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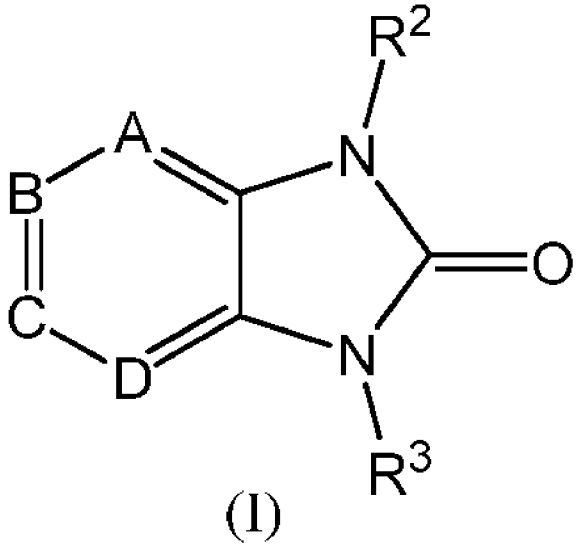
(54) **Title**: BRUTON'S TYROSINE KINASE INHIBITORS

(57) **Abstract**: Bruton's tyrosine kinase (Btk) inhibitors have the following Formula (I):



(I)

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TITLE OF THE INVENTION

BRUTON'S TYROSINE KINASE INHIBITORS

This application claims the benefit of US Provisional Application No. 62/241,184, filed on October 14, 2015, which is incorporated by reference for all purposes as if fully set forth herein.

FIELD OF THE INVENTION

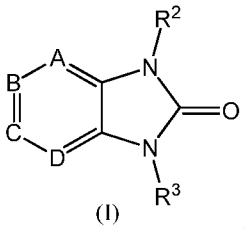
Described herein are Bruton's tyrosine kinase inhibitors, methods of making such inhibitors, and pharmaceutical compositions containing such inhibitors.

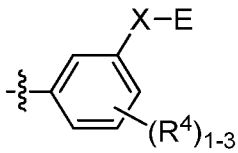
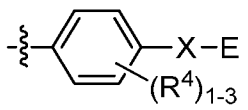
BACKGROUND OF THE INVENTION

Bruton's tyrosine kinase (Btk) plays an important role in signal transduction in B cells and is a factor that contributes to the survival, differentiation, proliferation, and activation of B cells. There is currently a need for methods of treating diseases in which B cells or mast cells participate. Btk is also known to participate in mast cell activation and in the physiological functions of platelets. Therefore, Btk inhibitors are effective for the treatment of diseases in which B cells or mast cells participate, for example, allergic diseases, autoimmune diseases, inflammatory diseases, thromboembolic diseases, and cancers.

SUMMARY OF THE INVENTION

The Btk inhibitors described herein have the following Formula (I):



(I) . In Formula (I), A is N or CR^1; B, C, and D are each N or C-H, with the proviso that only one or two of A, B, C, and D can be N. R^1 is hydrogen, amino, OH, CN, -NHOH or $CONH_2$; R^2 is  Or  .

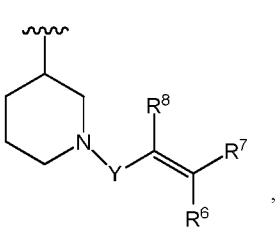
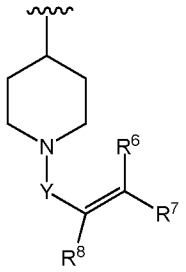
–X-E is one of the followings: (1) X is O, OCR^aR^b, S(O), $S(O)_2$, CR^aR^b, $NR^c(C=O)$, $C=ONR^c$ or a bond; and E is a hydrogen, an aryl or a heteroaryl substituted with one to three R^5 substituents; or a 3-7 membered saturated or partially unsaturated carbocyclic ring, an 8-10 membered bicyclic saturated, partially unsaturated or aryl ring, a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur,

a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, a 7-10 membered bicyclic saturated or partially unsaturated heterocyclic ring having 1-5 heteroatoms independently selected from nitrogen, oxygen , or sulfur , or an 8-10 membered bicyclic heteroaryl ring having 1-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; or (2) -X-E is hydrogen, halogen , $-OR^a$, $-O(CH_2)_{1-4}R^a$, -CN, $-NO_2$.R^4 and R^5 are each independently selected from the group consisting of hydrogen, halogen, hydroxy, cyano,OCF_3, OCF_2H, C_{1-6} alkyl, optionally substituted with one to five fluorines, C_{3-6} cycloalkyl, optionally substituted with one to five fluorines, C_{1-4} alkoxy, optionally substituted with one to five fluorines, C_{1-4} alkylthio, optionally substituted with one to five fluorines, C_{1-4} alkylsulfonyl, optionally substituted with one to five fluorines, carboxy, C_{1-4} alkyloxycarbonyl, and C_{1-4} alkylcarbonyl. R^a and R^b are each independently hydrogen, fluorine, or C_{1-3} alkyl, optionally substituted with one to five fluorines. R^c is hydrogen or C_{1-3} alkyl, optionally substituted with one to five fluorines. R^3 is a group having a double bond.

