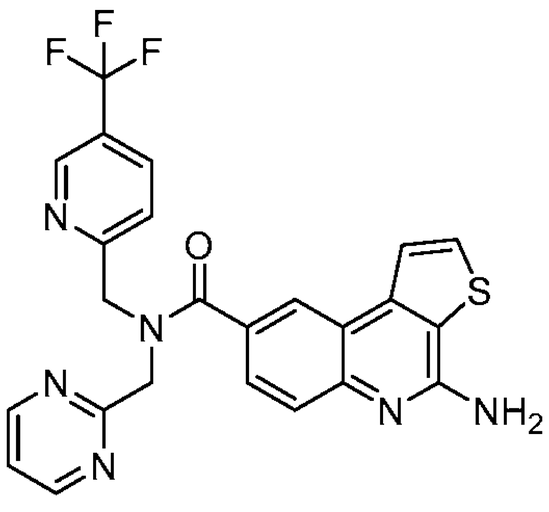
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
617		4-amino-3-methyl-N-(2-methylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)[1,2]oxazolo[4,5-c]quinoline-8-carboxamide	458.1
618		4-amino-3-methyl-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide and 4-amino-3-methyl-N-((1S)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide	507.2
619		4-amino-3-methyl-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)[1,2]oxazolo[4,5-c]quinoline-8-carboxamide and 4-amino-3-methyl-N-((1S)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)[1,2]oxazolo[4,5-c]quinoline-8-carboxamide	508.2

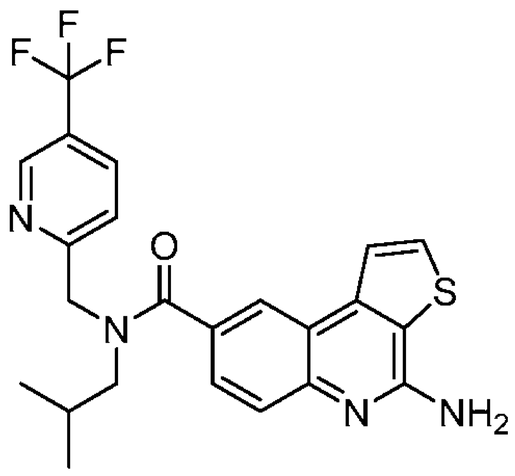
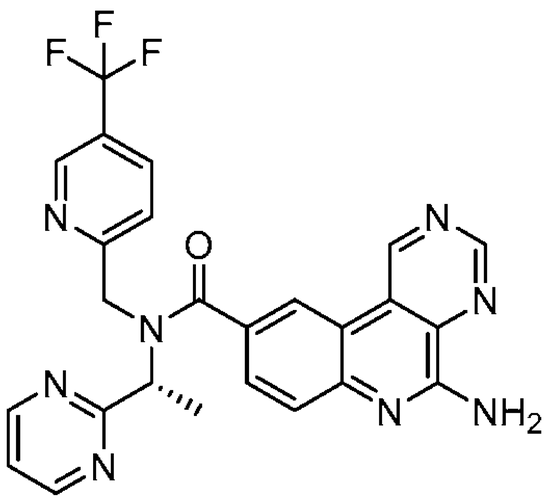
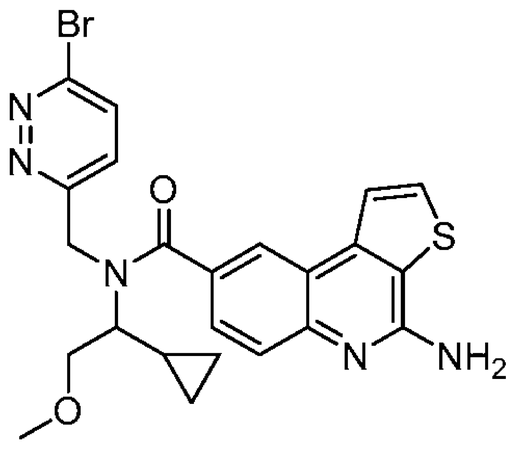
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
620		4-amino-N-(2-methylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	446.0
621		4-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	496.0
622		4-amino-N-((5-chloro-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-2,3-dihydro-1H-cyclopenta[c]quinoline-8-carboxamide	459.0
623		4-amino-N-((5-(difluoromethyl)-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-2,3-dihydro-1H-cyclopenta[c]quinoline-8-carboxamide	475.0

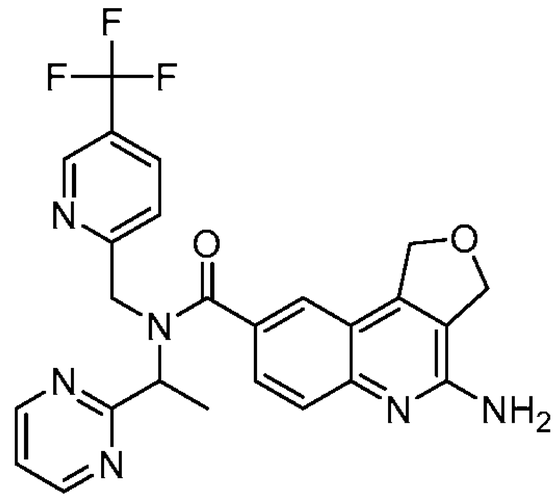
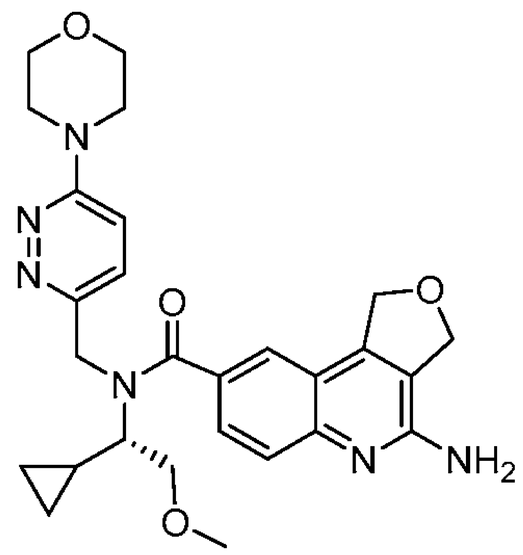
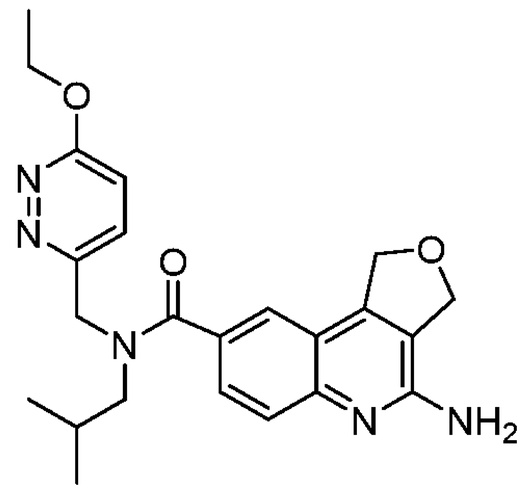
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
624		4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((1R)-1-(3-fluoro-2-pyridinyl)ethyl)-2,3-dihydro-1H-cyclopenta[c]quinoline-8-carboxamide	521.0
625		6-amino-N-((5-(difluoromethyl)-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-8,9-dihydro-7H-cyclopenta[c][1,8]naphthyridine-2-carboxamide	476.0
626		6-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-8,9-dihydro-7H-cyclopenta[c][1,8]naphthyridine-2-carboxamide	494.0
627		6-amino-N-((5-chloro-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-8,9-dihydro-7H-cyclopenta[c][1,8]naphthyridine-2-carboxamide	460.0

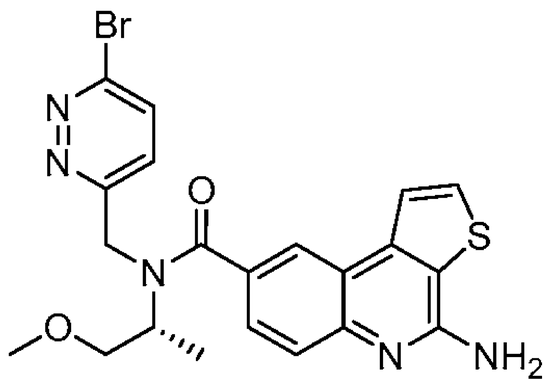
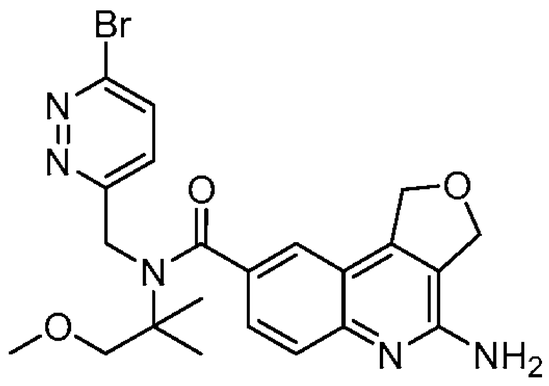
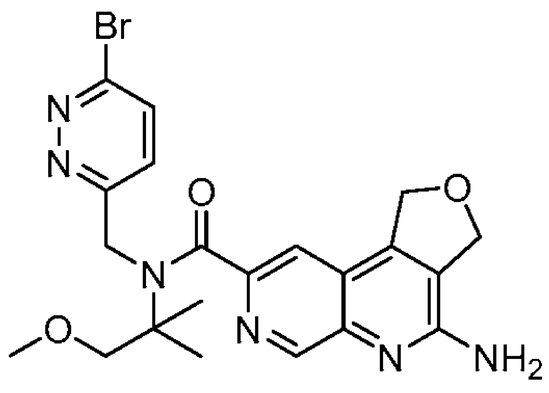
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
628		6-amino-N-((1R)-1-(3-fluoro-2-pyridinyl)ethyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-8,9-dihydro-7H-cyclopenta[c][1,8]naphthyridine-2-carboxamide	512.0
629		6-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-2-phenanthridinecarboxamide	503.0
630		6-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-2-phenanthridinecarboxamide	460.0

Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
631		5-amino-N-(2-pyrimidinylmethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)benzo[c][2,6]naphthyridine-9-carboxamide	490.0
632		5-amino-N-(2-methylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)benzo[c][2,6]naphthyridine-9-carboxamide	454.0
633		5-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)benzo[c][2,6]naphthyridine-9-carboxamide	504.0

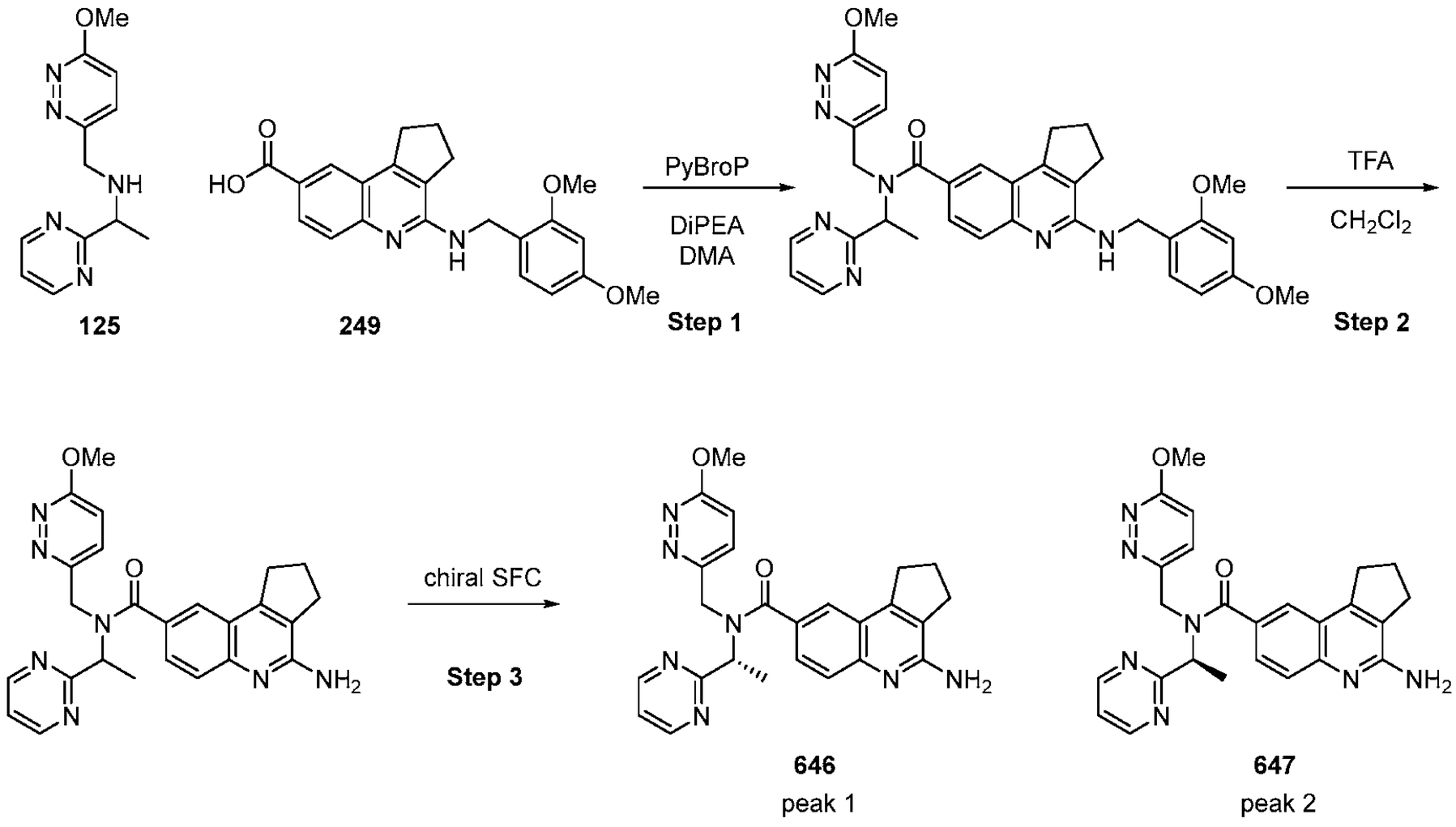
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
634		4-amino-N-((2R)-1-methoxy-2-propanyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)[1,2]oxazolo[4,5-c]quinoline-8-carboxamide and 4-amino-N-((2S)-1-methoxy-2-propanyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)[1,2]oxazolo[4,5-c]quinoline-8-carboxamide	474.2
635		4-amino-N-((3-fluoro-2-pyridinyl)methyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)thieno[2,3-c]quinoline-8-carboxamide	512.0
636		4-amino-N-(2-pyrimidinylmethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)thieno[2,3-c]quinoline-8-carboxamide	495.0

Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
637		4-amino-N-(2-methylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)thieno[2,3-c]quinoline-8-carboxamide	459.0
638		5-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)pyrimido[4,5-c]quinoline-9-carboxamide	505.0
639		4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((1R)-1-cyclopropyl-2-methoxyethyl)thieno[2,3-c]quinoline-8-carboxamide and 4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((1S)-1-cyclopropyl-2-methoxyethyl)thieno[2,3-c]quinoline-8-carboxamide	512.0

Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
640		4-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide and 4-amino-N-((1S)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	495.2
641		4-amino-N-((1S)-1-cyclopropyl-2-methoxyethyl)-N-((6-(4-morpholinyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	505.1
642		4-amino-N-((6-ethoxy-3-pyridazinyl)methyl)-N-(2-methylpropyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	422.1

Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
643		4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)thieno[2,3-c]quinoline-8-carboxamide	486.0 and 488.0
644		4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-(1-methoxy-2-methyl-2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	486.0 and 488.0
645		4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-(1-methoxy-2-methyl-2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	487.15 and 489.10

[0261] Example 646 and 647: (R) or (S)-4-amino-N-((6-methoxypyridazin-3-yl)methyl)-N-(1-(pyrimidin-2-yl)ethyl)-2,3-dihydro-1H-cyclopenta[c]quinoline-8-carboxamide.



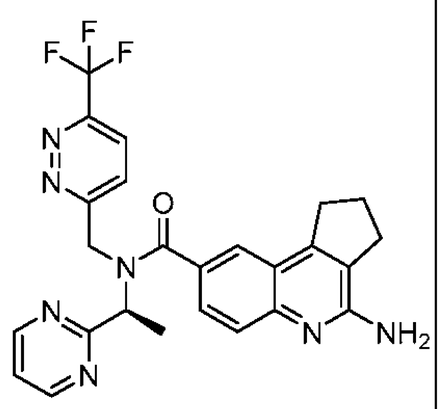
[0262] Step 1. To a solution of N-((6-methoxypyridazin-3-yl)methyl)-1-(pyrimidin-2-yl)ethan-1-amine (**125,** 0.150 g, 0.612 mmol), 4-((2,4-dimethoxybenzyl)amino)-2,3-dihydro-1H-cyclopenta[c]quinoline-8-carboxylic acid hydrochloride (**249,** 0.330 g, 0.795 mmol) and 1,1'-dimethyltriethylamine (0.790 g, 1.068 mL, 6.12 mmol, Sigma-Aldrich Corporation) in DMF (5 mL) was added bromotripyrrolidinophosphonium hexafluorophosphate (0.285 g, 0.612 mmol, Sigma-Aldrich Corporation) and the resulting mixture was heated at 50°C for 45 min. The reaction was brought to rt, diluted with water, sat.$NaHCO_3$ and extracted with EtOAc (3x). The combined organics were dried over Na_2SO_4, filtered and concentrated. The residue was then chromatographed on silica gel using 0-50% 3:1 EtOAc/EtOH in heptane to afford 4-((2,4-dimethoxybenzyl)amino)-N-((6-methoxypyridazin-3-yl)methyl)-N-(1-(pyrimidin-2-yl)ethyl)-2,3-dihydro-1H-cyclopenta[c]quinoline-8-carboxamide as a light yellow solid. *m/z* (ESI): 606.2 $(M+H)^+$.

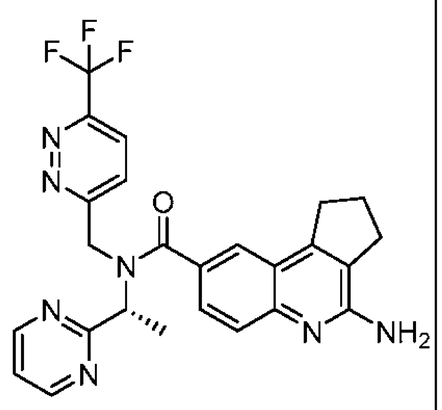
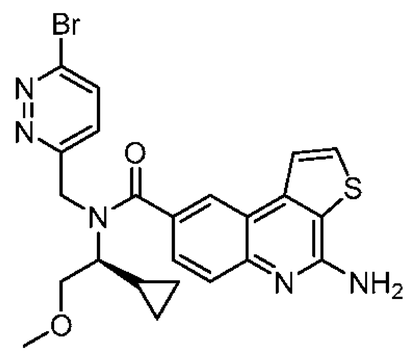
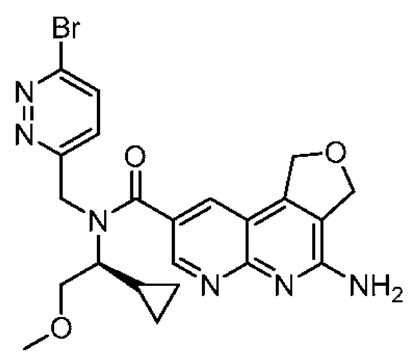
[0263] Step 2. To a solution of 4-((2,4-dimethoxybenzyl)amino)-N-((6-methoxypyridazin-3-yl)methyl)-N-(1-(pyrimidin-2-yl)ethyl)-2,3-dihydro-1H-cyclopenta[c]quinoline-8-carboxamide in DCM (2 mL) was added TFA (1.5 mL, 19.5 mmol, Aldrich) and the resulting mixture was heated at 50°C for 1 h. The reaction was concentrated, washed with 10% Na_2CO_3 and extracted with DCM. The combined organics were concentrated and chromatographed on silica gel using 0-50% 3:1 EtOAc/EtOH in heptane to afford 4-amino-N-((6-methoxypyridazin-3-yl)methyl)-N-(1-(pyrimidin-2-yl)ethyl)-2,3-dihydro-1H-cyclopenta[c]quinoline-8-carboxamide (0.067 g, 0.147 mmol, 24.05 % yield) as a light yellow solid.

[0264] Step 3. The racemic sample was purified via preparative SFC using a Chiral Technologies AD column (250 X 21 mm, 5mm) with a mobile phase of 50% Liquid CO_2 and 50% MeOH with 0.2% TEA using a flowrate of 50 mL/min. The more potent (measured by IC_{50} in HCT116 MTAP null cell viability assay) enantiomer was assigned as the *(R)*-; the less potent (measured by IC_{50} in HCT116 MTAP null cell viability assay) enantiomer was assigned as *(S)*-. The 1st eluting peak was (R)-4-amino-N-((6-methoxypyridazin-3-yl)methyl)-N-(1-(pyrimidin-2-yl)ethyl)-2,3-dihydro-1H-cyclopenta[c]quinoline-8-carboxamide (**646,** 0.016 g, 0.035 mmol), isolated as a light brown solid. The 2nd eluting peak was (S)-4-amino-N-((6-methoxypyridazin-3-yl)methyl)-N-(1-(pyrimidin-2-yl)ethyl)-2,3-dihydro-1H-cyclopenta[c]quinoline-8-carboxamide (**647,** 0.015 g, 0.033 mmol), isolated as a light yellow solid. *m/z* (ESI): 456 $(M+H)^+$. ^1H NMR (400 MHz, DMSO-d6) δ ppm 8.80 (d, J=5.0 Hz, 2 H), 7.71 (br d, J=1.9 Hz, 1 H), 7.47 - 7.62 (m, 3 H), 7.42 (t, J=4.9 Hz, 1 H), 7.14 (d, J=9.1 Hz, 1 H), 6.44 (br s, 2 H), 5.33 - 5.51 (m, 1 H), 4.94 (br d, J=16.0 Hz, 1 H), 4.52 - 4.72 (m, 1 H), 4.00 (s, 3 H), 2.89 - 3.16 (m, 2 H), 2.75 - 2.86 (m, 2 H), 2.16 (br t, J=7.6 Hz, 2 H), 1.60 (d, J=7.0 Hz, 3 H).

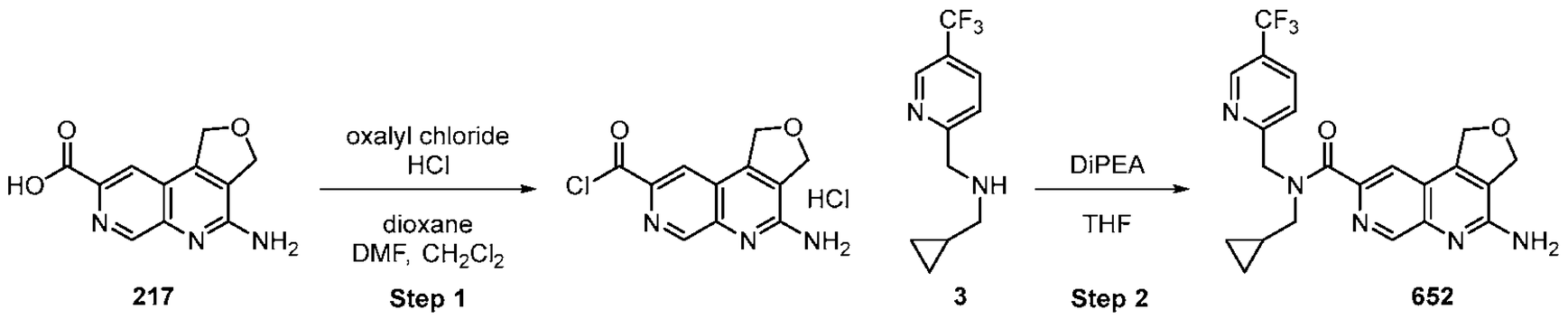
[0265] Compounds in Table 21 were prepared in a manner similar to that described above for Example **646** and **647.**

Table 21

Ex.	Structure	Name	m/z (ESI): $(M+H)^+$	SFC conditions
648		4-amino-N-((1S)-1-(2-pyrimidinyl)ethyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-2,3-dihydro-1H-cyclopenta[c]quinoline-8-carboxamide	494	1st peak, Chiral Technologies AD column (250 X 21 mm, 5mm) with a mobile phase of 80% Liquid CO_2 and 20% MeOH with 0.2% TEA using a flowrate of 80 mL/min

Ex.	Structure	Name	m/z (ESI): $(M+H)^+$	SFC conditions
649		4-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-2,3-dihydro-1H-cyclopenta[c]quinoline-8-carboxamide	494	2nd peak, Chiral Technologies AD column (250 X 21 mm, 5mm) with a mobile phase of 80% Liquid CO_2 and 20% MeOH with 0.2% TEA using a flowrate of 80 mL/min
650		4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((1S)-1-cyclopropyl-2-methoxyethyl)thieno[2,3-c]quinoline-8-carboxamide	512	1st peak, Chiral Technologies OD column (250 X 21 mm, 5mm) with a mobile phase of 50% Liquid CO_2 and 50% MeOH with 0.2% TEA using a flowrate of 60 mL/min
651		4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((1S)-1-cyclopropyl-2-methoxyethyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide	499	1st peak, Chiral Technologies OD column (250 X 21 mm, 5mm) with a mobile phase of 75% Liquid CO_2 and 25% MeOH with 0.2% TEA using a flowrate of 80 mL/min

[0266] Example 652: 4-amino-N-(cyclopropylmethyl)-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide.



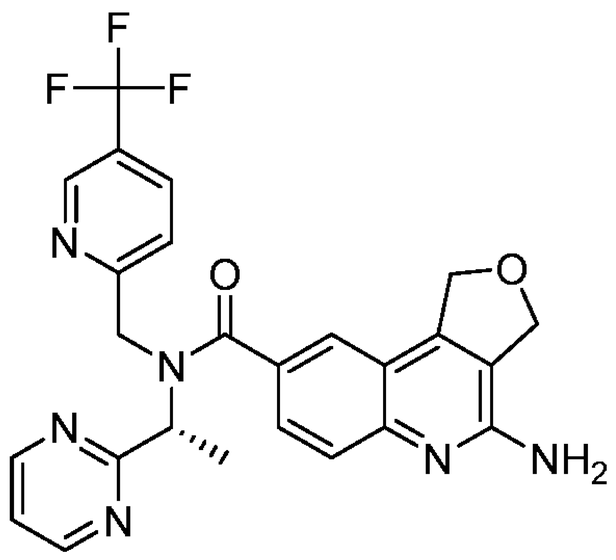
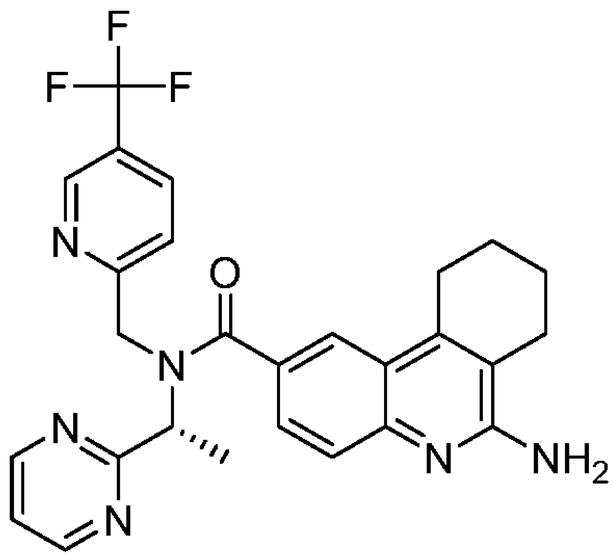
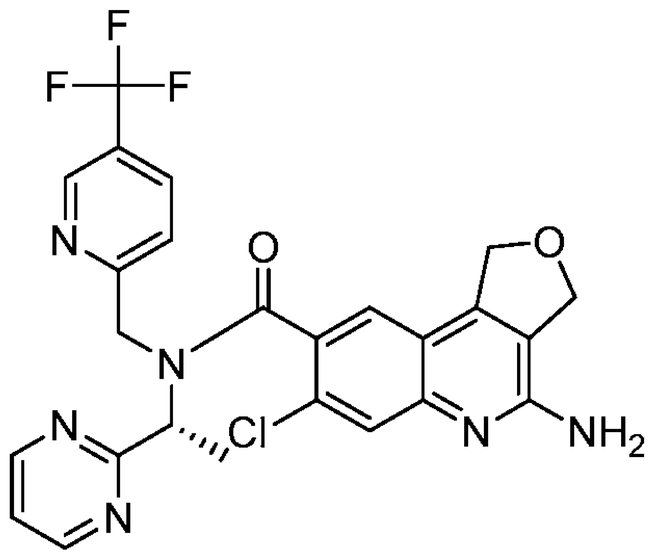
217 **Step 1** **3** **Step 2** **652**

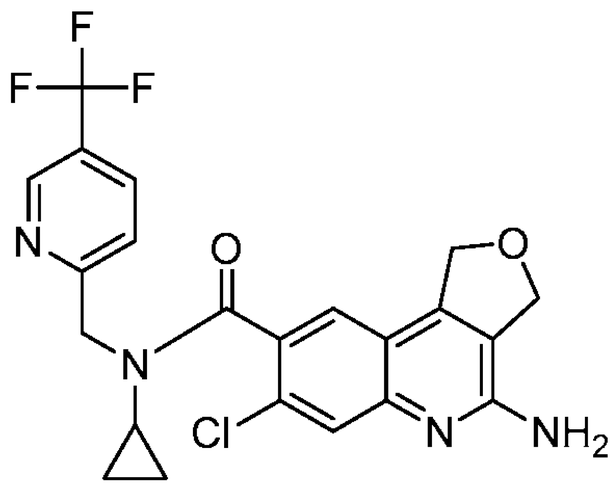
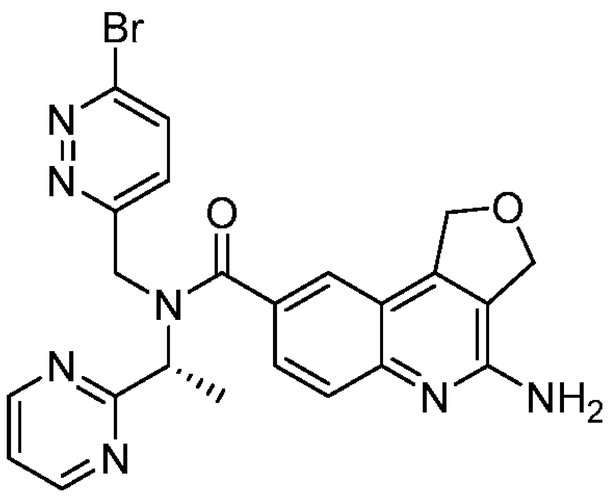
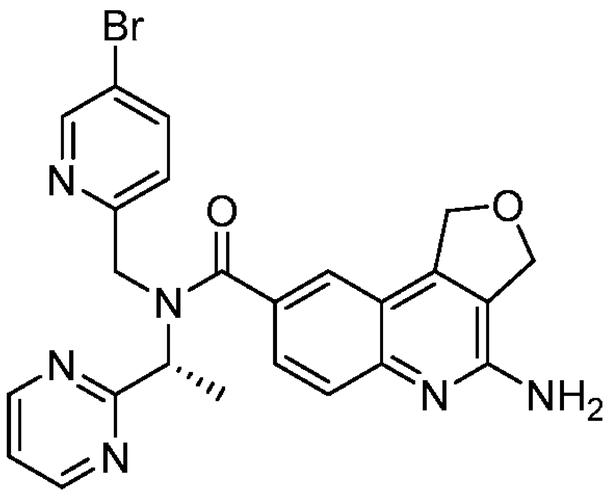
[0267] Step 1. To a stirred solution of 4-amino-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxylic acid (**217,** 0.500 g, 2.163 mmol) in dichloromethane (5.00 mL) was added HCl (4M in dioxane, 1.622 mL, 6.49 mmol) and the reaction mixture was stirred at room temperature for 30 min. Then, the reaction mixture was concentrated, co-distilled with toluene (3 x 50 mL), and dried. This crude material was taken up in dichloromethane (5.00 mL) and cooled to 0 °C. Oxalyl chloride (1.136 mL, 12.98 mmol) and DMF (0.033 mL, 0.433 mmol) were added dropwise at the same temperature and the reaction mixture was stirred room temperature for 16 h. The reaction mixture was concentrated under reduced pressure in nitrogen atmosphere, and the obtained crude material was triturated with heptane (3 x 5 mL), and dried under nitrogen atmosphere to give 4-amino-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carbonyl chloride hydrochloride (0.500 g, 1.748 mmol, 81 % yield) as yellow solid.

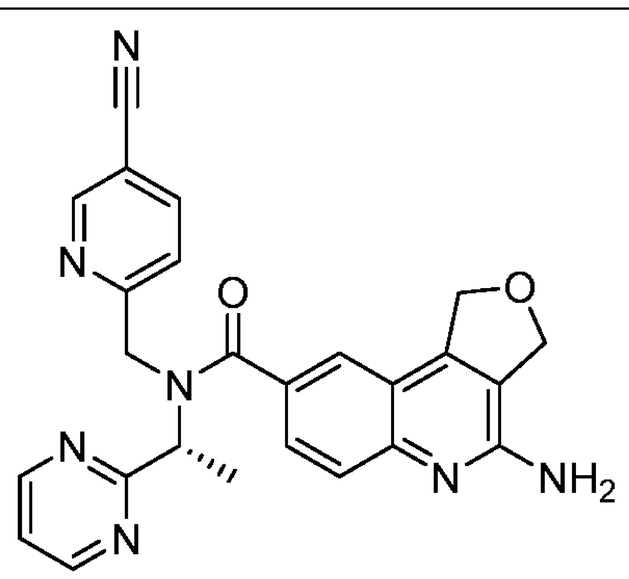
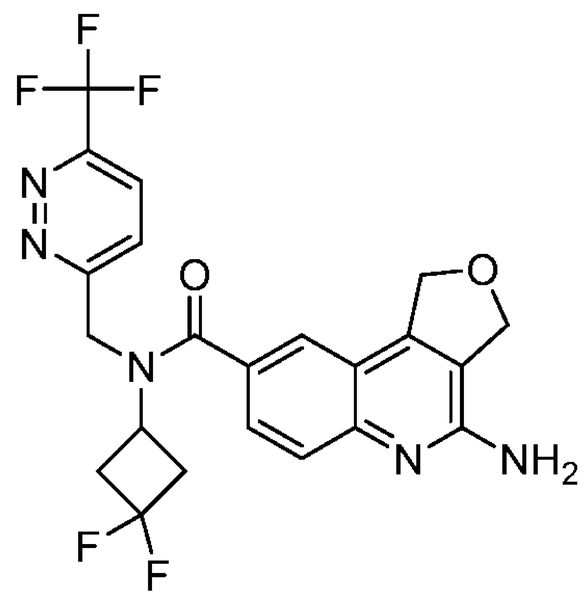
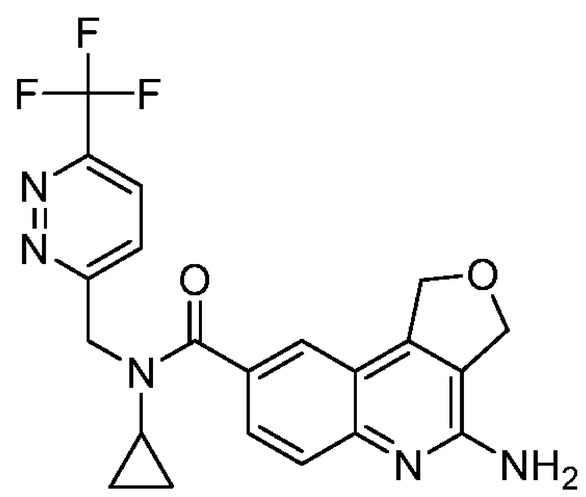
[0268] Step 2. To a mixture of 1-cyclopropyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)methanamine (**3**, 0.050 g, 0.217 mmol) , tetrahydrofuran (2 mL) and diisopropylethylamine (0.112 g, 0.151 mL, 0.869 mmol, Aldrich) was added 4-amino-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carbonyl chloride hydrochloride (0.065 g, 0.228 mmol). The mixture was stirred at rt until completion and then concentrated in vacuo. The crude product was purified by silica gel chromatography (0-100% EtOAc/EtOH (3/1) in heptane). 4-amino-N-(cyclopropylmethyl)-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide (**652**, 49.5 mg, 0.112 mmol, 51.4% yield) was isolated as an off-white solid. *m/z* (ESI): 444 $(M+H)^+$. ^{1}H NMR (400 MHz, METHANOL-d4) δ ppm 8.75 - 8.97 (m, 2 H), 8.02 - 8.16 (m, 1 H), 7.82 (br s, 1 H), 7.59 - 7.78 (m, 1 H), 5.31 - 5.49 (m, 2 H), 5.04 - 5.19 (m, 4 H), 3.44 - 3.54 (m, 2 H), 1.06 - 1.31 (m, 1 H), 0.37 - 0.55 (m, 2 H), 0.04 - 0.31 (m, 2 H). ^{19}F NMR (377 MHz, METHANOL-d4) δ ppm -63.86 (m, 3 F)**.**

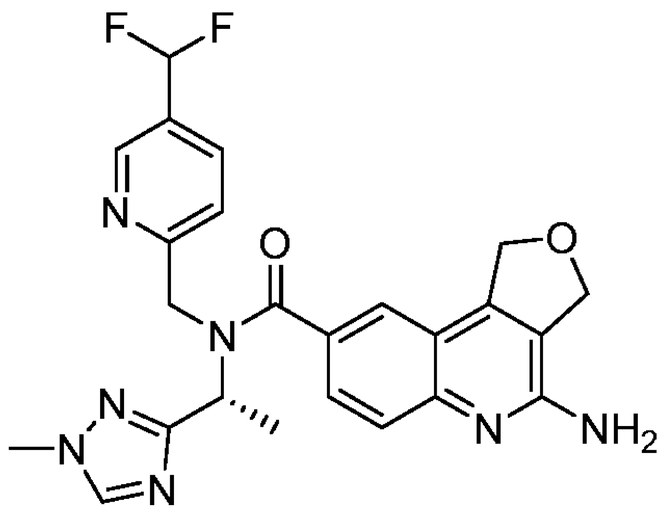
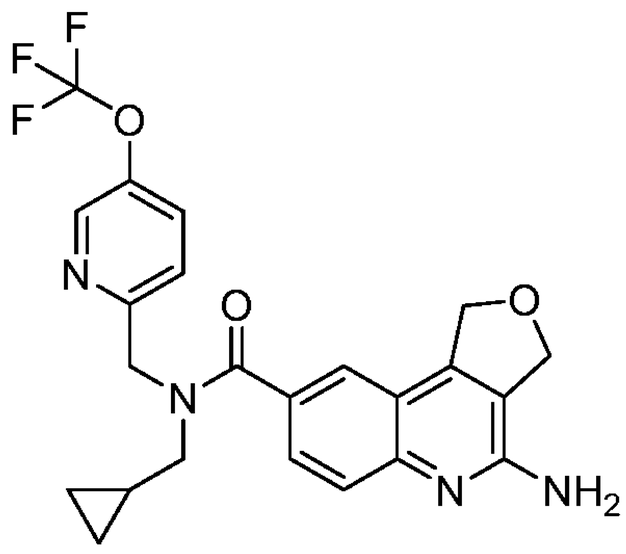
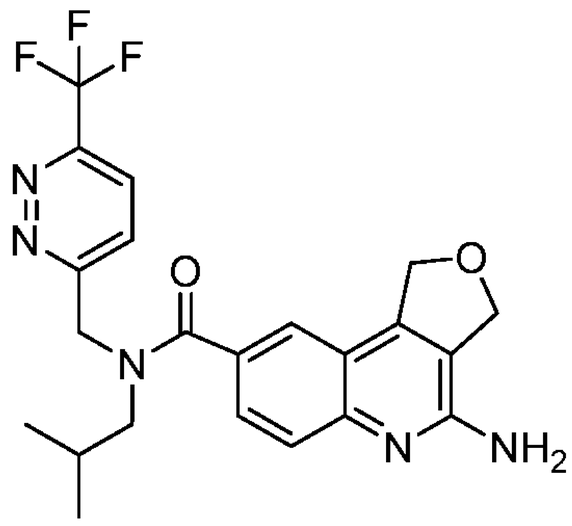
[0269] Compounds in Table 22 were prepared in a manner similar to that described above for Example **652**.

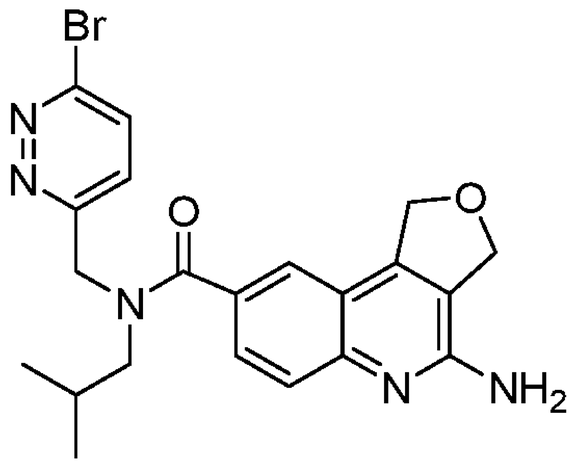
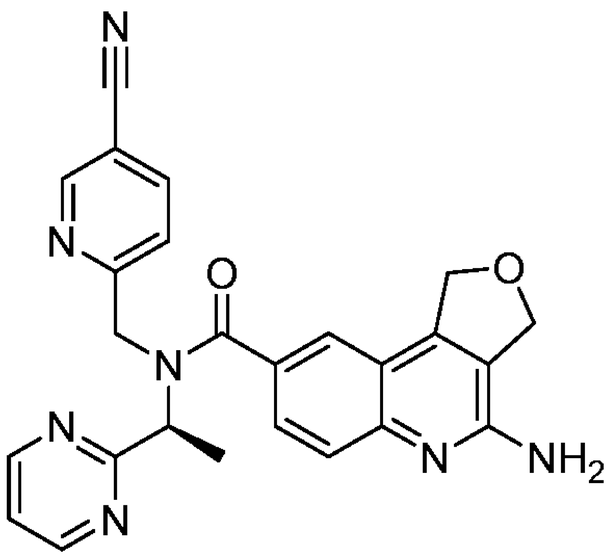
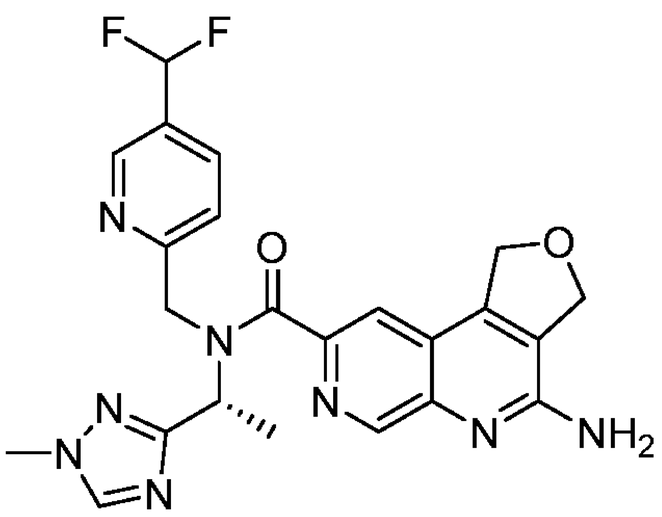
Table 22

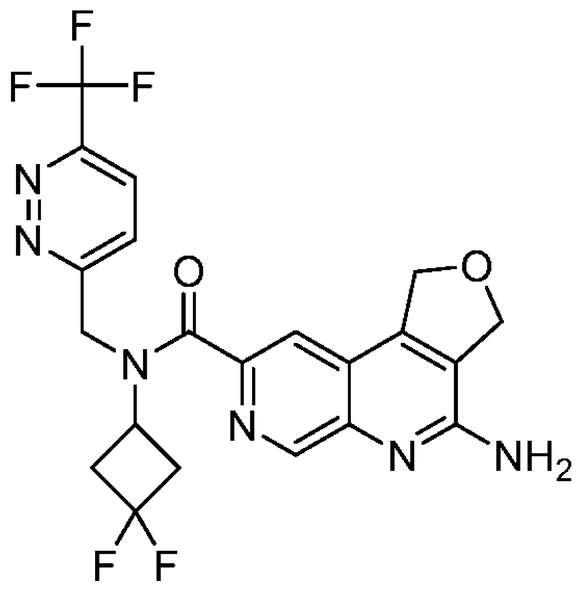
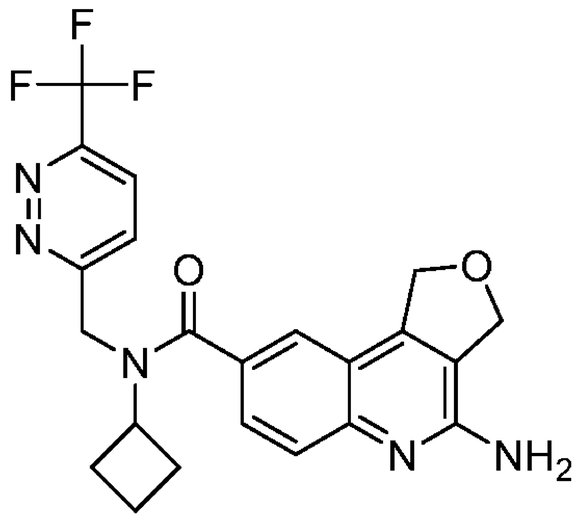
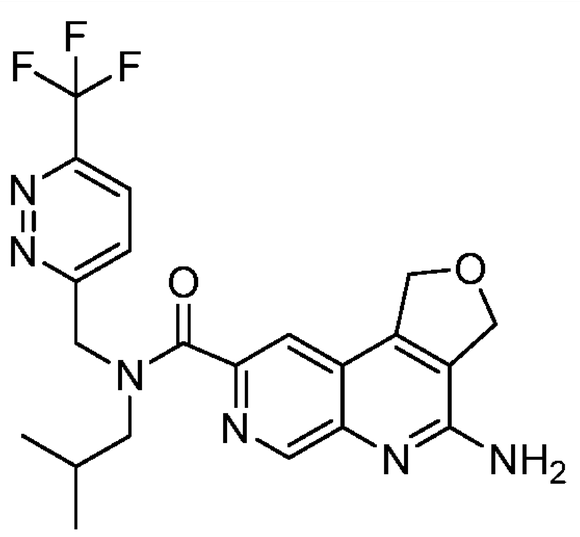
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
653		4-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	495.1
654		6-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-7,8,9,10-tetrahydro-2-phenanthridinecarboxamide	507.2
655		4-amino-7-chloro-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	529.1

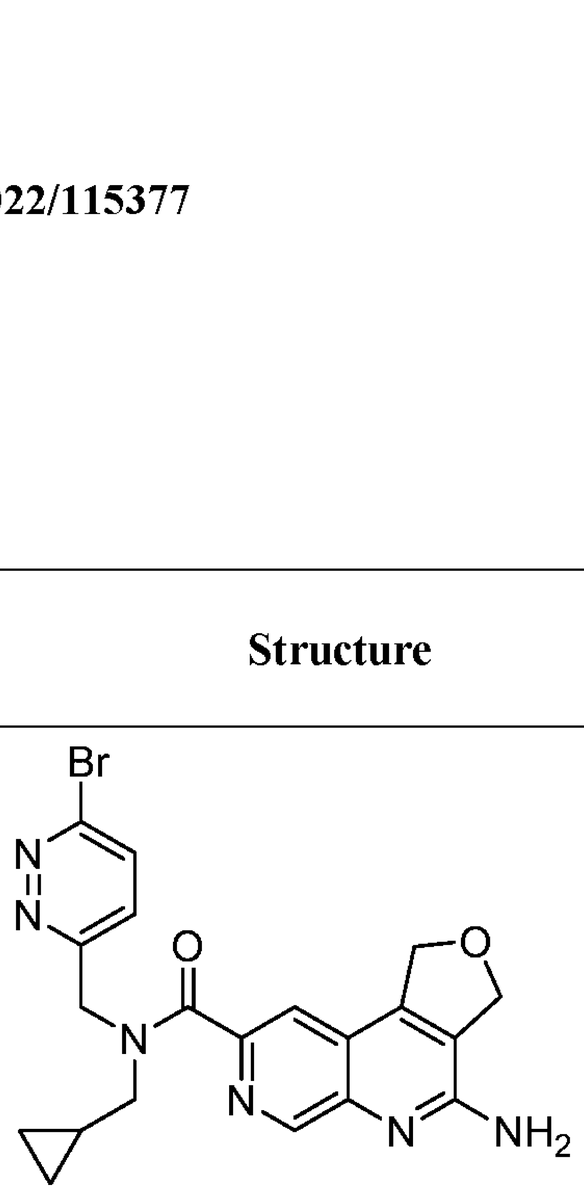
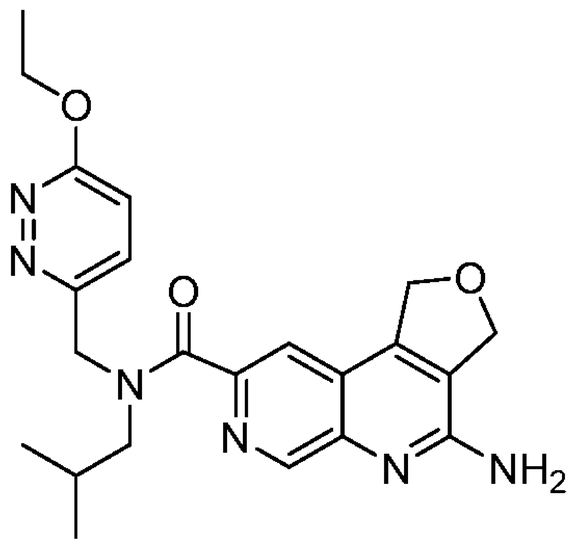
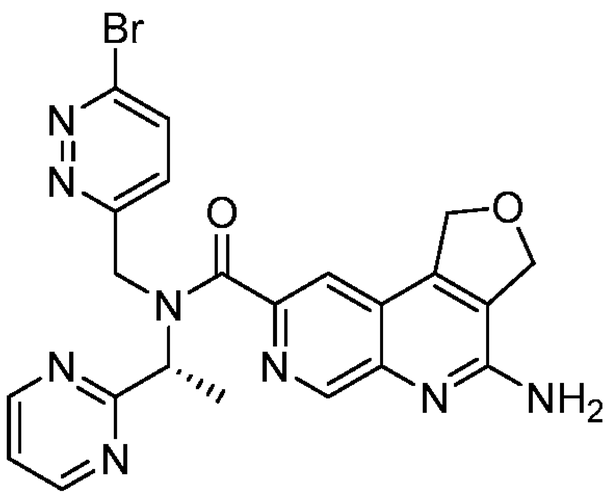
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
656		4-amino-7-chloro-N-cyclopropyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	463
657		4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	506 and 508
658		4-amino-N-((5-bromo-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	505 and 507

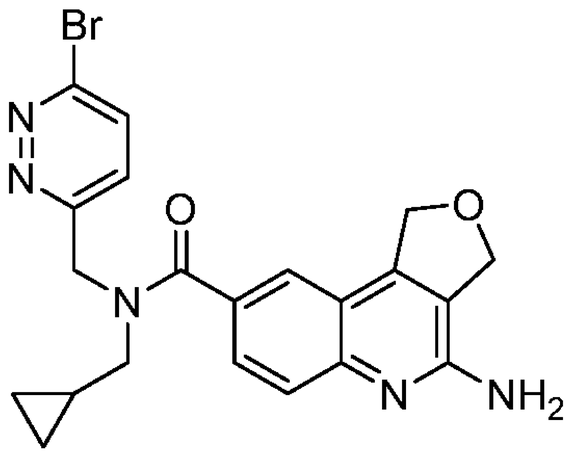
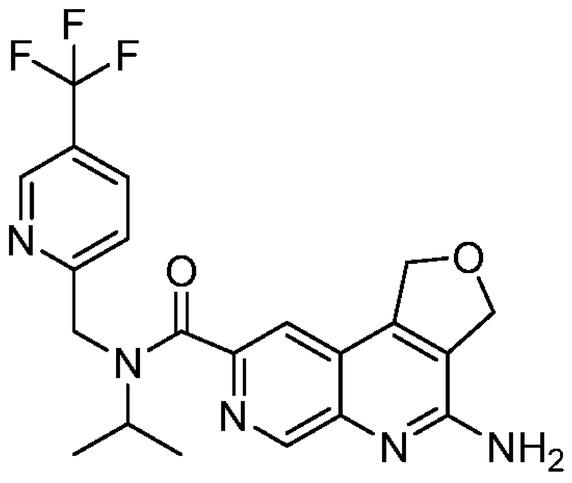
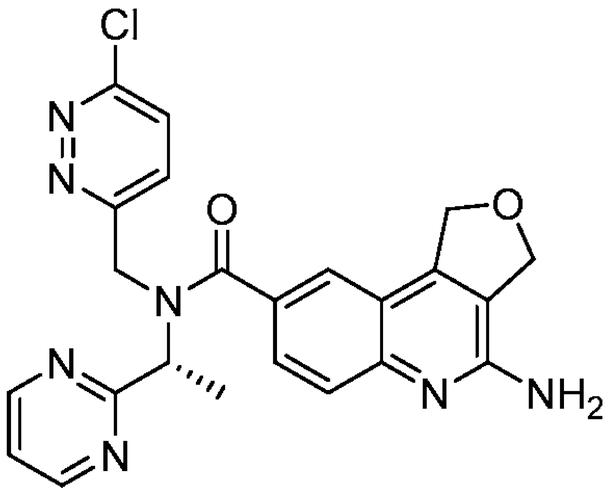
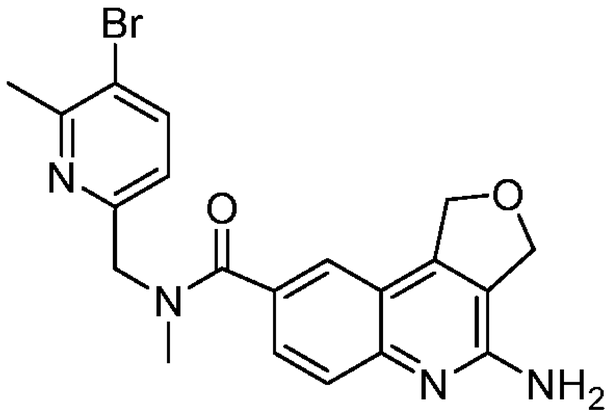
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
659		4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	452
660		4-amino-N-(3,3-difluorocyclobutyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	481.2
661		4-amino-N-cyclopropyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	430.2

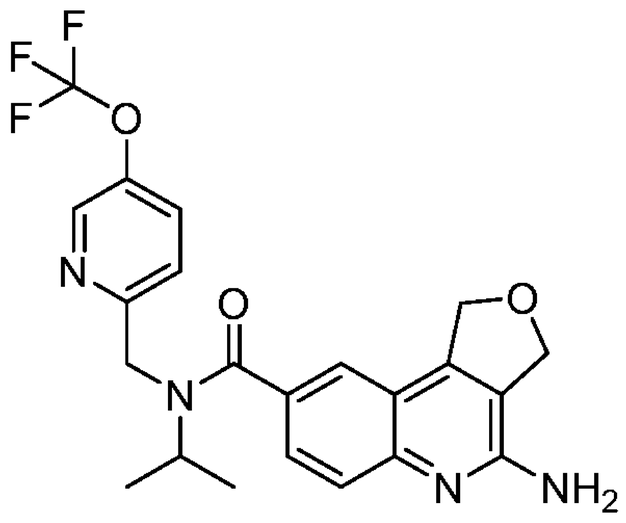
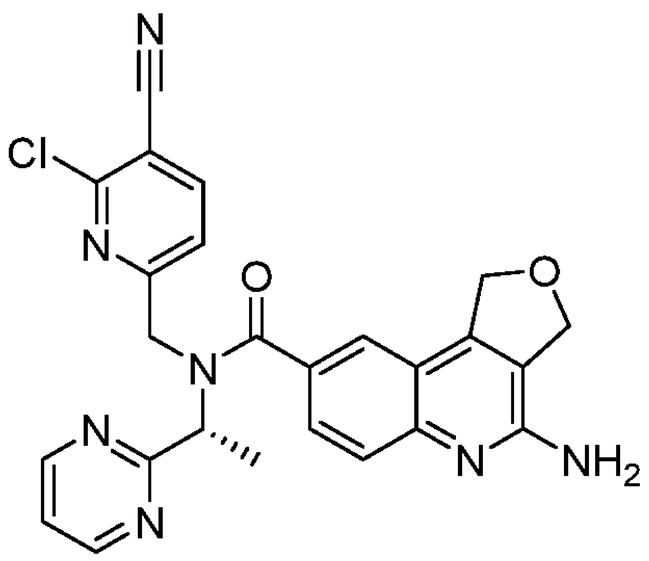
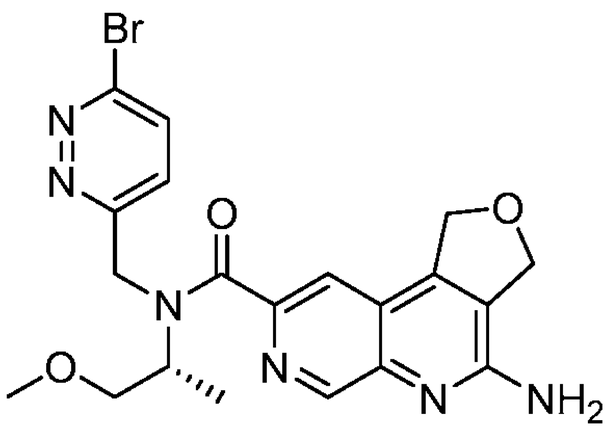
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
662		4-amino-N-((5-(difluoromethyl)-2-pyridinyl)methyl)-N-((1R)-1-(1-methyl-1H-1,2,4-triazol-3-yl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	480.3
663		4-amino-N-(cyclopropylmethyl)-N-((5-(trifluoromethoxy)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	459.2
664		4-amino-N-(2-methylpropyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	446.1

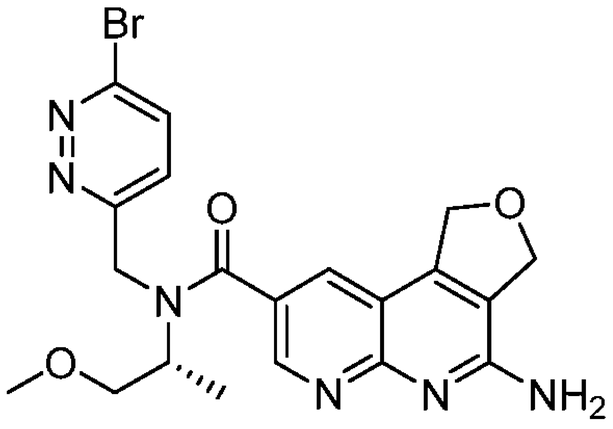
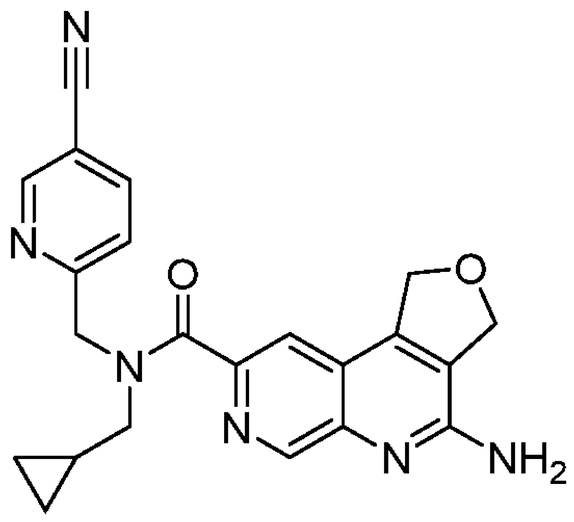
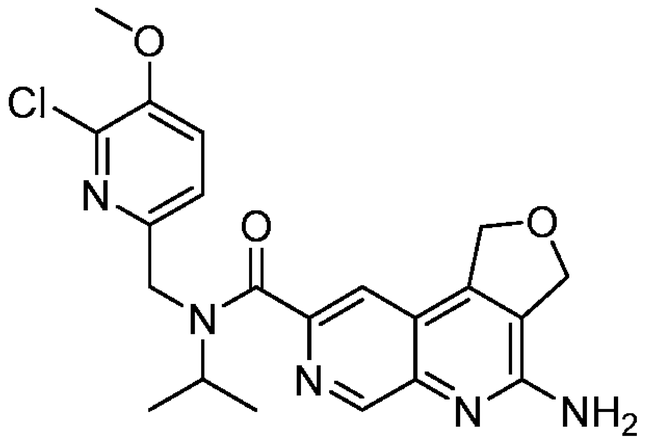
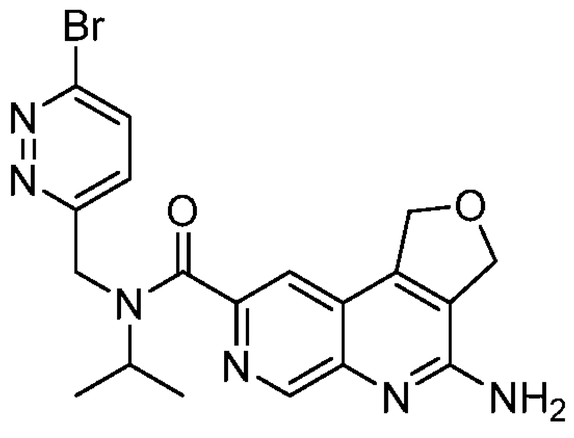
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
665		4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-(2-methylpropyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	456 and 458
666		4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((1S)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	452
667		4-amino-N-((5-(difluoromethyl)-2-pyridinyl)methyl)-N-((1R)-1-(1-methyl-1H-1,2,4-triazol-3-yl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	481.2

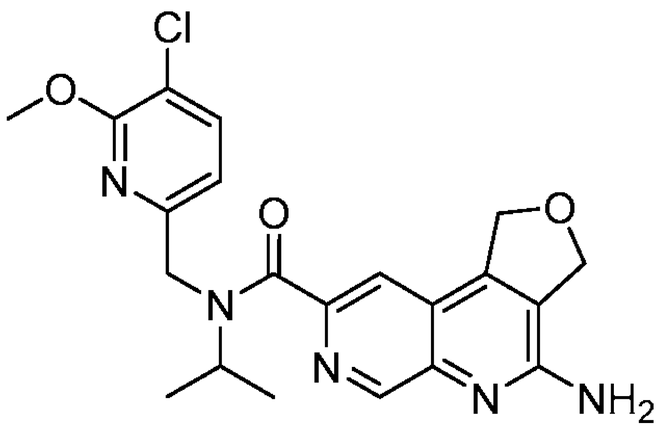
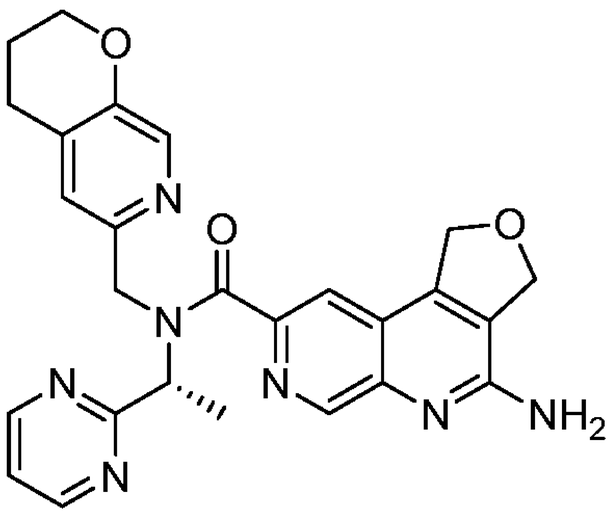
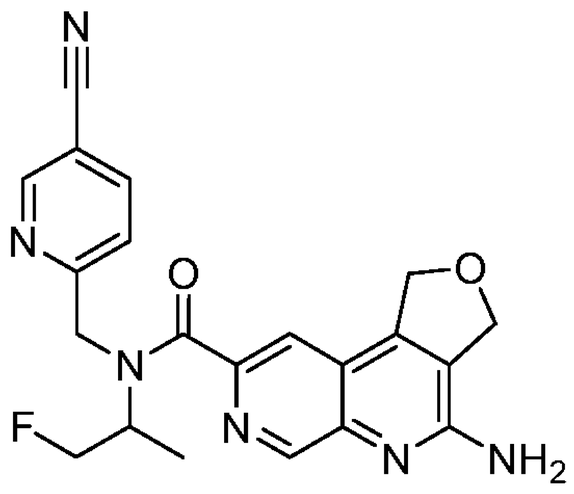
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
668		4-amino-N-(3,3-difluorocyclobutyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	481.2
669		4-amino-N-cyclobutyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	444.2
670		4-amino-N-(2-methylpropyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	447

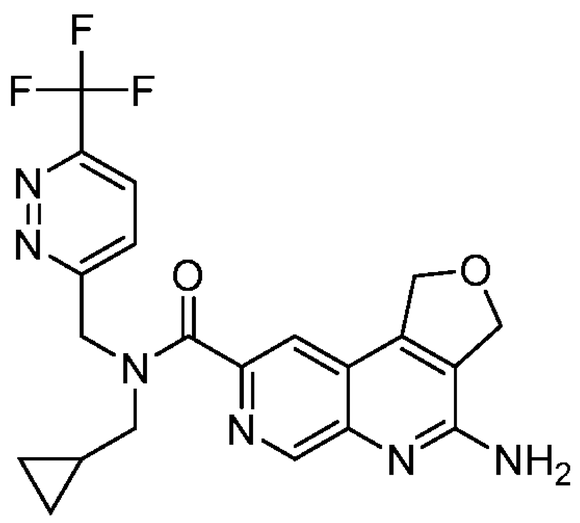
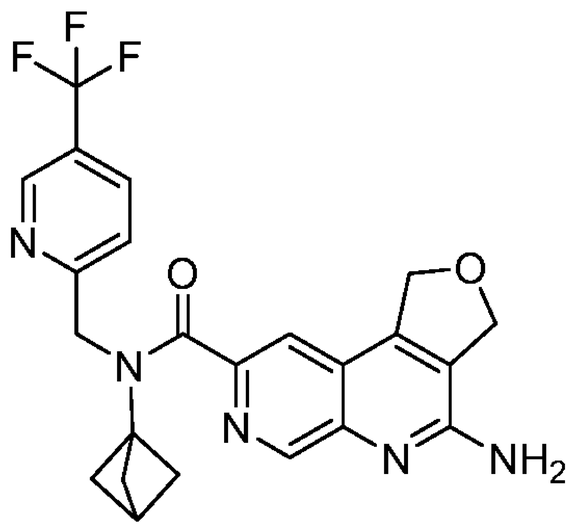
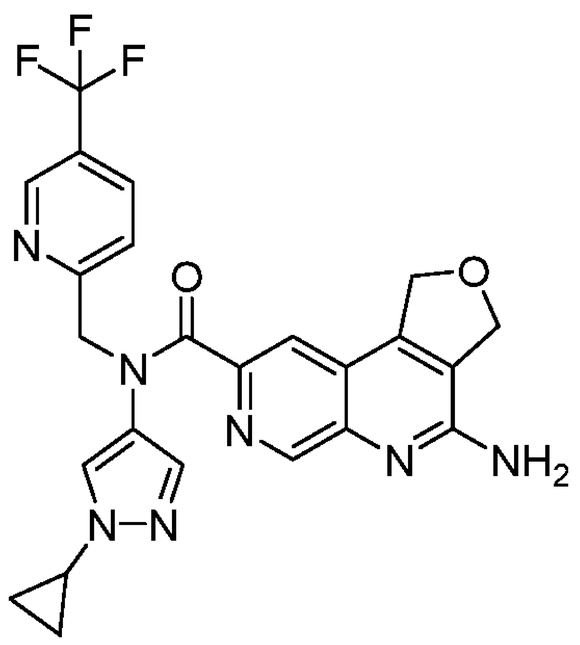
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
671		4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-(cyclopropylmethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	455 and 457
672		4-amino-N-((6-ethoxy-3-pyridazinyl)methyl)-N-(2-methylpropyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	423
673		4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	507 and 509

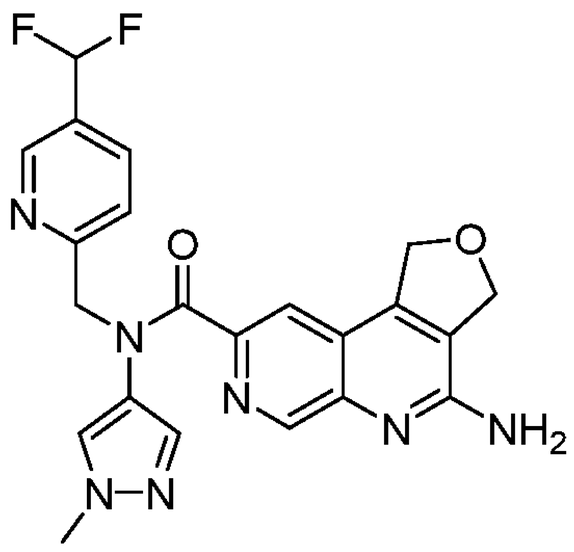
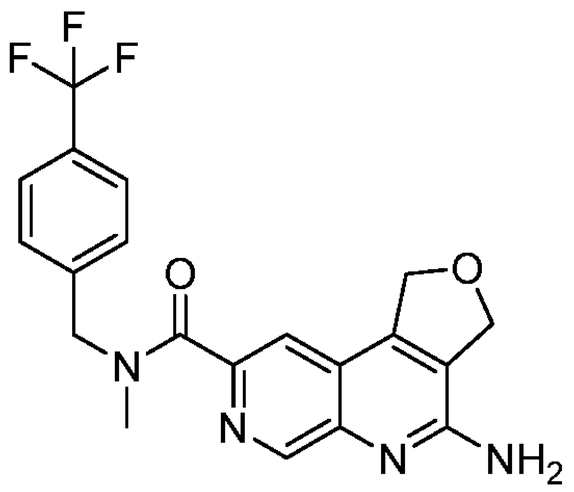
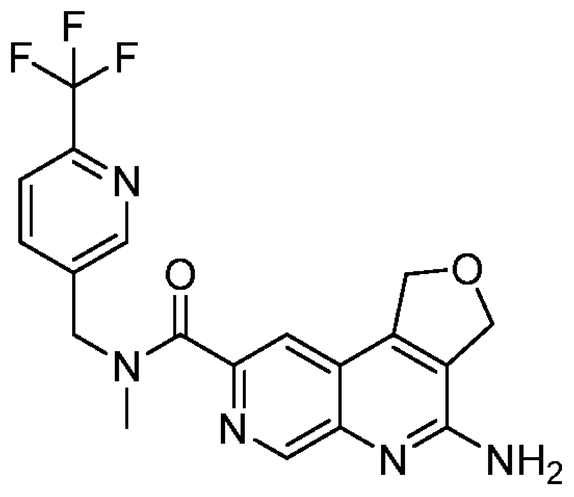
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
674		4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-(cyclopropylmethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	454 and 456
675		4-amino-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	432.2
676		4-amino-N-((6-chloro-3-pyridazinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	462
677		4-amino-N-((5-bromo-6-methyl-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	427.0 and 428.9

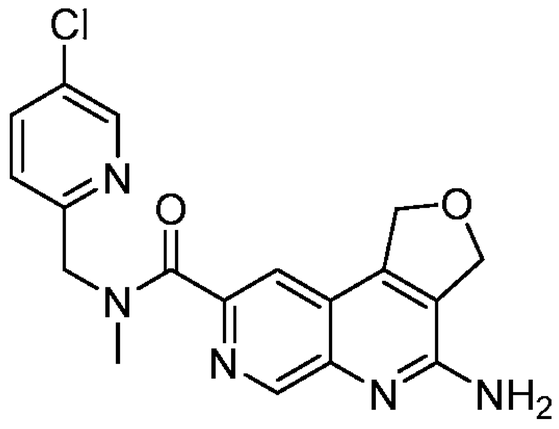
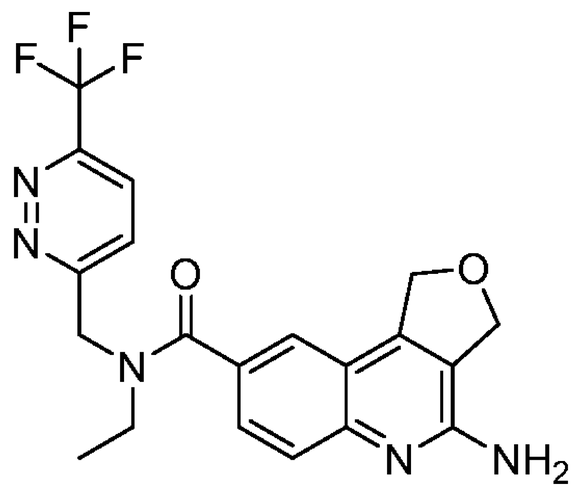
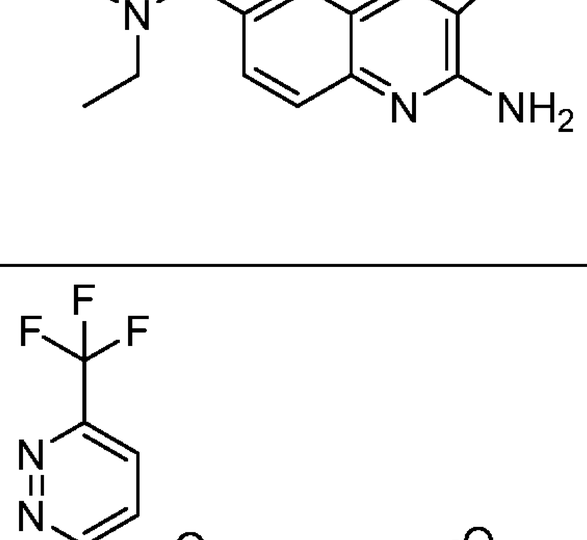
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
678		4-amino-N-(2-propanyl)-N-((5-(trifluoromethoxy)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	
679		4-amino-N-((6-chloro-5-cyano-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	486.2
680		4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	473.0 and 475.1

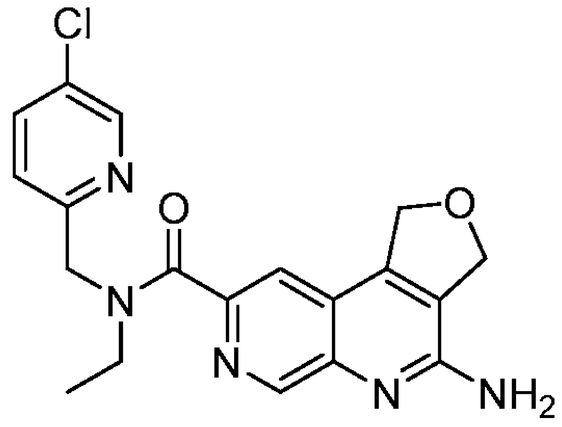
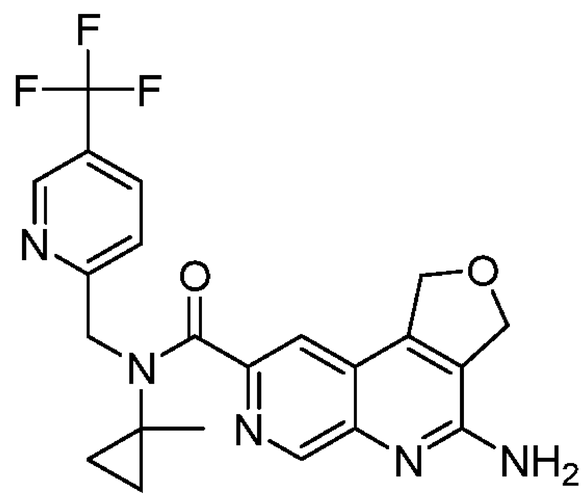
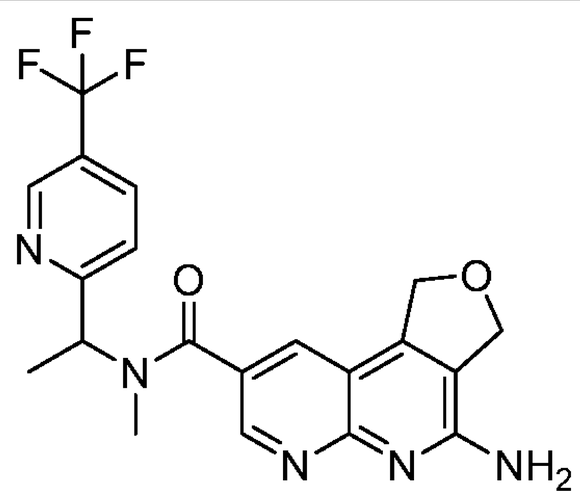
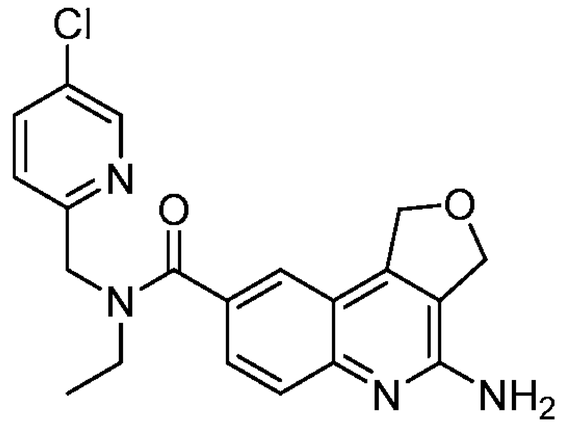
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
681		4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide	473.0 and 475.1
682		4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-(cyclopropylmethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	401
683		4-amino-N-((6-chloro-5-methoxy-2-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	428
684		4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	443 and 445

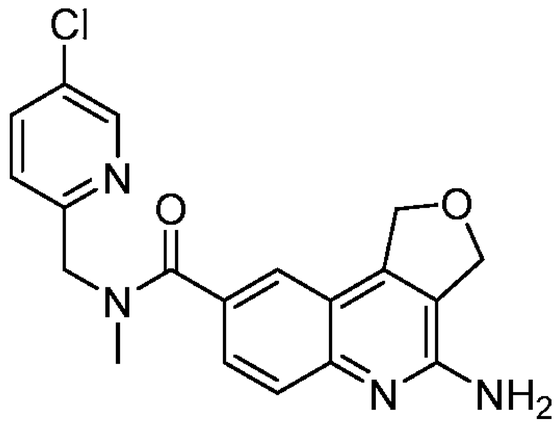
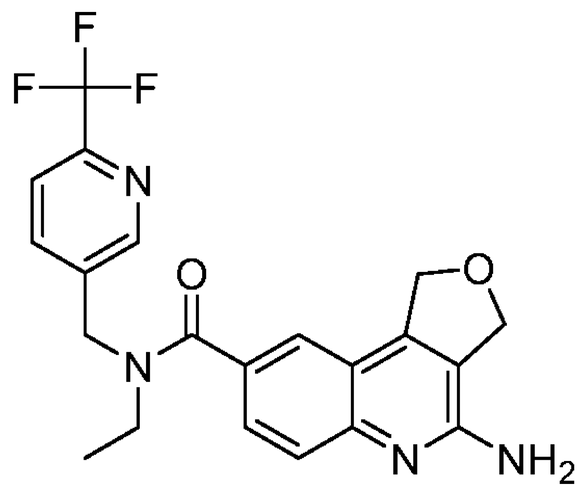
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
685		4-amino-N-((5-chloro-6-methoxy-2-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	428
686		4-amino-N-(3,4-dihydro-2H-pyrano[2,3-c]pyridin-6-ylmethyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	484.2
687		4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((2R)-1-fluoro-2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide and 4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((2S)-1-fluoro-2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	407.2

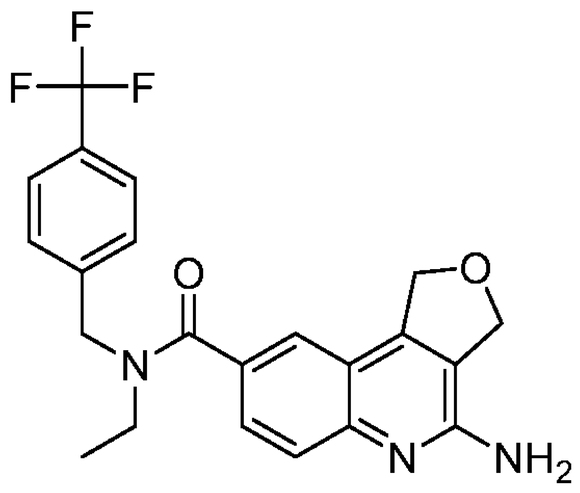
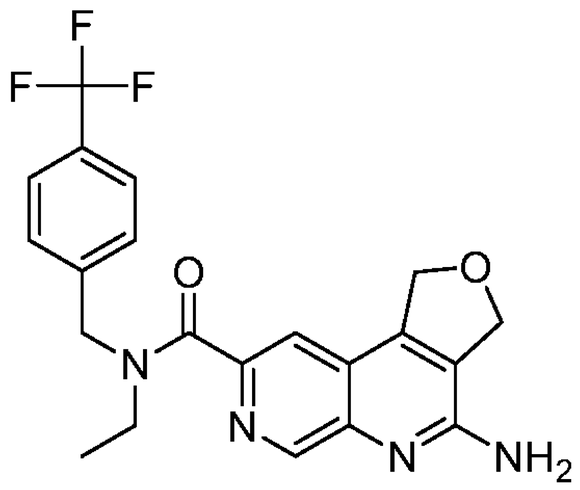
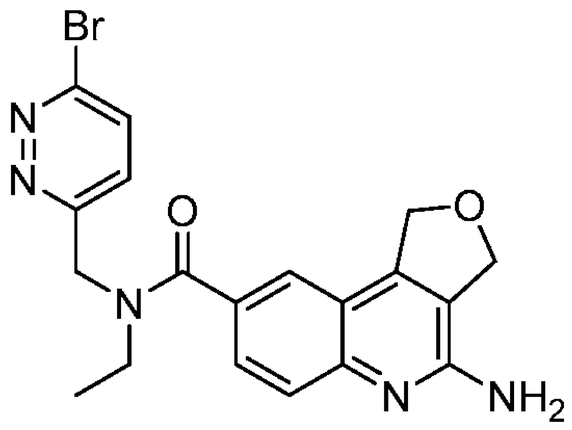
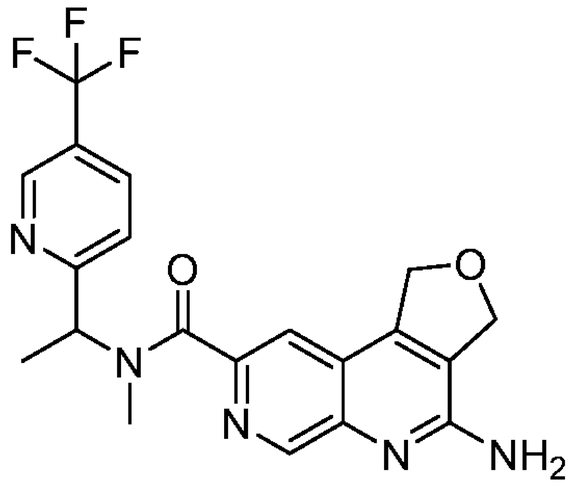
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
688		4-amino-N-(cyclopropylmethyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	445
689		4-amino-N-(bicyclo[1.1.1]pentan-1-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	456.2
690		4-amino-N-(1-cyclopropyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	496

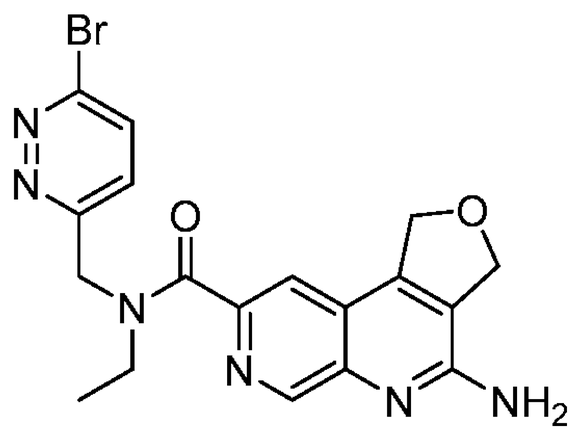
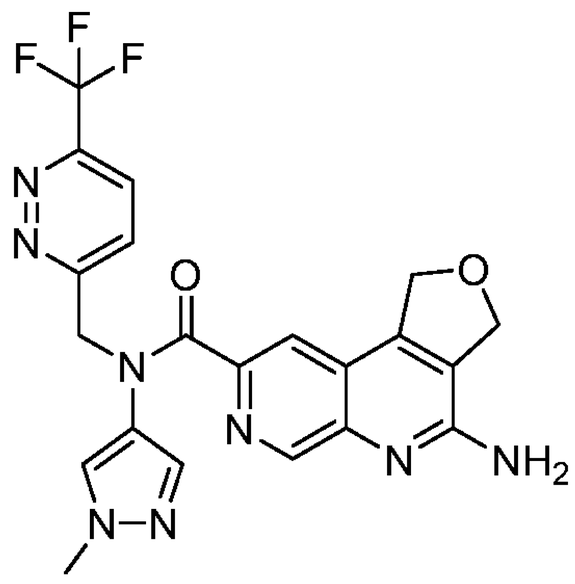
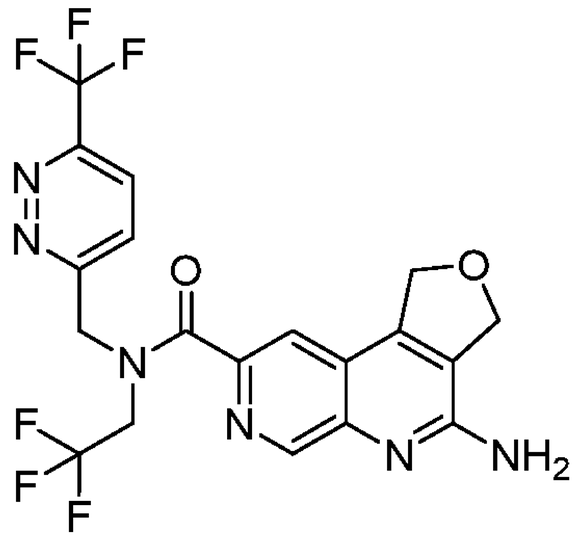
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
691		4-amino-N-((5-(difluoromethyl)-2-pyridinyl)methyl)-N-(1-methyl-1H-pyrazol-4-yl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	452.2
692		4-amino-N-methyl-N-(4-(trifluoromethyl)benzyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	403
693		4-amino-N-methyl-N-((6-(trifluoromethyl)-3-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	404

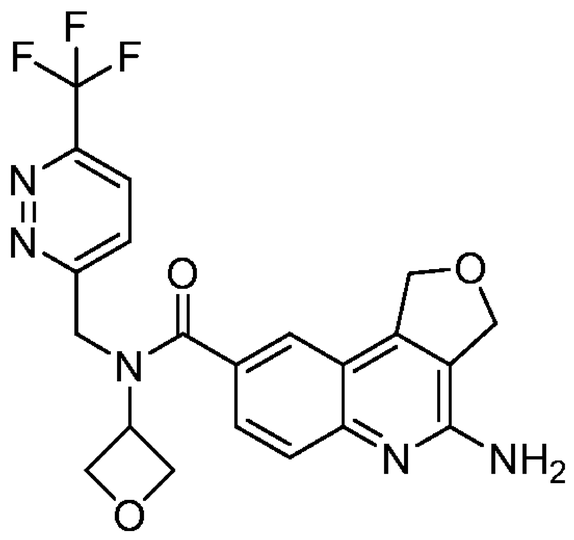
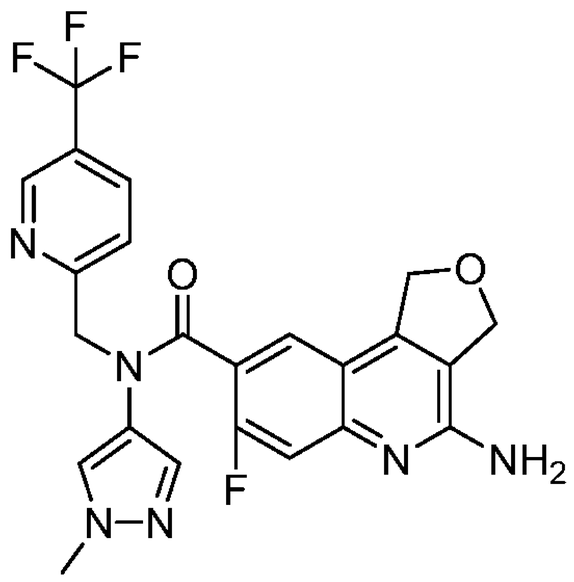
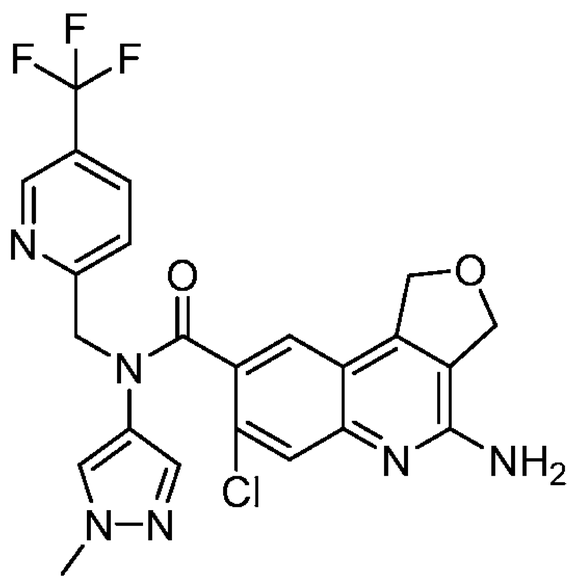
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
694		4-amino-N-((5-chloro-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	370
695		4-amino-N-ethyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	418.45
696		4-amino-N-ethyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	419.35
697		4-amino-N-methyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide and 4-amino-N-methyl-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	417.2

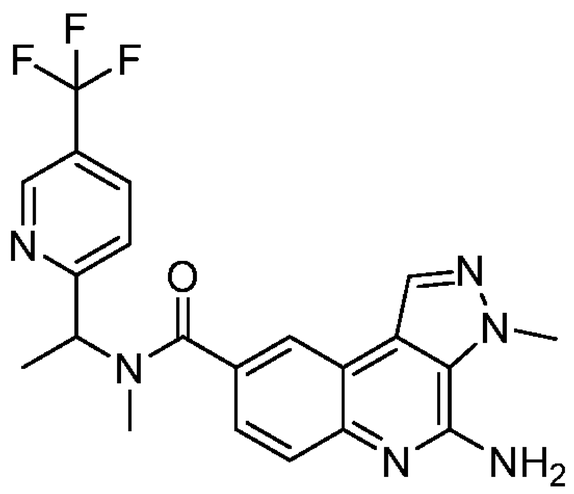
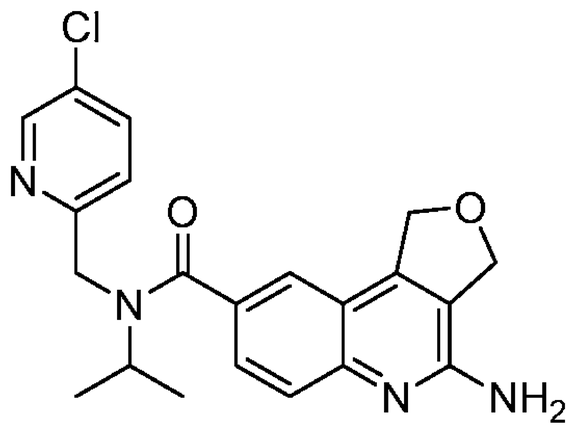
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
698		4-amino-N-((5-chloro-2-pyridinyl)methyl)-N-ethyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	384
699		4-amino-N-(1-methylcyclopropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	444.2
700		4-amino-N-methyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide and 4-amino-N-methyl-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide	418
701		4-amino-N-((5-chloro-2-pyridinyl)methyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	383

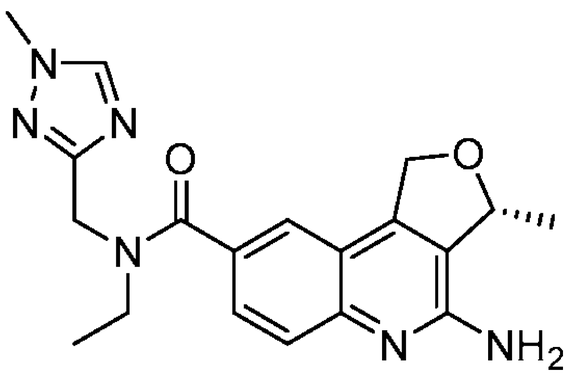
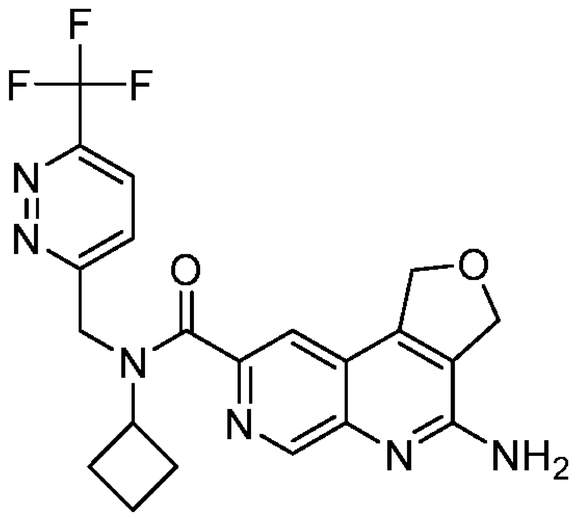
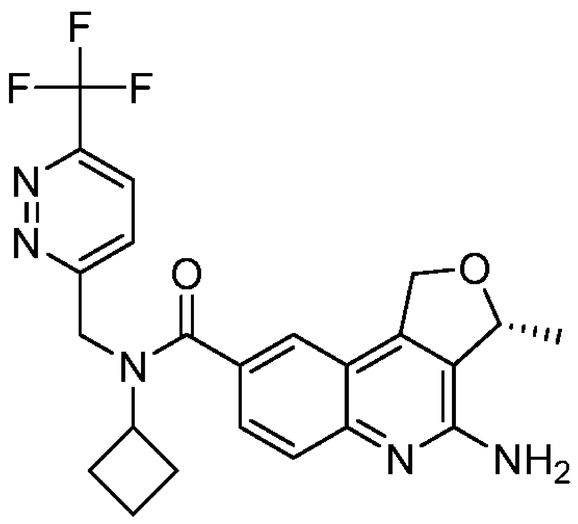
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
702		4-amino-N-((5-chloro-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	369
703		4-amino-N-ethyl-N-((6-(trifluoromethyl)-3-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	417
704		4-amino-N-ethyl-N-((6-(trifluoromethyl)-3-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	418
705		4-amino-N-ethyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide and 4-amino-N-ethyl-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide	432

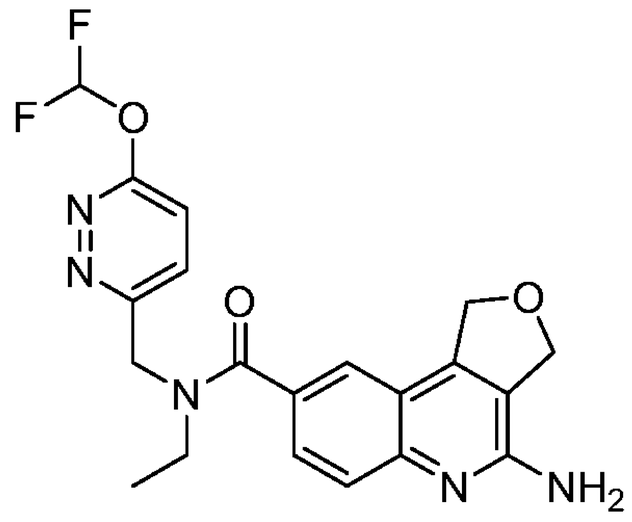
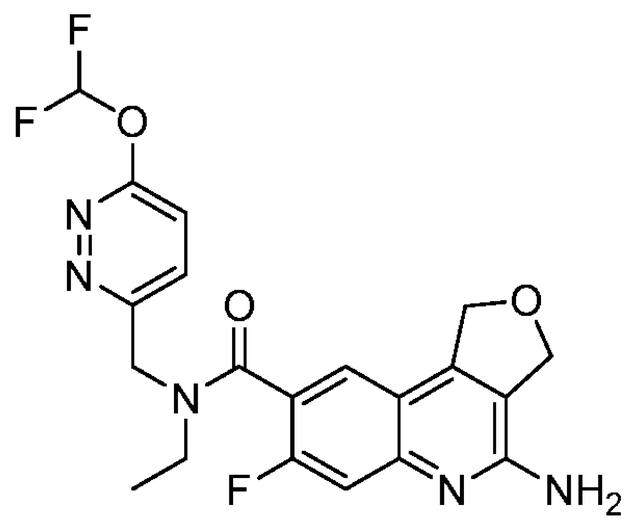
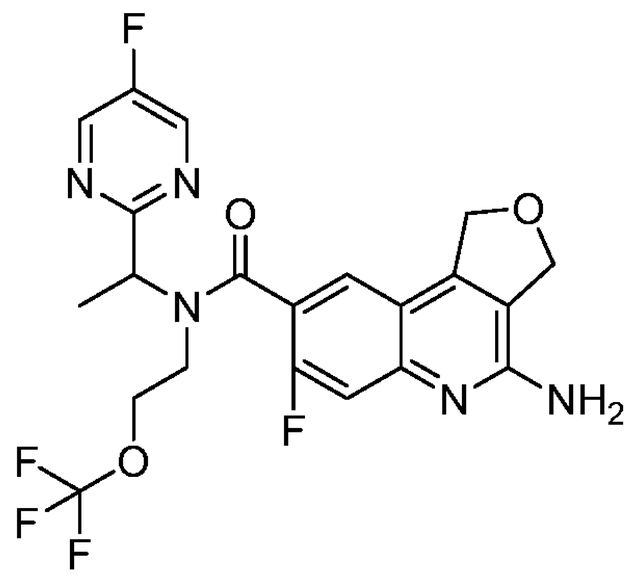
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
706		4-amino-N-ethyl-N-(4-(trifluoromethyl)benzyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	416
707		4-amino-N-ethyl-N-(4-(trifluoromethyl)benzyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	417
708		4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	428.05 and 430.15
709		4-amino-N-methyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide and 4-amino-N-methyl-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	418

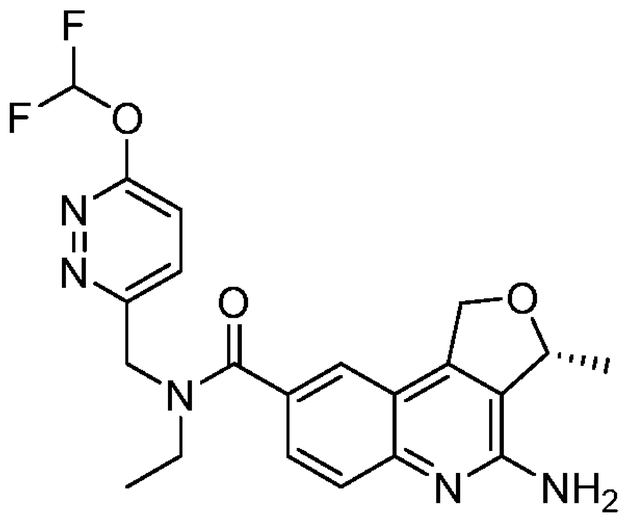
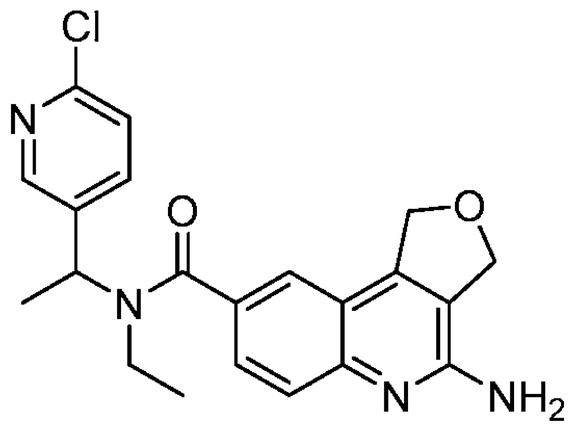
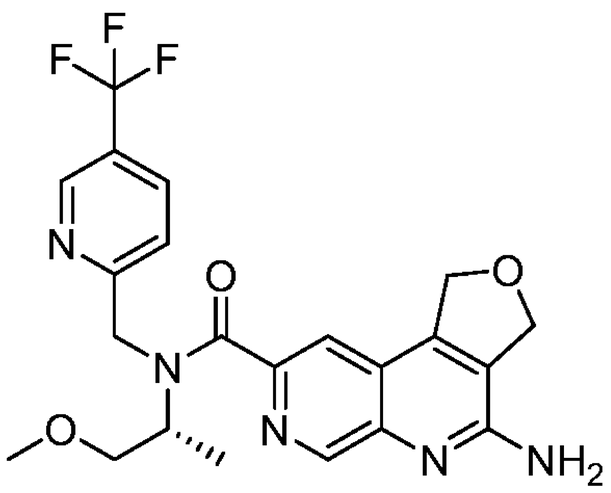
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
710		4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-ethyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	429.1 and 431.05
711		4-amino-N-(1-methyl-1H-pyrazol-4-yl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	471.1
712		4-amino-N-(2,2,2-trifluoroethyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	473.05