Further described is an isomer or tautomer thereof, a pharmaceutical acceptable solvate thereof, or a pharmaceutical acceptable prodrug thereof.

In one aspect, in Formula (I), E is selected from aryl, heteroaryl, carbocyclyl, heterocyclyl, any of which is optionally substituted with one to three R^5substituents.

In another aspect, in Formula (I), R^3 is selected from the group consisting of:


,

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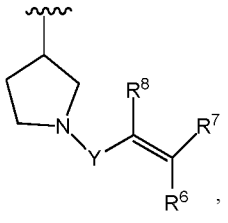
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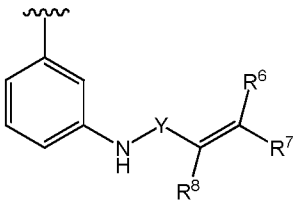
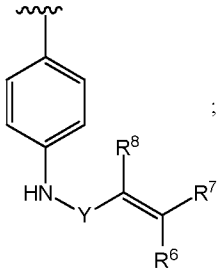
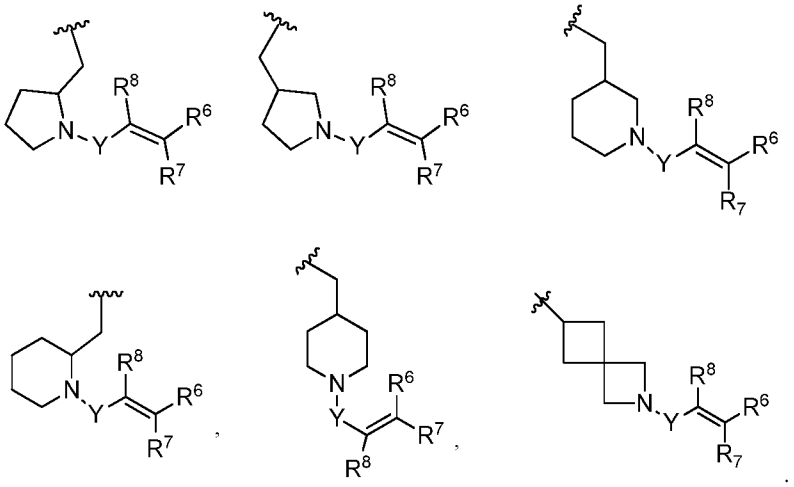

and

;

Y isC(=O); OC(=O), NHC(=O), S=O, $S(=O)_2$, or $NHS(=O)_2$; R^6, R^7, R^8 are each independently hydrogen, halogen, CN, C_{1-4} alkyl, C_{1-6} alkoxyalkyl, C_{1-8} alkylaminoalkyl, or C_{1-4} alkylphenyl; or R^7 and R^8 taken together form a bond.

In another aspect, in Formula (I), R^3 is selected from the group consisting of:



Y is C(=O); OC(=O), NHC(=O), S=O, $S(=O)_2$, or $NHS(=O)_2$; R^6, R^7, R^8 are each independently hydrogen, halogen, CN, C_{1-4} alkyl, C_{1-6} alkoxyalkyl, C_{1-8} alkylaminoalkyl, or C_{1-4} alkylphenyl; or R^7 and R^8 taken together form a bond.

In another aspect, in Formula (I), A is CR^1, and one of B, C, and D is N.

In another aspect, in Formula (I), A is CR^1, B is N, and C and D are CR^1.

In another aspect, described herein is a pharmaceutical composition including a therapeutically effective amount of the compound of Formula (I), and a pharmaceutically acceptable excipient.

In another aspect, described herein is a method for treating an autoimmune disease comprising administering to a subject in need thereof a composition containing a therapeutically effective amount of the compound of Fomula (I) and other therapeutic agents.