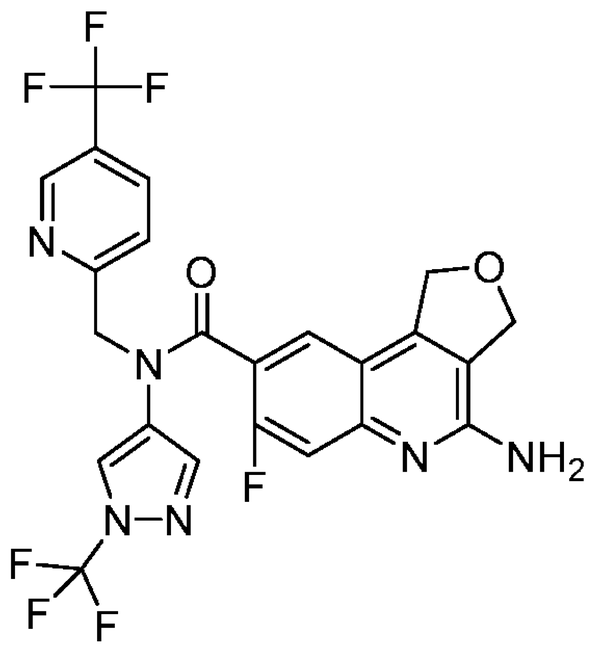
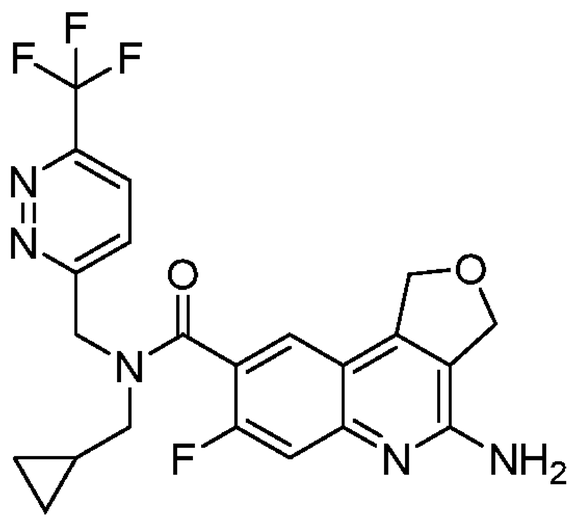
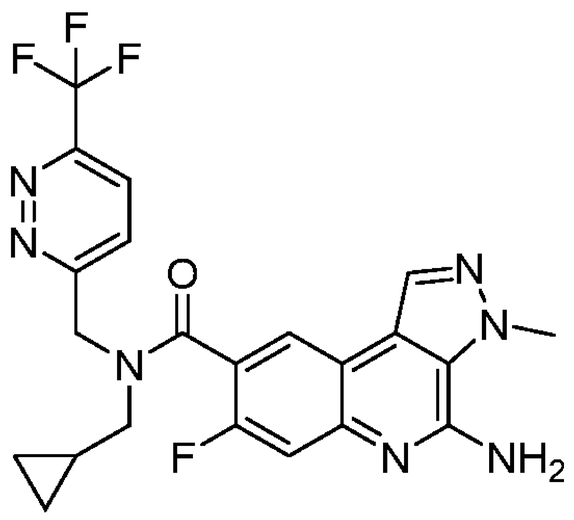
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
713		4-amino-N-(3-oxetanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	446.05
714		4-amino-7-fluoro-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	487.2
715		4-amino-7-chloro-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	503

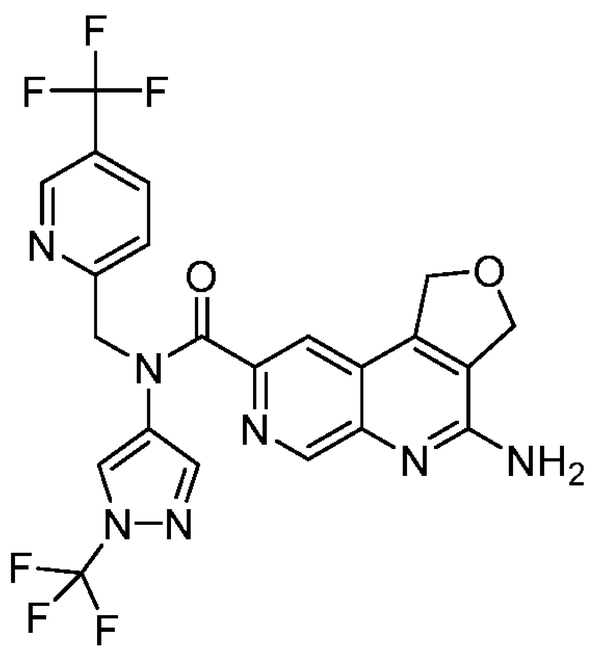
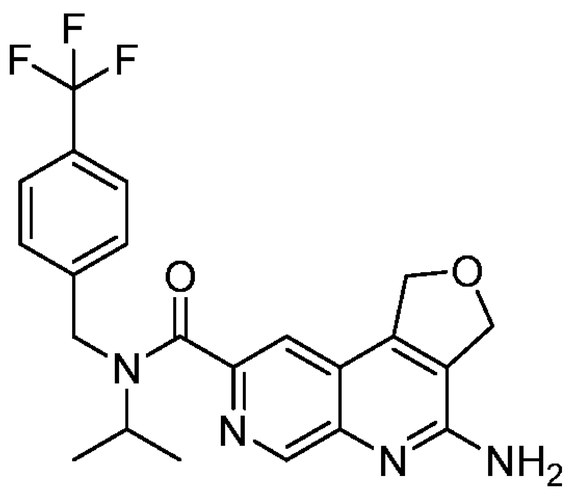
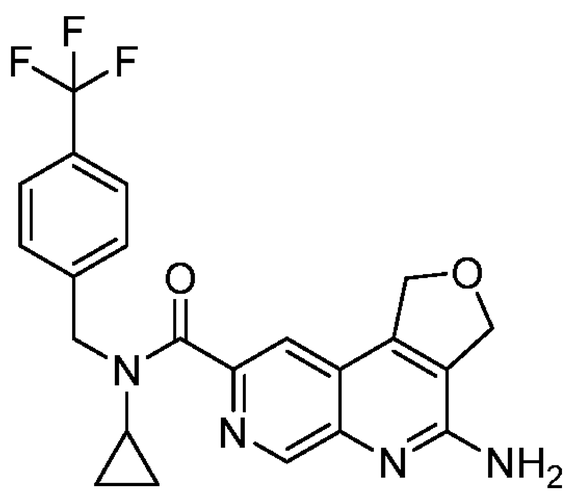
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
716		4-amino-N,3-dimethyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide and 4-amino-N,3-dimethyl-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide	429.2
717		4-amino-N-((5-chloro-2-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	397
718		4-amino-N-((5-chloro-2-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	398
719		4-amino-N-ethyl-7-fluoro-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide and 4-amino-N-ethyl-7-fluoro-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	449.1

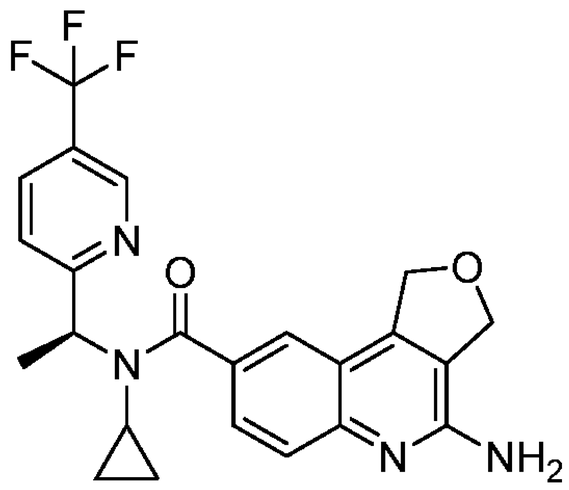
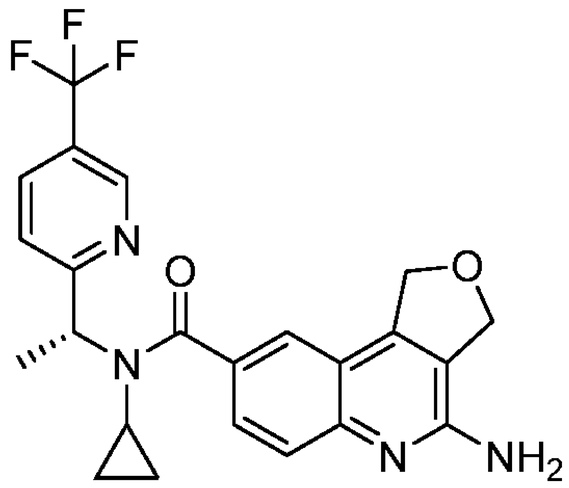
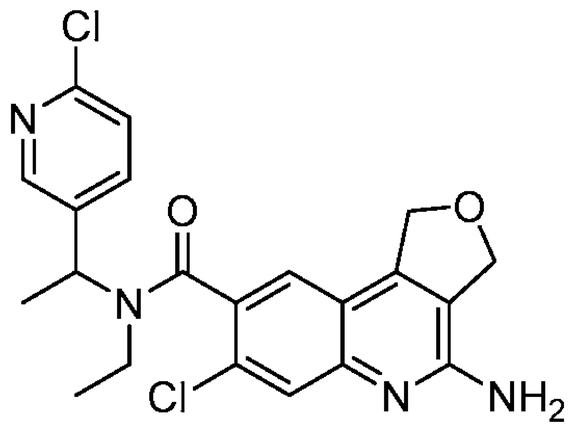
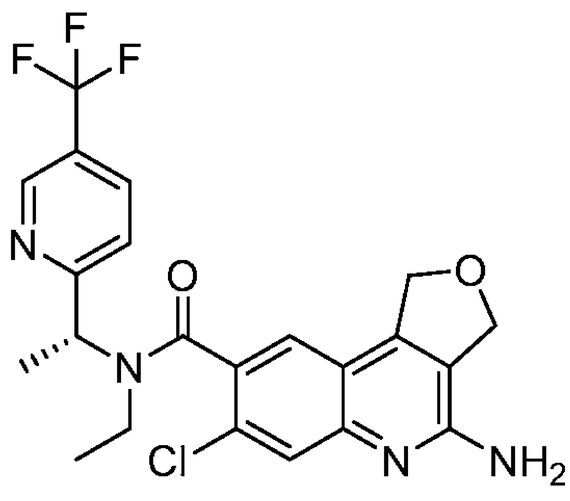
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
720		(3R)-4-amino-N-ethyl-3-methyl-N-((1-methyl-1H-1,2,4-triazol-3-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	366.95
721		4-amino-N-cyclobutyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	445.2
722		(3R)-4-amino-N-cyclobutyl-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	458.2

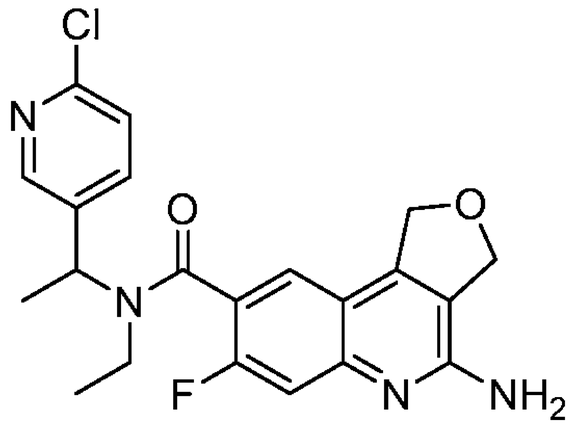
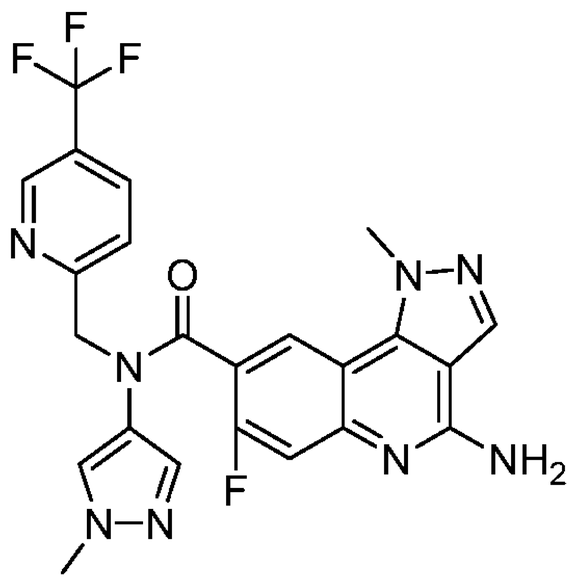
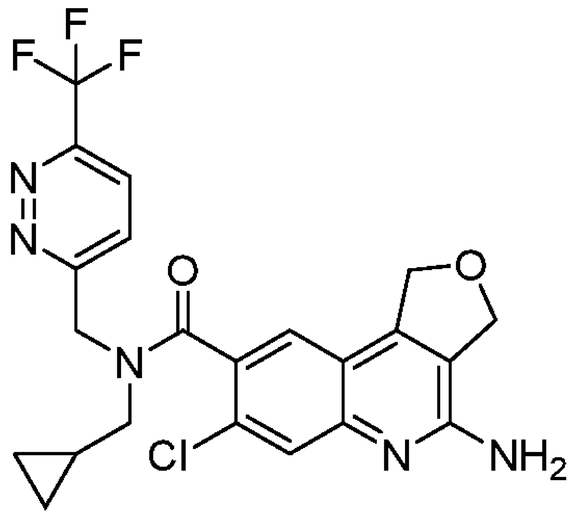
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
723		4-amino-N-((6-(difluoromethoxy)-3-pyridazinyl)methyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	416.2
724		4-amino-N-((6-(difluoromethoxy)-3-pyridazinyl)methyl)-N-ethyl-7-fluoro-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	434.05
725		4-amino-7-fluoro-N-((1R)-1-(5-fluoro-2-pyrimidinyl)ethyl)-N-(2-(trifluoromethoxy)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide and 4-amino-7-fluoro-N-((1S)-1-(5-fluoro-2-pyrimidinyl)ethyl)-N-(2-(trifluoromethoxy)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	484.15

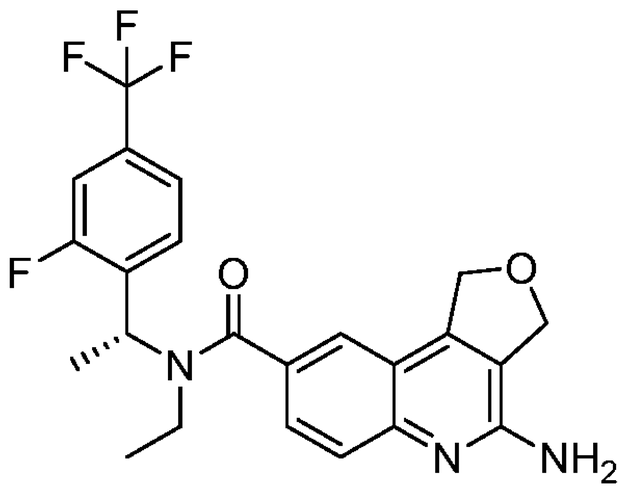
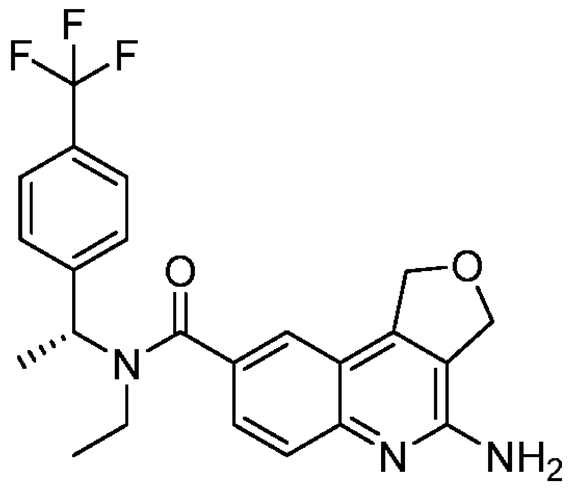
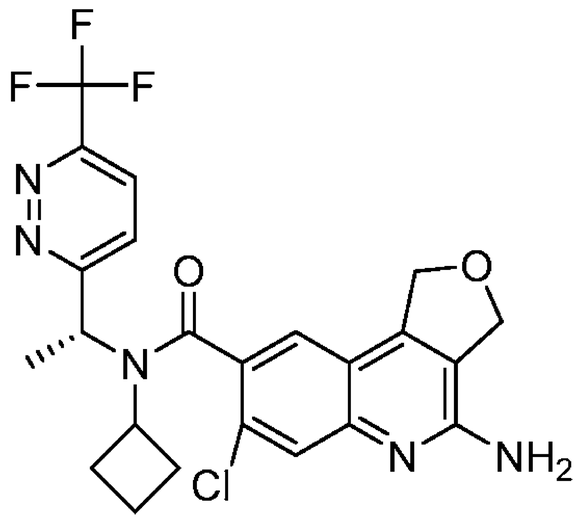
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
726		(3R)-4-amino-N-((6-(difluoromethoxy)-3-pyridazinyl)methyl)-N-ethyl-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	430.05
727		4-amino-N-((1R)-1-(6-chloro-3-pyridinyl)ethyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide and 4-amino-N-((1S)-1-(6-chloro-3-pyridinyl)ethyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	397.1
728		4-amino-N-((2R)-1-methoxy-2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	462

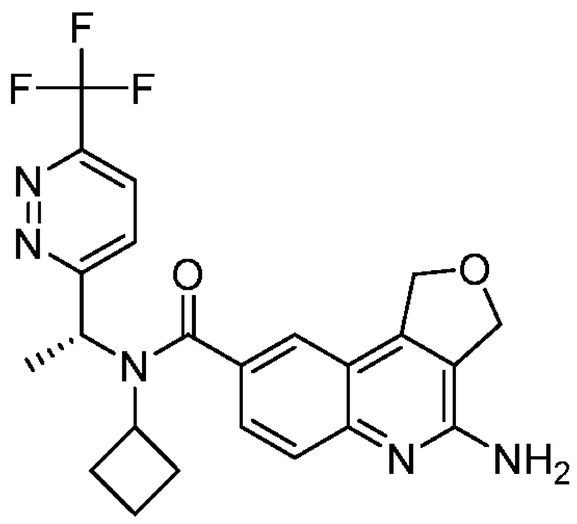
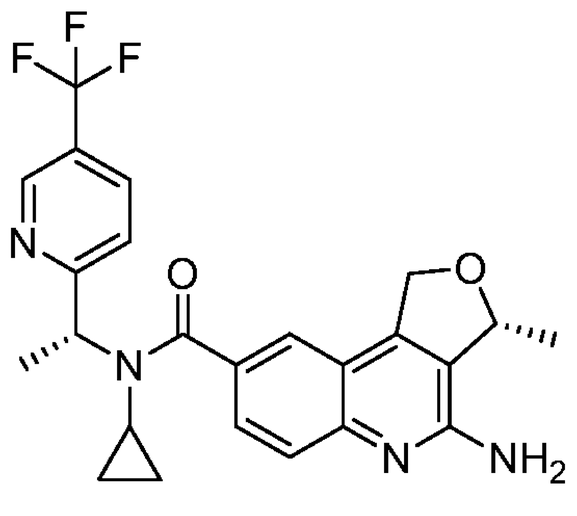
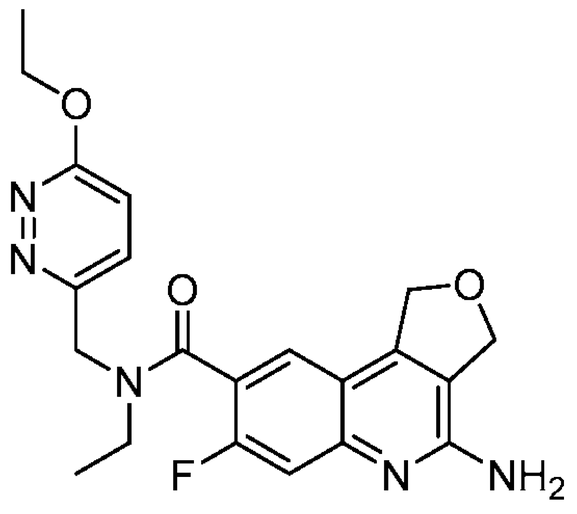
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
729		4-amino-7-fluoro-N-(1-(trifluoromethyl)-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	541.2
730		4-amino-N-(cyclopropylmethyl)-7-fluoro-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	462.1
731		4-amino-N-(cyclopropylmethyl)-7-fluoro-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide	474.1

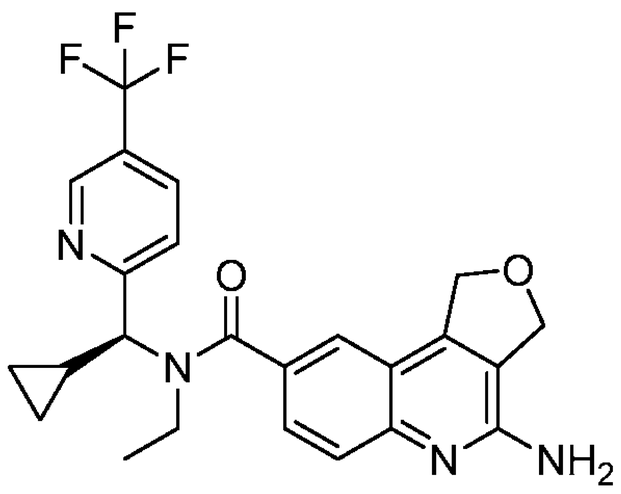
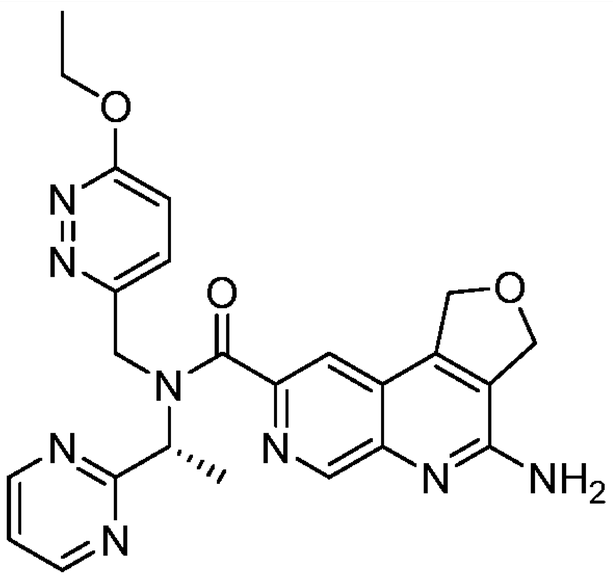
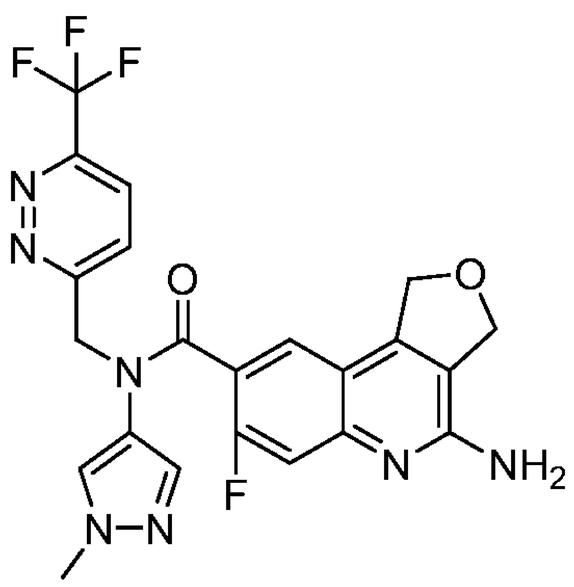
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
732		4-amino-N-(1-(trifluoromethyl)-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	524
733		4-amino-N-(2-propanyl)-N-(4-(trifluoromethyl)benzyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	431
734		4-amino-N-cyclopropyl-N-(4-(trifluoromethyl)benzyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	429

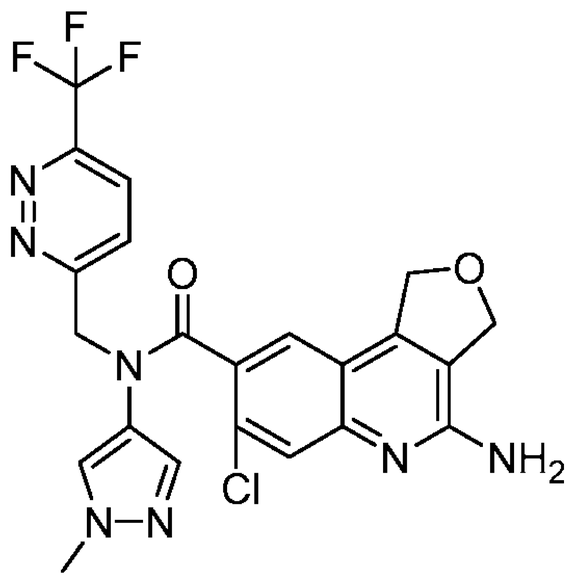
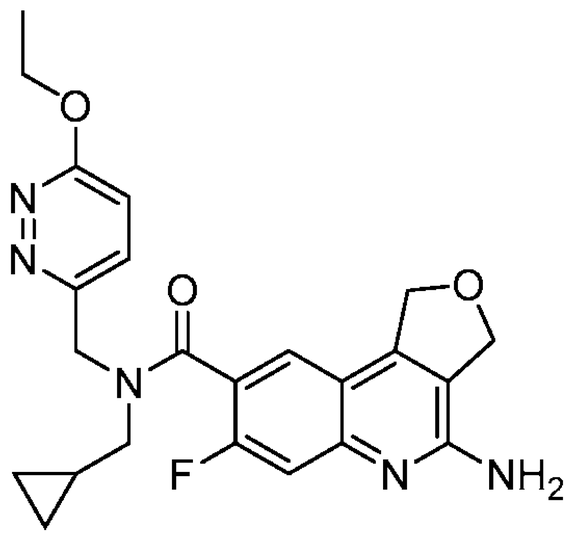
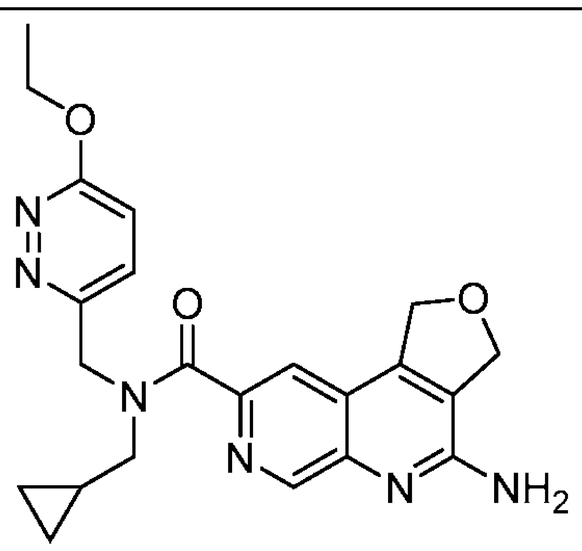
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
735		4-amino-N-cyclopropyl-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	443
736		4-amino-N-cyclopropyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	443
737		4-amino-7-chloro-N-((1R)-1-(6-chloro-3-pyridinyl)ethyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide and 4-amino-7-chloro-N-((1S)-1-(6-chloro-3-pyridinyl)ethyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	431
738		4-amino-7-chloro-N-ethyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	465.1

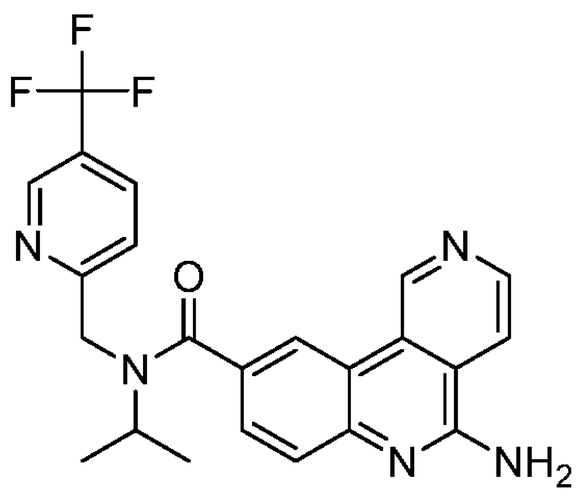
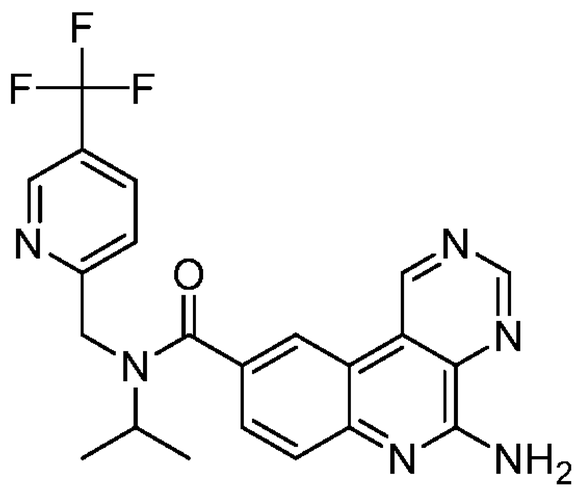
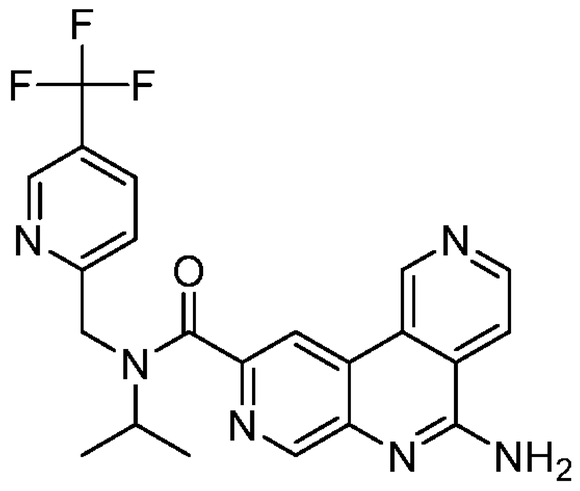
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
739		4-amino-N-((1R)-1-(6-chloro-3-pyridinyl)ethyl)-N-ethyl-7-fluoro-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide and 4-amino-N-((1S)-1-(6-chloro-3-pyridinyl)ethyl)-N-ethyl-7-fluoro-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	415
740		4-amino-7-fluoro-1-methyl-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	499.2
741		4-amino-7-chloro-N-(cyclopropylmethyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	478

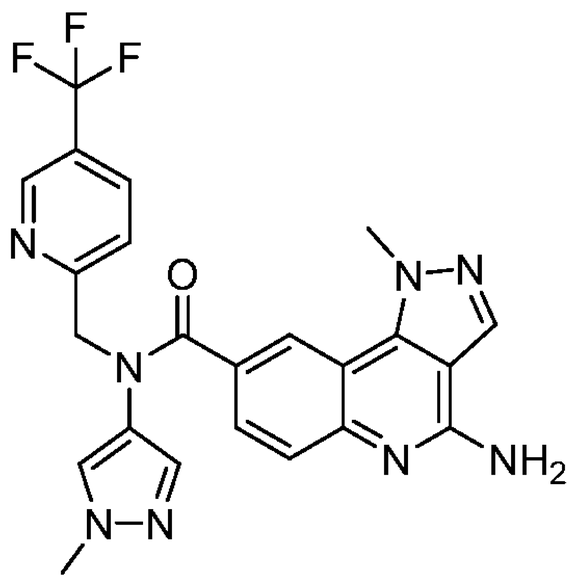
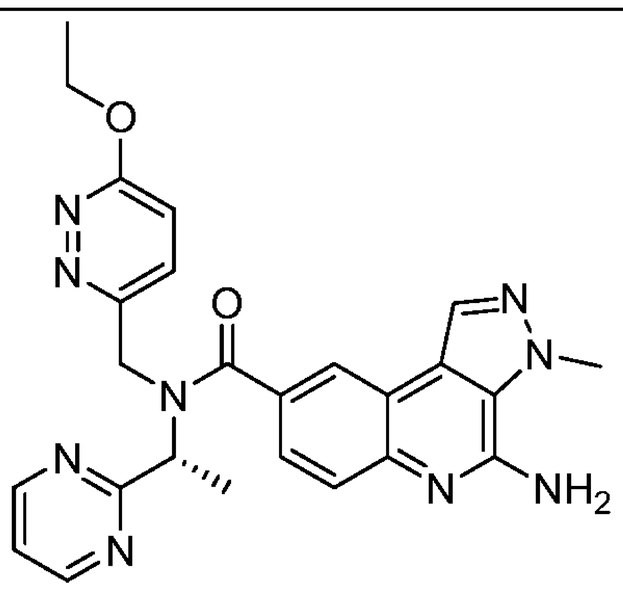
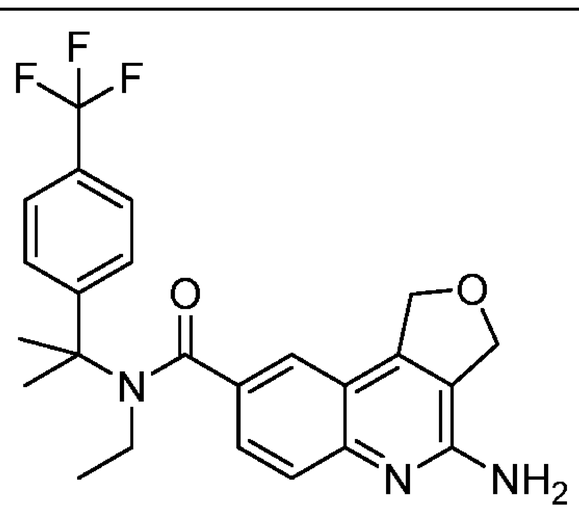
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
742		4-amino-N-ethyl-N-((1R)-1-(2-fluoro-4-(trifluoromethyl)phenyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	448.1
743		4-amino-N-ethyl-N-((1R)-1-(4-(trifluoromethyl)phenyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	430.2
744		4-amino-7-chloro-N-cyclobutyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	492.2

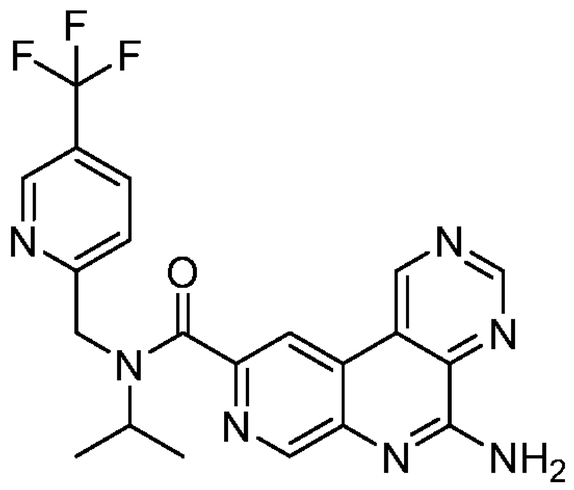
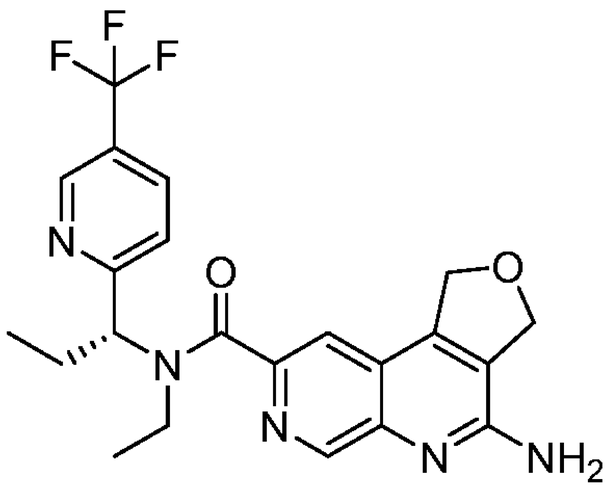
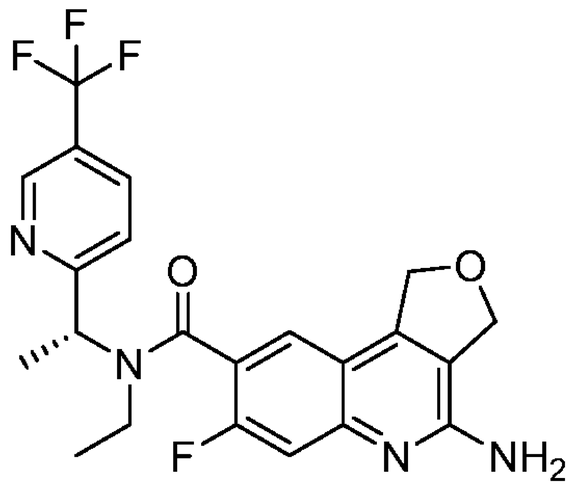
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
745		4-amino-N-cyclobutyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	457.9
746		(3R)-4-amino-N-cyclopropyl-3-methyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	457
747		4-amino-N-((6-ethoxy-3-pyridazinyl)methyl)-N-ethyl-7-fluoro-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	412.15

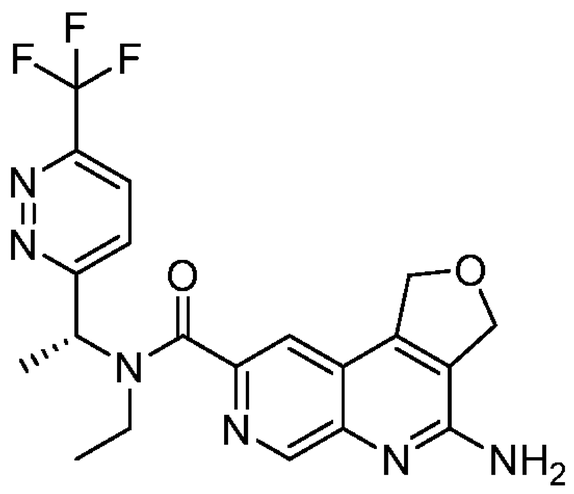
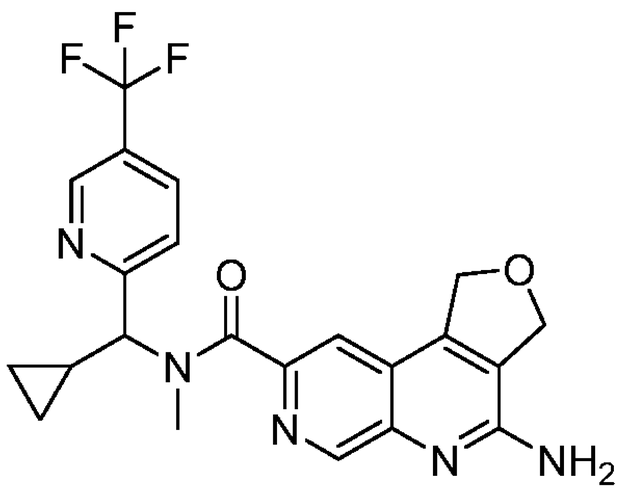
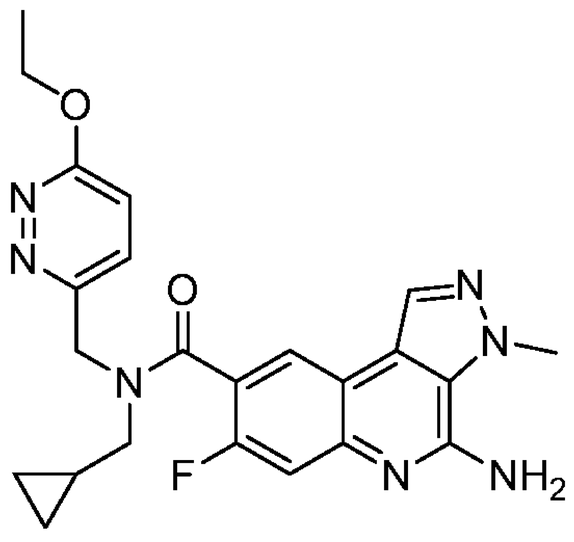
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
748		4-amino-N-((S)-cyclopropyl(5-(trifluoromethyl)-2-pyridinyl)methyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	457.2
749		4-amino-N-((6-ethoxy-3-pyridazinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	473.2
750		4-amino-7-fluoro-N-(1-methyl-1H-pyrazol-4-yl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	488.2

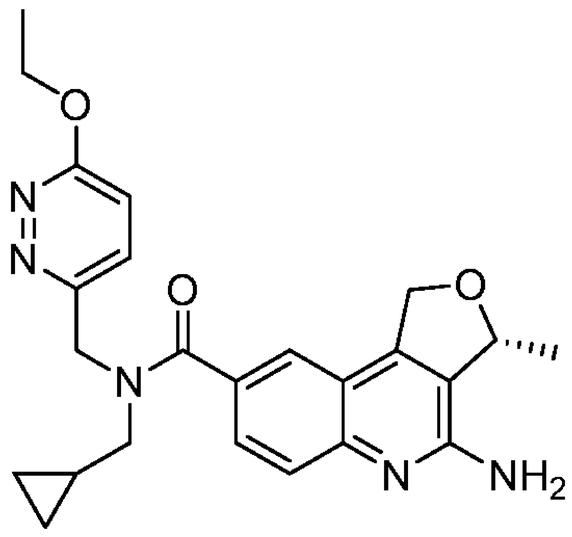
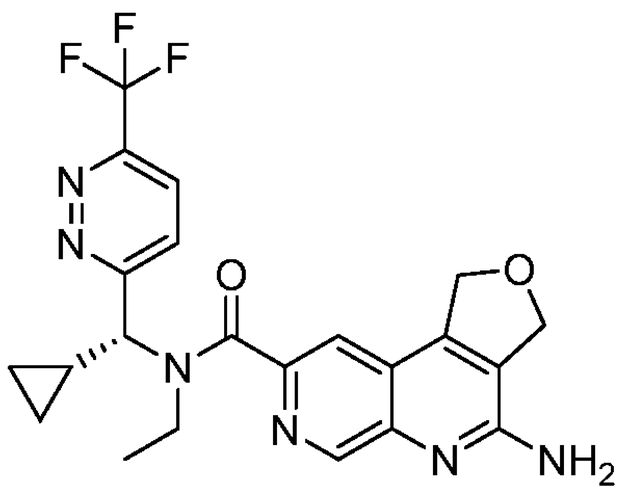
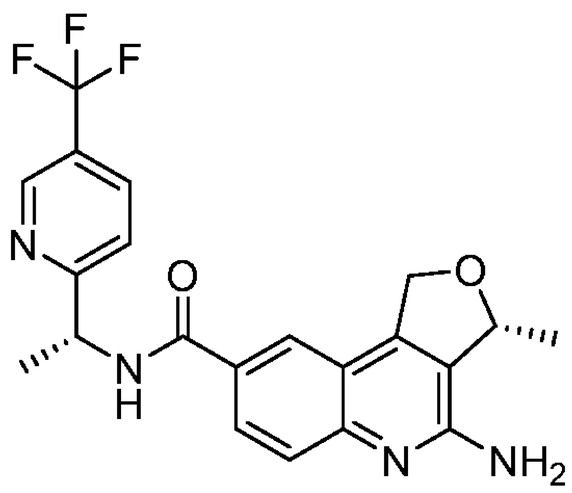
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
751		4-amino-7-chloro-N-(1-methyl-1H-pyrazol-4-yl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	504.1
752		4-amino-N-(cyclopropylmethyl)-N-((6-ethoxy-3-pyridazinyl)methyl)-7-fluoro-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	438.2
753		4-amino-N-(cyclopropylmethyl)-N-((6-ethoxy-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	421.25

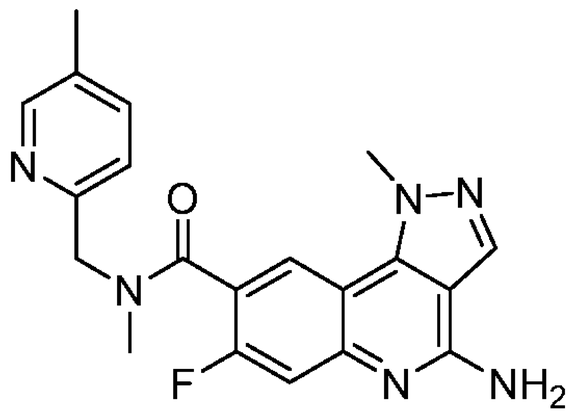
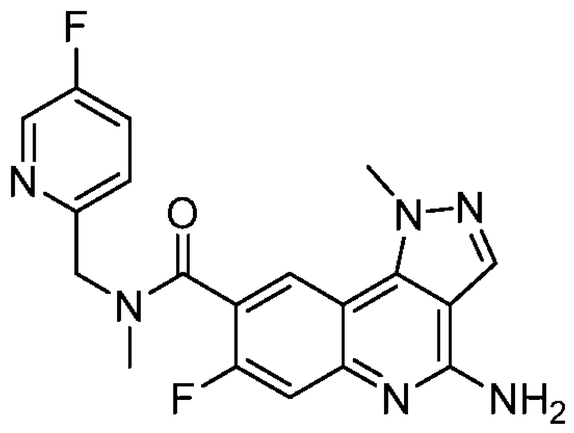
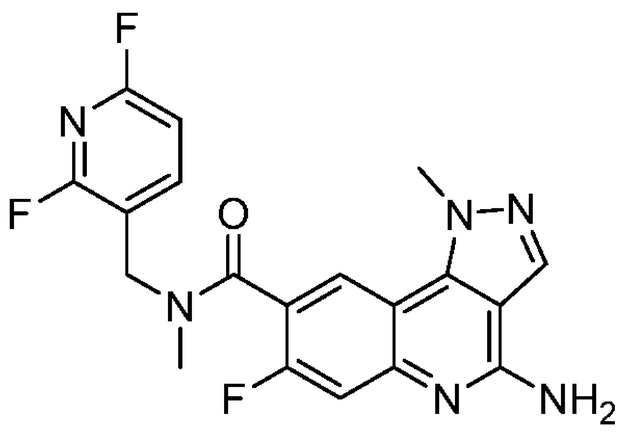
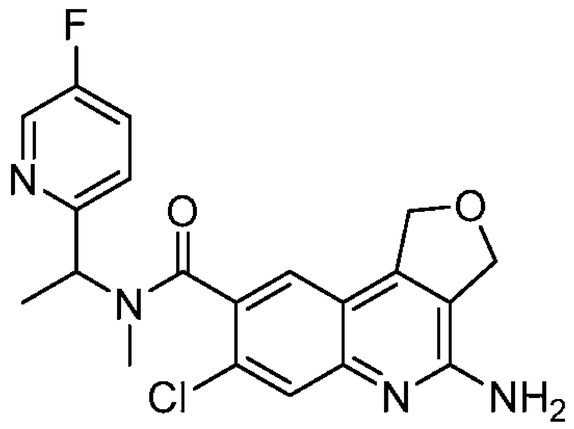
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
754		5-amino-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)benzo[c][2,6]naphthyridine-9-carboxamide	440.1
755		5-amino-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)pyrimido[4,5-c]quinoline-9-carboxamide	441.2
756		5-amino-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)pyrido[4,3-c][1,7]naphthyridine-9-carboxamide	441.1

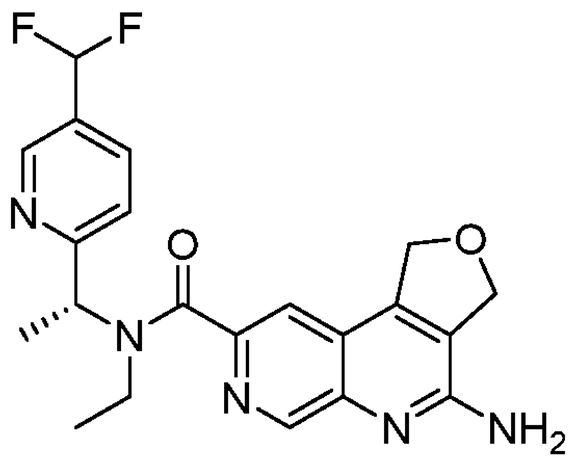
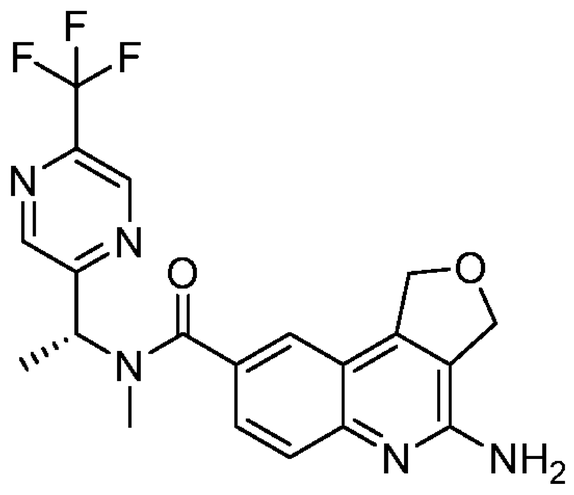
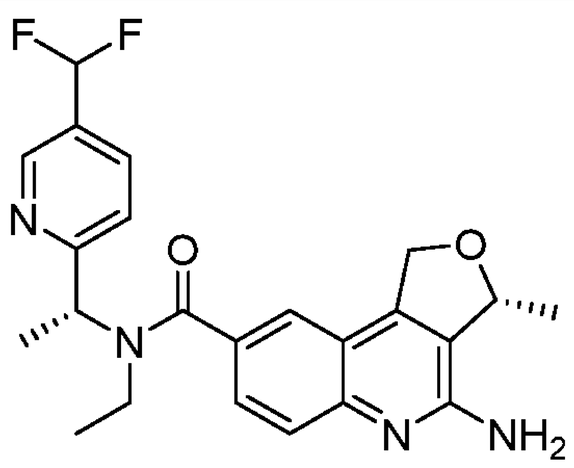
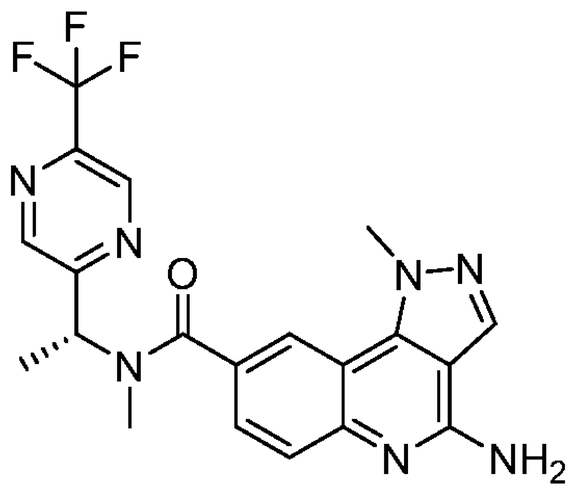
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
757		4-amino-1-methyl-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	481
758		4-amino-N-((6-ethoxy-3-pyridazinyl)methyl)-3-methyl-N-((1R)-1-(2-pyrimidinyl)ethyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide	484.25
759		4-amino-N-ethyl-N-(2-(4-(trifluoromethyl)phenyl)-2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	444.1

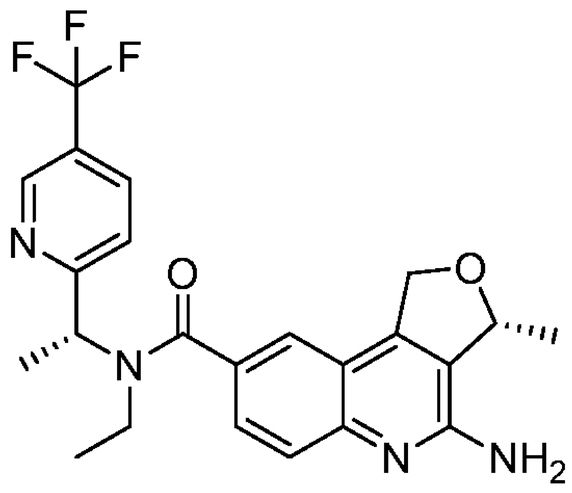
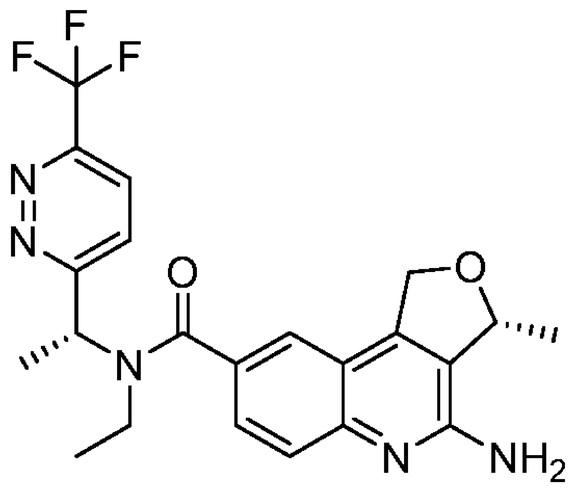
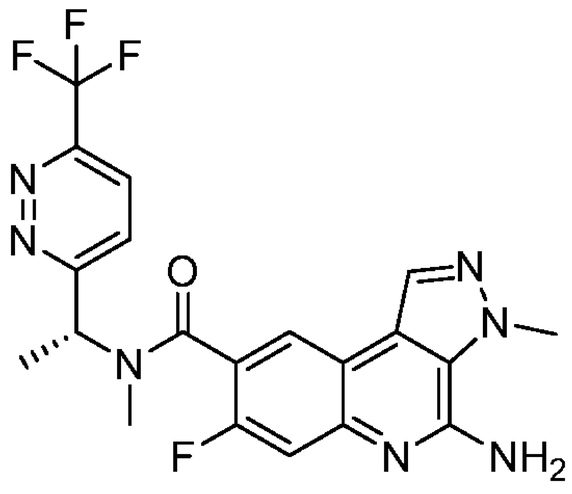
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
760		5-amino-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)pyrimido[4,5-c][1,7]naphthyridine-9-carboxamide	442.1
761		4-amino-N-ethyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)propyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	446.2
762		4-amino-N-ethyl-7-fluoro-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	449

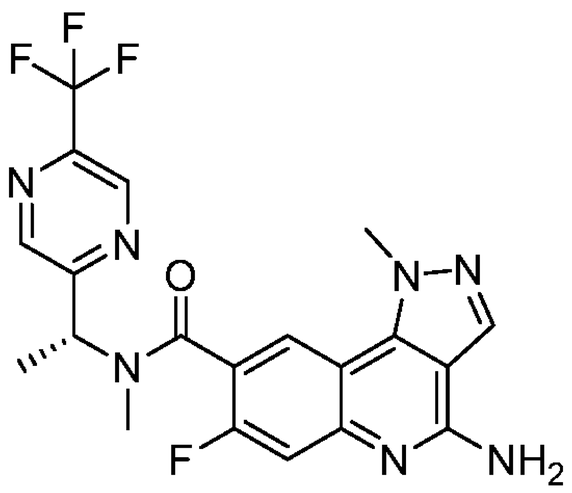
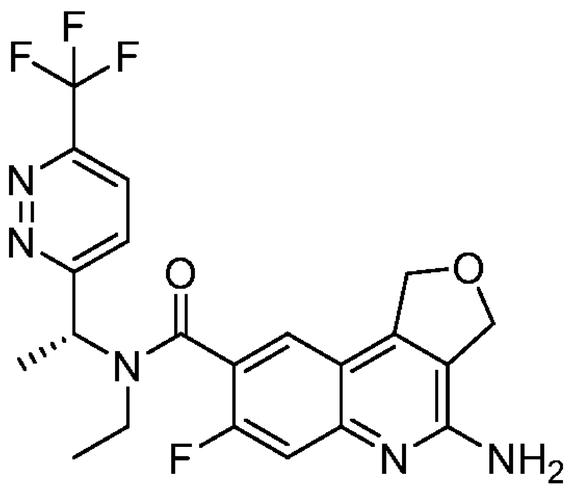
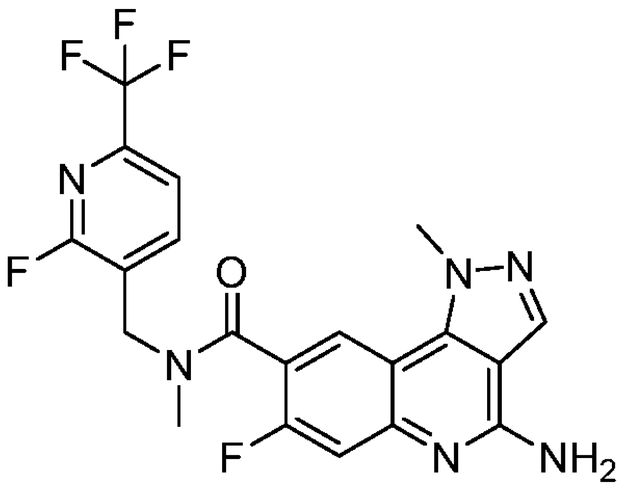
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
763		4-amino-N-ethyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	443
764		4-amino-N-((R)-cyclopropyl(5-(trifluoromethyl)-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide and 4-amino-N-((S)-cyclopropyl(5-(trifluoromethyl)-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	444.2
765		4-amino-N-(cyclopropylmethyl)-N-((6-ethoxy-3-pyridazinyl)methyl)-7-fluoro-3-methyl-3H-pyrazolo[3,4-c]quinoline-8-carboxamide	450.25

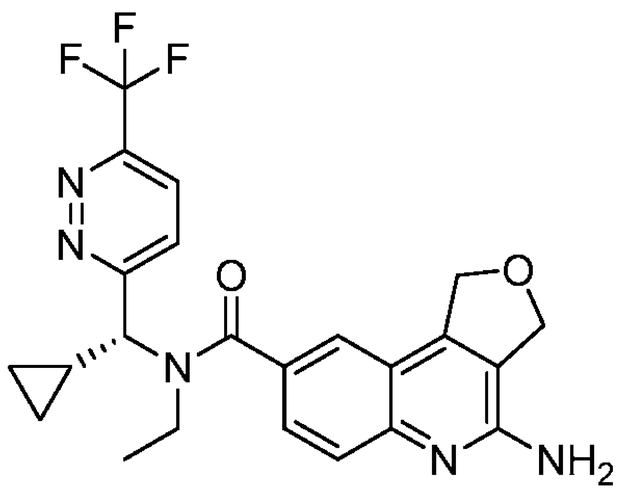
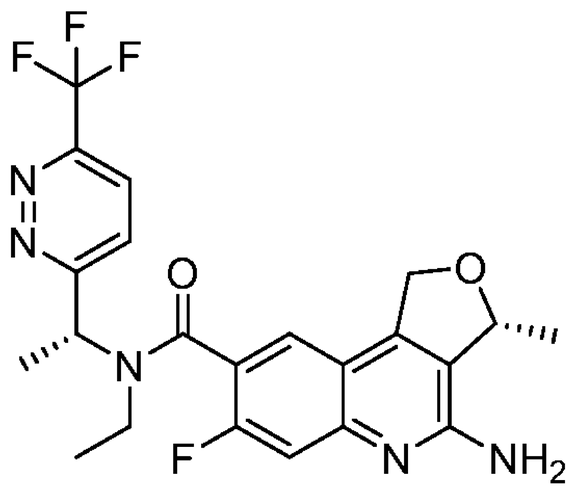
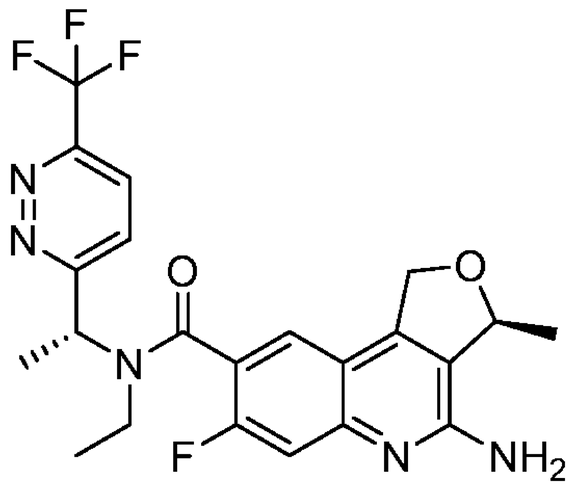
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
766		(3R)-4-amino-N-(cyclopropylmethyl)-N-((6-ethoxy-3-pyridazinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	434.2
767		4-amino-N-((R)-cyclopropyl(6-(trifluoromethyl)-3-pyridazinyl)methyl)-N-ethyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	459.1
768		(3R)-4-amino-3-methyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	417.2

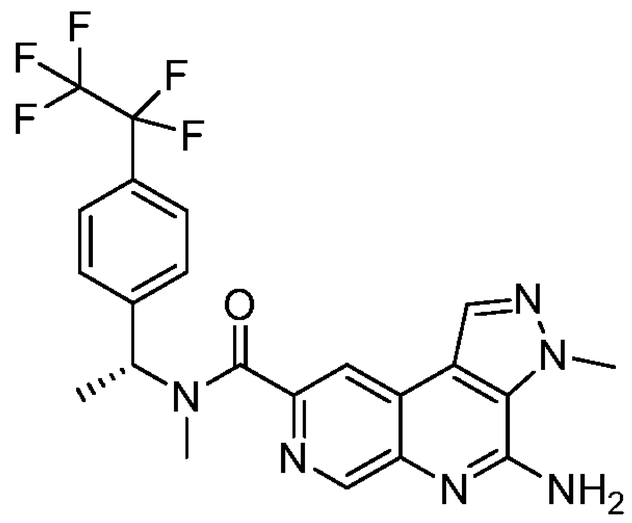
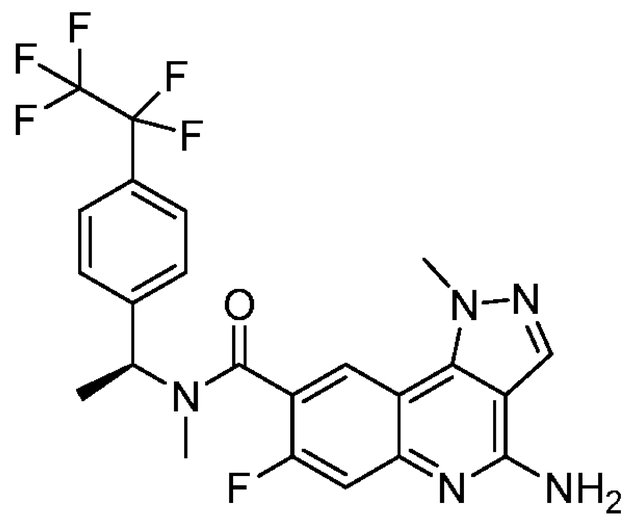
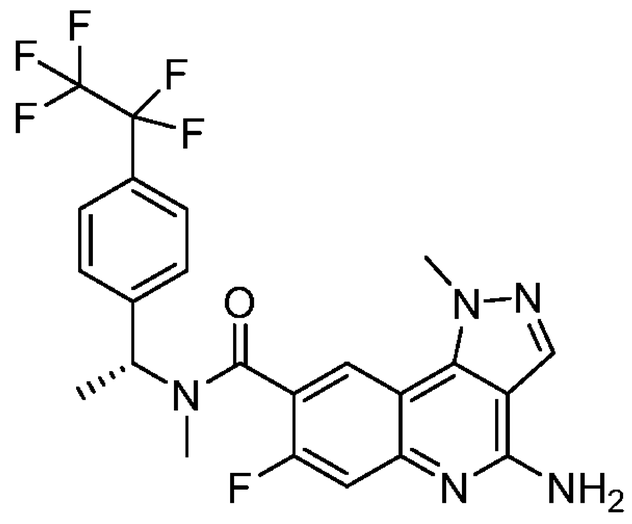
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
769		4-amino-7-fluoro-N,1-dimethyl-N-((5-methyl-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	379
770		4-amino-7-fluoro-N-((5-fluoro-2-pyridinyl)methyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	383.2
771		4-amino-N-((2,6-difluoro-3-pyridinyl)methyl)-7-fluoro-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	401.9
772		4-amino-7-chloro-N-((1R)-1-(5-fluoro-2-pyridinyl)ethyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide and 4-amino-7-chloro-N-((1S)-1-(5-fluoro-2-pyridinyl)ethyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	401

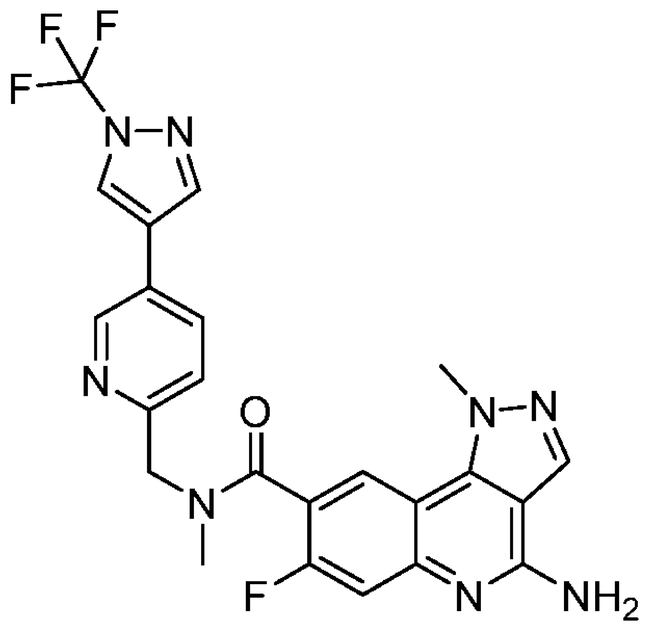
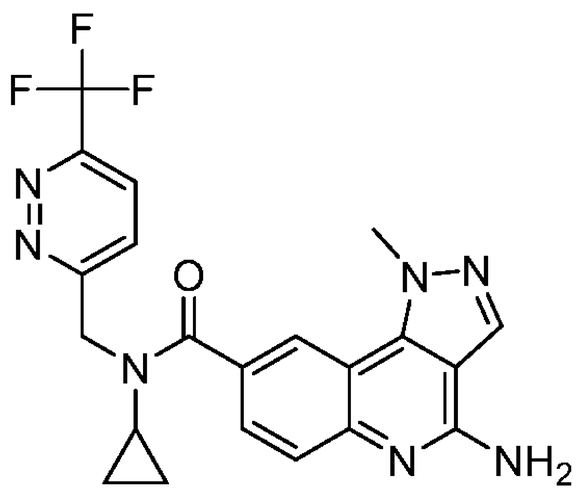
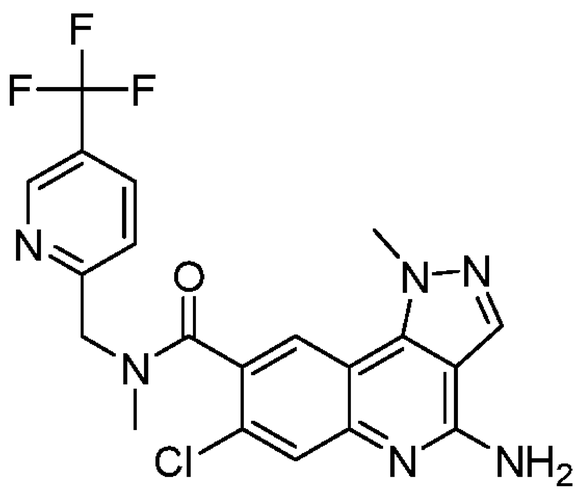
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
773		4-amino-N-((1R)-1-(5-(difluoromethyl)-2-pyridinyl)ethyl)-N-ethyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	414.1
774		4-amino-N-methyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyrazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	418.1
775		(3R)-4-amino-N-((1R)-1-(5-(difluoromethyl)-2-pyridinyl)ethyl)-N-ethyl-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	427.1
776		4-amino-N,1-dimethyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyrazinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	430.1

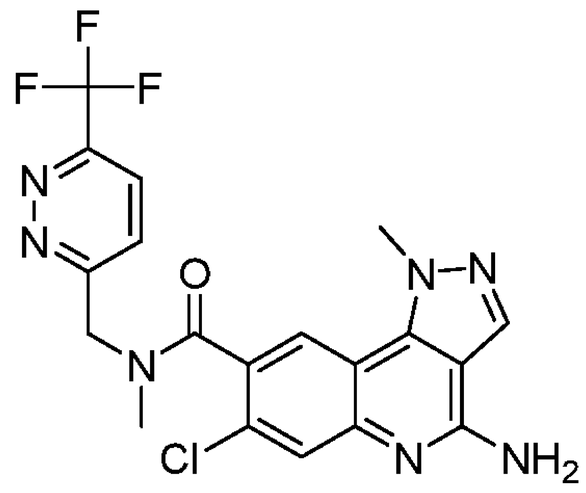
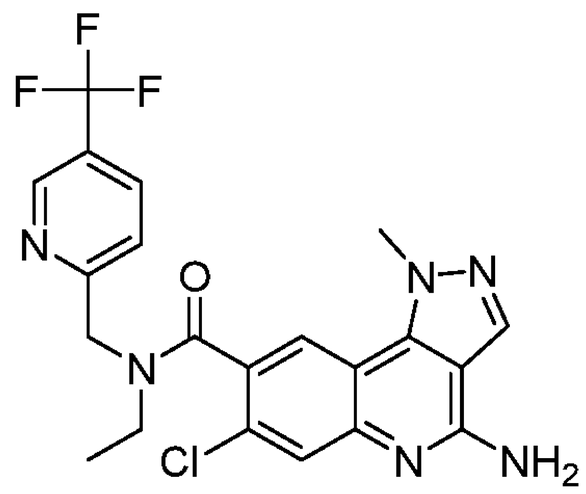
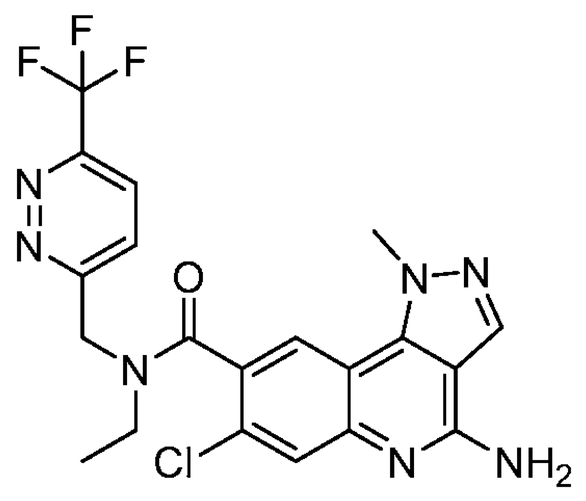
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
777		(3R)-4-amino-N-ethyl-3-methyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	445.1
778		(3R)-4-amino-N-ethyl-3-methyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	446.1
779		4-amino-7-fluoro-N,3-dimethyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide	448.1

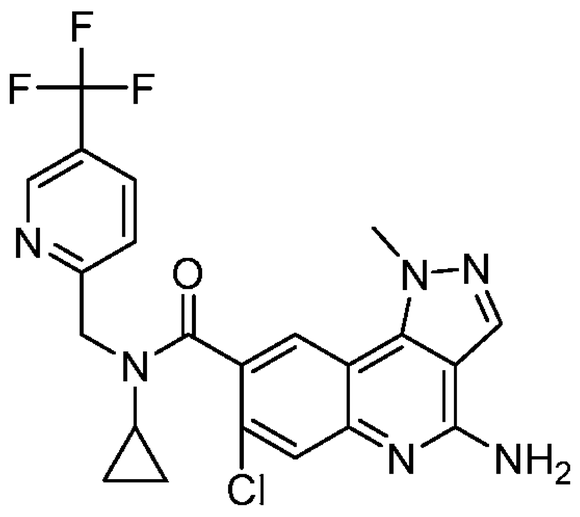
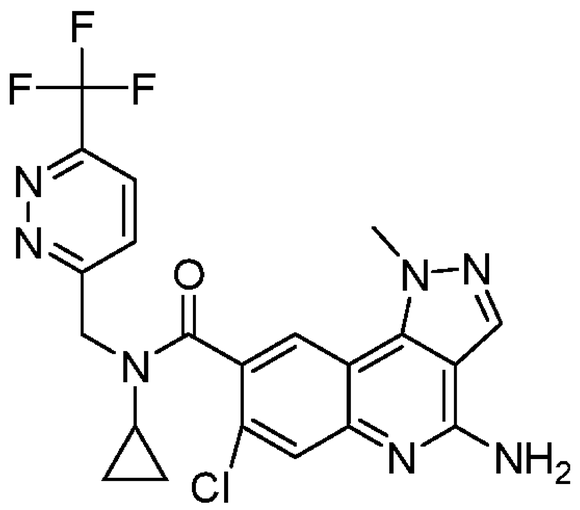
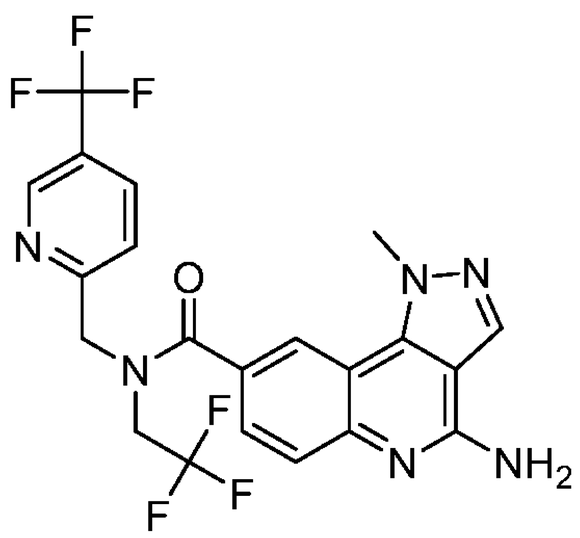
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
780		4-amino-7-fluoro-N,1-dimethyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyrazinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	448.1
781		4-amino-N-ethyl-7-fluoro-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	450.1
782		4-amino-7-fluoro-N-((2-fluoro-6-(trifluoromethyl)-3-pyridinyl)methyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	451.1

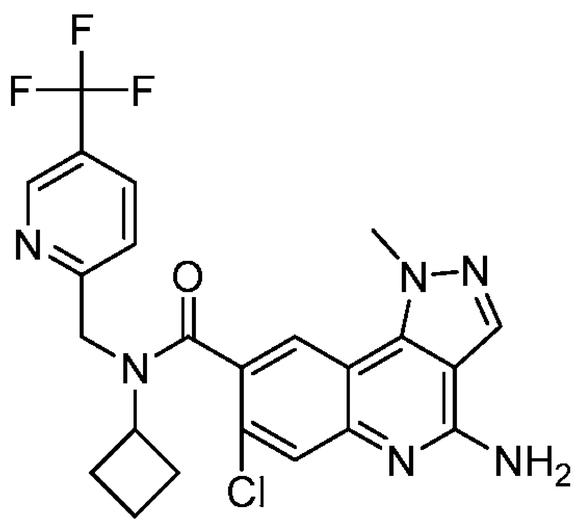
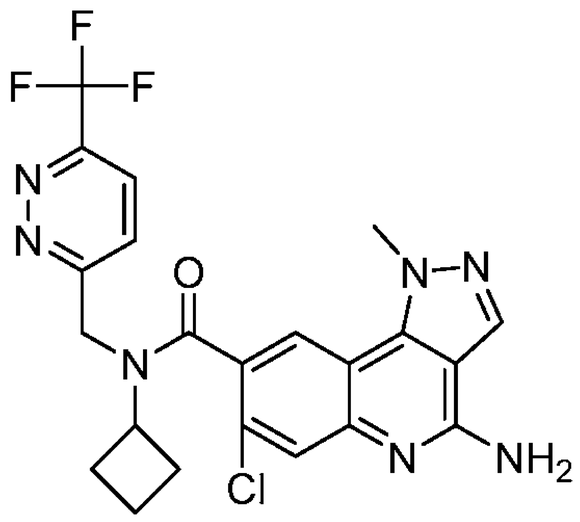
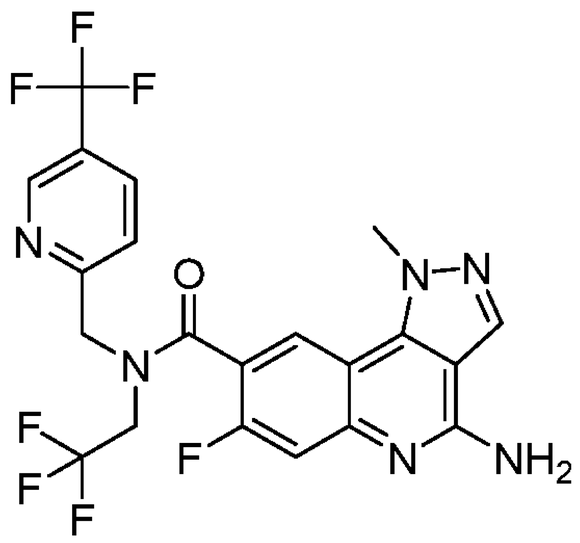
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
783		4-amino-N-((R)-cyclopropyl(6-(trifluoromethyl)-3-pyridazinyl)methyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	458.2
784		(3R)-4-amino-N-ethyl-7-fluoro-3-methyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	464.1
785		(3S)-4-amino-N-ethyl-7-fluoro-3-methyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	464.1

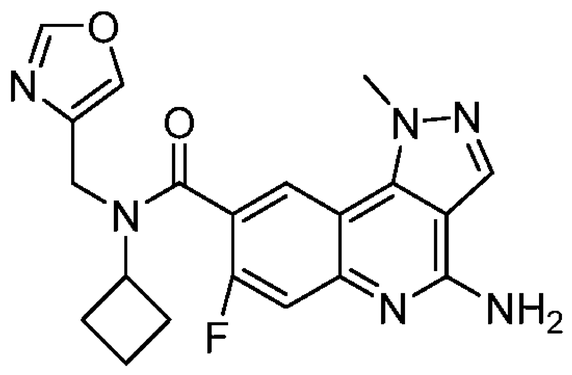
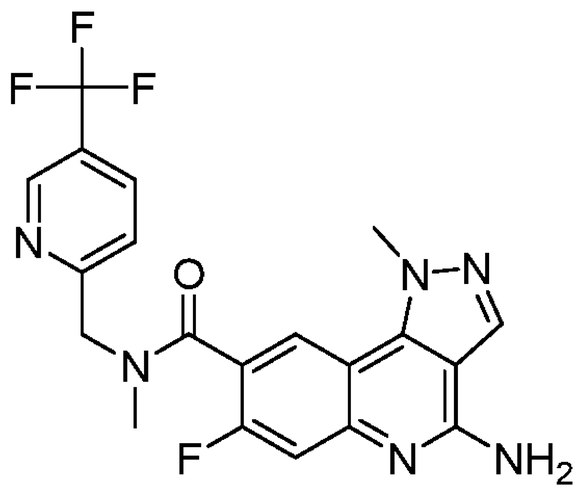
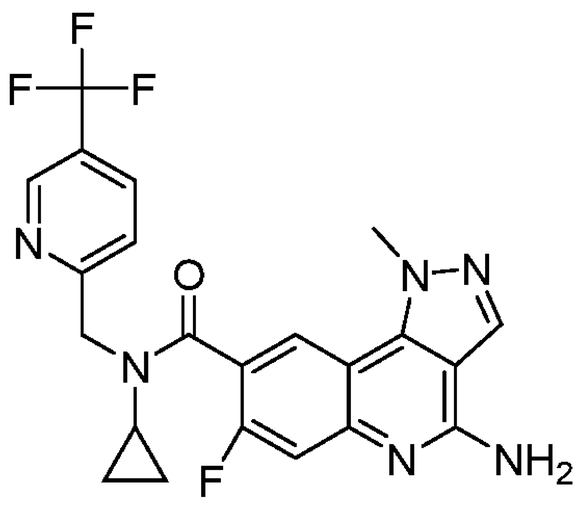
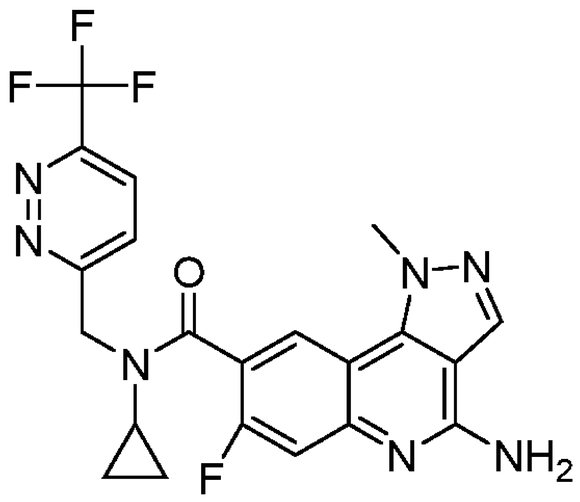
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
786		4-amino-N,3-dimethyl-N-((1R)-1-(4-(pentafluoroethyl)phenyl)ethyl)-3H-pyrazolo[3,4-c][1,7]naphthyridine-8-carboxamide	479.1
787		4-amino-7-fluoro-N,1-dimethyl-N-((1S)-1-(4-(pentafluoroethyl)phenyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	496.1
788		4-amino-7-fluoro-N,1-dimethyl-N-((1R)-1-(4-(pentafluoroethyl)phenyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	496.1

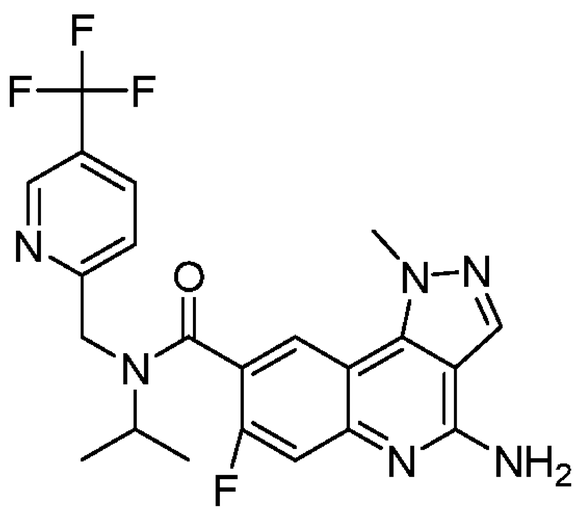
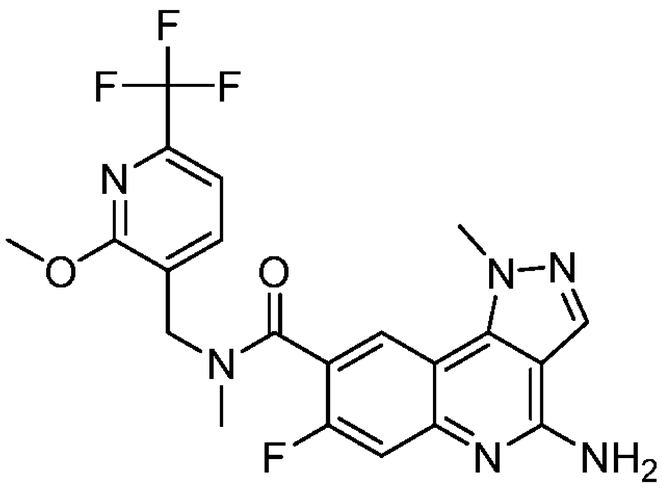
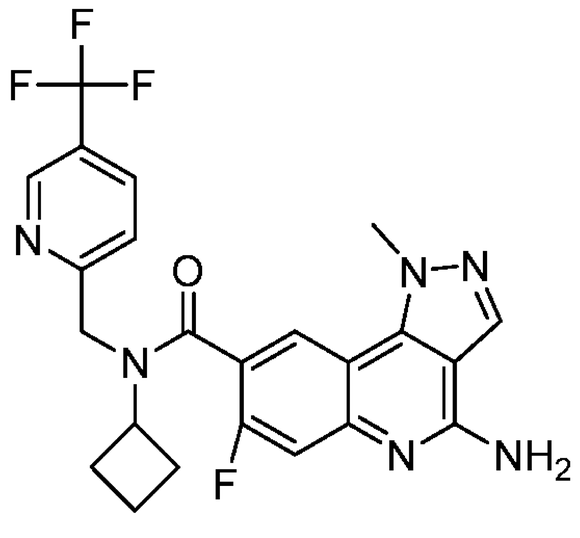
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
789		4-amino-7-fluoro-N,1-dimethyl-N-((5-(1-(trifluoromethyl)-1H-pyrazol-4-yl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	499.4
790		4-amino-N-cyclopropyl-1-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	442.1
791		4-amino-7-chloro-N,1-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	449.15

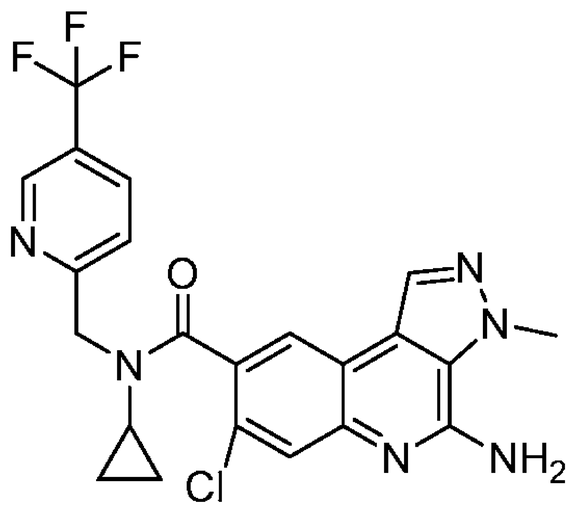
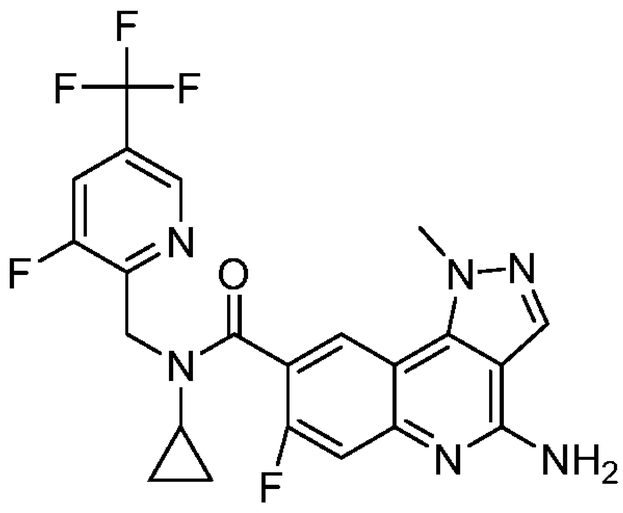
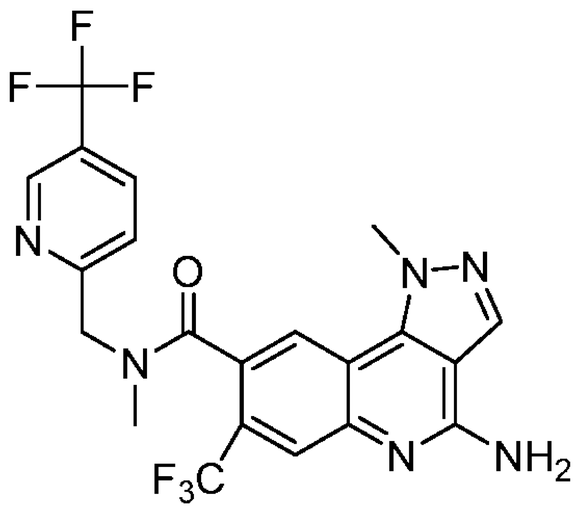
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
792		4-amino-7-chloro-N,1-dimethyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	450.1
793		4-amino-7-chloro-N-ethyl-1-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	463.1
794		4-amino-7-chloro-N-ethyl-1-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	464.2

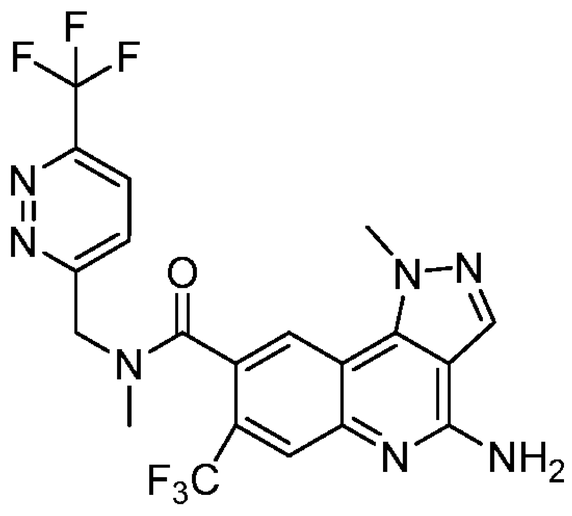
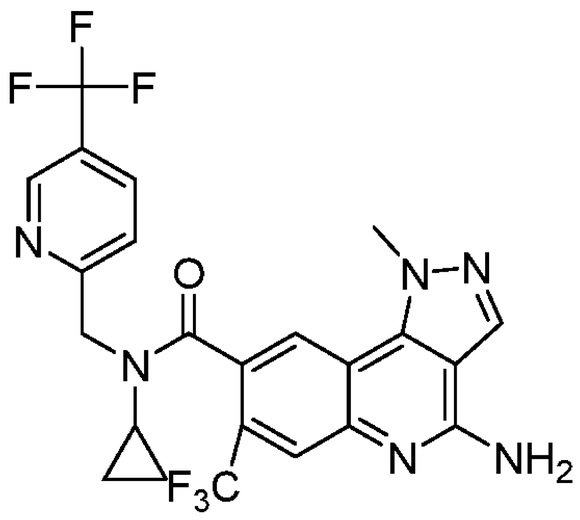
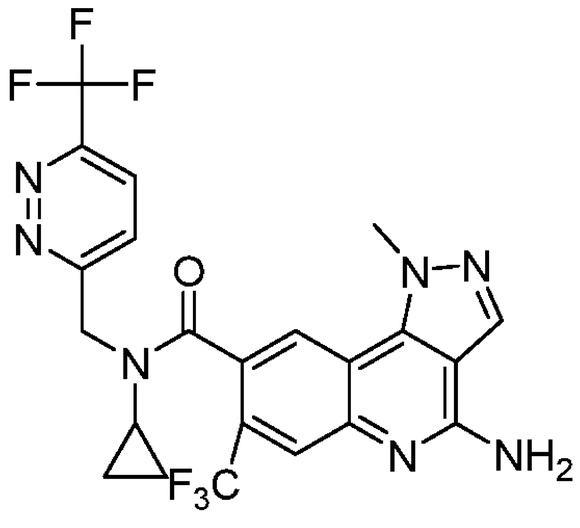
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
795		4-amino-7-chloro-N-cyclopropyl-1-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	475.1
796		4-amino-7-chloro-N-cyclopropyl-1-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	476.2
797		4-amino-1-methyl-N-(2,2,2-trifluoroethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	483

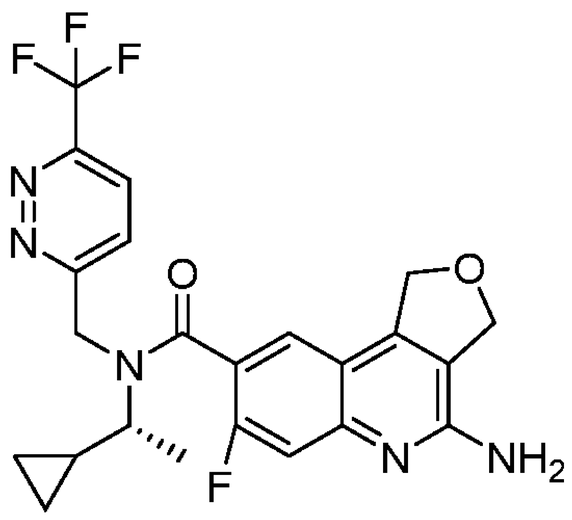
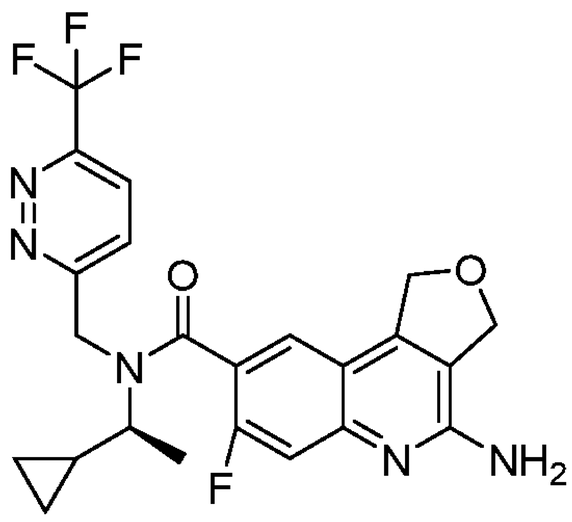
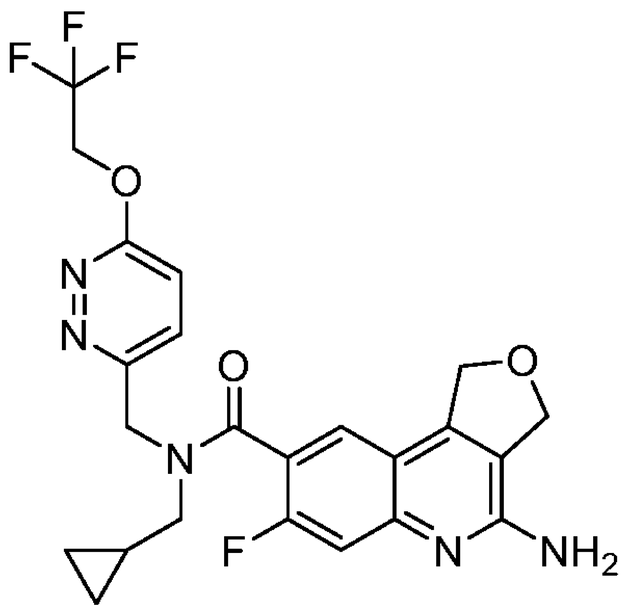
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
798		4-amino-7-chloro-N-cyclobutyl-1-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	489.2
799		4-amino-7-chloro-N-cyclobutyl-1-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	490.15
800		4-amino-7-fluoro-1-methyl-N-(2,2,2-trifluoroethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	501.1

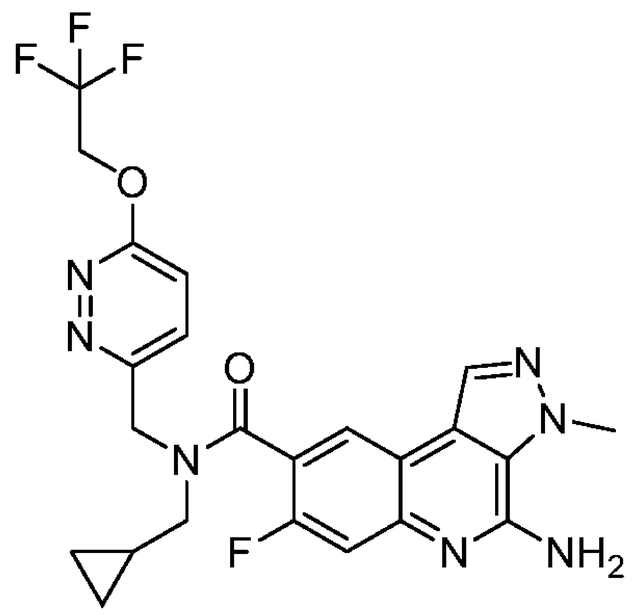
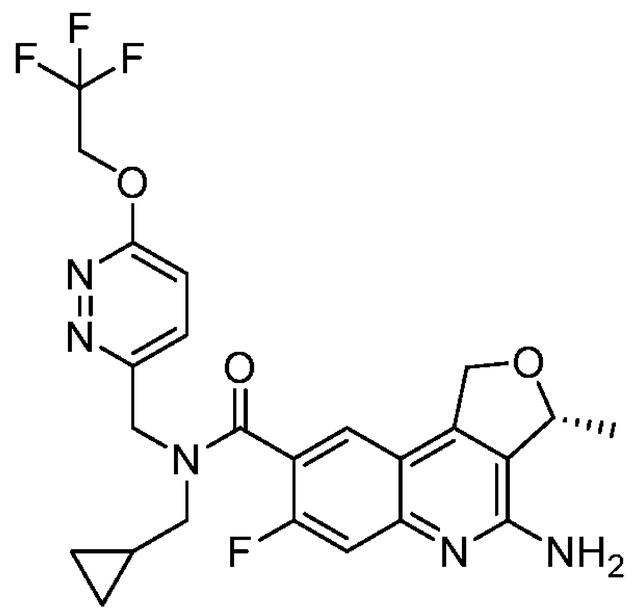
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
801		4-amino-N-cyclobutyl-7-fluoro-1-methyl-N-(1,3-oxazol-4-ylmethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	395
802		4-amino-7-fluoro-N,1-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	432.9
803		4-amino-N-cyclopropyl-7-fluoro-1-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	459
804		4-amino-N-cyclopropyl-7-fluoro-1-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	459.9

Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
805		4-amino-7-fluoro-1-methyl-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	460.9
806		4-amino-7-fluoro-N-((2-methoxy-6-(trifluoromethyl)-3-pyridinyl)methyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	462.9
807		4-amino-N-cyclobutyl-7-fluoro-1-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	473

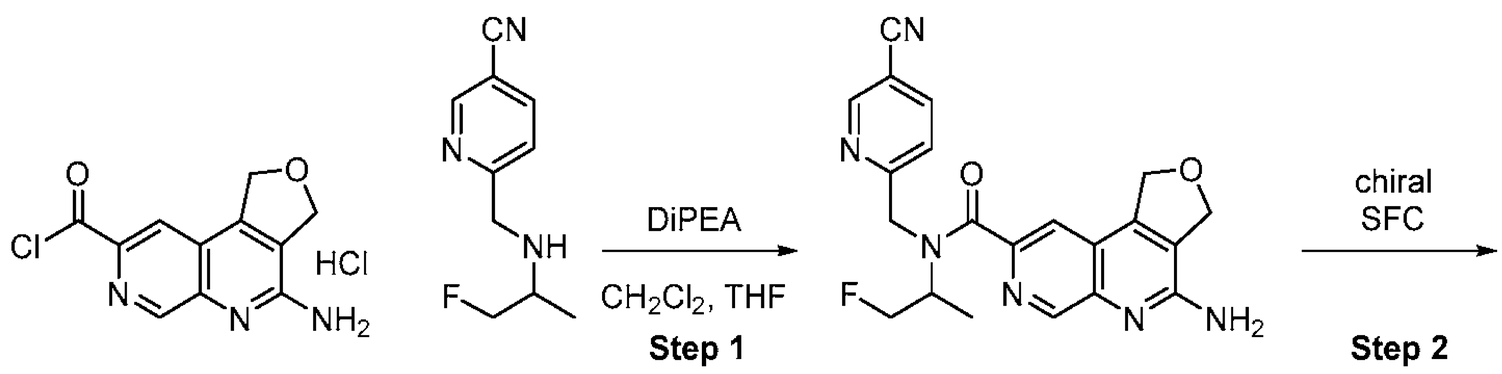
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
808		4-amino-7-chloro-N-cyclopropyl-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide	474.9
809		4-amino-N-cyclopropyl-7-fluoro-N-((3-fluoro-5-(trifluoromethyl)-2-pyridinyl)methyl)-1-methyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	477
810		4-amino-N,1-dimethyl-7-(trifluoromethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	483.2

Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
811		4-amino-N,1-dimethyl-7-(trifluoromethyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	484.1
812		4-amino-N-cyclopropyl-1-methyl-7-(trifluoromethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	508.8
813		4-amino-N-cyclopropyl-1-methyl-7-(trifluoromethyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	510.2

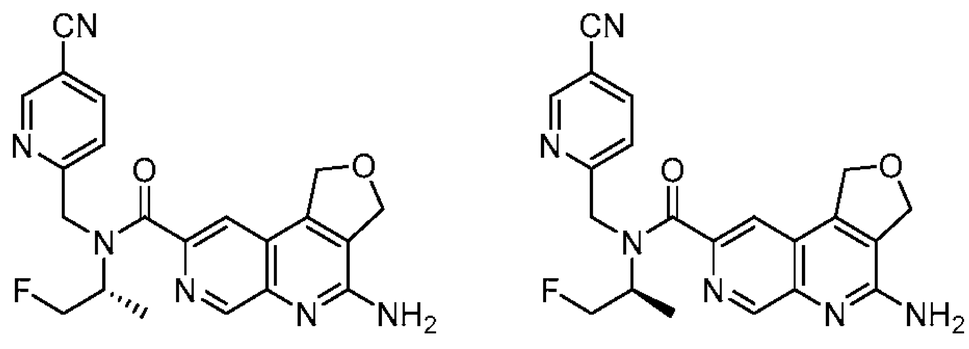
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
814		4-amino-N-((1R)-1-cyclopropylethyl)-7-fluoro-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	476.05
815		4-amino-N-((1S)-1-cyclopropylethyl)-7-fluoro-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	476.05
816		4-amino-N-(cyclopropylmethyl)-7-fluoro-N-((6-(2,2,2-trifluoroethoxy)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	492.1

Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
817		4-amino-N-(cyclopropylmethyl)-7-fluoro-3-methyl-N-((6-(2,2,2-trifluoroethoxy)-3-pyridazinyl)methyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide	504.1
818		(3R)-4-amino-N-(cyclopropylmethyl)-7-fluoro-3-methyl-N-((6-(2,2,2-trifluoroethoxy)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	506.2

[0270] Example 819: (S)-4-amino-N-((5-cyanopyridin-2-yl)methyl)-N-(1-fluoropropan-2-yl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide.



102



819
peak 1

820
peak 2

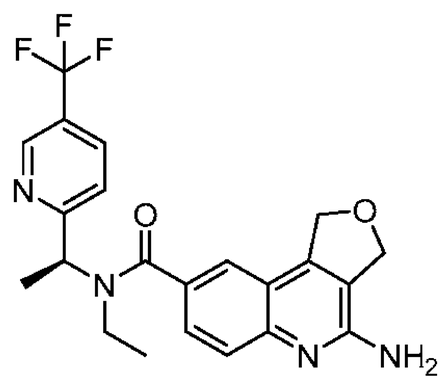
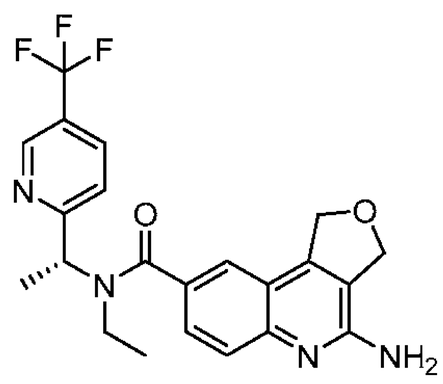
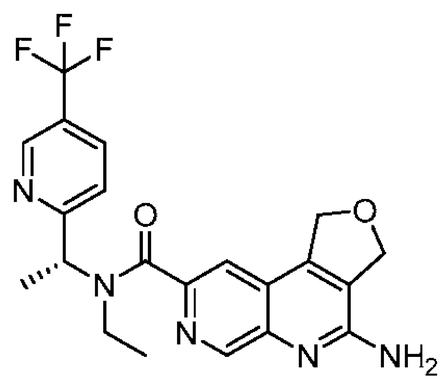
[0271] To a stirred ice-cooled solution of 6-(((1-fluoropropan-2-yl)amino)methyl)nicotinonitrile (**102,** 80 mg, 0.41 mmol) and N-ethyl-N-isopropylpropan-2-amine (107 mg, 0.145 mL, 0.828 mmol, Aldrich) in DCM (1 mL) and tetrahydrofuran (1 mL) was added 4-amino-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carbonyl chloride (derived from acid **217,** 119 mg, 0.476 mmol) in one portion as a solid. The resulting mixture was stirred at 0°C for 1 h. The crude mixture was directly loaded on a silica gel precolumn (25 g) and subjected to combi-flash column chromatography on a 12-g ISCO gold column, eluting with MeOH (with 0.5% ammonium hydroxide)/DCM (15 min from 0 to 18%) to give 4-amino-N-((5-cyanopyridin-2-yl)methyl)-N-(1-fluoropropan-2-yl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide (100 mg, 0.246 mmol, 59.4% yield) as a white solid.

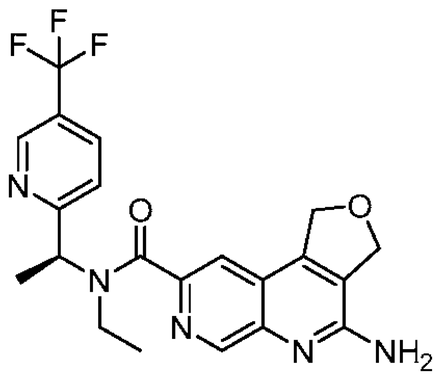
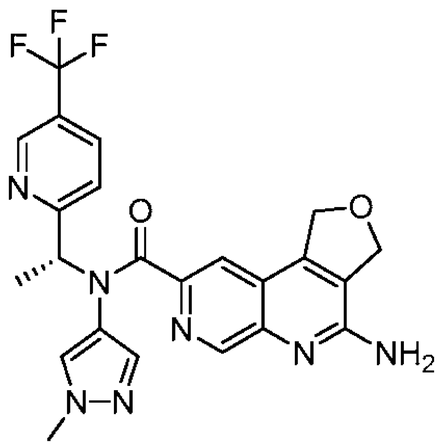
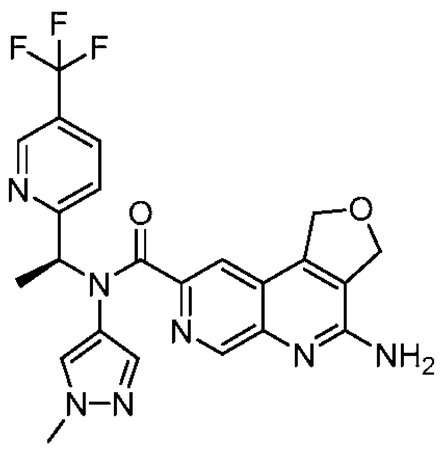
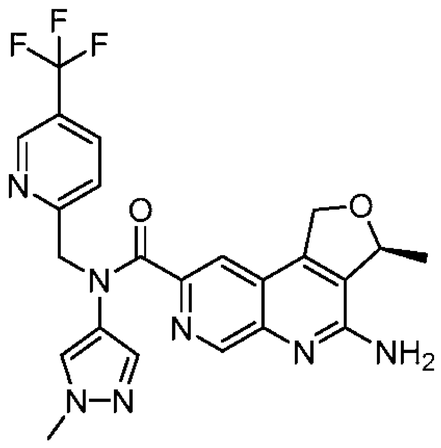
[0272] The racemic product was purified via preparative SFC using a Chiral Technologies OJ column (250 X 21 mm, 5mm) with a mobile phase of 80% Liquid CO_2 and 20% MeOH with 0.2% TEA using a flowrate of 80 mL/min. Stereochemistry was arbitrarily assigned. The 1st eluting peak was assigned (S)-4-amino-N-((5-cyanopyridin-2-yl)methyl)-N-(1-fluoropropan-2-yl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide (48.6 mg, 0.120 mmol, 28.9% yield), obtained as an off-white solid. The 1st eluting peak was arbitrarily assigned as (S)-4-amino-N-((5-cyanopyridin-2-yl)methyl)-N-(1-fluoropropan-2-yl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide and the 2nd eluting peak was arbitrarily assigned as (R)-4-amino-N-((5-cyanopyridin-2-yl)methyl)-N-(1-fluoropropan-2-yl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide (43.881 mg, 0.108 mmol, 26.1 % yield), obtained as an off-white solid. *m/z* (ESI): 407.2 $(M+H)^+$. ^1H NMR (DMSO-d6, 500 MHz) δ 8.6-9.1 (m, 2H), 8.1-8.3 (m, 1H), 7.5-7.8 (m, 2H), 6.9-7.2 (m, 2H), 5.2-5.4 (m, 2H), 4.3-5.1 (m, 7H), 3.2-3.3 (m, 1H), 1.20 (br d, 3H, J=6.4 Hz). ^1H NMR (METHANOL-d4 with some CDCl3, 400 MHz) δ 8.7-9.0 (m, 2H), 7.9-8.1 (m,

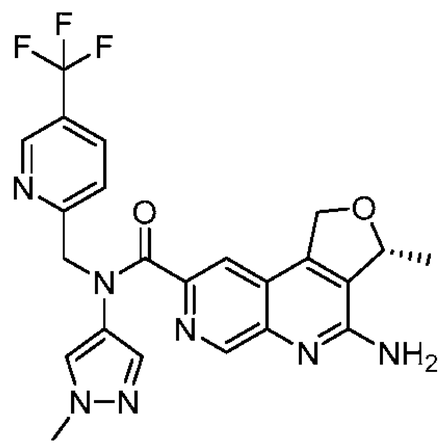
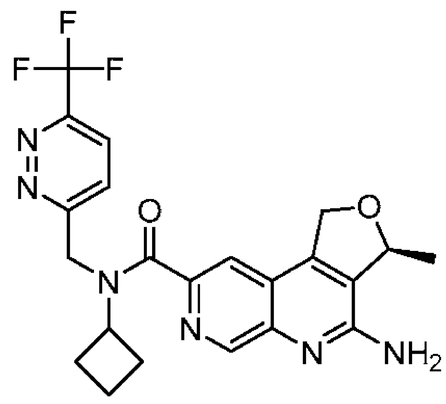
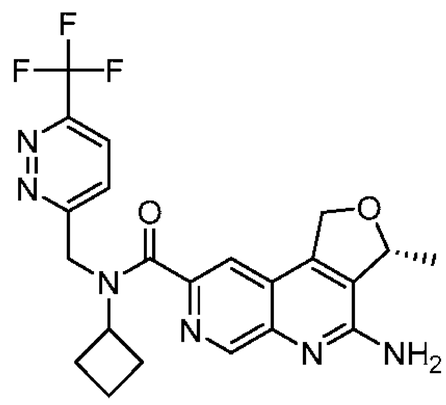
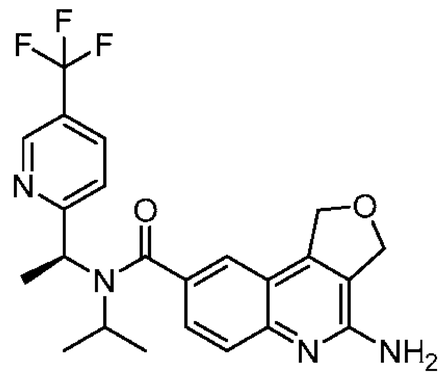
1H), 7.6-7.8 (m, 2H), 5.3-5.5 (m, 2H), 5.15 (br s, 2H), 4.8-5.1 (m, 2H), 4.7-4.8 (m, 1H), 4.3-4.6 (m, 2H), 1.2-1.4 (m, 3H). ^{19}F NMR (METHANOL-d4, 376 MHz) δ -227.9--221.0 (m, 1F).

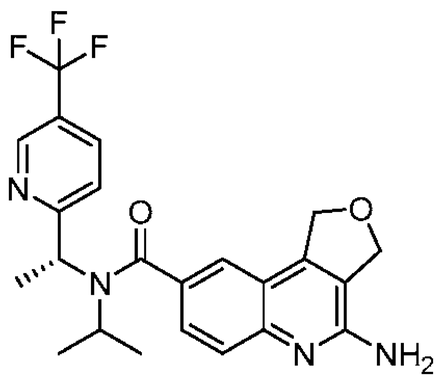
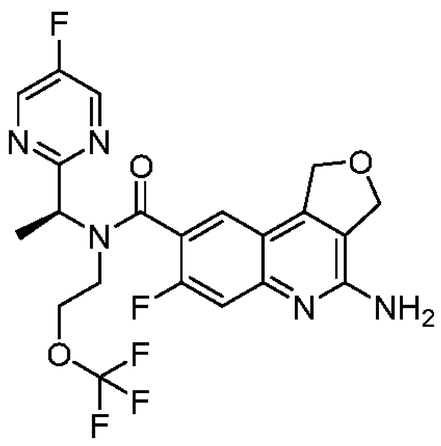
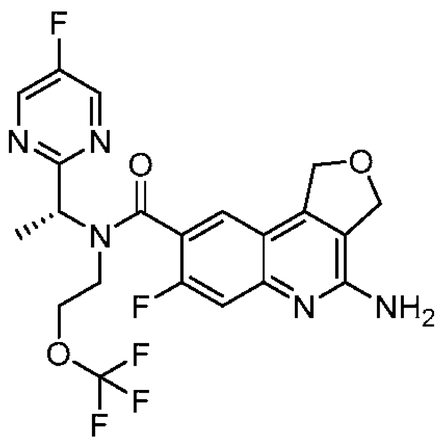
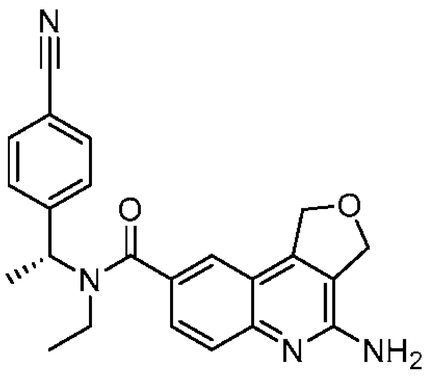
[0273] Compounds in Table 23 were prepared in a manner similar to that described above for Example **819** and **820**.

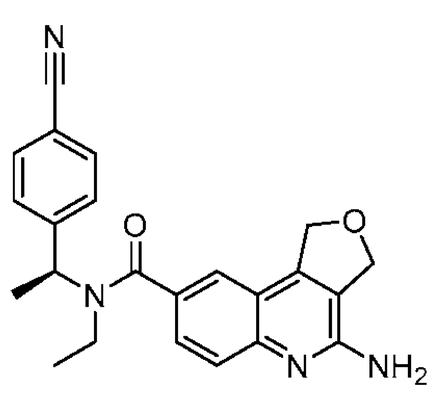
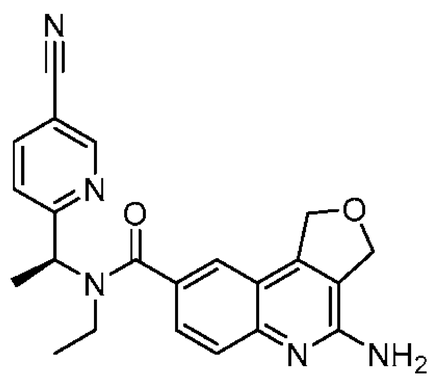
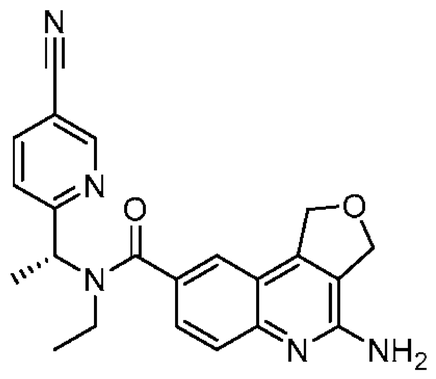
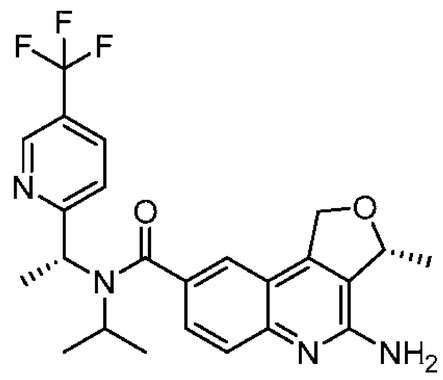
Table 23

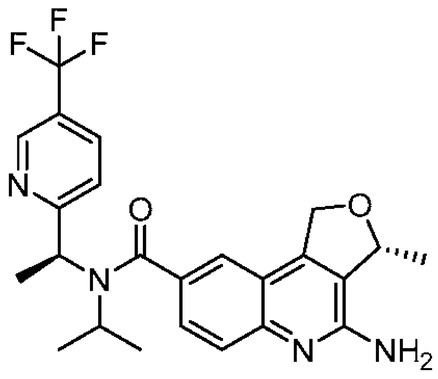
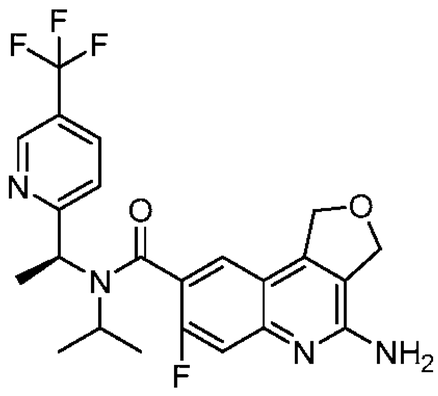
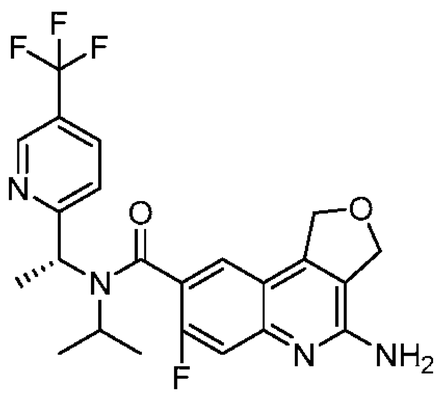
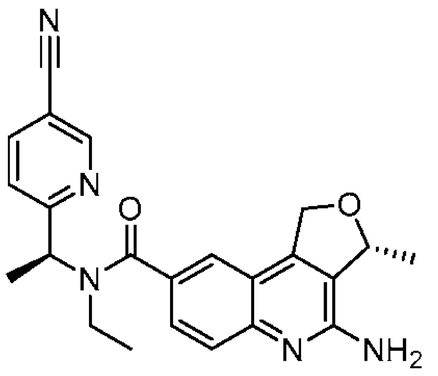
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$	SFC conditions
821		4-amino-N-ethyl-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	431.2	1st peak, Regis (S,S) Whelk-01 column (250 X 21 mm, 5mm) with a mobile phase of 70% Liquid CO_2 and 30% MeOH with 0.2% TEA using a flowrate of 80 mL/min
822		4-amino-N-ethyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	431.2	2nd peak, Regis (S,S) Whelk-01 column (250 X 21 mm, 5mm) with a mobile phase of 70% Liquid CO_2 and 30% MeOH with 0.2% TEA using a flowrate of 80 mL/min
823		4-amino-N-ethyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	432.2	1st peak, Chiralcel OZ-H column (250 X 21 mm, 5μm) with a mobile phase of 65% Liquid CO_2 and 35% MeOH and TEA using a flowrate of 60 mL/min

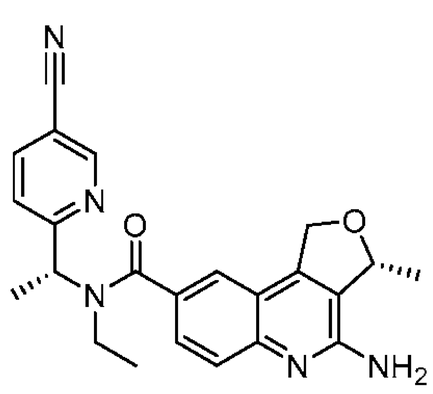
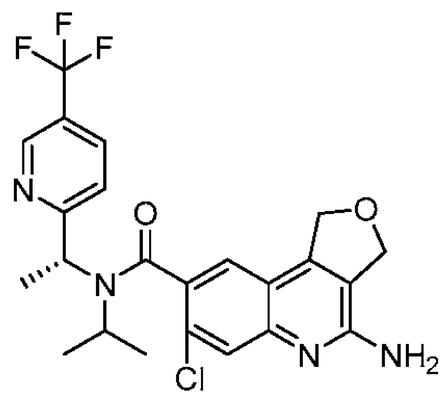
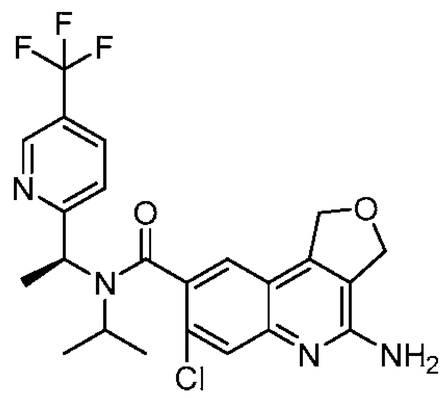
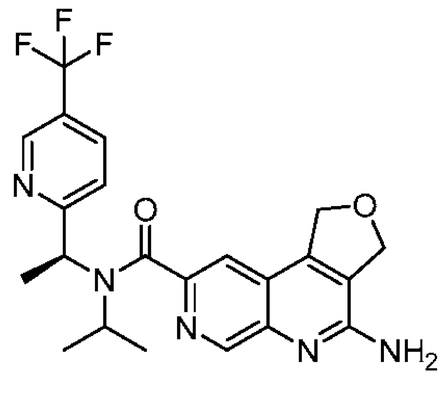
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$	SFC conditions
824		4-amino-N-ethyl-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	432.2	2nd peak, Chiralcel OZ-H column (250 X 21 mm, 5µm) with a mobile phase of 65% Liquid CO_2 and 35% MeOH and TEA using a flowrate of 60 mL/min
825		4-amino-N-(1-methyl-1H-pyrazol-4-yl)-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	484.2	1st peak, Regis (S,S) Whelk-01 column (250 X 21 mm) with a mobile phase of 70% Liquid CO_2 and 30% MeOH with 0.2% TEA
826		4-amino-N-(1-methyl-1H-pyrazol-4-yl)-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	484.2	2nd peak, Regis (S,S) Whelk-01 column (250 X 21 mm) with a mobile phase of 70% Liquid CO_2 and 30% MeOH with 0.2% TEA
827		(3S)-4-amino-3-methyl-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	484.2	1st peak, ChiralPak OZ (250 X 21 mm, 5µm) with a mobile phase of 70% Liquid CO_2 and 30% MeOH with 0.2% TEA

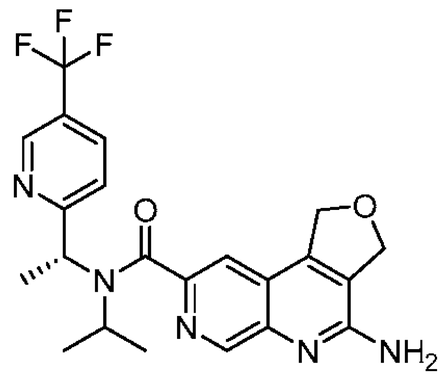
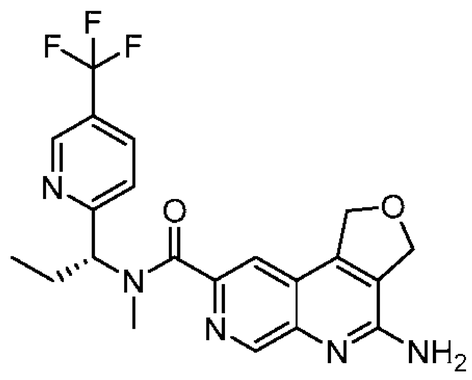
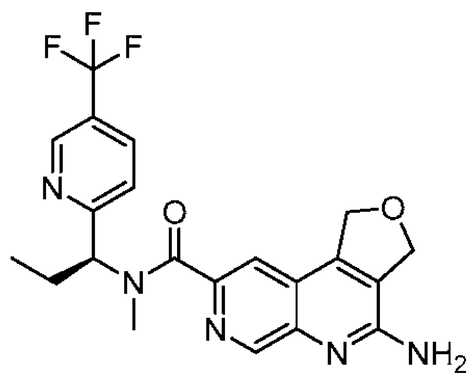
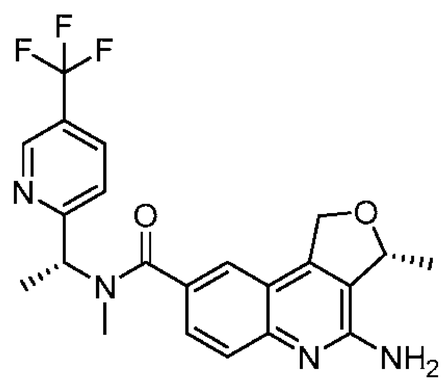
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$	SFC conditions
828		(3R)-4-amino-3-methyl-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	484.2	2nd peak, ChiralPak OZ (250 X 21 mm, 5µm) with a mobile phase of 70% Liquid CO_2 and 30% MeOH with 0.2% TEA
829		(3S)-4-amino-N-cyclobutyl-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	458.8	1st peak, Chiral Technologies AS column (250 X 21 mm, 5mm) with a mobile phase of 85% Liquid CO_2 and 15% MeOH with 0.2% TEA using a flowrate of 70 mL/min
830		(3R)-4-amino-N-cyclobutyl-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	458.8	2nd peak, Chiral Technologies AS column (250 X 21 mm, 5mm) with a mobile phase of 85% Liquid CO_2 and 15% MeOH with 0.2% TEA using a flowrate of 70 mL/min
831		4-amino-N-(2-propanyl)-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	445.0	1st peak, preparative SFC using a Regis (S,S) Whelk-01column (250 X 21 mm, 5mm) with a mobile phase of 70% Liquid CO_2 and 30% MeOH with 0.2% TEA using a flowrate of 80 mL/min

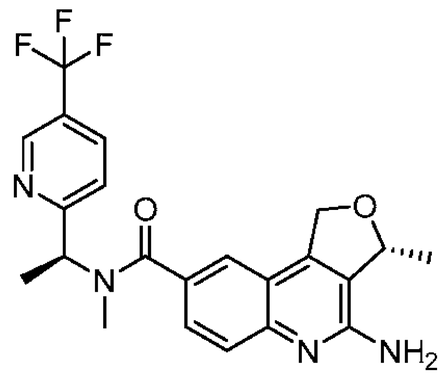
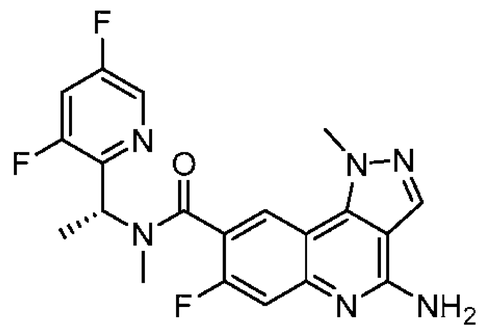
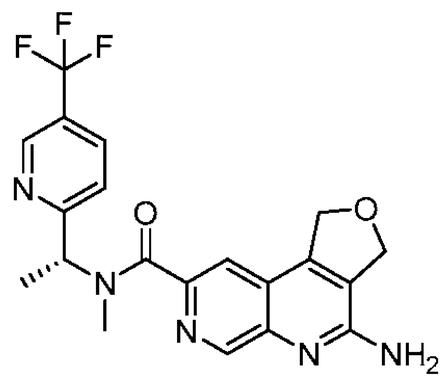
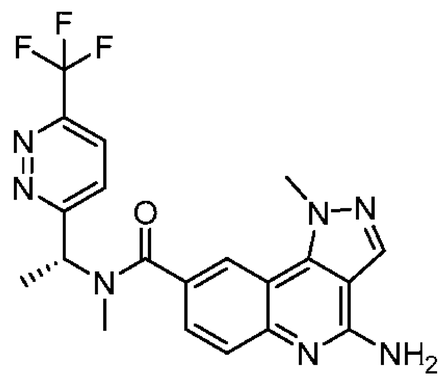
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$	SFC conditions
832		4-amino-N-(2-propanyl)-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	445.0	2nd peak, preparative SFC using a Regis (S,S) Whelk-01column (250 X 21 mm, 5mm) with a mobile phase of 70% Liquid CO_2 and 30% MeOH with 0.2% TEA using a flowrate of 80 mL/min
833		4-amino-7-fluoro-N-((1S)-1-(5-fluoro-2-pyrimidinyl)ethyl)-N-(2-(trifluoromethoxy)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	484.2	1st peak, Chiral Technologies OX column (250 X 21 mm, 5mm) with a mobile phase of 50% Liquid CO_2 and 50% MeOH with 0.2% TEA using a flowrate of 50 mL/min
834		4-amino-7-fluoro-N-((1R)-1-(5-fluoro-2-pyrimidinyl)ethyl)-N-(2-(trifluoromethoxy)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	484.2	2nd peak, Chiral Technologies OX column (250 X 21 mm, 5mm) with a mobile phase of 50% Liquid CO_2 and 50% MeOH with 0.2% TEA using a flowrate of 50 mL/min
835		4-amino-N-((1R)-1-(4-cyanophenyl)ethyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	387.0	1st peak, Chiral Technologies OX column (250 X 21 mm, 5mm) with a mobile phase of 50% Liquid CO_2 and 50% MeOH with 0.2% TEA using a flowrate of 50 mL/min

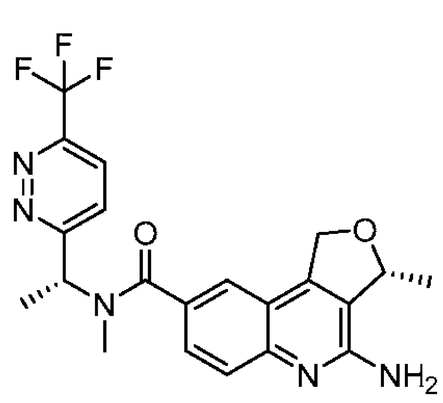
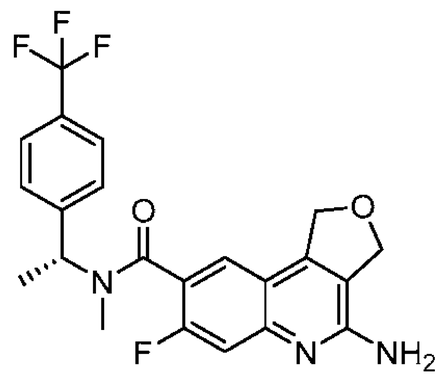
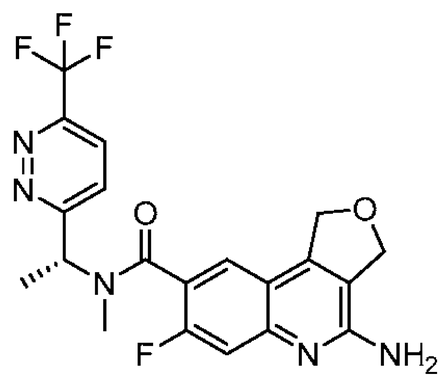
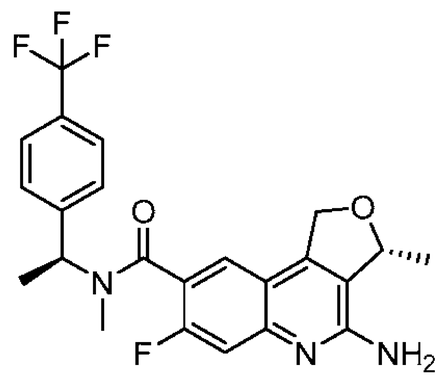
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$	SFC conditions
836		4-amino-N-((1S)-1-(4-cyanophenyl)ethyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	387.0	2nd peak, Chiral Technologies OX column (250 X 21 mm, 5mm) with a mobile phase of 50% Liquid CO_2 and 50% MeOH with 0.2% TEA using a flowrate of 50 mL/min
837		4-amino-N-((1S)-1-(5-cyano-2-pyridinyl)ethyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	388.0	1st peak, Chiral Technologies OX column (250 X 21 mm, 5mm) with a mobile phase of 50% Liquid CO_2 and 50% MeOH with 0.2% TEA using a flowrate of 50 mL/min
838		4-amino-N-((1R)-1-(5-cyano-2-pyridinyl)ethyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	388.0	2nd peak, Chiral Technologies OX column (250 X 21 mm, 5mm) with a mobile phase of 50% Liquid CO_2 and 50% MeOH with 0.2% TEA using a flowrate of 50 mL/min
839		(3R)-4-amino-3-methyl-N-(2-propanyl)-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	459.0	1st peak, Chiral Technologies IG column (250 X 21 mm, 5mm) with a mobile phase of 60% Liquid CO_2 and 40% MeOH with 0.2% TEA using a flowrate of 70 mL/min

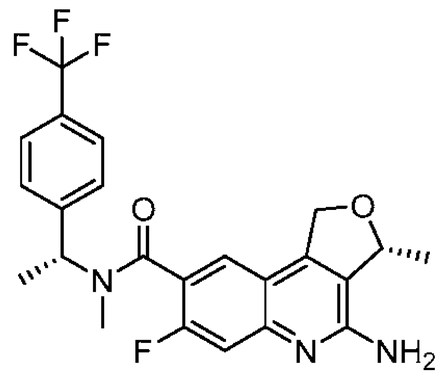
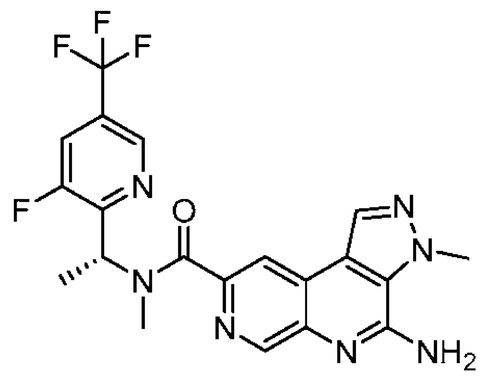
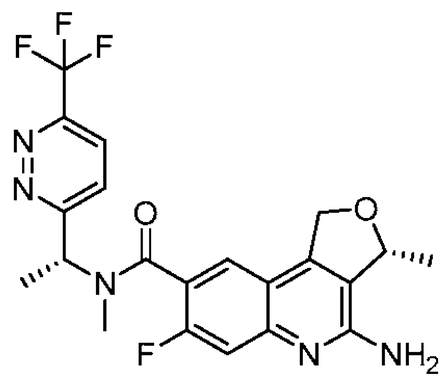
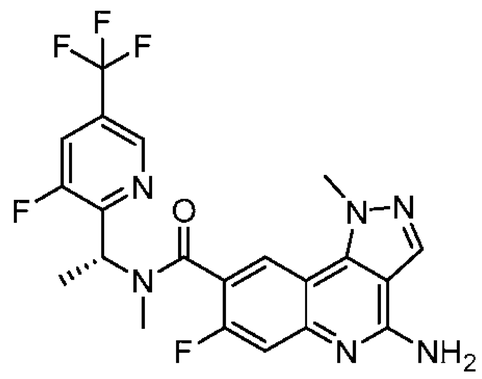
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$	SFC conditions
840		(3R)-4-amino-3-methyl-N-(2-propanyl)-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	459.0	2nd peak, Chiral Technologies IG column (250 X 21 mm, 5mm) with a mobile phase of 60% Liquid CO_2 and 40% MeOH with 0.2% TEA using a flowrate of 70 mL/min
841		4-amino-7-fluoro-N-(2-propanyl)-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	463.0	1st peak, Purified by Prep SFC using column Whelk-O-S,S (250 X 21 mm, 5µm) with a mobile phase of 75% Liquid CO_2 and 25% MeOH and 0.2%TEA using a flowrate 80 mL/min
842		4-amino-7-fluoro-N-(2-propanyl)-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	463.0	2nd peak, Purified by Prep SFC using column Whelk-O-S,S (250 X 21 mm, 5µm) with a mobile phase of 75% Liquid CO_2 and 25% MeOH and 0.2%TEA using a flowrate 80 mL/min
843		(3R)-4-amino-N-((1S)-1-(5-cyano-2-pyridinyl)ethyl)-N-ethyl-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	402.0	1st peak, Chiral Technologies IG column (250 X 21 mm, 5mm) X 2 with a mobile phase of 85% Liquid CO_2 and 15% MeOH with 0.2% TEA using a flowrate of 70 mL/min

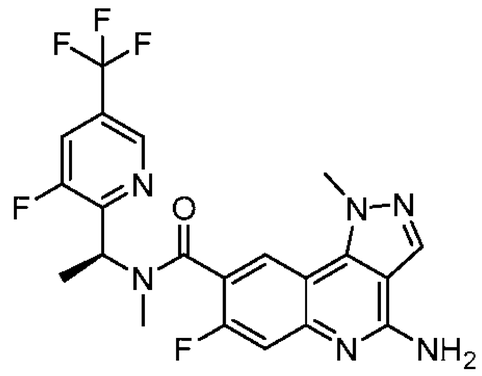
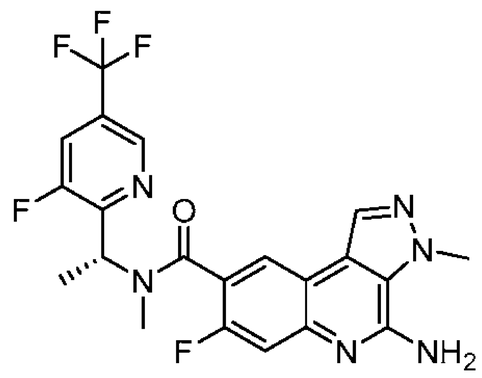
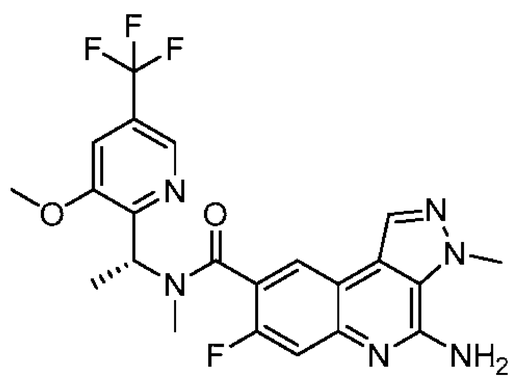
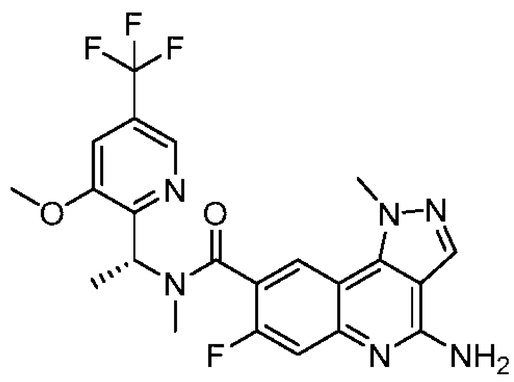
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$	SFC conditions
844		(3R)-4-amino-N-((1R)-1-(5-cyano-2-pyridinyl)ethyl)-N-ethyl-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	402.0	2nd peak, Chiral Technologies IG column (250 X 21 mm, 5mm) X 2 with a mobile phase of 85% Liquid CO_2 and 15% MeOH with 0.2% TEA using a flowrate of 70 mL/min
845		4-amino-7-chloro-N-(2-propanyl)-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	479.0	1st peak, Purified by Prep SFC using column Chiralpak IC (250 X 21 mm, 5µm) with a mobile phase of 65% Liquid CO_2 and 35% MeOH and 0.2%TEA using a flowrate 70 mL/min
846		4-amino-7-chloro-N-(2-propanyl)-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	479.0	2nd peak, Purified by Prep SFC using column Chiralpak IC (250 X 21 mm, 5µm) with a mobile phase of 65% Liquid CO_2 and 35% MeOH and 0.2%TEA using a flowrate 70 mL/min
847		4-amino-N-(2-propanyl)-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	446.0	1st peak, Regis (S,S) Whelk-01 column (250 X 21 mm, 5mm) with a mobile phase of 80% Liquid CO_2 and 20% EtOH with 0.2% TEA using a flowrate of 80 mL/min

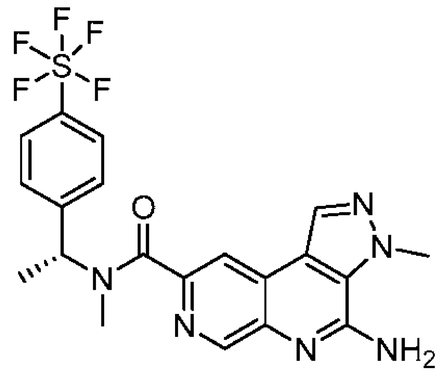
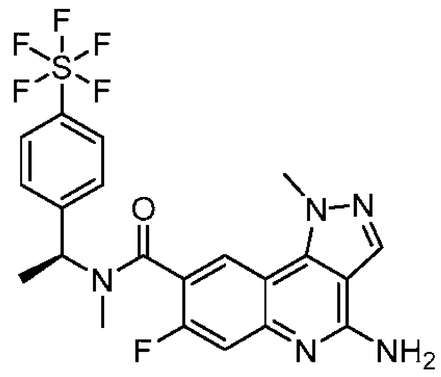
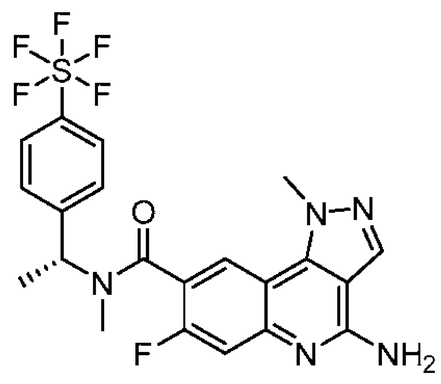
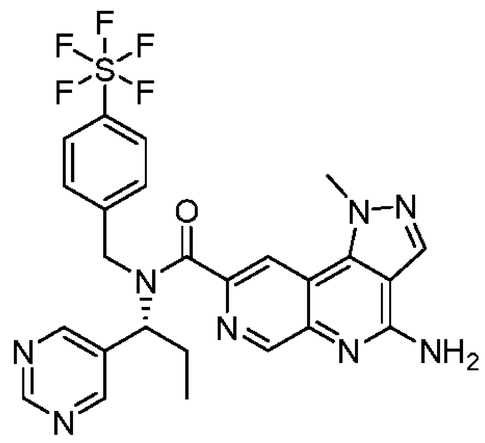
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$	SFC conditions
848		4-amino-N-(2-propanyl)-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	446.0	2nd peak, Regis (S,S) Whelk-01 column (250 X 21 mm, 5mm) with a mobile phase of 80% Liquid CO_2 and 20% EtOH with 0.2% TEA using a flowrate of 80 mL/min
849		4-amino-N-methyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)propyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	432.1	1st peak, Purified by Prep SFC using column Chiralcel OX (250 X 21 mm, 5μm) with a mobile phase of 70% Liquid CO_2 and 30% MeOH and 0.2%TEA using a flowrate 100 mL/min
850		4-amino-N-methyl-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)propyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	432.1	2nd peak, Purified by Prep SFC using column Chiralcel OX (250 X 21 mm, 5μm) with a mobile phase of 70% Liquid CO_2 and 30% MeOH and 0.2%TEA using a flowrate 100 mL/min
851		(3R)-4-amino-N,3-dimethyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	431.0	1st peak, Regis (S,S) Whelk-01 column (250 X 21 mm, 5mm) with a mobile phase of 60% Liquid CO_2 and 40% MeOH with 0.2% TEA using a flowrate of 80 mL/min

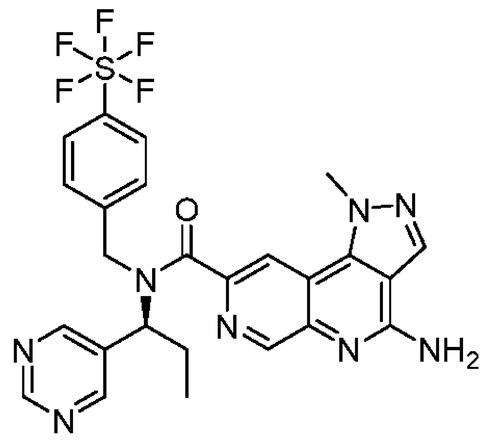
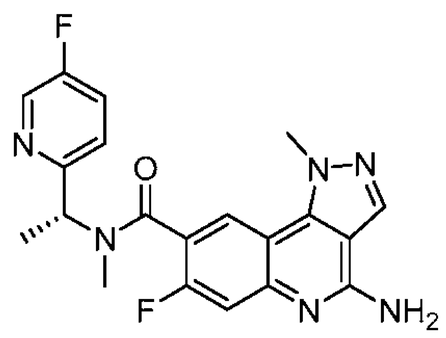
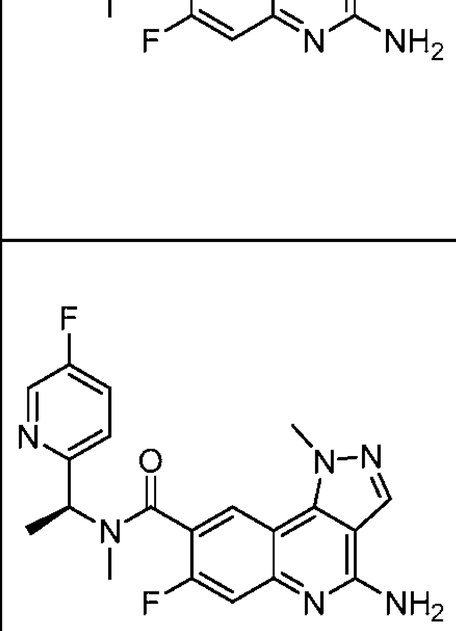
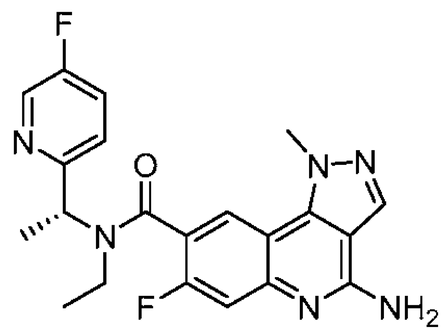
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$	SFC conditions
852		(3R)-4-amino-N,3-dimethyl-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	431.2	2nd peak, Regis (S,S) Whelk-01 column (250 X 21 mm, 5mm) with a mobile phase of 60% Liquid CO_2 and 40% MeOH with 0.2% TEA using a flowrate of 80 mL/min
853		4-amino-N-((1R)-1-(3,5-difluoro-2-pyridinyl)ethyl)-7-fluoro-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	415	2nd peak, Chiralcel OD column (2 x 25 cm, 5 micron) with a mobile phase of 80% Liquid CO_2 and 20% methanol with 0.15% triethylamine using a flowrate of 50 mL/min
854		4-amino-N-methyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	418.2	1st peak, Chiral Technologies OX column (250 X 21 mm, 5mm) with a mobile phase of 65% Liquid CO_2 and 35% MeOH with 0.2% TEA using a flowrate of 70 mL/min
855		4-amino-N,1-dimethyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	430.1	1st peak, Chiralpak AD column (21 x 250 mm) with a mobile phase of 75% Liquid CO_2 and 25% EtOH with 0.2% diethylamine using a flowrate of 80 mL/min

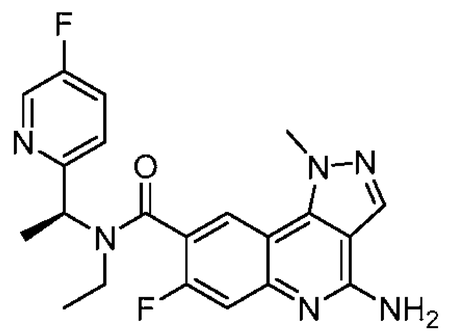
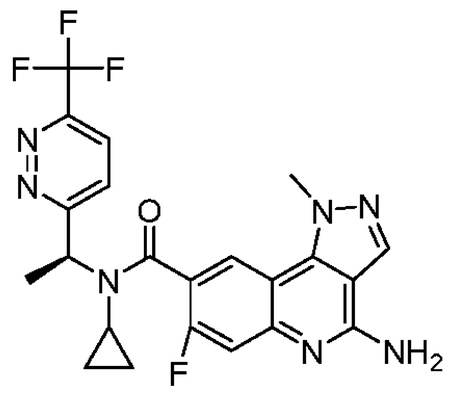
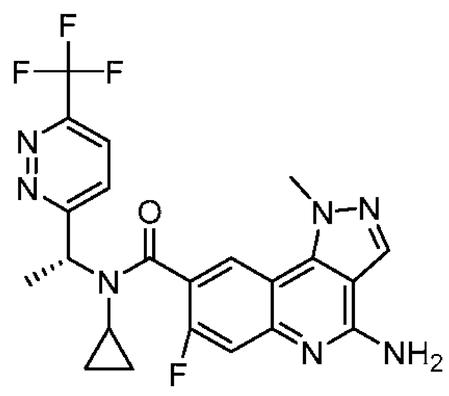
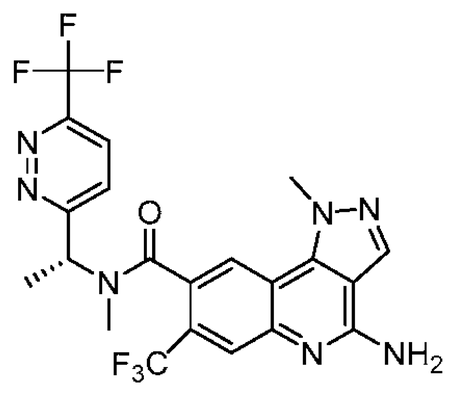
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$	SFC conditions
856		(3R)-4-amino-N,3-dimethyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	432	2nd peak, Chiral Technologies OX column (250 X 30 mm, 5mm) with a mobile phase of 80% Liquid CO_2 and 20% MeOH with 0.2% TEA using a flowrate of 170 mL/min
857		4-amino-7-fluoro-N-methyl-N-((1R)-1-(4-(trifluoromethyl)phenyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	433.9	1st peak, Chiralpak AZ column (21 x 250mm, 5μm) with a mobile phase of 55% Liquid CO_2 and 45% MeOH with 0.2% DEA using a flowrate of 80 mL/min
858		4-amino-7-fluoro-N-methyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	436.2	1st peak, Whelk-O S,S column (250 X 21 mm, 5um) with a mobile phase of 65% Liquid CO_2 and 35% methanol with 0.2%TEA using a flowrate 100 mL/min
859		(3R)-4-amino-7-fluoro-N,3-dimethyl-N-((1S)-1-(4-(trifluoromethyl)phenyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	448.1	2nd peak, Chiralpak ID column (21 x 250 mm, 5 micron) with a mobile phase of 75% Liquid CO_2 and 25% MeOH with 0.2% diethylamine using a flowrate of 80 mL/min

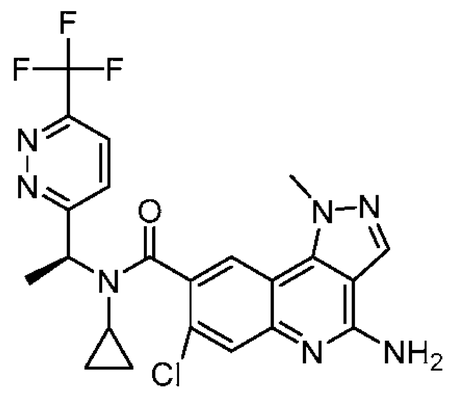
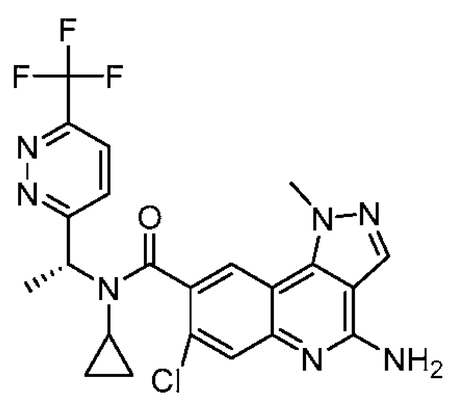
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$	SFC conditions
860		(3R)-4-amino-7-fluoro-N,3-dimethyl-N-((1R)-1-(4-(trifluoromethyl)phenyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	448.1	1st peak, Chiralpak ID column (21 x 250 mm, 5 micron) with a mobile phase of 75% Liquid CO_2 and 25% MeOH with 0.2% diethylamine using a flowrate of 80 mL/min
861		4-amino-N-((1R)-1-(3-fluoro-5-(trifluoromethyl)-2-pyridinyl)ethyl)-N,3-dimethyl-3H-pyrazolo[3,4-c][1,7]naphthyridine-8-carboxamide	448.2	1st peak, Lux Cellulose-2 column (2 x 15 cm, 5 micron) with a mobile phase of 65% Liquid CO_2 and 35% methanol with 0.1% diethylamine using a flowrate of 60 mL/min
862		(3R)-4-amino-7-fluoro-N,3-dimethyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	450.2	1st peak, Whelk-O S,S column (250 X 21 mm, 5um) with a mobile phase of 70% Liquid CO_2 and 30% methanol with 0.2%TEA using a flowrate 100 mL/min
863		4-amino-7-fluoro-N-((1R)-1-(3-fluoro-5-(trifluoromethyl)-2-pyridinyl)ethyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	465.1	1st peak, (S,S) Whelk-O column (2 x 25 cm, 5 micron) with a mobile phase of 75% Liquid CO_2 and 25% methanol with 0.2 triethylamine using a flowrate of 65 mL/min

Ex.	Structure	Name	m/z (ESI): $(M+H)^+$	SFC conditions
864		4-amino-7-fluoro-N-((1S)-1-(3-fluoro-5-(trifluoromethyl)-2-pyridinyl)ethyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	465.1	2nd peak, (S,S) Whelk-O column (2 x 25 cm, 5 micron) with a mobile phase of 75% Liquid CO_2 and 25% methanol with 0.2 triethylamine using a flowrate of 65 mL/min
865		4-amino-7-fluoro-N-((1R)-1-(3-fluoro-5-(trifluoromethyl)-2-pyridinyl)ethyl)-N,3-dimethyl-3H-pyrazolo[3,4-c]quinoline-8-carboxamide	465.1	1st peak, Enantiocel AS-5 column (2 x 25 cm, 5 micron) with a mobile phase of 60% Liquid CO_2 and 40% methanol with 0.1% diethyalmine using a flowrate of 60 mL/min
866		4-amino-7-fluoro-N-((1R)-1-(3-methoxy-5-(trifluoromethyl)-2-pyridinyl)ethyl)-N,3-dimethyl-3H-pyrazolo[3,4-c]quinoline-8-carboxamide	477.2	1st peak, Chiralpak IG column (2 x 25 cm, 5 micron) with a mobile phase of 50% Liquid CO_2 and 50% methanol with 0.1% diethylamine using a flowrate of 60 mL/min
867		4-amino-7-fluoro-N-((1R)-1-(3-methoxy-5-(trifluoromethyl)-2-pyridinyl)ethyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	477.2	2nd peak, ChiralPak IC column (2 x 15 cm 5 μm) with a mobile phase of 65% Liquid CO_2 and 35% MeOH with 0.2% diethylamine using a flowrate of 60 mL/min

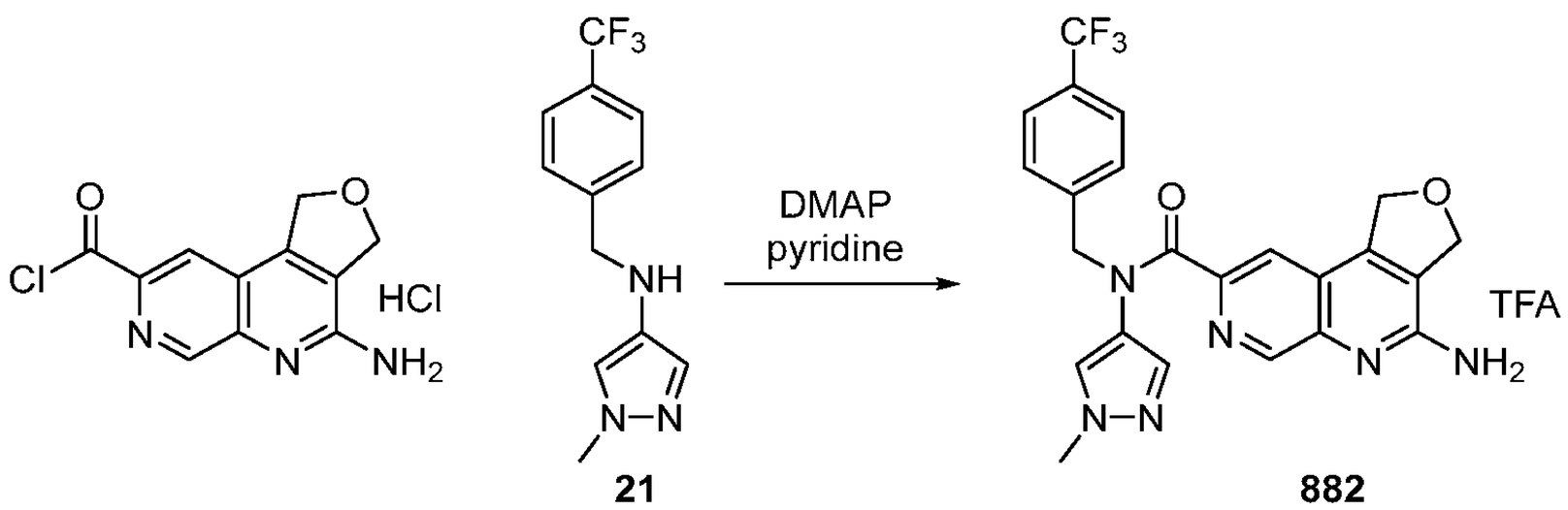
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$	SFC conditions
868		4-amino-N,3-dimethyl-N-((1R)-1-(4-(pentafluoro-lambda~6~-sulfanyl)phenyl)ethyl)-3H-pyrazolo[3,4-c][1,7]naphthyridine-8-carboxamide	487.2	1st peak, Chiralcel OD column (2 x 25 cm, 5 micron) with a mobile phase of 65% Liquid CO_2 and 35% methanol with 01.% deithylamine using a flowrate of 60 mL/min
869		4-amino-7-fluoro-N,1-dimethyl-N-((1S)-1-(4-(pentafluoro-lambda~6~-sulfanyl)phenyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	504.1	2nd peak, (S,S) Whelk-O column (2 x 25 cm, 5 micron) with a mobile phase of 70% Liquid CO_2 and 30% methanol with 0.2 triethylamine using a flowrate of 65 mL/min
870		4-amino-7-fluoro-N,1-dimethyl-N-((1R)-1-(4-(pentafluoro-lambda~6~-sulfanyl)phenyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	504.1	1st peak, (S,S) Whelk-O column (2 x 25 cm, 5 micron) with a mobile phase of 70% Liquid CO_2 and 30% methanol with 0.2 triethylamine using a flowrate of 65 mL/min
871		4-amino-1-methyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-N-((1R)-1-(5-pyrimidinyl)propyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide	579.2	1st peak, Chiralpak IC column (21x150 mm) with a mobile phase of 55% Liquid CO_2 and 45% methanol with 0.2% diethylamine using a flow rate of 80 mL/min

Ex.	Structure	Name	m/z (ESI): $(M+H)^+$	SFC conditions
872		4-amino-1-methyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-N-((1S)-1-(5-pyrimidinyl)propyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide	579.2	2nd peak, Chiralpak IC column (21x150 mm) with a mobile phase of 55% Liquid CO_2 and 45% methanol with 0.2% diethylamine using a flow rate of 80 mL/min
873		4-amino-7-fluoro-N-((1R)-1-(5-fluoro-2-pyridinyl)ethyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	397.2	1st peak, Chiralpak IC column (2 x 15 cm, 5 micron) with a mobile phase of 60% Liquid CO_2 and 40% isopropanol with 0.1% diethylamine using a flowrate of 65 mL/min
874		4-amino-7-fluoro-N-((1S)-1-(5-fluoro-2-pyridinyl)ethyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	397.2	2nd peak, Chiralpak IC column (2 x 15 cm, 5 micron) with a mobile phase of 60% Liquid CO_2 and 40% isopropanol with 0.1% diethylamine using a flowrate of 65 mL/min
875		4-amino-N-ethyl-7-fluoro-N-((1R)-1-(5-fluoro-2-pyridinyl)ethyl)-1-methyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	411.2	1st peak, Chiralpak IC column (2 x 15 cm, 5 micron) with a mobile phase of 55% Liquid CO_2 and 45% isopropanol with 0.1% diethylamine using a flowrate of 65 mL/min

Ex.	Structure	Name	m/z (ESI): $(M+H)^+$	SFC conditions
876		4-amino-N-ethyl-7-fluoro-N-((1S)-1-(5-fluoro-2-pyridinyl)ethyl)-1-methyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	411.2	2nd peak, Chiralpak IC column (2 x 15 cm, 5 micron) with a mobile phase of 55% Liquid CO_2 and 45% isopropanol with 0.1% diethylamine using a flowrate of 65 mL/min
877		4-amino-N-cyclopropyl-7-fluoro-1-methyl-N-((1S)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	474	1st peak, Chiralpak AZ column (21x250 mm) with a mobile phase of 70% Liquid CO_2 and 30% methanol with 0.2% diethylamine using a flow rate of 80 mL/min
878		4-amino-N-cyclopropyl-7-fluoro-1-methyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	474.2	2nd peak, Chiralpak AZ column (21x250 mm) with a mobile phase of 70% Liquid CO_2 and 30% methanol with 0.2% diethylamine using a flow rate of 80 mL/min
879		4-amino-N,1-dimethyl-7-(trifluoromethyl)-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	498.2	1st peak, Chiralpak IG 21x 500 mm, 5 micron) with a mobile phase of 75% Liquid CO_2 and 25% 2-propanol with 0.2% triethylamine using a flowrate of 55 mL/min

Ex.	Structure	Name	m/z (ESI): $(M+H)^+$	SFC conditions
880		4-amino-7-chloro-N-cyclopropyl-1-methyl-N-((1S)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	490.1	2nd peak, (S,S) Whelk-O column (2 x 25 cm, 5 micron) with a mobile phase of 70% Liquid CO_2 and 30% methanol with 0.1% diethylamine using a flowrate of 60 mL/min
881		4-amino-7-chloro-N-cyclopropyl-1-methyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide	490.1	1st peak, (S,S) Whelk-O column (2 x 25 cm, 5 micron) with a mobile phase of 70% Liquid CO_2 and 30% methanol with 0.1% diethylamine using a flowrate of 60 mL/min

[0274] Example 882: 4-amino-N-(1-methyl-1H-pyrazol-4-yl)-N-(4-(trifluoromethyl)benzyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide 2,2,2-trifluoroacetate.

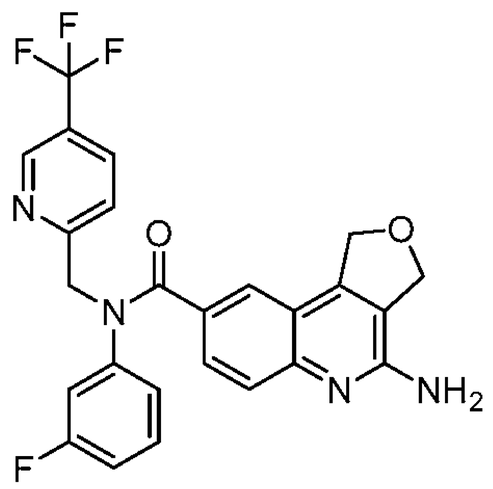
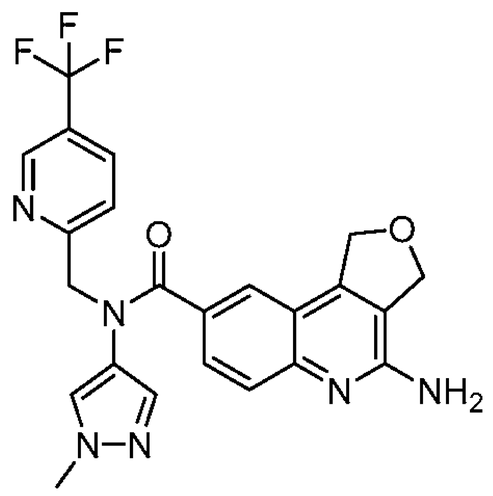
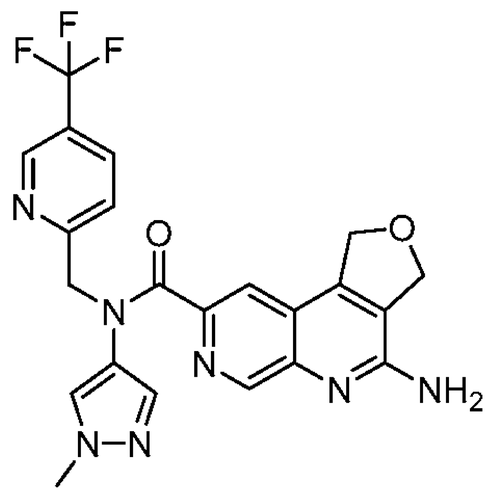


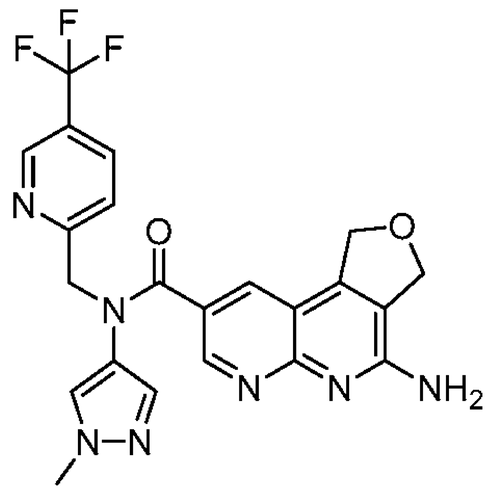
[0275] 4-amino-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carbonyl chloride hydrochloride (168 mg, 0.588 mmol) prepared as above, was added to a stirred suspension of 1-methyl-N-(4-(trifluoromethyl)benzyl)-1H-pyrazol-4-amine (**21,** 100 mg, 0.392 mmol) and N,N-dimethylpyridin-4-amine (14.36 mg, 0.118 mmol, Aldrich) in pyridine (930 mg, 1000 µL, 11.75 mmol, Sigma-Aldrich Corporation). The mixture was heated in an oil bath for 6 h at 60 °C. The resulting residue was partitioned between 50 mL of EtOAc and 5 mL of 1 N NaOH. The organic layer was concentrated and the residue was purified via reverse phase HPLC (10% to 80% CH_3CN in water with 0.1% TFA) to give 4-amino-N-

(1-methyl-1H-pyrazol-4-yl)-N-(4-(trifluoromethyl)benzyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide 2,2,2-trifluoroacetate (**882,** 100 mg, 0.172 mmol, 43.8 % yield) as a brown solid. *m/z* (ESI): 469.0 $(M+H)^+$. ^1H NMR (METHANOL-d_4, 400 MHz) δ 8.88 (s, 1H), 7.88 (s, 1H), 7.68 (m, 2H), 7.60 (m, 2H), 7.40 (s, 1H), 7.12 (s, 1H), 5.47 (m, 2H), 5.1-5.2 (m, 4H), 3.65 (s, 3H). ^{19}F NMR (METHANOL-d_4, 376 MHz) δ -64.04 (s, 3F), -77.30 (s, 3F).

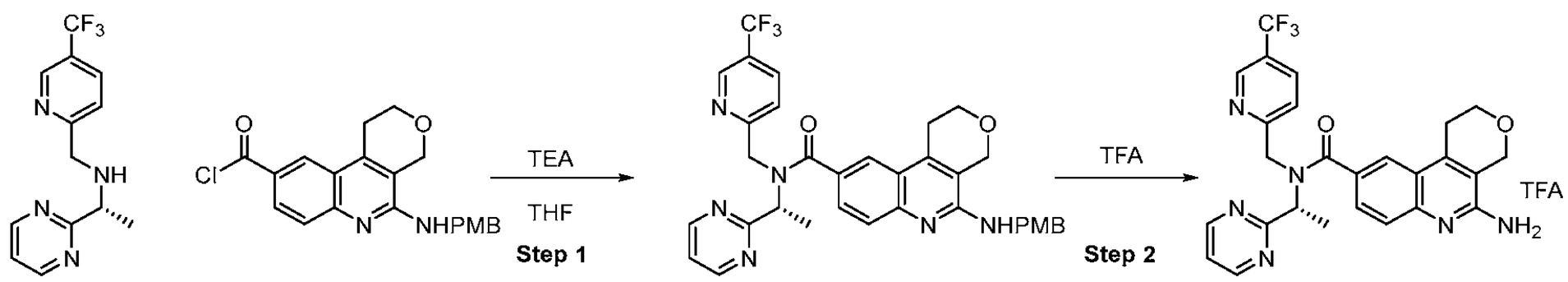
[0276] Compounds in Table 24 were prepared in a manner similar to that described above for Example **882**.

Table 24

Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
883		4-amino-N-(3-fluorophenyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	483.2
884		4-amino-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	469.2
885		4-amino-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide	470.2

Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
886		4-amino-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide	470.0

[0277] Example 887: 5-amino-N-[(1R)-1-pyrimidin-2-ylethyl]-N-[[5-(trifluoromethyl)-2-pyridyl]methyl]-2,4-dihydro-1H-pyrano[3,4-c]quinoline-9-carboxamide.

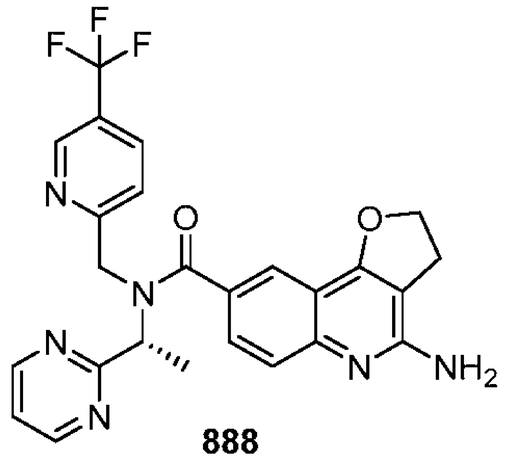


[0278] Step 1. (R)-1-(pyrimidin-2-yl)-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)ethan-1-amine (**112,** 0.123 g, 0.436 mmol) and triethylamine (0.240 g, 0.334 mL, 2.376 mmol, Sigma-Aldrich Corporation) were added to a stirred mixture of crude 5-((4-methoxybenzyl)amino)-1,4-dihydro-2H-pyrano[3,4-c]quinoline-9-carbonyl chloride (0.152 g, 0.396 mmol, from acid **258**) in tetrahydrofuran (3 mL). The reaction mixture was stirred at rt for 15 min. The reaction mixture was diluted with EtOAc (75 mL) and washed with saturated aqueous NH_4Cl (50 mL). The organic layer was separated, washed with brine (50 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo to give crude (R)-5-((4-methoxybenzyl)amino)-N-(1-(pyrimidin-2-yl)ethyl)-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,4-dihydro-2H-pyrano[3,4-c]quinoline-9-carboxamide as a brown oil that was used directly in the next step, assuming 100% yield. *m/z* (ESI): 629.1 $(M+H)^+$.

[0279] Step 2. Crude (R)-5-((4-methoxybenzyl)amino)-N-(1-(pyrimidin-2-yl)ethyl)-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,4-dihydro-2H-pyrano[3,4-c]quinoline-9-carboxamide (249 mg, 0.396 mmol) was mixed in trifluoroacetic acid (1530 mg, 1 mL, 13.42 mmol, Sigma-Aldrich Corporation). The reaction mixture was stirred at 60 °C for 24 h then concentrated and purified on a XBridge column (19x100mm, 5um) using 0.1% NH_4OH in H_2O (A) and ACN (B) as mobile phase. (R)-5-amino-N-(1-(pyrimidin-2-yl)ethyl)-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,4-dihydro-2H-

pyrano[3,4-c]quinoline-9-carboxamide 2,2,2-trifluoroacetate (80 mg, 0.129 mmol, 32.5 % yield) was isolated as a brown solid. *m/z* (ESI): 509.2 $[M + H]^+$.

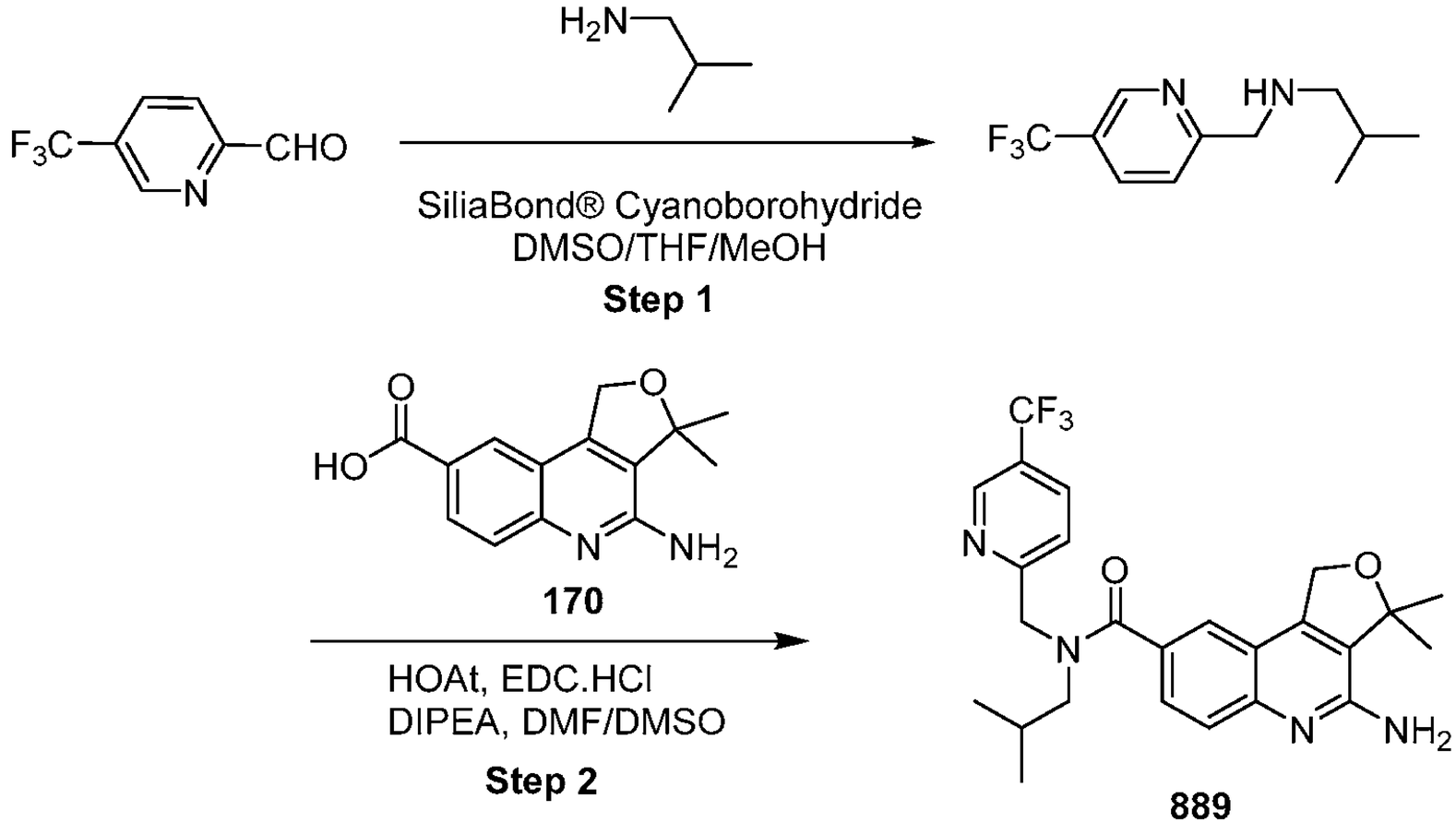
[0280] Example 888: 4-amino-N-[(1R)-1-pyrimidin-2-ylethyl]-N-[[5-(trifluoromethyl)-2-pyridyl]methyl]-2,3-dihydrofuro[3,2-c]quinoline-8-carboxamide.



888

[0281] Example 888 was prepared in a manner similar to that described above for Example **887**. *m/z* (ESI): 495.0 $(M+H)^+$

[0282] Example 889: 2-amino-N-(cyclobutylmethyl)-3-methyl-N-[[5-(trifluoromethyl)-2-pyridyl]methyl]quinoline-6-carboxamide



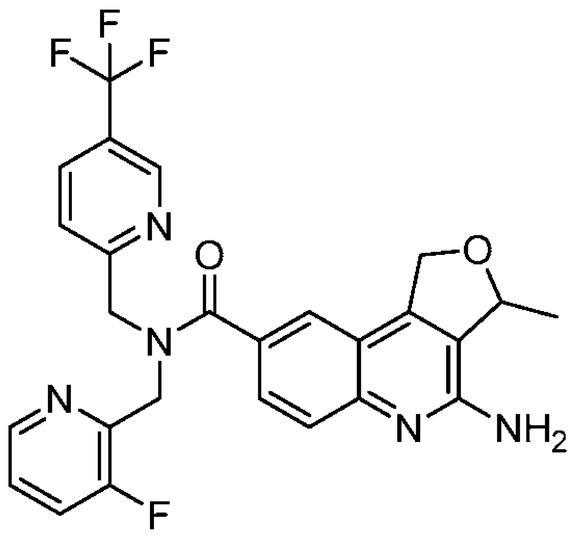
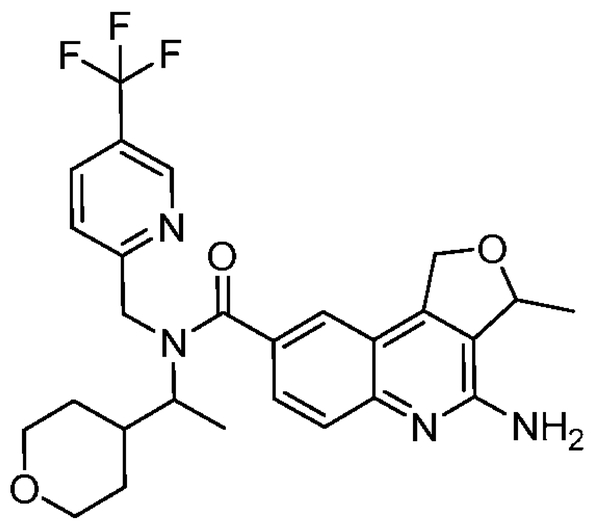
[0283] Step 1. A solution of isobutylamine (1 eq, 100 mM in dry DMSO) and a solution of 5-(trifluoromethyl)picolinaldehyde (1 eq, 100 mM in dry DMSO) were mixed together with equal amounts of dry THF and dry MeOH (25 mM final conc) and MS 3Å. The mixture was shaken at rt. Thereafter, SiliaBond® Cyanoborohydride (2.5 eq) was added and the reaction mixture was shaken at rt. The reaction mixture was filtered, and the filter-cake was rinsed with CH_3CN. The combined washings and filtrate

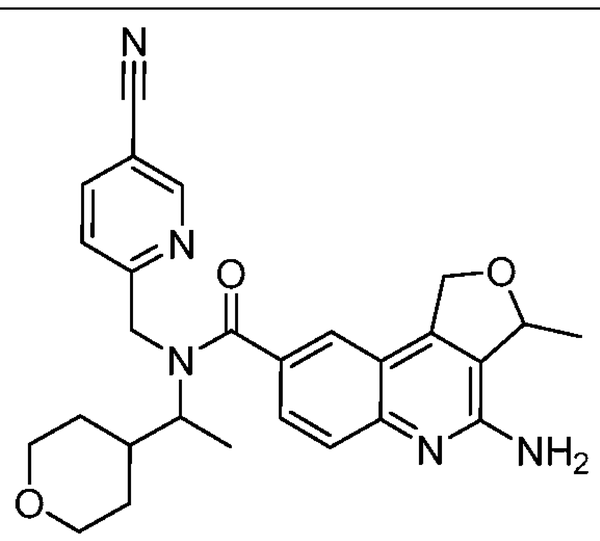
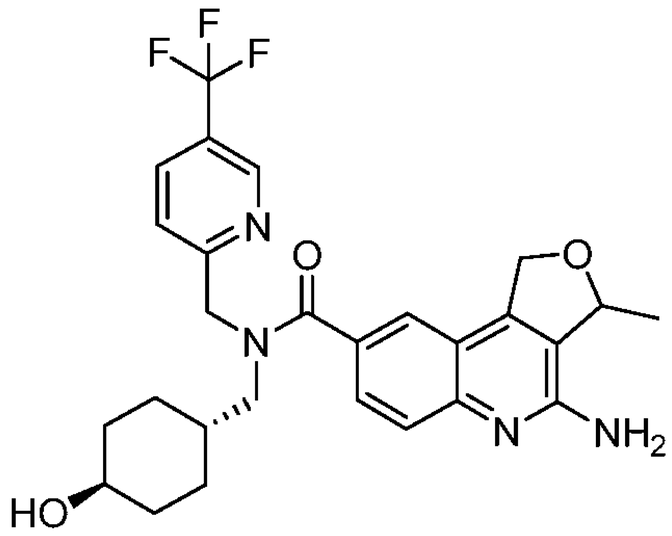
were concentrated under reduced pressure to give 2-methyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)propan-1-amine.

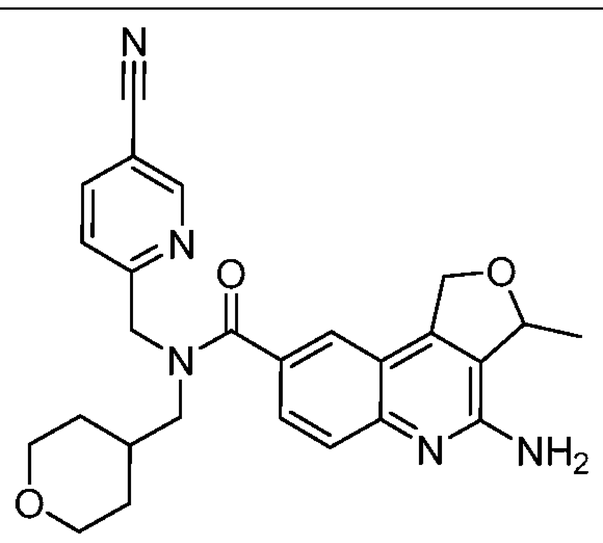
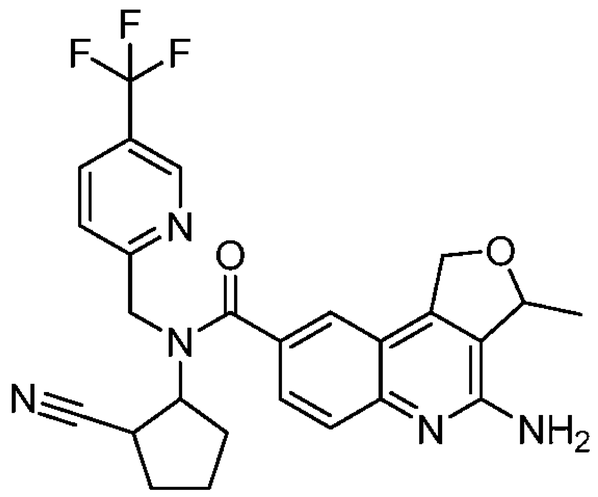
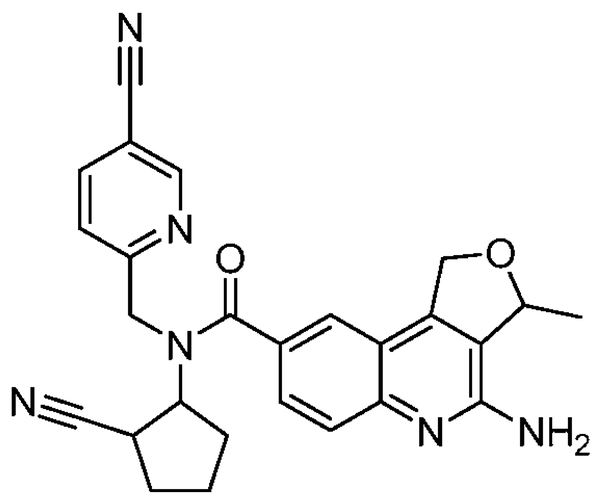
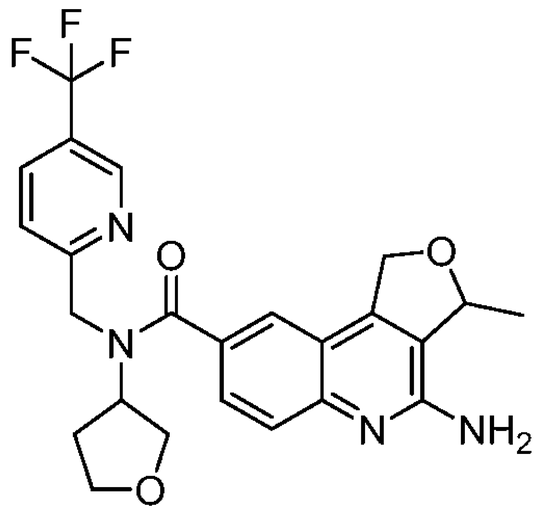
[0284] Step 2. 4-amino-3,3-dimethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxylic acid (**170**, 1 eq, 100 mM in dry DMSO), HOAt (1 eq, 100 mM in dry DMSO) and a solution of EDC and DIPEA (100 mM and 200 mM, respectively in dry DMF) were added in sequence to the crude mixture of amine. The reaction was then shaken at rt overnight and then concentrated under reduced pressure to give crude product that was purified by HPLC to yield the final product, 4-amino-N-isobutyl-3,3-dimethyl-N-[[5-(trifluoromethyl)-2-pyridyl]methyl]-1H-furo[3,4-c]quinoline-8-carboxamide with 99 % purity by UV. *m/z* (ESI): 473.2 $(M+H)^+$.

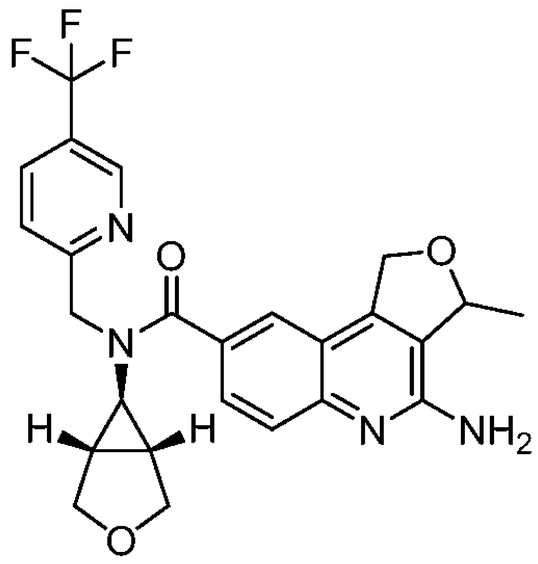
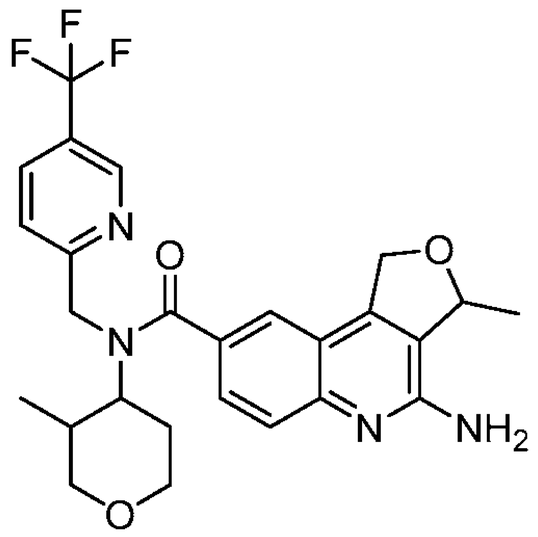
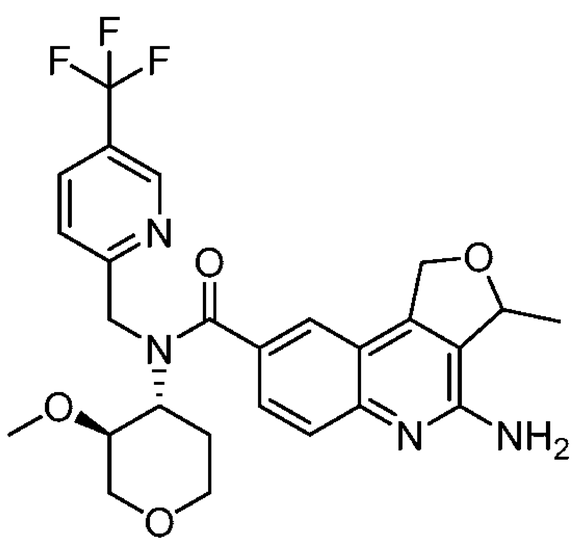
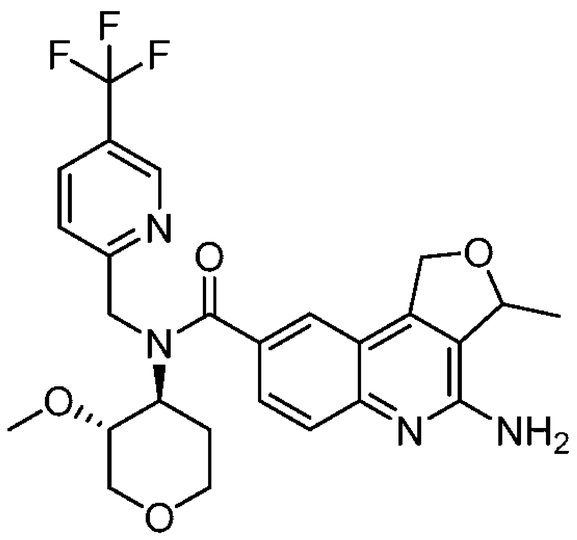
[0285] Compounds in Table 25 were prepared in a manner similar to that described above for Example 889.

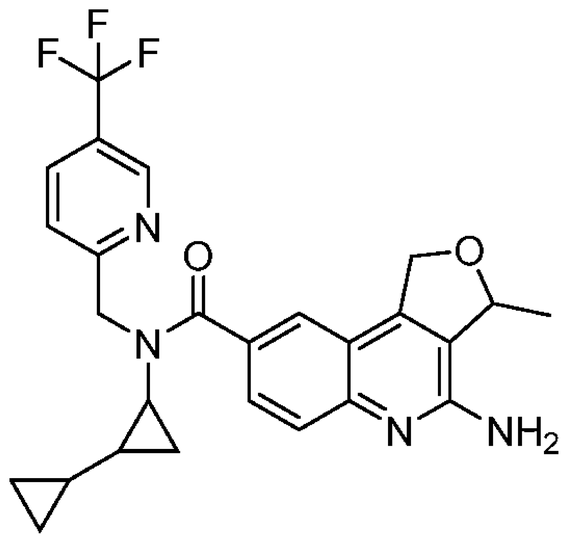
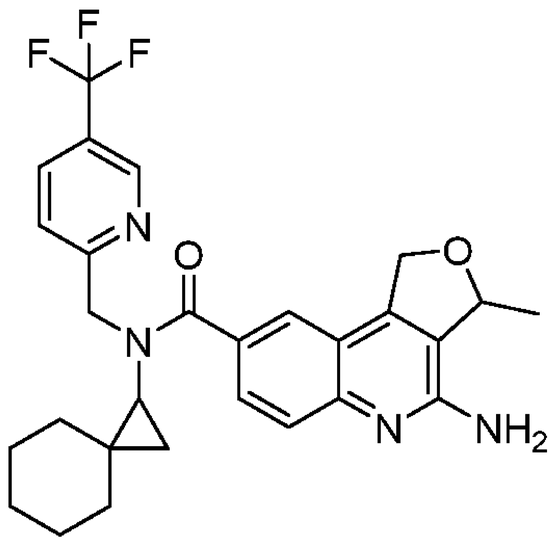
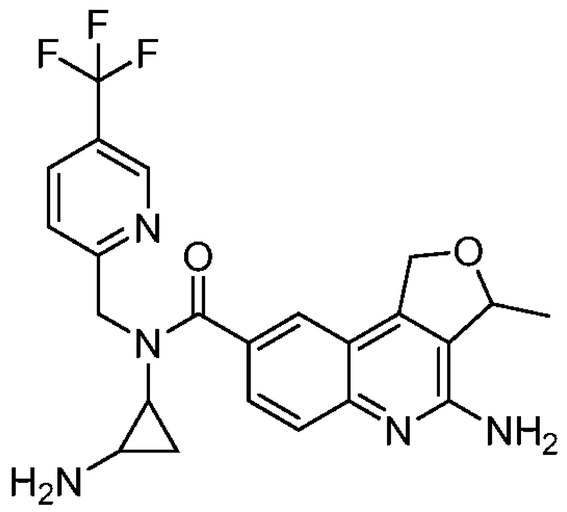
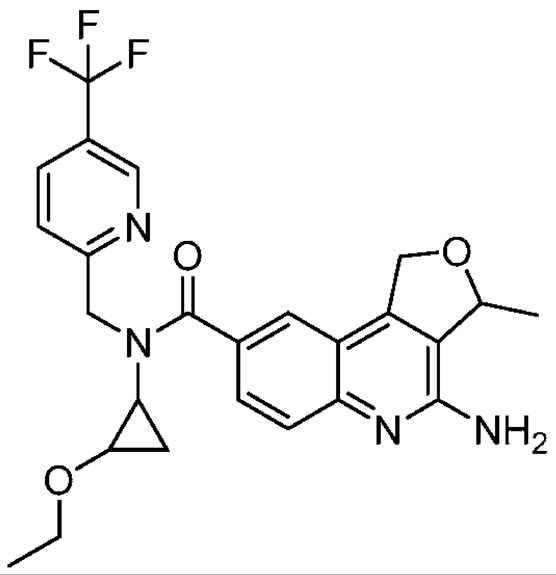
Table 25

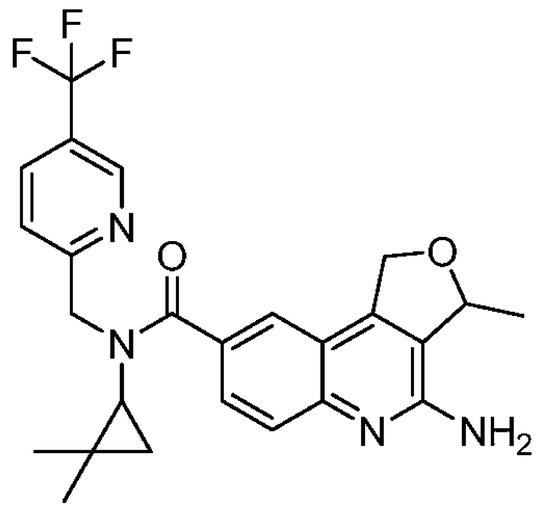
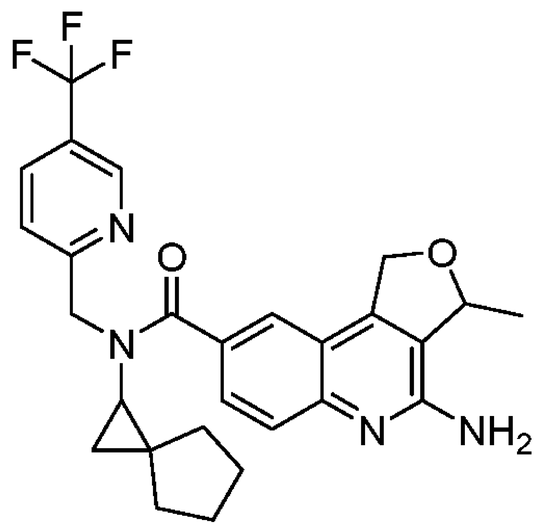
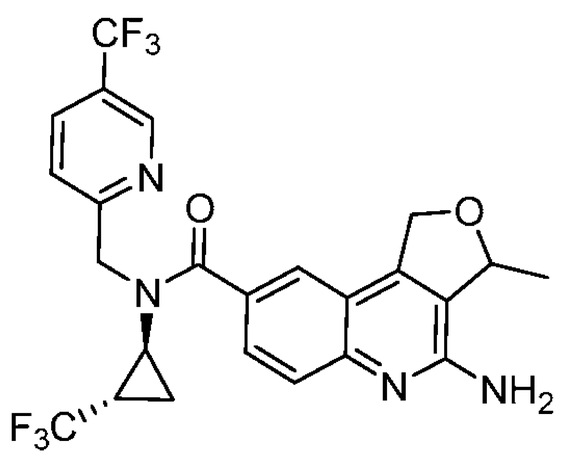
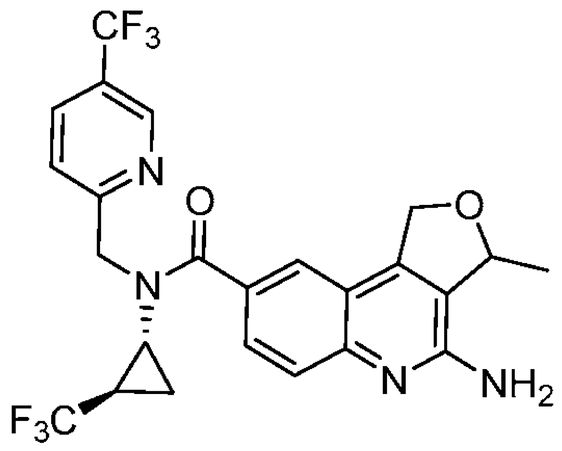
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
890		4-amino-N-((3-fluoropyridin-2-yl)methyl)-3-methyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	512.2
891		4-amino-3-methyl-N-(1-(tetrahydro-2H-pyran-4-yl)ethyl)-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	515.2

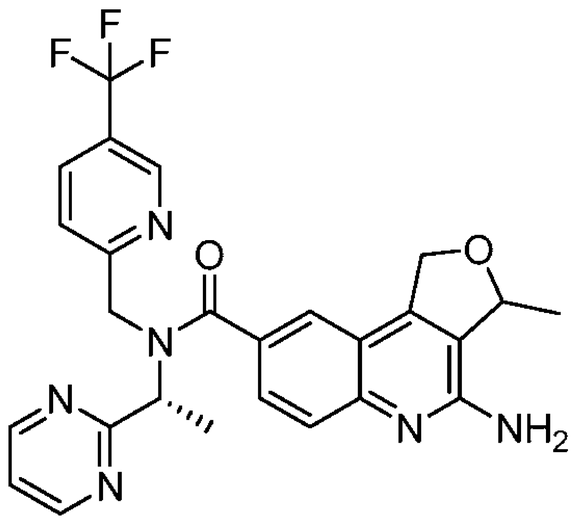
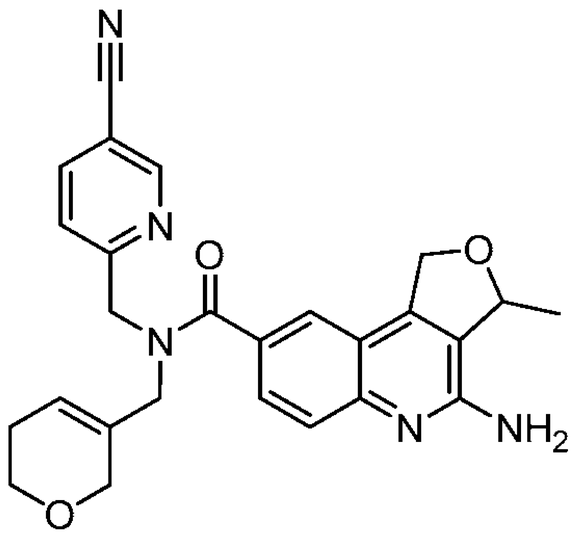
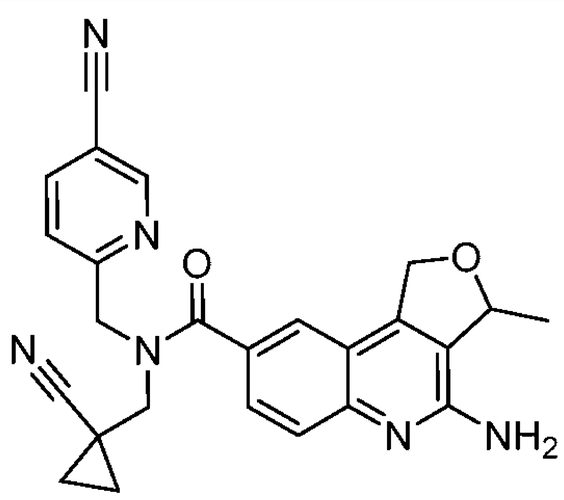
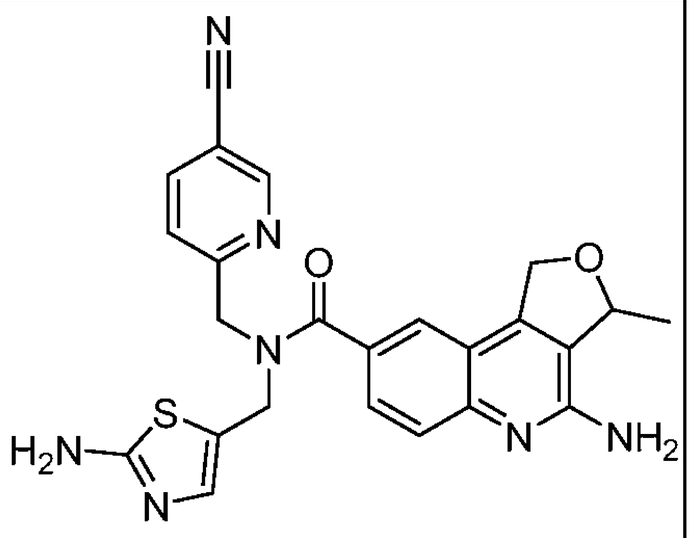
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
892		4-amino-N-((5-cyanopyridin-2-yl)methyl)-3-methyl-N-(1-(tetrahydro-2H-pyran-4-yl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	472.2
893		4-amino-N-(((1r,4r)-4-hydroxycyclohexyl)methyl)-3-methyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	515.2
894		4-amino-N-((5-cyanopyridin-2-yl)methyl)-N-(((1r,4r)-4-hydroxycyclohexyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	472.2
895		4-amino-3-methyl-N-((tetrahydro-2H-pyran-4-yl)methyl)-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	501.2

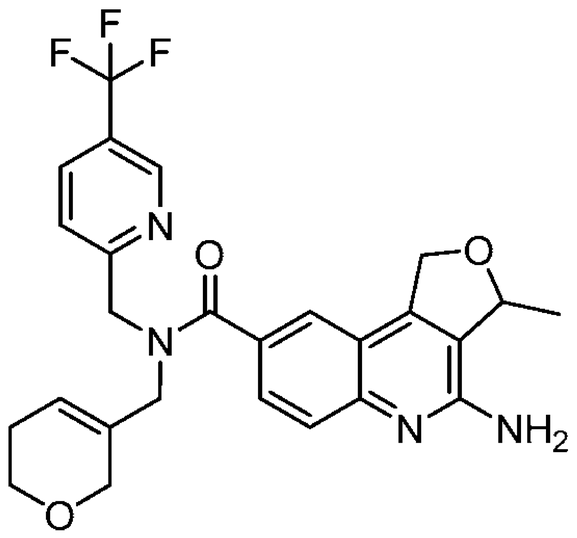
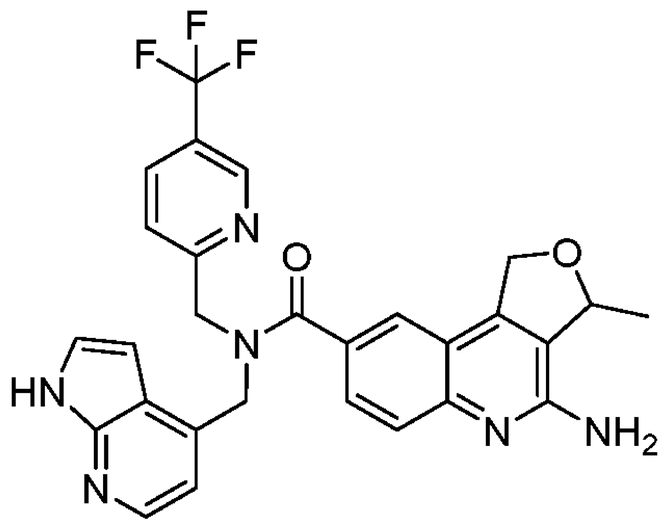
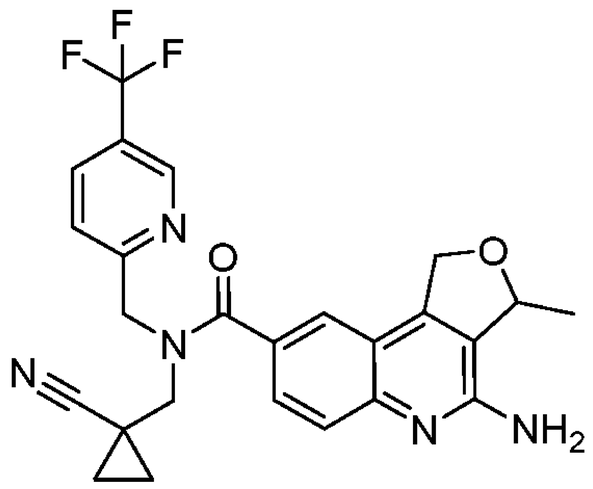
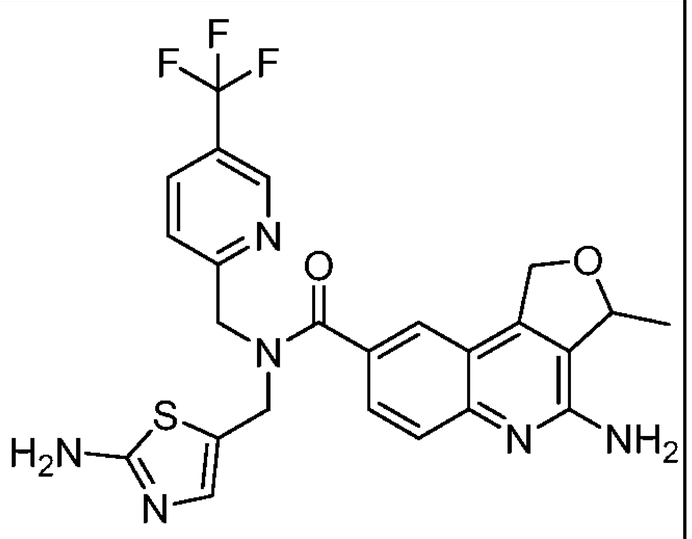
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
896		4-amino-N-((5-cyanopyridin-2-yl)methyl)-3-methyl-N-((tetrahydro-2H-pyran-4-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	458.2
897		4-amino-N-(2-cyanocyclopentyl)-3-methyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	496.2
898		4-amino-N-(2-cyanocyclopentyl)-N-((5-cyanopyridin-2-yl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	453.2
899		4-amino-3-methyl-N-(tetrahydrofuran-3-yl)-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	473.2

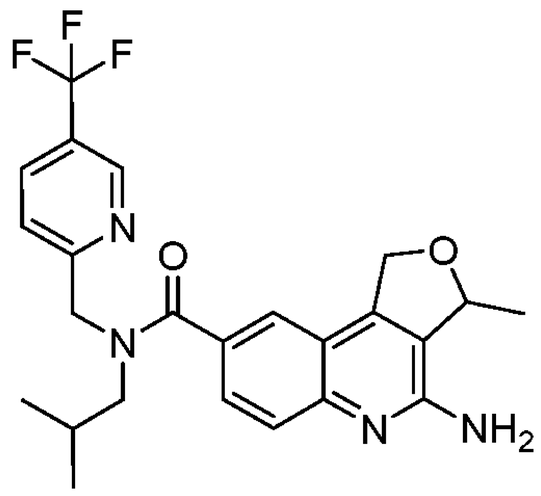
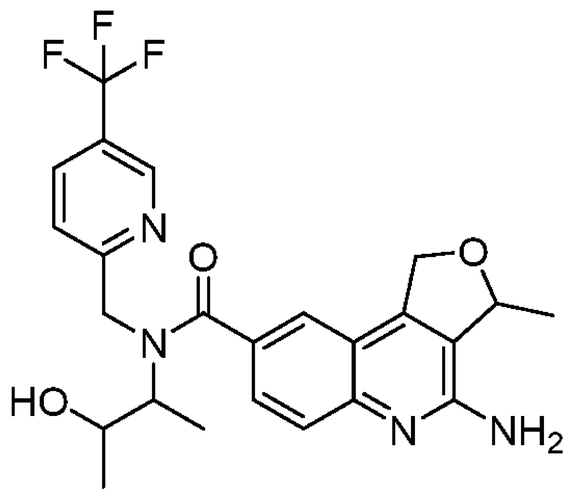
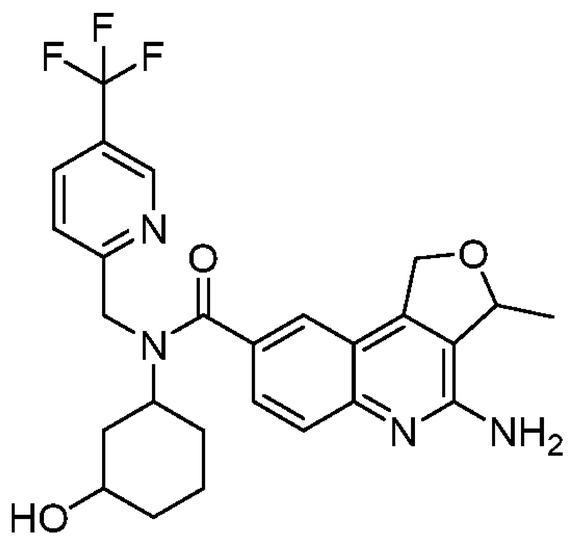
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
900		4-amino-N-((1R,5S,6r)-3-oxabicyclo[3.1.0]hexan-6-yl)-3-methyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	485.2
901		4-amino-3-methyl-N-(3-methyltetrahydro-2H-pyran-4-yl)-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	501.2
902		4-amino-N-((3S,4R)-3-methoxytetrahydro-2H-pyran-4-yl)-3-methyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	517.2
903		4-amino-N-((3R,4S)-3-methoxytetrahydro-2H-pyran-4-yl)-3-methyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	517.2

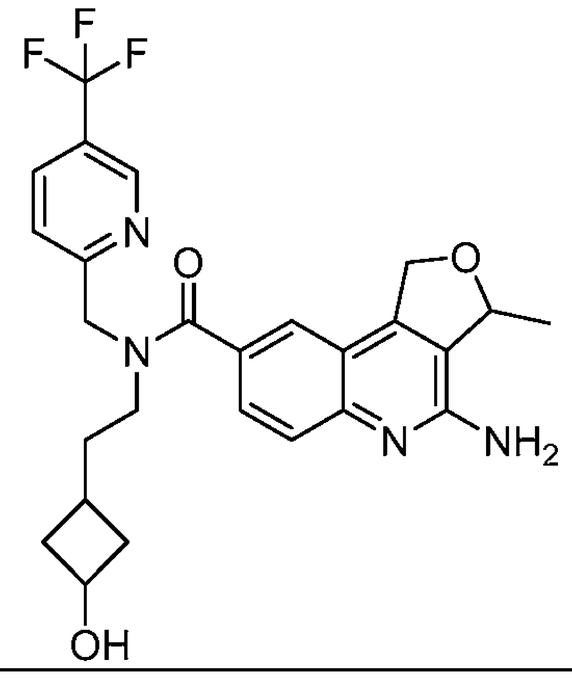
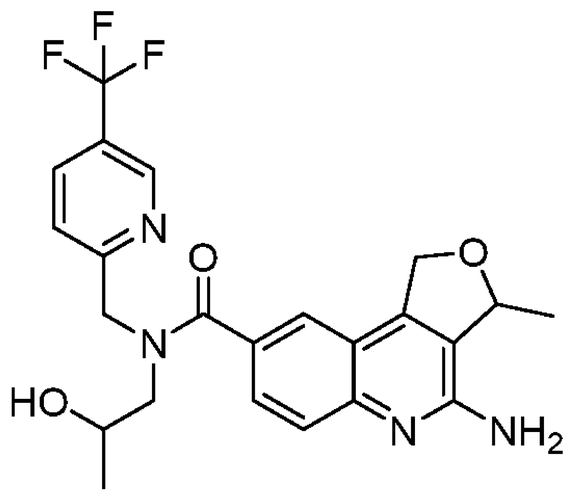
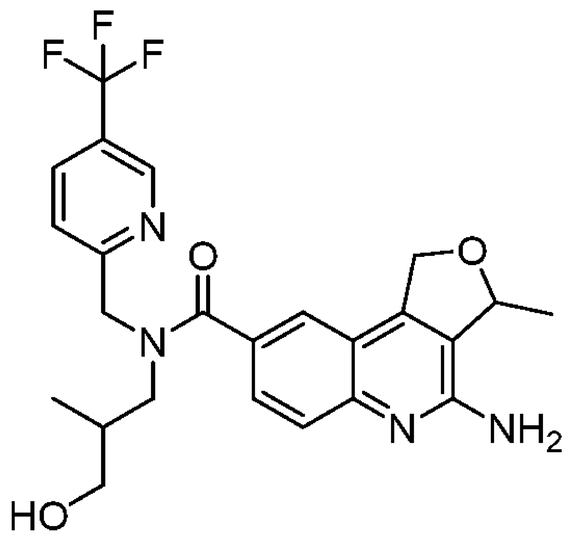
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
904		N-([1,1'-bi(cyclopropan)]-2-yl)-4-amino-3-methyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	483.2
905		4-amino-3-methyl-N-(spiro[2.5]octan-1-yl)-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	511.2
906		4-amino-N-(2-aminocyclopropyl)-3-methyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	458.2
907		4-amino-N-(2-ethoxycyclopropyl)-3-methyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	487.2

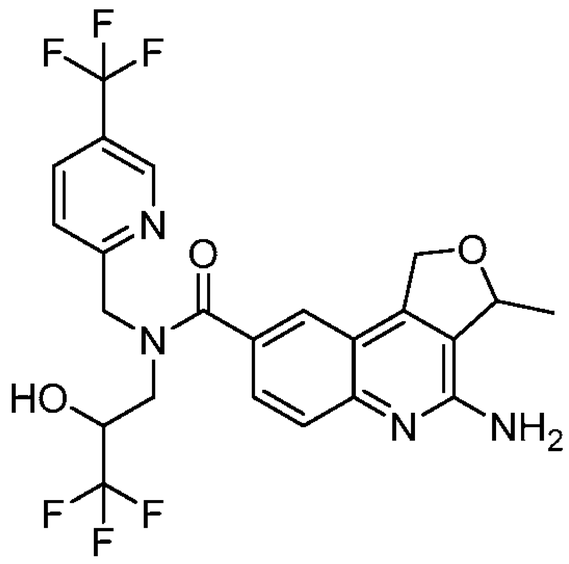
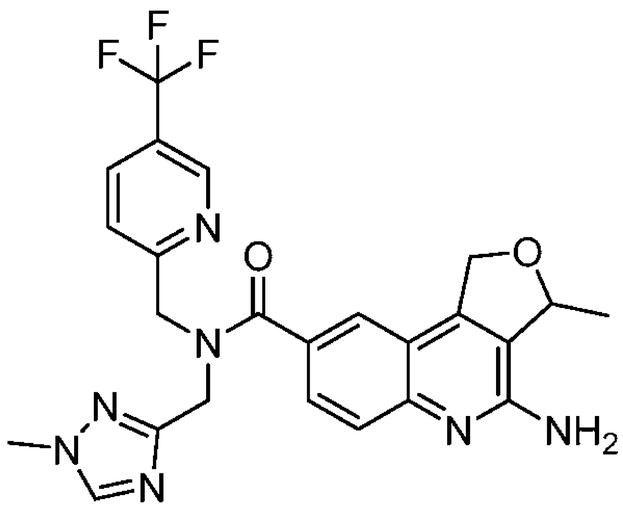
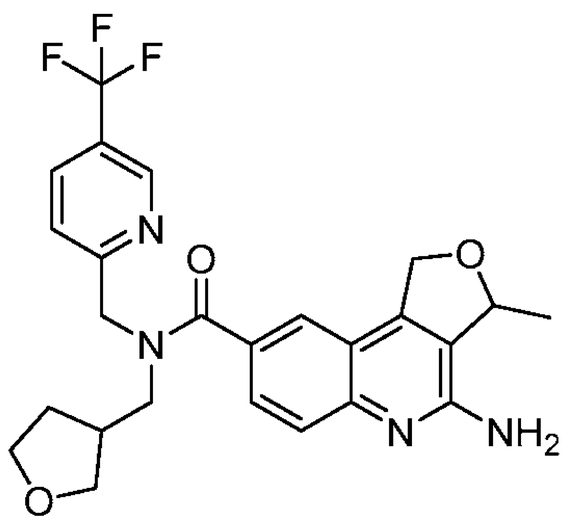
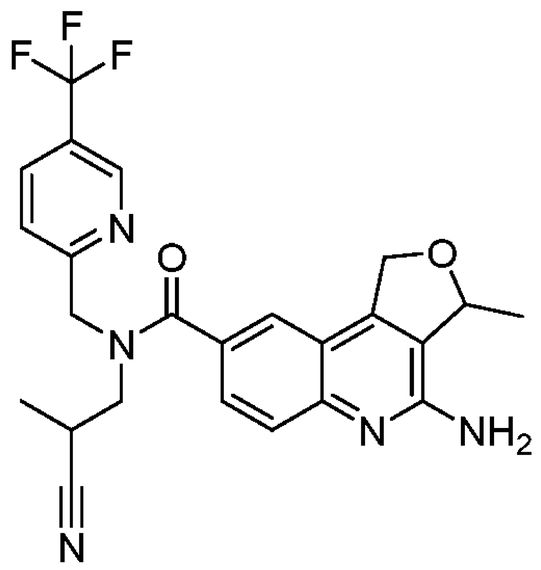
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
908		4-amino-N-(2,2-dimethylcyclopropyl)-3-methyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	471.2
909		4-amino-3-methyl-N-(spiro[2.4]heptan-1-yl)-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	497.2
910	 	4-amino-3-methyl-N-((1R,2R)-2-(trifluoromethyl)cyclopropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide and 4-amino-3-methyl-N-((1S,2S)-2-(trifluoromethyl)cyclopropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	511.2

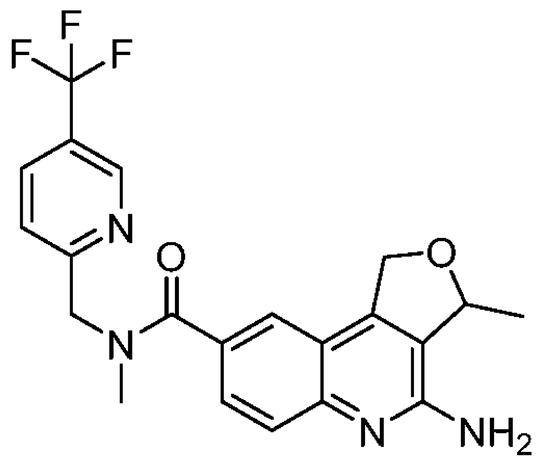
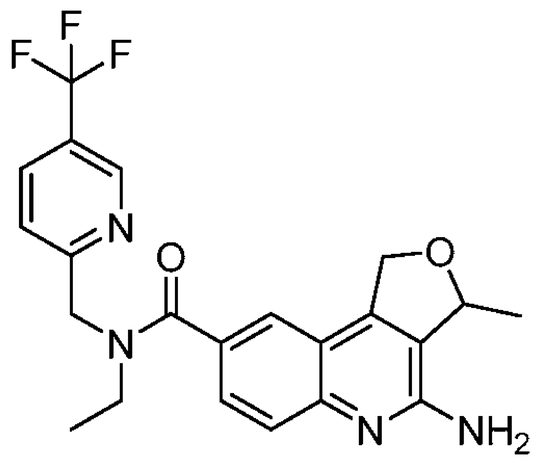
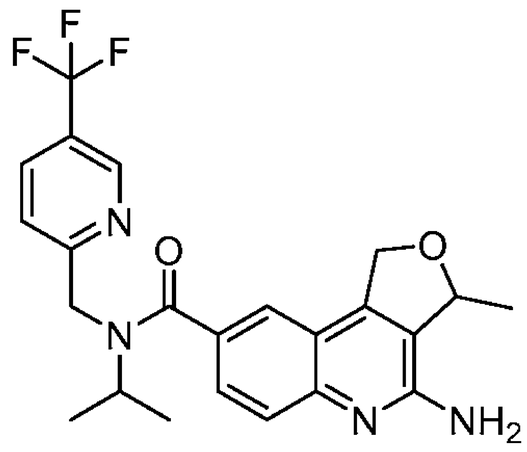
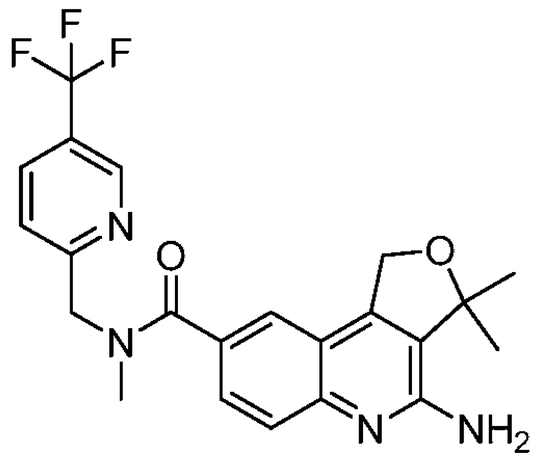
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
911		4-amino-3-methyl-N-((R)-1-(pyrimidin-2-yl)ethyl)-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	509.6
912		4-amino-N-((5-cyanopyridin-2-yl)methyl)-N-((5,6-dihydro-2H-pyran-3-yl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	456.2
913		4-amino-N-((1-cyanocyclopropyl)methyl)-N-((5-cyanopyridin-2-yl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	439.2
914		4-amino-N-((2-aminothiazol-5-yl)methyl)-N-((5-cyanopyridin-2-yl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	572.2

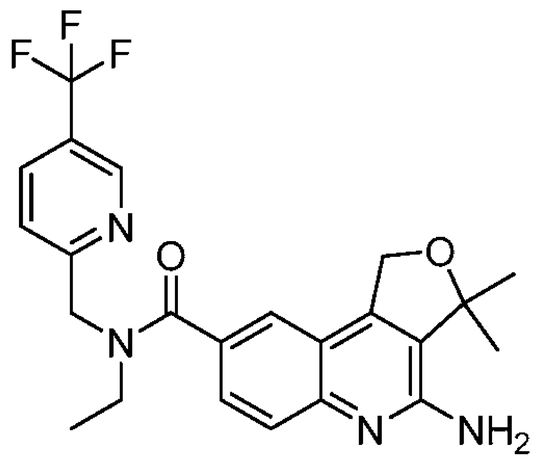
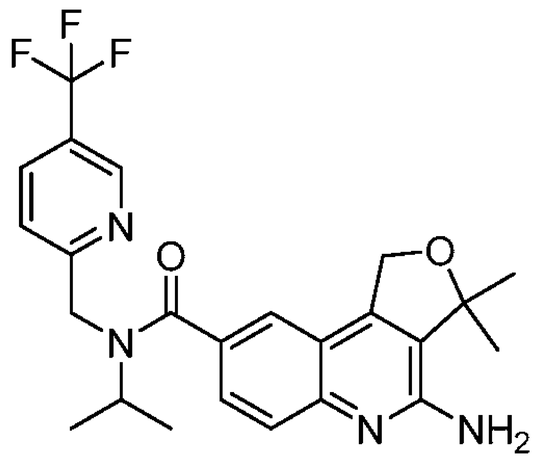
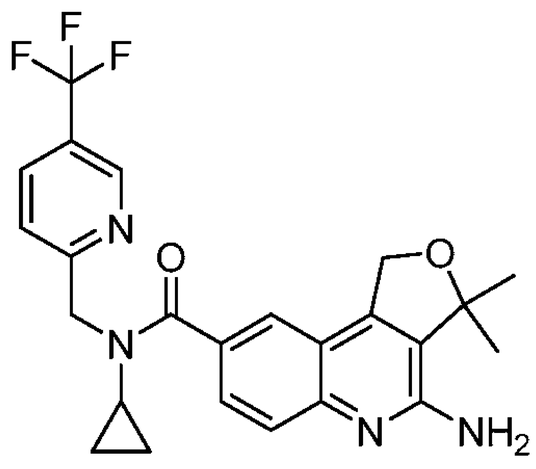
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
915		4-amino-N-((5,6-dihydro-2H-pyran-3-yl)methyl)-3-methyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	499.2
916		N-((1H-pyrrolo[2,3-b]pyridin-4-yl)methyl)-4-amino-3-methyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	533.2
917		4-amino-N-((1-cyanocyclopropyl)methyl)-3-methyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	482.2
918		4-amino-N-((2-aminothiazol-5-yl)methyl)-3-methyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	515.1

Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
919		4-amino-N-isobutyl-3-methyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	459.2
920		4-amino-N-(3-hydroxybutan-2-yl)-3-methyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	475.2
921		4-amino-N-(3-hydroxycyclohexyl)-3-methyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	501.2

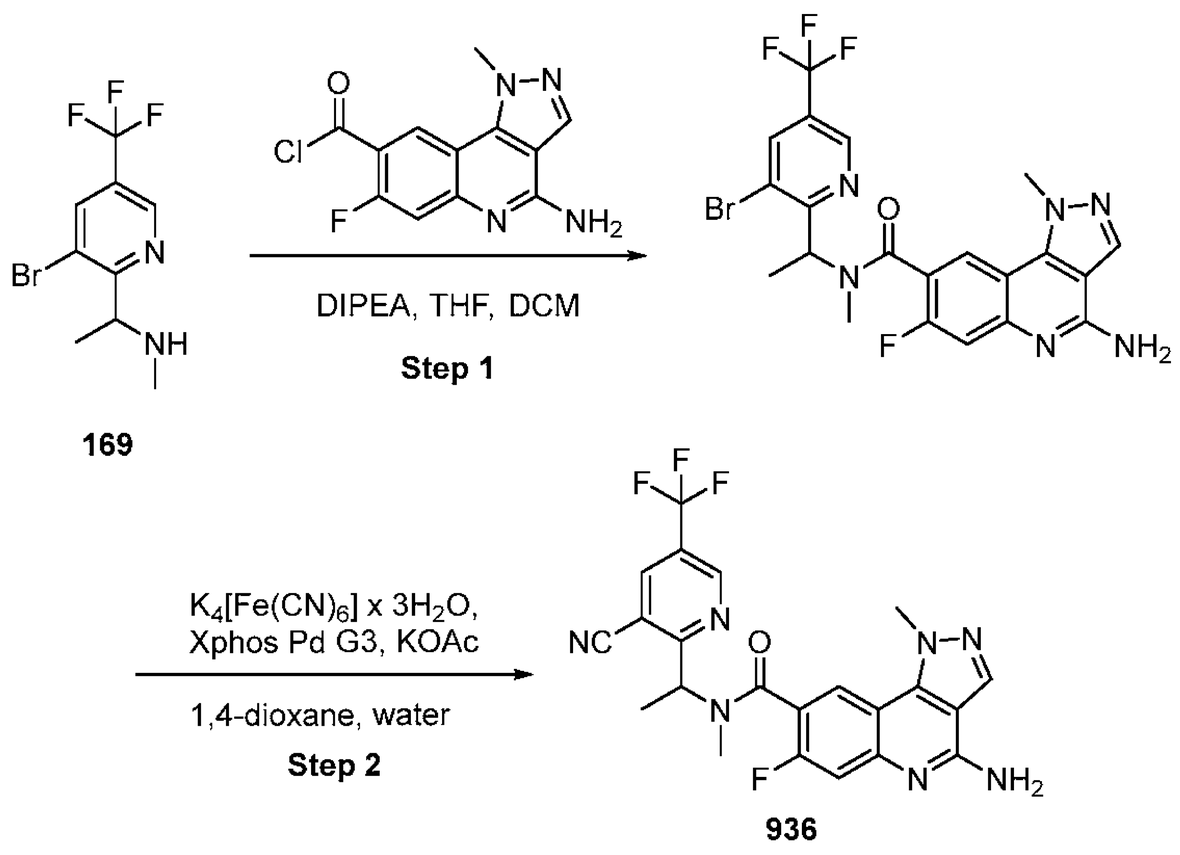
Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
922		4-amino-N-(2-(3-hydroxycyclobutyl)ethyl)-3-methyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	501.2
923		4-amino-N-(2-hydroxypropyl)-3-methyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	461.2
924		4-amino-N-(3-hydroxy-2-methylpropyl)-3-methyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	475.2

Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
925		4-amino-3-methyl-N-(3,3,3-trifluoro-2-hydroxypropyl)-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	515.2
926		4-amino-3-methyl-N-((1-methyl-1H-1,2,4-triazol-3-yl)methyl)-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	498.2
927		4-amino-3-methyl-N-((tetrahydrofuran-3-yl)methyl)-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	487.2
928		4-amino-N-(2-cyanopropyl)-3-methyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	470.2

Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
929		4-amino-N,3-dimethyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	417.2
930		4-amino-N-ethyl-3-methyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	431.2
931		4-amino-N-isopropyl-3-methyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	445.2
932		4-amino-N,3,3-trimethyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	431.2

Ex.	Structure	Name	m/z (ESI): $(M+H)^+$
933		4-amino-N-ethyl-3,3-dimethyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	445.2
934		4-amino-N-isopropyl-3,3-dimethyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	459.2
935		4-amino-N-cyclopropyl-3,3-dimethyl-N-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide	457.2

[0286] Example 936: 4-amino-N-(1-(3-cyano-5-(trifluoromethyl)pyridin-2-yl)ethyl)-7-fluoro-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide



169

936

[0287] Step 1. To a 50-mL round-bottomed flask was added 1-(3-bromo-5-(trifluoromethyl)pyridin-2-yl)-N-methylethan-1-amine (0.090 g, 0.318 mmol) and n,n-diisoproylethylamine (0.123 g, 0.167 mL, 0.954 mmol, Sigma-Aldrich Corporation) in tetrahydrofuran (1.590 mL) and dichloromethane (1.590 mL). The reaction mixture was cooled to 0 °C, then 4-amino-7-fluoro-1-methyl-1H-pyrazolo[4,3-c]quinoline-8-carbonyl chloride hydrochloride (0.110 g, 0.350 mmol) was added slowly to the reaction mixture. The overall reaction mixture was stirred at rt for 30 min. The reaction mixture was concentrated in vacuo. The crude material was absorbed onto a plug of silica gel and purified by chromatography through a silica-gel column, eluting with a gradient of 0-8% MeOH in CH_2Cl_2, then isocratic at 8% MeOH in CH_2Cl_2, to provide 4-amino-N-(1-(3-bromo-5-(trifluoromethyl)pyridin-2-yl)ethyl)-7-fluoro-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide (0.040 g, 0.076 mmol, 23.95 % yield) as off-white solid. *m/z* (ESI): 525.0 $(M+H)^+$.

[0288] Step 2. A resealable reaction vessel was charged with 4-amino-N-(1-(3-bromo-5-(trifluoromethyl)pyridin-2-yl)ethyl)-7-fluoro-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide (0.040 g, 0.076 mmol), potassium ferrocyanide trihydrate (0.257 g, 0.609 mmol, Toronto Research Chemicals) and potassium acetate (0.022 g, 0.228 mmol, Sigma-Aldrich Corporation) in 1,4-dioxane (0.190 mL) and water (0.190 mL). The reaction mixture was sparged with Argon (gas) for 5 min, then methanesulfonato(2-dicyclohexylphosphino-2',4',6'-tri-i-propyl-1,1'-biphenyl)(2'-amino-1,1'-biphenyl-2-yl)palladium (ii) (XPhos Pd G3) (0.012 g, 0.015 mmol, Strem Chemicals, Inc.) was added to the mixture and the vial was sealed. The mixture was stirred and heated at 100°C for 2 h. The reaction mixture was concentrated in vacuo. The crude material was absorbed onto a plug of silica gel and purified by chromatography through a silica-gel column, eluting with a gradient of 0-8% MeOH in CH_2Cl_2, to provide 4-amino-N-(1-(3-cyano-5-(trifluoromethyl)pyridin-2-yl)ethyl)-7-fluoro-N,1-dimethyl-1H-

pyrazolo[4,3-c]quinoline-8-carboxamide (0.020 g, 0.042 mmol, 55.7 % yield) as off-white solid. *m/z* (ESI): 472.1 $(M+H)^+$.

HCT116 Proliferation Activity

[0289] HCT116 MTAP null and WT cells were seeded in 96-well tissue culture plates in RPMI 1640 media + 10% fetal bovine serum. Plates were incubated overnight at 37°C and 5% CO_2. Cells were then treated with an 8- or 9-point serial dilution of compound, using a top concentration of 1, or 10 μM, 1:3 serial dilution steps and, a DMSO-only control. Cells were incubated in the presence of drug for 6 days. Effects on cell viability were measured with the CellTiter-Glo® Luminescent Cell Viability Assay (Promega) per manufacturer's recommendation. Assay plates were read on an EnVision™ Multilabel Reader using the Ultra-Sensitive luminescence module. IC_{50} values were calculated with GraphPad Prism v 5.01 using symmetrical sigmoidal dose-response least squares fit with Hill slope fixed to -1 and top constrain to 100% or GeneData Screener using a 4-parameter logistic model to fit dose response curves.

[0290] Alternatively, compounds could be assayed with a 384 well plate format:

[0291] Compounds were pre-spotted into 384 well plates with a 22-point serial dilution of compound, using a top concentration of 10 or 50 μM, 1:2 serial dilution steps and, a DMSO-only control. HCT116 MTAP null and WT cells were then seeded as above and after 6 days effects on cell viability were measured with the CellTiter-Glo® Luminescent Cell Viability Assay (Promega). Assay plates were read as above and IC_{50} values were calculated with GeneData Screener using a 4-parameter logistic model to fit dose response curves. The reported IC_{50} represents the value where the curve transits 50% of control.

Table 26

HCT116-MTAP null and WT cell line proliferation

Ex.	HCT-116 MTAP null IC_{50} (μM)	HCT-116 WT IC_{50} (μM)
300	0.041	1.340
301	0.259	11.000
302	0.900	17.267
303	0.024	0.574
304	0.026	0.352
305	0.027	0.861

Ex.	HCT-116 MTAP null IC_{50} (μM)	HCT-116 WT IC_{50} (μM)
306	0.217	7.990
307	0.018	0.471
308	0.124	5.095
309	4.000	>10
310	0.071	4.050
311	0.056	2.205

Ex.	HCT-116 MTAP null IC_{50} (μM)	HCT-116 WT IC_{50} (μM)
312	1.090	>10
313	0.200	3.680
314	0.254	15.200
315	0.137	11.060
316	0.570	23.650
317	0.432	49.700
318	4.930	36.300
319	27.700	>50
320	0.303	15.800
321	0.226	3.790
322	0.081	1.030
323	0.358	15.033
324	0.908	51.600
325	0.073	2.280
326	0.019	1.280
327	0.811	>10
328	0.129	19.400
329	0.022	0.160
330	0.204	>10
331	0.028	2.300
332	0.120	6.095
333	0.024	1.408
334	0.010	0.509
335	0.361	
336	0.087	2.571
337	0.033	0.714
338	0.406	5.830
339	0.025	0.611
340	2.950	>10
341	0.212	3.790
342	1.310	
343	0.270	8.240
344	0.244	>10

Ex.	HCT-116 MTAP null IC_{50} (μM)	HCT-116 WT IC_{50} (μM)
345	0.011	0.210
346	1.090	19.429
347	0.712	43.800
348	0.155	9.035
349	0.325	9.190
350	0.332	22.100
351	0.048	3.510
352	0.872	>10
353	0.124	>10
354	0.623	21.400
355	0.171	19.000
356	0.092	5.360
357	0.115	4.270
358	0.121	8.161
359	0.226	10.200
360	0.053	3.072
361	0.173	7.753
362	0.076	2.210
363	0.036	1.180
364	0.058	1.760
365	0.076	6.500
366	0.175	12.500
367	2.280	>50
368	0.065	3.260
369	0.124	5.039
370	0.029	1.370
371	0.010	0.288
372	0.110	5.610
373	0.022	2.975
374	0.014	0.286
375	1.500	6.890
376	0.222	15.150
377	0.049	2.065

Ex.	HCT-116 MTAP null IC_{50} (μM)	HCT-116 WT IC_{50} (μM)
378	0.294	9.430
379	0.025	0.764
380	0.056	4.100
381	0.008	1.560
382	1.160	22.800
383	1.310	43.000
384	0.053	1.380
385	0.157	7.285
386	0.455	30.300
387	0.175	4.040
388	0.054	1.280
389	0.050	3.393
390	0.262	9.900
391	0.091	4.540
392	0.057	1.539
393	0.113	6.933
394	0.030	0.831
395	0.031	0.535
396	0.020	0.629
397	0.055	1.101
398	0.049	1.390
399	0.393	4.430
400	0.970	>10
401	0.084	3.075
402	0.027	2.207
403	10.000	>10
404	0.180	11.400
405	0.362	>10
406	0.097	4.135
407	3.660	>10
408	0.086	3.353
409	0.056	5.873
410	0.087	3.255

Ex.	HCT-116 MTAP null IC_{50} (μM)	HCT-116 WT IC_{50} (μM)
411	0.181	13.600
412	0.397	25.550
413	0.870	20.300
414	5.865	>50
415	0.449	25.132
416	0.062	8.233
417	5.610	17.600
418	0.171	6.337
419	0.152	3.793
420	0.248	8.358
421	0.116	10.035
422	6.740	10.675
423	0.064	3.980
424	0.032	1.340
425	2.710	>50
426	0.096	4.220
427	0.044	1.675
428	0.101	1.250
429	1.260	31.800
430	0.312	12.850
431	14.335	23.500
432	0.203	6.390
433	0.344	21.200
434	0.584	23.900
435	0.014	0.065
436	0.029	0.187
437	0.031	0.353
438	0.012	0.187
439	0.007	0.138
440	0.461	>10
441	0.012	0.204
442	0.009	0.177
443	0.127	7.214

Ex.	HCT-116 MTAP null IC_{50} (μM)	HCT-116 WT IC_{50} (μM)
444	0.013	0.343
445	0.008	0.153
446	0.012	0.237
447	0.031	0.256
448	0.124	2.100
449	0.042	1.230
450	0.159	11.465
451	0.032	4.377
452	0.047	1.570
453	0.035	0.543
454	0.550	17.900
455	0.148	4.780
456	0.287	>10
457	0.132	3.175
458	0.026	0.361
459	0.029	0.305
460	0.019	0.287
461	0.069	4.500
462	0.105	3.935
463	0.014	0.440
464	0.007	0.240
465	0.031	1.230
466	0.028	0.217
467	0.014	0.332
468	0.008	0.208
469	0.025	0.550
470	0.041	3.023
471	0.043	1.161
472	0.267	14.900
473	0.809	>10
474	0.030	1.330
475	0.375	7.811
476	1.370	4.460

Ex.	HCT-116 MTAP null IC_{50} (μM)	HCT-116 WT IC_{50} (μM)
477	0.655	19.428
478	0.082	9.580
479	0.328	17.100
480	0.272	1.446
481	0.074	5.710
482	0.052	2.640
483	0.458	7.290
484	0.020	0.402
485	0.365	32.100
486	0.445	17.500
487	0.088	1.371
488	0.049	0.696
489	0.276	5.210
490	0.087	3.475
492	0.048	0.622
493	0.124	1.165
494	0.282	9.070
495	0.079	6.355
496	1.272	2.238
497	0.250	3.525
498	0.266	12.700
499	0.164	4.140
500	0.595	32.467
501	0.046	1.200
502	3.930	47.300
503	0.056	2.005
504	0.056	1.850
505	0.022	0.662
506	0.009	0.369
507	0.025	0.373
508	0.060	2.840
509	0.040	0.878
510	0.065	2.660

Ex.	HCT-116 MTAP null IC_{50} (μM)	HCT-116 WT IC_{50} (μM)
511	0.122	4.920
512	0.038	1.380
513	0.019	0.848
514	0.071	3.250
515	0.080	3.350
516	0.167	9.320
517	0.706	45.400
518	0.106	6.270
519	0.187	14.000
520	0.149	9.060
521	0.018	0.698
522	0.014	0.380
523	0.072	6.790
524	0.183	16.350
525	0.032	2.125
526	0.169	6.950
527	0.183	13.500
528	0.111	5.420
529	0.887	28.500
530	0.165	6.560
531	0.188	2.340
532	0.037	2.030
533	0.459	3.190
534	0.581	5.580
535	0.860	6.990
536	0.050	0.325
537	0.222	5.390
538	0.040	0.735
539	0.106	2.100
540	0.039	1.480
541	0.037	0.548
542	0.035	1.540
543	0.057	2.010

Ex.	HCT-116 MTAP null IC_{50} (μM)	HCT-116 WT IC_{50} (μM)
544	0.056	2.320
545	0.007	0.140
546	0.019	0.976
547	0.668	24.500
548	0.078	6.873
549	0.020	0.487
550	0.066	1.800
551	0.125	5.570
552	0.025	1.880
553	0.247	12.400
554	0.008	0.181
555	0.023	2.043
556	0.014	0.458
557	0.375	12.300
558	0.019	0.421
559	0.030	1.179
560	0.056	4.140
561	0.089	5.330
562	0.086	3.530
563	0.028	2.080
564	0.021	0.925
565	0.019	0.653
566	0.013	0.181
567	0.090	6.790
568	0.091	5.390
569	0.031	3.890
570	0.757	0.329
571	0.071	4.930
572	0.939	>50
573	0.085	3.730
574	0.025	0.878
575	0.012	0.354
576	0.107	2.080

Ex.	HCT-116 MTAP null IC_{50} (μM)	HCT-116 WT IC_{50} (μM)
577	3.260	>10
578	0.338	4.930
579	0.348	5.620
580	0.321	10.800
581	0.809	10.200
582	0.036	0.558
583	0.173	4.815
584	0.014	0.164
585	0.149	1.980
586	0.012	0.150
587	0.076	1.710
588	0.079	1.950
589	0.029	0.815
590	2.230	>50
591	0.563	32.100
592	0.025	2.410
593	0.012	0.908
594	0.638	29.100
595	0.010	0.676
596	0.888	37.300
597	0.200	15.200
598	0.008	0.415
599	0.536	27.200
600	0.018	0.663
601	0.997	21.200
602	0.006	0.209
603	0.276	11.800
604	0.238	24.600
605	0.014	0.793
606	0.263	3.700
607	0.154	1.370
608	0.226	3.790
609	0.081	1.030

Ex.	HCT-116 MTAP null IC_{50} (μM)	HCT-116 WT IC_{50} (μM)
610	0.006	0.135
611	0.084	0.474
612	0.176	3.060
613	0.023	0.761
614	0.042	0.255
615	0.019	0.271
616	0.018	0.419
617	0.245	>10
618	0.033	0.264
619	0.061	1.060
620	0.077	3.560
621	0.108	1.230
622	0.011	0.156
623	0.015	0.148
624	0.021	0.189
625	0.130	1.590
626	0.043	0.444
627	0.045	0.583
628	0.119	1.190
629	0.016	0.398
630	0.019	0.408
631	0.010	0.215
632	0.011	0.231
633	0.013	0.071
634	0.034	0.953
635	0.073	1.210
636	0.149	2.990
637	0.212	3.220
638	0.022	0.378
639	0.238	3.150
640	0.013	0.110
641	0.016	0.242
642	0.041	1.304

Ex.	HCT-116 MTAP null IC_{50} (μM)	HCT-116 WT IC_{50} (μM)
643	0.178	1.615
644	2.790	>10
645	50.000	>50
646	0.019	0.263
647	0.673	4.200
648	0.279	2.500
649	0.014	0.181
650	0.053	0.811
651	0.234	3.520
652	0.050	1.390
653	0.008	0.073
654	0.009	0.171
655	0.016	0.294
656	0.019	1.260
657	0.013	0.196
658	0.006	0.071
659	0.014	0.378
660	0.354	>10
661	0.303	26.200
662	0.029	0.290
663	0.035	1.025
664	0.038	1.390
665	0.037	1.250
666	0.687	>10
667	0.929	7.130
668	0.304	>10
669	0.073	3.070
670	0.170	8.020
671	0.080	3.970
672	0.145	7.460
673	0.110	3.265
674	0.073	2.575
675	0.066	12.733

Ex.	HCT-116 MTAP null IC_{50} (μM)	HCT-116 WT IC_{50} (μM)
676	0.012	0.316
677	0.243	>10
678	0.040	1.175
679	0.005	0.108
680	0.091	2.840
681	0.367	6.490
682	0.087	3.400
683	0.235	>10
684	0.342	>10
685	0.201	>10
686	0.445	8.800
687	>10	>10
688	0.081	3.445
689	0.096	2.585
690	0.071	4.170
691	0.127	3.880
692	0.449	>10
693	2.020	>10
694	0.415	>10
695	0.210	4.990
696	0.261	>10
697	0.121	4.430
698	0.206	4.500
699	0.249	
700	1.100	>10
701	0.193	7.250
702	0.470	4.120
703	0.337	8.150
704	0.549	>10
705	0.637	28.500
706	0.172	3.450
707	0.106	2.870
708	0.153	8.220

Ex.	HCT-116 MTAP null IC_{50} (μM)	HCT-116 WT IC_{50} (μM)
709	0.076	4.250
710	0.484	>10
711	0.148	4.780
712	2.000	>50
713	5.110	>50
714	0.008	0.124
715	0.006	0.070
716	0.917	33.300
717	0.609	7.759
718	0.281	16.443
719	1.031	21.798
720	14.900	>50
721	0.209	9.410
722	0.085	3.350
723	0.157	6.020
724	0.054	2.440
725	0.854	>50
726	0.109	7.520
727	0.279	12.300
728	0.047	0.663
729	0.019	0.534
730	0.017	0.620
731	0.047	2.090
732	0.087	2.850
733	0.290	6.300
734	0.383	14.400
735	5.500	36.200
736	0.127	4.890
737	0.059	2.380
738	0.013	0.430
739	0.071	2.220
740	0.005	0.100
741	0.042	1.023

Ex.	HCT-116 MTAP null IC_{50} (μM)	HCT-116 WT IC_{50} (μM)
742	0.066	2.500
743	0.015	1.090
744	0.038	0.967
745	0.246	14.800
746	0.034	3.457
747	0.161	5.090
748	5.350	36.400
749	0.177	3.345
750	0.023	0.767
751	0.017	0.337
752	0.033	0.771
753	0.124	3.890
754	0.024	0.370
755	0.892	6.420
756	0.049	0.744
757	0.026	1.315
758	0.037	0.658
759	6.730	11.800
760	0.743	6.100
761	0.305	13.600
762	0.026	0.621
763	0.113	4.813
764	6.380	>50
765	0.049	1.980
766	0.061	1.910
767	2.270	>50
768	4.230	>50
769	0.115	7.500
770	0.253	19.400
771	0.395	31.100
772	0.374	18.200
773	0.106	2.630
774	0.736	40.600

Ex.	HCT-116 MTAP null IC_{50} (μM)	HCT-116 WT IC_{50} (μM)
775	0.033	2.680
776	0.150	>10
777	0.025	1.380
778	0.049	2.657
779	0.364	28.900
780	0.022	1.185
781	0.037	1.310
782	0.080	7.767
783	0.868	16.400
784	0.022	0.609
785	0.851	19.800
786	0.126	7.330
787	0.865	8.970
788	0.008	0.134
789	0.083	6.930
790	0.776	47.100
791	0.011	0.341
792	0.030	2.330
793	0.011	0.296
794	0.020	0.499
795	0.008	0.379
796	0.034	1.670
797	0.041	0.755
798	0.010	0.152
799	0.008	0.263
800	0.007	0.245
801	0.153	13.550
802	0.021	1.376
803	0.012	0.384
804	0.026	1.803
805	0.008	0.121
806	0.056	3.160
807	0.005	0.114

Ex.	HCT-116 MTAP null IC_{50} (μM)	HCT-116 WT IC_{50} (μM)
808	0.052	3.130
809	0.031	1.790
810	0.226	13.800
811	0.645	>50
812	0.237	14.100
813	0.676	29.300
814	0.044	1.170
815	0.018	0.301
816	0.078	2.490
817	0.028	0.689
818	0.007	0.161
819		
820	7.070	>10
821	4.190	>50
822	0.323	11.950
823	0.528	16.233
824	2.390	26.300
825	0.022	0.276
826	6.720	27.100
827	1.250	47.200
828	0.026	0.294
829	7.790	>50
830	0.080	2.970
831	2.570	31.700
832	0.454	12.600
833	2.565	27.200
834	0.817	19.700
835	0.126	3.760
836	3.635	38.700
837	7.080	>50
838	0.161	8.590
839	0.213	9.520
840	0.638	22.950

Ex.	HCT-116 MTAP null IC_{50} (μM)	HCT-116 WT IC_{50} (μM)
841	0.613	11.650
842	0.115	3.275
843	3.355	>50
844	0.105	6.225
845	0.105	2.240
846	0.212	3.940
847	1.865	36.050
848	0.453	11.450
849	0.879	24.400
850	8.345	>50
851	0.047	4.003
852	3.160	>50
853	0.167	14.350
854	0.086	3.280
855	0.164	28.850
856	0.087	8.480
857	0.026	1.090
858	0.041	3.333
859	0.583	17.500
860	0.017	0.849
861	0.205	13.600
862	0.031	2.195
863	0.007	0.340
864	0.618	22.700
865	0.059	2.810
866	0.309	11.300
867	0.157	7.840
868	0.059	3.840
869	0.627	8.430
870	0.007	0.162
871	0.025	0.078
872	0.075	4.500
873	0.066	7.317

Ex.	HCT-116 MTAP null IC_{50} (μM)	HCT-116 WT IC_{50} (μM)
874	0.929	36.000
875	0.025	1.415
876	0.334	30.450
877	0.756	44.100
878	0.010	0.709
879	0.181	12.300
880	0.137	8.310
881	0.007	0.370
882	0.062	1.340
883	0.020	0.514
884	0.027	0.733
885	0.025	0.596
886	1.690	>10
887	0.025	0.496
888	0.021	0.231
889	0.202	4.740
890	0.014	0.156
891	0.040	
892	0.073	1.900
893	0.041	
894	0.180	
895	0.051	0.550
896	0.088	1.800
897	0.024	0.110
898	0.052	0.290
899	0.130	9.700
900	0.290	>10
901	0.042	0.430
902	0.034	0.330
903	0.058	4.000
904	0.031	1.600
905	0.080	4.600
906	0.790	

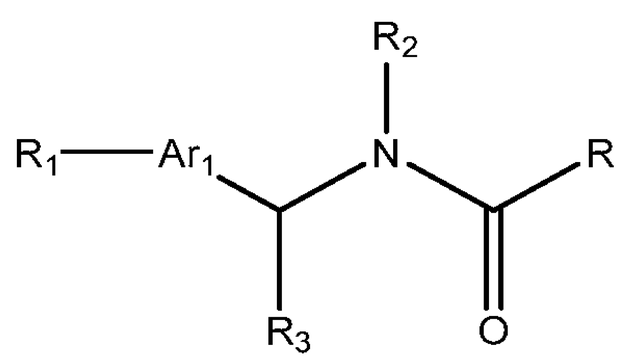
Ex.	HCT-116 MTAP null IC_{50} (μM)	HCT-116 WT IC_{50} (μM)
907	0.040	>1
908	0.123	6.200
909	0.215	8.000
910	0.022	3.000
911	0.021	0.173
912	0.140	
913	0.049	1.700
914	0.200	
915	0.029	4.200
916	0.006	0.200
917	0.017	1.563
918	0.054	>1
919	0.025	
920	0.076	
921	0.093	

Ex.	HCT-116 MTAP null IC_{50} (μM)	HCT-116 WT IC_{50} (μM)
922	0.048	
923	0.056	
924	0.043	
925	0.035	
926	0.030	
927	0.069	
928	0.039	
929	0.200	>1
930	0.061	>10
931	0.072	9.600
932	0.860	1.700
933	0.560	>10
934	0.079	>1
935	0.630	>1
936	0.721	18.700

[0292] All publications and patent applications cited in this specification are hereby incorporated by reference herein in their entireties and for all purposes as if each individual publication or patent application were specifically and individually indicated as being incorporated by reference and as if each reference was fully set forth in its entirety. Although the foregoing invention has been described in some detail by way of illustration and example for purposes of clarity of understanding, it will be readily apparent to those of ordinary skill in the art in light of the teachings of this invention that certain changes and modifications may be made thereto without departing from the spirit or scope of the appended claims.

WHAT IS CLAIMED:

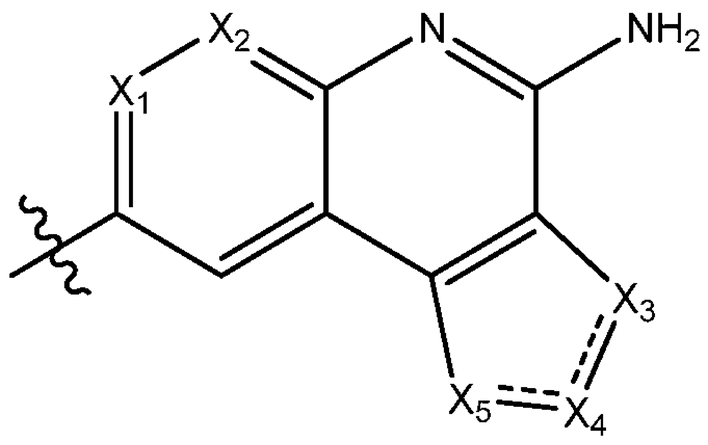
1. A compound of Formula **I**



I

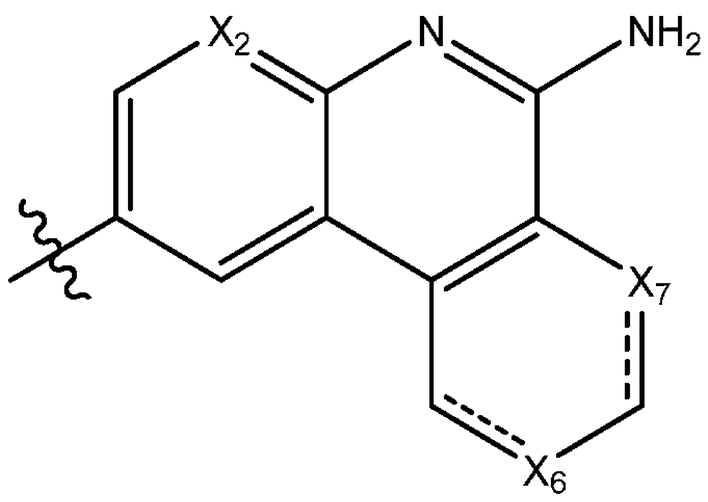
a tautomer thereof, a stereoisomer thereof, or a pharmaceutically acceptable salt of any of the foregoing, wherein:

R is a tricycle independently selected from the formulae **IA** and **IB**:



IA

and



IB,

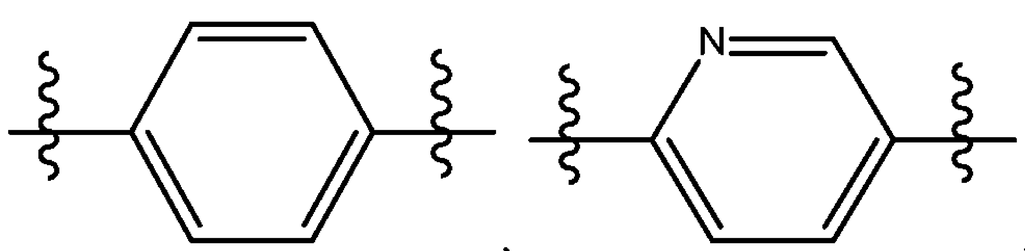
wherein  is a single or double bond,

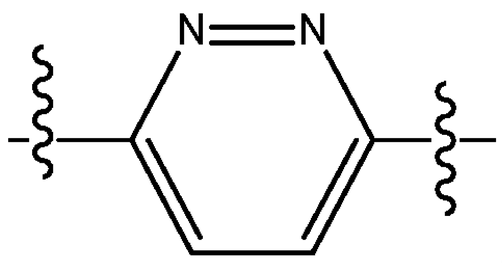
X^1, X^2, X^6 and X^7 are in each instance N or C, wherein both X^1 and X^2 cannot be N at the same time, and wherein if X^1 is C, it can be optionally substituted with halo;

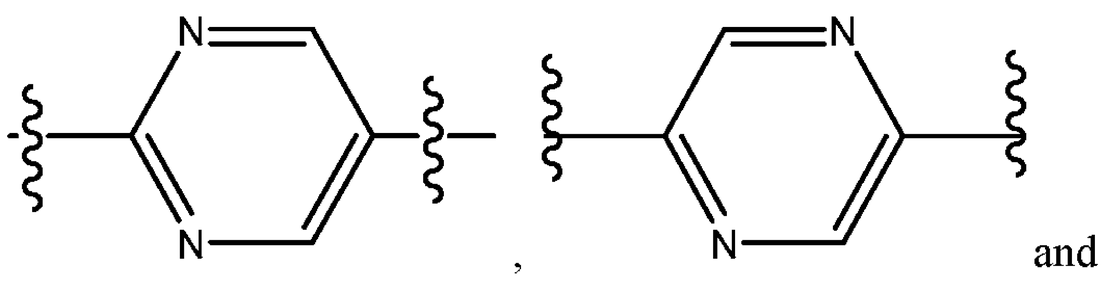
X^3, X^4 and X^5 are at each instance independently selected from an optionally substituted C, O, N and S; wherein the substituents are independently selected from C_{1-3} alkyl, C_{1-3} alkyl(OH), wherein alkyl can be optionally substituted with halo;

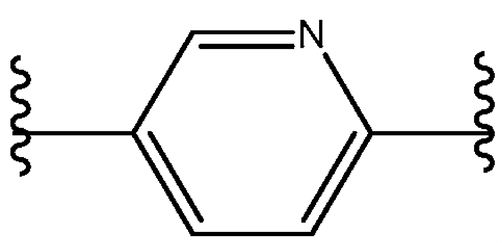
R^3 in each instance is independently selected from H or C_{1-3} alkyl;

Ar^1 is a six membered optionally substituted aryl or heteroaryl independently selected from:


,


,


, and


;

wherein the substituents are independently selected from C_{1-3} alkyl, -OC_{1-3} alkyl or halo;

R^1 in each instance is independently selected from H, halo, optionally substituted C_{1-3} alkyl, wherein the substituents are selected from halo; -CN, optionally substituted -O-C_{1-3} alkyl, wherein the substituents are selected from halo; -C(O)OC_{1-3} alkyl, wherein C_{1-3} alkyl can be optionally substituted with halo, and morpholinyl; and

R^2 in each instance is independently selected from an optionally substituted C_{1-8} alkyl, wherein the substituents are selected from halo, hydroxy, amino, -O- C_{1-3} alkyl or -CN; 5 or 6 membered cycle or heterocycle, optionally substituted with hydroxy, amino, an optionally substituted C_{1-6} alkyl, wherein the substituents are selected from halo; an optionally substituted C_{1-6} alkyl-O- C_{1-3} alkyl, wherein the substituents are selected from halo; 5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridinyl; C_{1-3} alkyl-heterocyclyl, wherein the heterocyclyl is selected from optionally substituted 3,4-dihydro-2H-pyrano[2,3-c]pyridinyl; pyradazinyl, triazolyl, pyrimidinyl, tetrahydrofuranyl, 1H-pyrrolo[2,3-b]pyridinyl, cyclohexyl; wherein the substituents are selected from C_{1-3} alkyl, -CN, and halo, or an optionally substituted C_{1-6} alkyl-O- C_{1-3} alkyl, wherein the substituents are selected from halo; optionally substituted phenyl, wherein the substituents are selected from halo or C_{1-3} alkyl.

2. The compound of claim 1, the tautomer thereof, the stereoisomer thereof, or the pharmaceutically acceptable salt of any of the foregoing, wherein R^1 is a tricycle of formulae **IA**.

3. The compound of claim 1, the tautomer thereof, the stereoisomer thereof, or the pharmaceutically acceptable salt of any of the foregoing, wherein R^1 is a tricycle of formulae **IB**.

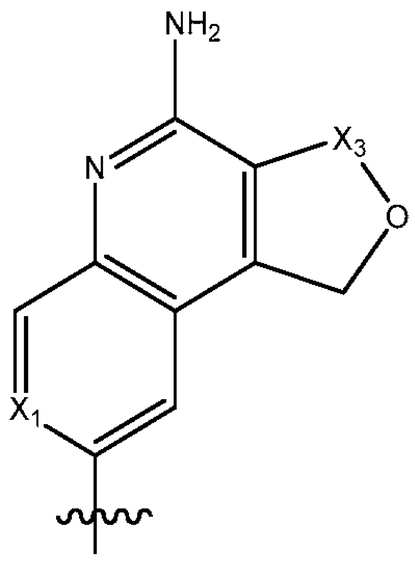
4. The compound of claim 2, the tautomer thereof, the stereoisomer thereof, or the pharmaceutically acceptable salt of any of the foregoing, wherein X^1 and X^2 are both C.

5. The compound of claim 4, the tautomer thereof, the stereoisomer thereof, or the pharmaceutically acceptable salt of any of the foregoing, wherein X^1 is unsubstituted or substituted with halo.

6. The compound of claim 3, the tautomer thereof, the stereoisomer thereof, or the pharmaceutically acceptable salt of any of the foregoing, wherein X^2 is C.

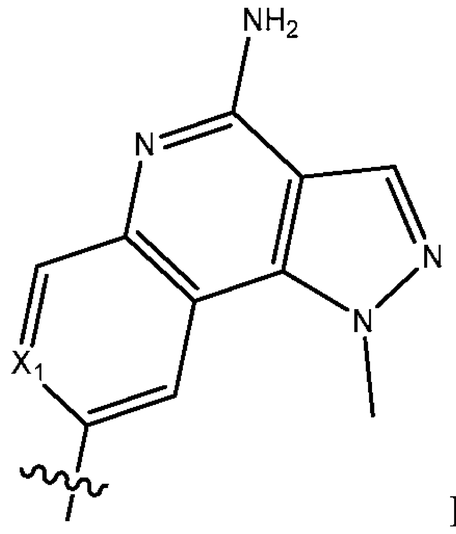
7. The compound of claim 3, the tautomer thereof, the stereoisomer thereof, or the pharmaceutically acceptable salt of any of the foregoing, wherein X^2 is N.

8. The compound of claim 4, the tautomer thereof, the stereoisomer thereof, or the pharmaceutically acceptable salt of any of the foregoing, wherein R is a tricycle of the formulae **IA1**



IA1

9. The compound of claim 4, the tautomer thereof, the stereoisomer thereof, or the pharmaceutically acceptable salt of any of the foregoing, wherein R is a tricycle of the formulae **IA2**



IA2

10. The compound of claim 8, the tautomer thereof, the stereoisomer thereof, or the pharmaceutically acceptable salt of any of the foregoing, wherein X^3 is C, unsubstituted or substituted with methyl.

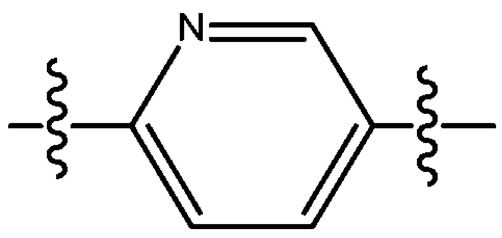
11. The compound of claim 1, the tautomer thereof, the stereoisomer thereof, or the pharmaceutically acceptable salt of any of the foregoing, wherein R^3 is H.

12. The compound of claim 1, the tautomer thereof, the stereoisomer thereof, or the pharmaceutically acceptable salt of any of the foregoing, wherein R^3 is methyl.

13. The compound of claim 8, the tautomer thereof, the stereoisomer thereof, or the pharmaceutically acceptable salt of any of the foregoing, wherein R^2 is an optionally substituted $C_{1\text{-}8}$ alkyl.

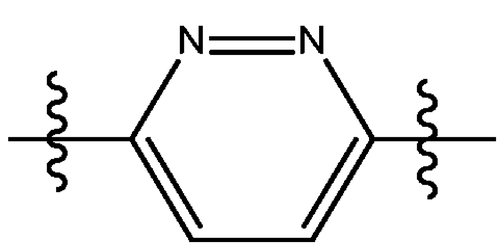
14. The compound of claim 8, the tautomer thereof, the stereoisomer thereof, or the pharmaceutically acceptable salt of any of the foregoing, wherein R^2 is an optionally substituted methyl, ethyl, isopropyl, or cyclo$C_{1\text{-}6}$alkyl.

15. The compound of claim 14, the tautomer thereof, the stereoisomer thereof, or the pharmaceutically acceptable salt of any of the foregoing, wherein Ar^1 is



.

16. The compound of claim 14, the tautomer thereof, the stereoisomer thereof, or the pharmaceutically acceptable salt of any of the foregoing, wherein Ar^1 is



17. The compound of claim 15, the tautomer thereof, the stereoisomer thereof, or the pharmaceutically acceptable salt of any of the foregoing, wherein R^1 is halo.

18. The compound of claim 15, the tautomer thereof, the stereoisomer thereof, or the pharmaceutically acceptable salt of any of the foregoing, wherein R^1 is optionally substituted C_{1-3} alkyl or -CN.

19. The compound of claim 3, the tautomer thereof, the stereoisomer thereof, or the pharmaceutically acceptable salt of any of the foregoing, wherein R^1 is halo, optionally substituted C_{1-3} alkyl or -CN.

20. A compound, the tautomer thereof, the stereoisomer thereof, or the pharmaceutically acceptable salt of any of the foregoing, wherein the compound is selected from:
4-amino-N-(cyclopropylmethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-cyclopropyl-3-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((2R)-1-methoxy-2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((2S)-1-methoxy-2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((2R)-1-methoxy-2-propanyl)-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((2S)-1-methoxy-2-propanyl)-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-N-((6-chloro-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-chloro-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-((6-chloro-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((6-chloro-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-3-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3S)-4-amino-N-(bicyclo[1.1.1]pentan-1-yl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-3-methyl-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-(bicyclo[1.1.1]pentan-1-yl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-N,3-dimethyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-3-methyl-N-(2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-((2R)-1-methoxy-2-propanyl)-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-((2S)-1-methoxy-2-propanyl)-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-cyclopropyl-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-cyclopropyl-3-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N,3-dimethyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3S)-4-amino-N-cyclopropyl-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3S)-4-amino-N,3-dimethyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-3-methyl-N-(2,2,2-trifluoroethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;

4-amino-N-(cyclopropylmethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide;
4-amino-N-((2R)-1-methoxy-2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide;
4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-(cyclopropylmethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-(cyclopropylmethyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((5-bromo-2-pyridinyl)methyl)-N,3-dimethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((6-cyclopropyl-3-pyridazinyl)methyl)-3-methyl-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-bromo-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-(cyclopropylmethyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((6-bromo-3-pyridazinyl)methyl)-3-methyl-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-(cyclopropylmethyl)-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-(cyclopropylmethyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(cyclopropylmethyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1-methylcyclopropyl)methyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3R)-4-amino-N-(2,2-dimethylpropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((1-methylcyclopropyl)methyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(2,2-dimethylpropyl)-3,3-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-3,3-dimethyl-N-((1-methylcyclopropyl)methyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(2,2-dimethylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-N-((5-cyclopropyl-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-7-fluoro-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-cyclopropyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-cyclopropyl-N-((5-cyclopropyl-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-((6-cyclopropyl-3-pyridinyl)methyl)-3-methyl-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-cyclopropyl-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-cyclopropyl-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3R)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-cyclopropyl-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-N,3-dimethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-7-fluoro-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-(2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-ethyl-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-ethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-ethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-cyclopropyl-3-pyridinyl)methyl)-7-fluoro-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-cyclopropyl-N-((5-cyclopropyl-2-pyridinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-7-fluoro-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-N-((5-cyclopropyl-2-pyridinyl)methyl)-7-fluoro-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-7-fluoro-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-7-fluoro-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-ethoxy-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((6-ethoxy-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N,3-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-3-methyl-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(bicyclo[1.1.1]pentan-1-yl)-N-((6-ethoxy-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-7-chloro-N-((5-cyclopropyl-2-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-(bicyclo[1.1.1]pentan-1-yl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(bicyclo[1.1.1]pentan-1-yl)-7-fluoro-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((6-cyclopropyl-3-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-3-methyl-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-N,3-dimethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(bicyclo[1.1.1]pentan-1-yl)-N-((6-ethoxy-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-ethoxy-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;

4-amino-7-chloro-N-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((2R)-1-methoxy-2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((2S)-1-methoxy-2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-((5-cyano-2-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-(2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-(2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(bicyclo[1.1.1]pentan-1-yl)-7-chloro-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-(cyclopropylmethyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-((6-ethoxy-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-3-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((1-methylcyclopropyl)methyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-methyl-N-(4-(trifluoromethyl)benzyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-methyl-N-((6-(trifluoromethyl)-3-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-((6-cyclopropyl-3-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-(cyclopropylmethyl)-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3S)-4-amino-N-((6-cyclopropyl-3-pyridinyl)methyl)-3-methyl-N-(2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-N-(2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;

(3R)-4-amino-N-cyclopropyl-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-3-methyl-N-(2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3S)-4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-3-methyl-N-(2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-ethyl-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-(bicyclo[1.1.1]pentan-1-yl)-N-((6-ethoxy-3-pyridazinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-3-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N,3-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-((6-cyclopropyl-3-pyridinyl)methyl)-3-methyl-N-(2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
methyl 4-(6-((((4-amino-1,3-dihydrofuro[3,4-c]quinolin-8-yl)carbonyl)(methyl)amino)methyl)-3-pyridinyl)-1-piperazinecarboxylate;
(3S)-4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-N,3-dimethyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-N,3-dimethyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-cyclopropyl-N-((5-cyclopropyl-2-pyridinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3S)-4-amino-N-cyclopropyl-N-((5-cyclopropyl-2-pyridinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(cyclopropylmethyl)-N-((6-(difluoromethoxy)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-ethyl-7-fluoro-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-ethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((5-chloro-2-pyridinyl)methyl)-N-ethyl-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-N-ethyl-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((5-chloro-2-pyridinyl)methyl)-3-methyl-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-(cyclopropylmethyl)-N-((6-(difluoromethoxy)-3-pyridazinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3S)-4-amino-N-(cyclopropylmethyl)-N-((6-(difluoromethoxy)-3-pyridazinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(cyclopropylmethyl)-N-((6-(difluoromethoxy)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-ethyl-7-fluoro-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
5-amino-N-ethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)benzo[c][2,6]naphthyridine-9-carboxamide;
4-amino-N-((5-(3,6-dihydro-2H-pyran-4-yl)-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
methyl 6-((((4-amino-1,3-dihydrofuro[3,4-c]quinolin-8-yl)carbonyl)(methyl)amino)methyl)-3',6'-dihydro[3,4'-bipyridine]-1'(2'H)-carboxylate;
5-oxo-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-5,6-dihydropyrazolo[1,5-c]quinazoline-9-carboxamide;
4-amino-1,3-dimethyl-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((5-bromo-2-pyridinyl)methyl)-N,3-dimethyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3S)-4-amino-N-((5-bromo-2-pyridinyl)methyl)-N,3-dimethyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-3-methyl-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyrazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-7-fluoro-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-7-fluoro-N-((1R)-1-(3-fluoro-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-N-((5-(difluoromethyl)-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-chloro-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1S)-1-(2-pyrimidinyl)ethyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1R)-1-(3-fluoro-2-pyridinyl)ethyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(1,3-dimethoxy-2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((2R)-1-methoxy-2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-methoxy-3-pyridazinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((8R)-5,6,7,8-tetrahydro[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((8S)-5,6,7,8-tetrahydro[1,2,4]triazolo[1,5-a]pyridin-8-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((8R)-5,6,7,8-tetrahydro[1,2,4]triazolo[1,5-a]pyridin-8-yl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((8S)-5,6,7,8-tetrahydro[1,2,4]triazolo[1,5-a]pyridin-8-yl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(4-(3-oxetanyl)benzyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(4-(3-oxetanyl)benzyl)-N-((1S)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-N-(cyclopropylmethyl)-N-((6-(4-morpholinyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((6-(2,2,2-trifluoroethoxy)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-cyclopropyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-bromo-2-pyridinyl)methyl)-N-cyclopropyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-N-((5-(difluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1-cyanocyclopropyl)methyl)-N-((5-cyano-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-cyclopropyl-3-pyridazinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((3R,4S)-3-methoxytetrahydro-2H-pyran-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((3S,4R)-3-methoxytetrahydro-2H-pyran-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((3R,4R)-4-methoxytetrahydro-2H-pyran-3-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((3S,4S)-4-methoxytetrahydro-2H-pyran-3-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-((5-cyano-2-pyridinyl)methyl)-N-cyclopropyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-chloro-5-methoxy-2-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-(cyclopropylmethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-(2-propanyl)-N-((5-(trifluoromethoxy)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((5-(difluoromethyl)-2-pyridinyl)methyl)-3-methyl-N-((1R)-1-(1-methyl-1H-1,2,4-triazol-3-yl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3R)-4-amino-3-methyl-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(3,4-dihydro-2H-pyrano[2,3-c]pyridin-6-ylmethyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(bicyclo[1.1.1]pentan-1-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-((5-cyano-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((2R)-1-fluoro-2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((2S)-1-fluoro-2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-((5-cyano-2-pyridinyl)methyl)-N-(cyclopropylmethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-cyclopropyl-7-fluoro-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-7-fluoro-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-((5-cyclopropyl-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-7-fluoro-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-cyclopropyl-N-((5-cyclopropyl-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-(2,2,2-trifluoroethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-(bicyclo[1.1.1]pentan-1-yl)-N-((6-ethoxy-3-pyridazinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-N-(2,2,2-trifluoroethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N,3-dimethyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(2,2,2-trifluoroethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-7-chloro-N-((2R)-1-methoxy-2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-((2S)-1-methoxy-2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((2R)-1-methoxy-2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((2S)-1-methoxy-2-propanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-(tetrahydro-2H-pyran-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-cyclopropyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
6-amino-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-8,9-dihydro-7H-cyclopenta[c][1,7]naphthyridine-2-carboxamide;
6-amino-N-((5-(difluoromethyl)-2-pyridinyl)methyl)-N-(1-methyl-1H-pyrazol-4-yl)-8,9-dihydro-7H-cyclopenta[c][1,7]naphthyridine-2-carboxamide;
4-amino-3-methyl-N-(1-methylcyclopropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
4-amino-3-methyl-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyrazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-ethyl-7-fluoro-N-((5-(trifluoromethyl)-2-pyrazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-ethyl-N-((5-(trifluoromethyl)-2-pyrazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-7-chloro-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyrazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-ethyl-3-methyl-N-((5-(trifluoromethyl)-2-pyrazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-cyclobutyl-7-fluoro-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-methoxy-N-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N,7-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-cyclobutyl-7-fluoro-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-cyclobutyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-3-methyl-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
4-amino-1-methyl-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-cyclopropyl-7-fluoro-3-methyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
4-amino-N-cyclobutyl-N-((6-(difluoromethoxy)-3-pyridazinyl)methyl)-7-fluoro-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-methyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-methyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-7-fluoro-N-methyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-methyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N,3-dimethyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N,3-dimethyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;

4-amino-N-((5-fluoro-2-pyridinyl)methyl)-N,1,7-trimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-((6-cyclopropyl-3-pyridazinyl)methyl)-7-fluoro-N,3-dimethyl-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-cyclopropyl-3-pyridazinyl)methyl)-7-fluoro-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-((6-cyclopropyl-3-pyridazinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N,3,7-trimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
4-amino-N,1,7-trimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-7-fluoro-3-methyl-N-(2-propanyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-chloro-2-pyridinyl)methyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-((5-(difluoromethyl)-2-pyridinyl)methyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-((5-(difluoromethyl)-2-pyridinyl)methyl)-7-fluoro-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-(3-fluoro-4-(trifluoromethyl)benzyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-((3-fluoro-5-(trifluoromethyl)-2-pyridinyl)methyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((3-fluoro-5-(trifluoromethyl)-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N,1-dimethyl-N-((6-(1-(trifluoromethyl)-1H-pyrazol-4-yl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N,1-dimethyl-N-((6-(4-(trifluoromethyl)phenyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N,1-dimethyl-N-((1R)-1-(4'-(trifluoromethyl)[biphenyl]-4-yl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N,1-dimethyl-N-((1R)-1-(6-(4-(trifluoromethyl)phenyl)-3-pyridazinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;

4-amino-N,1-dimethyl-N-((1R)-1-(4'-(pentafluoro-lambda~6~-sulfanyl)[biphenyl]-4-yl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-2,3-dihydrofuro[3,2-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(2-(5-chloro-2-pyridinyl)-2,2-difluoroethyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-2,3-dihydrofuro[3,2-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-ethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide;
4-amino-7-fluoro-1,3-dimethyl-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-N-ethyl-1-methyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-N-ethyl-1-methyl-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-N-ethyl-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N,1-dimethyl-N-(4-(trifluoromethyl)benzyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N,1-dimethyl-N-(4-(trifluoromethyl)benzyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((5-cyclopropyl-2-pyridinyl)methyl)-N-ethyl-7-fluoro-1-methyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-ethyl-1-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-ethyl-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)[1,2]oxazolo[4,5-c]quinoline-8-carboxamide;
4-amino-N-ethyl-1-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-ethyl-1-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide;

4-amino-N-ethyl-1-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-ethyl-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N,1-dimethyl-N-(4-(trifluoromethyl)benzyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-ethyl-1,3-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-ethyl-7-fluoro-1-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-ethyl-7-fluoro-1-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
(3R)-4-amino-N-ethyl-7-fluoro-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-ethyl-7-fluoro-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N,1-dimethyl-N-(4-(trifluoromethyl)benzyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
(3R)-4-amino-N-ethyl-7-fluoro-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-ethyl-7-fluoro-1,3-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N,1-dimethyl-N-(4-(pentafluoroethyl)benzyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N,1-dimethyl-N-(4-(pentafluoroethyl)benzyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide;
4-amino-7-fluoro-N,1-dimethyl-N-(4-(pentafluoroethyl)benzyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-ethyl-1-methyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-ethyl-1-methyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-ethyl-7-fluoro-1-methyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;

4-amino-N,1-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N,1-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-cyclopropyl-1-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-7-fluoro-1-(2,2,2-trifluoroethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N,1-dimethyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-methyl-7-(trifluoromethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N,1-dimethyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N,1-dimethyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide;
4-amino-7-fluoro-N,1-dimethyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-(2-hydroxy-4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((2R)-1-fluoro-2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((2S)-1-fluoro-2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-(hydroxymethyl)-N-(2-methylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-(hydroxymethyl)-N-(2-methylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1R)-2-cyano-1-cyclopropylethyl)-N-((5-cyano-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1S)-2-cyano-1-cyclopropylethyl)-N-((5-cyano-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-6-methyl-2-pyridinyl)methyl)-N-((3R,4R)-4-methoxytetrahydro-2H-pyran-3-yl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-N-((5-cyano-6-methyl-2-pyridinyl)methyl)-N-((3S,4S)-4-methoxytetrahydro-2H-pyran-3-yl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((3S,4R)-3-methoxytetrahydro-2H-pyran-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((3R,4S)-3-methoxytetrahydro-2H-pyran-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((3R,4R)-4-methoxytetrahydro-2H-pyran-3-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((3S,4S)-4-methoxytetrahydro-2H-pyran-3-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-6-methyl-2-pyridinyl)methyl)-N-((3R,4R)-4-methoxytetrahydro-2H-pyran-3-yl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-cyclopropyl-3-methyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3S)-4-amino-N-cyclopropyl-3-methyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((1S)-1-(5-fluoro-2-pyridinyl)ethyl)-N,1,7-trimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-((1R)-1-(5-fluoro-2-pyridinyl)ethyl)-N,1,7-trimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-((1R)-1-(5-fluoro-2-pyridinyl)ethyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-((1S)-1-(5-fluoro-2-pyridinyl)ethyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((1R)-1-(3-fluoro-5-(trifluoromethyl)-2-pyridinyl)ethyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-ethyl-3-(fluoromethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((5-bromo-2-pyridinyl)methyl)-N,3-dimethyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N,1-dimethyl-N-((1R)-1-(4-(trifluoromethyl)phenyl)ethyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide;
4-amino-N,1-dimethyl-N-((1S)-1-(4-(trifluoromethyl)phenyl)ethyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide;

4-amino-N,1-dimethyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N,1-dimethyl-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N,1-dimethyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N,1-dimethyl-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-((1R)-1-(5-fluoro-2-pyridinyl)ethyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N,1-dimethyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
6-amino-N-(2-methylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-8,9-dihydro-7H-cyclopenta[c][1,8]naphthyridine-2-carboxamide;
4-amino-N-(cyclopropylmethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide;
4-amino-N-((2R)-1-methoxy-2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide;
4-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-2,3-dihydro-1H-cyclopenta[c]quinoline-8-carboxamide;
4-amino-N-(2-methylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-2,3-dihydro-1H-cyclopenta[c]quinoline-8-carboxamide;
4-amino-N-(2-methylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide;
4-amino-N-(2-methylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-2,3-dihydro-1H-cyclopenta[c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((1S)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-3-methyl-N-(2-methylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)[1,2]oxazolo[4,5-c]quinoline-8-carboxamide;
4-amino-3-methyl-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
4-amino-3-methyl-N-((1S)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
4-amino-3-methyl-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)[1,2]oxazolo[4,5-c]quinoline-8-carboxamide;
4-amino-3-methyl-N-((1S)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)[1,2]oxazolo[4,5-c]quinoline-8-carboxamide;
4-amino-N-(2-methylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((5-chloro-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-2,3-dihydro-1H-cyclopenta[c]quinoline-8-carboxamide;
4-amino-N-((5-(difluoromethyl)-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-2,3-dihydro-1H-cyclopenta[c]quinoline-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((1R)-1-(3-fluoro-2-pyridinyl)ethyl)-2,3-dihydro-1H-cyclopenta[c]quinoline-8-carboxamide;
6-amino-N-((5-(difluoromethyl)-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-8,9-dihydro-7H-cyclopenta[c][1,8]naphthyridine-2-carboxamide;
6-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-8,9-dihydro-7H-cyclopenta[c][1,8]naphthyridine-2-carboxamide;
6-amino-N-((5-chloro-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-8,9-dihydro-7H-cyclopenta[c][1,8]naphthyridine-2-carboxamide;
6-amino-N-((1R)-1-(3-fluoro-2-pyridinyl)ethyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-8,9-dihydro-7H-cyclopenta[c][1,8]naphthyridine-2-carboxamide;
6-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-2-phenanthridinecarboxamide;
6-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-2-phenanthridinecarboxamide;

5-amino-N-(2-pyrimidinylmethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)benzo[c][2,6]naphthyridine-9-carboxamide;
5-amino-N-(2-methylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)benzo[c][2,6]naphthyridine-9-carboxamide;
5-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)benzo[c][2,6]naphthyridine-9-carboxamide;
4-amino-N-((2R)-1-methoxy-2-propanyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)[1,2]oxazolo[4,5-c]quinoline-8-carboxamide;
4-amino-N-((2S)-1-methoxy-2-propanyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)[1,2]oxazolo[4,5-c]quinoline-8-carboxamide;
4-amino-N-((3-fluoro-2-pyridinyl)methyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)thieno[2,3-c]quinoline-8-carboxamide;
4-amino-N-(2-pyrimidinylmethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)thieno[2,3-c]quinoline-8-carboxamide;
4-amino-N-(2-methylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)thieno[2,3-c]quinoline-8-carboxamide;
5-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)pyrimido[4,5-c]quinoline-9-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((1R)-1-cyclopropyl-2-methoxyethyl)thieno[2,3-c]quinoline-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((1S)-1-cyclopropyl-2-methoxyethyl)thieno[2,3-c]quinoline-8-carboxamide;
4-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1S)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1S)-1-cyclopropyl-2-methoxyethyl)-N-((6-(4-morpholinyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-ethoxy-3-pyridazinyl)methyl)-N-(2-methylpropyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)thieno[2,3-c]quinoline-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-(1-methoxy-2-methyl-2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-(1-methoxy-2-methyl-2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((6-methoxy-3-pyridazinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-2,3-dihydro-1H-cyclopenta[c]quinoline-8-carboxamide;
4-amino-N-((6-methoxy-3-pyridazinyl)methyl)-N-((1S)-1-(2-pyrimidinyl)ethyl)-2,3-dihydro-1H-cyclopenta[c]quinoline-8-carboxamide;
4-amino-N-((1S)-1-(2-pyrimidinyl)ethyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-2,3-dihydro-1H-cyclopenta[c]quinoline-8-carboxamide;
4-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-2,3-dihydro-1H-cyclopenta[c]quinoline-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((1S)-1-cyclopropyl-2-methoxyethyl)thieno[2,3-c]quinoline-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((1S)-1-cyclopropyl-2-methoxyethyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide;
4-amino-N-(cyclopropylmethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
6-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-7,8,9,10-tetrahydro-2-phenanthridinecarboxamide;
4-amino-7-chloro-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-cyclopropyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-bromo-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(3,3-difluorocyclobutyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-N-((5-(difluoromethyl)-2-pyridinyl)methyl)-N-((1R)-1-(1-methyl-1H-1,2,4-triazol-3-yl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(cyclopropylmethyl)-N-((5-(trifluoromethoxy)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(2-methylpropyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-(2-methylpropyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((1S)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-(difluoromethyl)-2-pyridinyl)methyl)-N-((1R)-1-(1-methyl-1H-1,2,4-triazol-3-yl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(3,3-difluorocyclobutyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-cyclobutyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(2-methylpropyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-(cyclopropylmethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((6-ethoxy-3-pyridazinyl)methyl)-N-(2-methylpropyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-(cyclopropylmethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((6-chloro-3-pyridazinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-bromo-6-methyl-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(2-propanyl)-N-((5-(trifluoromethoxy)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-N-((6-chloro-5-cyano-2-pyridinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-((2R)-1-methoxy-2-propanyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-(cyclopropylmethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((6-chloro-5-methoxy-2-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((5-chloro-6-methoxy-2-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(3,4-dihydro-2H-pyrano[2,3-c]pyridin-6-ylmethyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((2R)-1-fluoro-2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((2S)-1-fluoro-2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(cyclopropylmethyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(bicyclo[1.1.1]pentan-1-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(1-cyclopropyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((5-(difluoromethyl)-2-pyridinyl)methyl)-N-(1-methyl-1H-pyrazol-4-yl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-methyl-N-(4-(trifluoromethyl)benzyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-methyl-N-((6-(trifluoromethyl)-3-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((5-chloro-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;

4-amino-N-ethyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-ethyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-methyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-methyl-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-chloro-2-pyridinyl)methyl)-N-ethyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(1-methylcyclopropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-methyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide;
4-amino-N-methyl-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide;
4-amino-N-((5-chloro-2-pyridinyl)methyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-chloro-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-ethyl-N-((6-(trifluoromethyl)-3-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-ethyl-N-((6-(trifluoromethyl)-3-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-ethyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide;
4-amino-N-ethyl-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide;
4-amino-N-ethyl-N-(4-(trifluoromethyl)benzyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-ethyl-N-(4-(trifluoromethyl)benzyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-N-methyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-methyl-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((6-bromo-3-pyridazinyl)methyl)-N-ethyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(1-methyl-1H-pyrazol-4-yl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(2,2,2-trifluoroethyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(3-oxetanyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N,3-dimethyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
4-amino-N,3-dimethyl-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-chloro-2-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((5-chloro-2-pyridinyl)methyl)-N-(2-propanyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-ethyl-7-fluoro-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-ethyl-7-fluoro-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-ethyl-3-methyl-N-((1-methyl-1H-1,2,4-triazol-3-yl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-cyclobutyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-cyclobutyl-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-N-((6-(difluoromethoxy)-3-pyridazinyl)methyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-(difluoromethoxy)-3-pyridazinyl)methyl)-N-ethyl-7-fluoro-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((1R)-1-(5-fluoro-2-pyrimidinyl)ethyl)-N-(2-(trifluoromethoxy)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((1S)-1-(5-fluoro-2-pyrimidinyl)ethyl)-N-(2-(trifluoromethoxy)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((6-(difluoromethoxy)-3-pyridazinyl)methyl)-N-ethyl-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1R)-1-(6-chloro-3-pyridinyl)ethyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1S)-1-(6-chloro-3-pyridinyl)ethyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((2R)-1-methoxy-2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-7-fluoro-N-(1-(trifluoromethyl)-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(cyclopropylmethyl)-7-fluoro-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(cyclopropylmethyl)-7-fluoro-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
4-amino-N-(1-(trifluoromethyl)-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(2-propanyl)-N-(4-(trifluoromethyl)benzyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-cyclopropyl-N-(4-(trifluoromethyl)benzyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-cyclopropyl-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-((1R)-1-(6-chloro-3-pyridinyl)ethyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-7-chloro-N-((1S)-1-(6-chloro-3-pyridinyl)ethyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-ethyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1R)-1-(6-chloro-3-pyridinyl)ethyl)-N-ethyl-7-fluoro-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1S)-1-(6-chloro-3-pyridinyl)ethyl)-N-ethyl-7-fluoro-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-1-methyl-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-(cyclopropylmethyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-ethyl-N-((1R)-1-(2-fluoro-4-(trifluoromethyl)phenyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-ethyl-N-((1R)-1-(4-(trifluoromethyl)phenyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-cyclobutyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-cyclobutyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-cyclopropyl-3-methyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-ethoxy-3-pyridazinyl)methyl)-N-ethyl-7-fluoro-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((S)-cyclopropyl(5-(trifluoromethyl)-2-pyridinyl)methyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((6-ethoxy-3-pyridazinyl)methyl)-N-((1R)-1-(2-pyrimidinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-7-fluoro-N-(1-methyl-1H-pyrazol-4-yl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-(1-methyl-1H-pyrazol-4-yl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(cyclopropylmethyl)-N-((6-ethoxy-3-pyridazinyl)methyl)-7-fluoro-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-N-(cyclopropylmethyl)-N-((6-ethoxy-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
5-amino-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)benzo[c][2,6]naphthyridine-9-carboxamide;
5-amino-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)pyrimido[4,5-c]quinoline-9-carboxamide;
5-amino-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)pyrido[4,3-c][1,7]naphthyridine-9-carboxamide;
4-amino-1-methyl-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-((6-ethoxy-3-pyridazinyl)methyl)-3-methyl-N-((1R)-1-(2-pyrimidinyl)ethyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
4-amino-N-ethyl-N-(2-(4-(trifluoromethyl)phenyl)-2-propanyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
5-amino-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)pyrimido[4,5-c][1,7]naphthyridine-9-carboxamide;
4-amino-N-ethyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)propyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-ethyl-7-fluoro-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-ethyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((R)-cyclopropyl(5-(trifluoromethyl)-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-((S)-cyclopropyl(5-(trifluoromethyl)-2-pyridinyl)methyl)-N-methyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(cyclopropylmethyl)-N-((6-ethoxy-3-pyridazinyl)methyl)-7-fluoro-3-methyl-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-(cyclopropylmethyl)-N-((6-ethoxy-3-pyridazinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((R)-cyclopropyl(6-(trifluoromethyl)-3-pyridazinyl)methyl)-N-ethyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-3-methyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-7-fluoro-N,1-dimethyl-N-((5-methyl-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((5-fluoro-2-pyridinyl)methyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-((2,6-difluoro-3-pyridinyl)methyl)-7-fluoro-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-((1R)-1-(5-fluoro-2-pyridinyl)ethyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-((1S)-1-(5-fluoro-2-pyridinyl)ethyl)-N-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1R)-1-(5-(difluoromethyl)-2-pyridinyl)ethyl)-N-ethyl-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-methyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyrazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1R)-1-(5-(difluoromethyl)-2-pyridinyl)ethyl)-N-ethyl-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N,1-dimethyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyrazinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
(3R)-4-amino-N-ethyl-3-methyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-ethyl-3-methyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N,3-dimethyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N,1-dimethyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyrazinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-ethyl-7-fluoro-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((2-fluoro-6-(trifluoromethyl)-3-pyridinyl)methyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-((R)-cyclopropyl(6-(trifluoromethyl)-3-pyridazinyl)methyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-ethyl-7-fluoro-3-methyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3S)-4-amino-N-ethyl-7-fluoro-3-methyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N,3-dimethyl-N-((1R)-1-(4-(pentafluoroethyl)phenyl)ethyl)-3H-pyrazolo[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-7-fluoro-N,1-dimethyl-N-((1S)-1-(4-(pentafluoroethyl)phenyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N,1-dimethyl-N-((1R)-1-(4-(pentafluoroethyl)phenyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N,1-dimethyl-N-((5-(1-(trifluoromethyl)-1H-pyrazol-4-yl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-1-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-chloro-N,1-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-chloro-N,1-dimethyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-ethyl-1-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-ethyl-1-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-cyclopropyl-1-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-cyclopropyl-1-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-1-methyl-N-(2,2,2-trifluoroethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-cyclobutyl-1-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-cyclobutyl-1-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-1-methyl-N-(2,2,2-trifluoroethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-cyclobutyl-7-fluoro-1-methyl-N-(1,3-oxazol-4-ylmethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;

4-amino-7-fluoro-N,1-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-7-fluoro-1-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-7-fluoro-1-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-1-methyl-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((2-methoxy-6-(trifluoromethyl)-3-pyridinyl)methyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-cyclobutyl-7-fluoro-1-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-cyclopropyl-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-7-fluoro-N-((3-fluoro-5-(trifluoromethyl)-2-pyridinyl)methyl)-1-methyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N,1-dimethyl-7-(trifluoromethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N,1-dimethyl-7-(trifluoromethyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-1-methyl-7-(trifluoromethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-1-methyl-7-(trifluoromethyl)-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-((1R)-1-cyclopropylethyl)-7-fluoro-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1S)-1-cyclopropylethyl)-7-fluoro-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(cyclopropylmethyl)-7-fluoro-N-((6-(2,2,2-trifluoroethoxy)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(cyclopropylmethyl)-7-fluoro-3-methyl-N-((6-(2,2,2-trifluoroethoxy)-3-pyridazinyl)methyl)-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-(cyclopropylmethyl)-7-fluoro-3-methyl-N-((6-(2,2,2-trifluoroethoxy)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-N-ethyl-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-ethyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-ethyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-ethyl-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(1-methyl-1H-pyrazol-4-yl)-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(1-methyl-1H-pyrazol-4-yl)-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3S)-4-amino-3-methyl-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-3-methyl-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3S)-4-amino-N-cyclobutyl-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N-cyclobutyl-3-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(2-propanyl)-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(2-propanyl)-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((1S)-1-(5-fluoro-2-pyrimidinyl)ethyl)-N-(2-(trifluoromethoxy)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((1R)-1-(5-fluoro-2-pyrimidinyl)ethyl)-N-(2-(trifluoromethoxy)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1R)-1-(4-cyanophenyl)ethyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1S)-1-(4-cyanophenyl)ethyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1S)-1-(5-cyano-2-pyridinyl)ethyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

4-amino-N-((1R)-1-(5-cyano-2-pyridinyl)ethyl)-N-ethyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-(2-propanyl)-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-(2-propanyl)-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-(2-propanyl)-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-(2-propanyl)-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1S)-1-(5-cyano-2-pyridinyl)ethyl)-N-ethyl-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1R)-1-(5-cyano-2-pyridinyl)ethyl)-N-ethyl-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-(2-propanyl)-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-(2-propanyl)-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(2-propanyl)-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(2-propanyl)-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-methyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)propyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-methyl-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)propyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-N,3-dimethyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N,3-dimethyl-N-((1S)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1R)-1-(3,5-difluoro-2-pyridinyl)ethyl)-7-fluoro-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-methyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;

4-amino-N,1-dimethyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
(3R)-4-amino-N,3-dimethyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-methyl-N-((1R)-1-(4-(trifluoromethyl)phenyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-methyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-7-fluoro-N,3-dimethyl-N-((1S)-1-(4-(trifluoromethyl)phenyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-7-fluoro-N,3-dimethyl-N-((1R)-1-(4-(trifluoromethyl)phenyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-((1R)-1-(3-fluoro-5-(trifluoromethyl)-2-pyridinyl)ethyl)-N,3-dimethyl-3H-pyrazolo[3,4-c][1,7]naphthyridine-8-carboxamide;
(3R)-4-amino-7-fluoro-N,3-dimethyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((1R)-1-(3-fluoro-5-(trifluoromethyl)-2-pyridinyl)ethyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((1S)-1-(3-fluoro-5-(trifluoromethyl)-2-pyridinyl)ethyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((1R)-1-(3-fluoro-5-(trifluoromethyl)-2-pyridinyl)ethyl)-N,3-dimethyl-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((1R)-1-(3-methoxy-5-(trifluoromethyl)-2-pyridinyl)ethyl)-N,3-dimethyl-3H-pyrazolo[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((1R)-1-(3-methoxy-5-(trifluoromethyl)-2-pyridinyl)ethyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N,3-dimethyl-N-((1R)-1-(4-(pentafluoro-lambda~6~-sulfanyl)phenyl)ethyl)-3H-pyrazolo[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-7-fluoro-N,1-dimethyl-N-((1S)-1-(4-(pentafluoro-lambda~6~-sulfanyl)phenyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N,1-dimethyl-N-((1R)-1-(4-(pentafluoro-lambda~6~-sulfanyl)phenyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-1-methyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-N-((1R)-1-(5-pyrimidinyl)propyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide;

4-amino-1-methyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-N-((1S)-1-(5-pyrimidinyl)propyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide;
4-amino-7-fluoro-N-((1R)-1-(5-fluoro-2-pyridinyl)ethyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((1S)-1-(5-fluoro-2-pyridinyl)ethyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-ethyl-7-fluoro-N-((1R)-1-(5-fluoro-2-pyridinyl)ethyl)-1-methyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-ethyl-7-fluoro-N-((1S)-1-(5-fluoro-2-pyridinyl)ethyl)-1-methyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-7-fluoro-1-methyl-N-((1S)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-7-fluoro-1-methyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N,1-dimethyl-7-(trifluoromethyl)-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-cyclopropyl-1-methyl-N-((1S)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-cyclopropyl-1-methyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-(1-methyl-1H-pyrazol-4-yl)-N-(4-(trifluoromethyl)benzyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(3-fluorophenyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,7]naphthyridine-8-carboxamide;
4-amino-N-(1-methyl-1H-pyrazol-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c][1,8]naphthyridine-8-carboxamide;
5-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,4-dihydro-2H-pyrano[3,4-c]quinoline-9-carboxamide;
4-amino-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-2,3-dihydrofuro[3,2-c]quinoline-8-carboxamide;

4-amino-3,3-dimethyl-N-(2-methylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((3-fluoro-2-pyridinyl)methyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((3-fluoro-2-pyridinyl)methyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((1R)-1-(tetrahydro-2H-pyran-4-yl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((1S)-1-(tetrahydro-2H-pyran-4-yl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((1R)-1-(tetrahydro-2H-pyran-4-yl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((1S)-1-(tetrahydro-2H-pyran-4-yl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-N-((1R)-1-(tetrahydro-2H-pyran-4-yl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-N-((1S)-1-(tetrahydro-2H-pyran-4-yl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-N-((1R)-1-(tetrahydro-2H-pyran-4-yl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-N-((1S)-1-(tetrahydro-2H-pyran-4-yl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((trans-4-hydroxycyclohexyl)methyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((trans-4-hydroxycyclohexyl)methyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((trans-4-hydroxycyclohexyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-((trans-4-hydroxycyclohexyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-(tetrahydro-2H-pyran-4-ylmethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-(tetrahydro-2H-pyran-4-ylmethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3R)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-N-(tetrahydro-2H-pyran-4-ylmethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-N-(tetrahydro-2H-pyran-4-ylmethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1R,2R)-2-cyanocyclopentyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1R,2S)-2-cyanocyclopentyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1S,2R)-2-cyanocyclopentyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1S,2S)-2-cyanocyclopentyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1R,2R)-2-cyanocyclopentyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1R,2S)-2-cyanocyclopentyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1S,2R)-2-cyanocyclopentyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1S,2S)-2-cyanocyclopentyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1R,2R)-2-cyanocyclopentyl)-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1R,2S)-2-cyanocyclopentyl)-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1S,2R)-2-cyanocyclopentyl)-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1S,2S)-2-cyanocyclopentyl)-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1R,2R)-2-cyanocyclopentyl)-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1R,2S)-2-cyanocyclopentyl)-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1S,2R)-2-cyanocyclopentyl)-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3S)-4-amino-N-((1S,2S)-2-cyanocyclopentyl)-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((3R)-tetrahydro-3-furanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((3S)-tetrahydro-3-furanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((3R)-tetrahydro-3-furanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((3S)-tetrahydro-3-furanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((1R,5S,6r)-3-oxabicyclo[3.1.0]hexan-6-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((1R,5S,6r)-3-oxabicyclo[3.1.0]hexan-6-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((3R,4R)-3-methyltetrahydro-2H-pyran-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((3R,4S)-3-methyltetrahydro-2H-pyran-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((3S,4R)-3-methyltetrahydro-2H-pyran-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((3S,4S)-3-methyltetrahydro-2H-pyran-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((3R,4R)-3-methyltetrahydro-2H-pyran-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((3R,4S)-3-methyltetrahydro-2H-pyran-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((3S,4R)-3-methyltetrahydro-2H-pyran-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((3S,4S)-3-methyltetrahydro-2H-pyran-4-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((3S,4R)-3-methoxytetrahydro-2H-pyran-4-yl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((3S,4R)-3-methoxytetrahydro-2H-pyran-4-yl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3R)-4-amino-N-((3R,4S)-3-methoxytetrahydro-2H-pyran-4-yl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((3R,4S)-3-methoxytetrahydro-2H-pyran-4-yl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1R,2R)-[1,1'-bi(cyclopropyl)]-2-yl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1R,2S)-[1,1'-bi(cyclopropyl)]-2-yl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1S,2R)-[1,1'-bi(cyclopropyl)]-2-yl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1S,2S)-[1,1'-bi(cyclopropyl)]-2-yl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1R,2R)-[1,1'-bi(cyclopropyl)]-2-yl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1R,2S)-[1,1'-bi(cyclopropyl)]-2-yl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1S,2R)-[1,1'-bi(cyclopropyl)]-2-yl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1S,2S)-[1,1'-bi(cyclopropyl)]-2-yl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((1R)-spiro[2.5]octan-1-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((1S)-spiro[2.5]octan-1-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((1R)-spiro[2.5]octan-1-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((1S)-spiro[2.5]octan-1-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1R,2R)-2-aminocyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1R,2S)-2-aminocyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1S,2R)-2-aminocyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3R)-4-amino-N-((1S,2S)-2-aminocyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1R,2R)-2-aminocyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1R,2S)-2-aminocyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1S,2R)-2-aminocyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1S,2S)-2-aminocyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1R,2R)-2-ethoxycyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1R,2S)-2-ethoxycyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1S,2R)-2-ethoxycyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1S,2S)-2-ethoxycyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1R,2R)-2-ethoxycyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1R,2S)-2-ethoxycyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1S,2R)-2-ethoxycyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1S,2S)-2-ethoxycyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1R)-2,2-dimethylcyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1S)-2,2-dimethylcyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1R)-2,2-dimethylcyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1S)-2,2-dimethylcyclopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3R)-4-amino-3-methyl-N-((1R)-spiro[2.4]heptan-1-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((1S)-spiro[2.4]heptan-1-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((1R)-spiro[2.4]heptan-1-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((1S)-spiro[2.4]heptan-1-yl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((1R,2R)-2-(trifluoromethyl)cyclopropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((1S,2S)-2-(trifluoromethyl)cyclopropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((1R,2R)-2-(trifluoromethyl)cyclopropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((1S,2S)-2-(trifluoromethyl)cyclopropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((1R)-1-(2-pyrimidinyl)ethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-(5,6-dihydro-2H-pyran-3-ylmethyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((5-cyano-2-pyridinyl)methyl)-N-(5,6-dihydro-2H-pyran-3-ylmethyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1-cyanocyclopropyl)methyl)-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1-cyanocyclopropyl)methyl)-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((2-amino-1,3-thiazol-5-yl)methyl)-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((2-amino-1,3-thiazol-5-yl)methyl)-N-((5-cyano-2-pyridinyl)methyl)-3-methyl-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-(5,6-dihydro-2H-pyran-3-ylmethyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3S)-4-amino-N-(5,6-dihydro-2H-pyran-3-ylmethyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-(1H-pyrrolo[2,3-b]pyridin-4-ylmethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-(1H-pyrrolo[2,3-b]pyridin-4-ylmethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1-cyanocyclopropyl)methyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1-cyanocyclopropyl)methyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((2-amino-1,3-thiazol-5-yl)methyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((2-amino-1,3-thiazol-5-yl)methyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-(2-methylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-(2-methylpropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((2R,3R)-3-hydroxy-2-butanyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((2R,3S)-3-hydroxy-2-butanyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((2S,3R)-3-hydroxy-2-butanyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((2S,3S)-3-hydroxy-2-butanyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((2R,3R)-3-hydroxy-2-butanyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((2R,3S)-3-hydroxy-2-butanyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((2S,3R)-3-hydroxy-2-butanyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((2S,3S)-3-hydroxy-2-butanyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3R)-4-amino-N-((1R,3R)-3-hydroxycyclohexyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1R,3S)-3-hydroxycyclohexyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1S,3R)-3-hydroxycyclohexyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((1S,3S)-3-hydroxycyclohexyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1R,3R)-3-hydroxycyclohexyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1R,3S)-3-hydroxycyclohexyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1S,3R)-3-hydroxycyclohexyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((1S,3S)-3-hydroxycyclohexyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-(2-(cis-3-hydroxycyclobutyl)ethyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-(2-(trans-3-hydroxycyclobutyl)ethyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-(2-(cis-3-hydroxycyclobutyl)ethyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-(2-(trans-3-hydroxycyclobutyl)ethyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((2R)-2-hydroxypropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((2S)-2-hydroxypropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((2R)-2-hydroxypropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((2S)-2-hydroxypropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((2R)-3-hydroxy-2-methylpropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3R)-4-amino-N-((2S)-3-hydroxy-2-methylpropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((2R)-3-hydroxy-2-methylpropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((2S)-3-hydroxy-2-methylpropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((2R)-3,3,3-trifluoro-2-hydroxypropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((2S)-3,3,3-trifluoro-2-hydroxypropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((2R)-3,3,3-trifluoro-2-hydroxypropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((2S)-3,3,3-trifluoro-2-hydroxypropyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((1-methyl-1H-1,2,4-triazol-3-yl)methyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((1-methyl-1H-1,2,4-triazol-3-yl)methyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((3R)-tetrahydro-3-furanylmethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-((3S)-tetrahydro-3-furanylmethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((3R)-tetrahydro-3-furanylmethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-((3S)-tetrahydro-3-furanylmethyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((2R)-2-cyanopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-((2S)-2-cyanopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((2R)-2-cyanopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-((2S)-2-cyanopropyl)-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;

(3R)-4-amino-N,3-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N,3-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-N-ethyl-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-N-ethyl-3-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3R)-4-amino-3-methyl-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
(3S)-4-amino-3-methyl-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N,3,3-trimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-ethyl-3,3-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-3,3-dimethyl-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-3,3-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide; and
4-amino-N-((1R)-1-(3-cyano-5-(trifluoromethyl)-2-pyridinyl)ethyl)-7-fluoro-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide.

21. A compound, the tautomer thereof, the stereoisomer thereof, or the pharmaceutically acceptable salt of any of the foregoing, wherein the compound is selected from:
(3R)-4-amino-N-ethyl-7-fluoro-3-methyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N,1-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-((1R)-1-(3-fluoro-5-(trifluoromethyl)-2-pyridinyl)ethyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N,1-dimethyl-N-(4-(pentafluoro-lambda~6~-sulfanyl)benzyl)-1H-pyrazolo[4,3-c][1,7]naphthyridine-8-carboxamide;

4-amino-7-fluoro-N,1-dimethyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
(3R)-4-amino-7-fluoro-N,3-dimethyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N-methyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
5-amino-N-(2-propanyl)-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)pyrido[4,3-c][1,7]naphthyridine-9-carboxamide;
4-amino-N-ethyl-7-fluoro-1-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-chloro-N-((1R)-1-(5-fluoro-2-pyridinyl)ethyl)-N,1-dimethyl-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-cyclobutyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-1-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-ethyl-7-fluoro-1-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-7-fluoro-1-methyl-N-((6-(trifluoromethyl)-3-pyridazinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N,1-dimethyl-N-((1R)-1-(5-(trifluoromethyl)-2-pyridinyl)ethyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
(3R)-4-amino-N-ethyl-3-methyl-N-((1R)-1-(6-(trifluoromethyl)-3-pyridazinyl)ethyl)-1,3-dihydrofuro[3,4-c]quinoline-8-carboxamide;
4-amino-N-cyclopropyl-7-fluoro-1-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide;
4-amino-7-fluoro-N,1-dimethyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide and
4-amino-N-ethyl-1-methyl-N-((5-(trifluoromethyl)-2-pyridinyl)methyl)-1H-pyrazolo[4,3-c]quinoline-8-carboxamide.

22. A method of treating a cancer, the method comprising administering to a subject an effective amount of the compound of any of claims 1, 20 or 21, the tautomer thereof, the stereoisomer thereof, or the pharmaceutically acceptable salt of any of the foregoing.

23. The method of claim 22, wherein the cancer is selected from ovarian, lung, lymphoid, glioblastoma, colon, melanoma, gastric, pancreatic or bladder cancer.

23. A pharmaceutical composition, comprising the compound of amy of claims 1, 20 or 21, the tautomer thereof, the stereoisomer thereof, or the pharmaceutically acceptable salt of any of the foregoing or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable excipient.