In another aspect, the Btk inhibitors described herein are selected from the group consisting of (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(2-oxo-3-(4-phenoxyphenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl), (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(m-tolyloxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-phenoxyphenyl)-1H-imidazo[4,5-c] pyridin-2(3H)-one, 1-(1-acryloylpyrrolidin-3-yl)-3-(3-

chloro-4-(3-(trifluoromethyl)phenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(2-oxo-3-(3-phenoxyphenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (S)-1-(1-acryloylpiperidin-3-yl)-3-(4-(2-chloro-3-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-chloro-5-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-cyclopropylphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(3-(2-thioxo-3-(4-(m-tolyloxy)phenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)pyrrolidin-1-yl)prop-2-en-1-one, (R)-1-(1-acryloylpiperidin-3-yl)-3-(3-fluoro-4-phenoxyphenyl) -1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(m-tolyloxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, 1-((1-acryloylpiperidin-4-yl)methyl)-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, 1-((1-acryloylpiperidin-4-yl)methyl)-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-(p-tolyloxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-(4-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R,E)-3-(3-chloro-4-phenoxyphenyl)-1-(1-(3-morpholinoacryloyl)pyrrolidin-3-yl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3- (3-chloro-4-(m-tolyloxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, 1-((1-acryloylpyrrolidin-2-yl)methyl)-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R,E)-3-(3-chloro-4-phenoxyphenyl)-1-(1-cinnamoylpyrrolidin-3-yl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-3-(3-chloro-4-phenoxyphenyl)-1-(1-(vinylsulfonyl)pyrrolidin-3-yl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-ethoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-isopropoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-(3-chlorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(3-(3-methyl-4-phenoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl) acrylamide, (R)-1-(1-methacryloylpyrrolidin-3-yl)-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R,E)-1-(1-cinnamoylpyrrolidin-3-yl)-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, 1-(1-acryloylpiperidin-4-yl)-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(phenylthio)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acetylpyrrolidin-3-yl)-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-(but-2-

ynoyl)pyrrolidin-3-yl)-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(4-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(4-(trifluoromethyl)phenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3,4-dichlorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(phenylthio)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-(3,5-difluorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3,4-dimethoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-(3-fluorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-(4-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-(4-(trifluoromethyl)phenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4- (3,4-dichlorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-(3-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(3-(4-(3-isopropoxyphenoxy)- 3-methylphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c] pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(3-methyl-4-(m-tolyloxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl) acrylamide, N-(3-(3-(3-fluoro-4-(3-isopropoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo [4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(3-fluoro-4-(m-tolyloxy) phenyl)-2-oxo-2,3-dihydro-1H-imidazo [4,5-c]pyridin-1-yl)phenyl)acrylamide, (N-(3-(3-(4-(3-chlorophenoxy)-3-fluorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(2,3-dimethylphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3- (3-fluoro-4-(3-isopropoxyphenoxy) phenyl) -1H-imidazo [4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-fluoro-4-(3-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-fluoro-4-(3-methoxyphenoxy) phenyl) -1H-imidazo [4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-(3-fluoro-2-methylphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-(3-cyclopropoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(3-fluoro-2-methylphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(2,3-dimethylphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(3-chloro-2-

fluorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(2,3-difluorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(2,3-difluorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(3-(4-(3-methoxyphenoxy)-3-methylphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-chloro-2-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(3-chloro-2-methoxyphenoxy)phenyl) -1H-imidazo[4,5-c]pyridin-2(3H)-one, ((R)-1-(1-acryloylpyrrolidin-3-yl)-2-oxo-3-(4-phenoxyphenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridine-4-carbonitrile, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(2-methoxy-3-methylphenoxy)phenyl)-1H-imidazo[4,5-c] pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(2-methoxy-3-methylphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3- (4-(2-methoxy-3-methylphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(3-(4-(3-chlorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(2-oxo-3-(4-(3-(trifluoromethoxy)phenoxy)phenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(3-chloro-5-methoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-chlorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(3-(3-chloro-4-phenoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(3-chlorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(3-(3-fluorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(2-oxo-3-(3-(p-tolyloxy)phenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-fluoro-4-(3-fluorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-fluoro-4-(m-tolyloxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(3-(4-(3-fluoro-2-methylphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(4-methoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(4-fluorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(4-chlorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(o-tolyloxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-fluorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(3-(4-(3-isopropoxyphenoxy)phenyl)-2-oxo-2,3-

dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(3-chloro-4-(3-methoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(3-(3-methoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(2-oxo-3-(3-(o-tolyloxy)phenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(3-(2-methoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(3-fluoro-4-(3-fluorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, 1-(1-acryloylpyrrolidin-3-yl)-3-(3-methyl-4-phenoxyphenyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one, 1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-methoxyphenoxy)-3-methylphenyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one, N-(3-(3-(3-fluoro-4-phenoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(3-fluoro-4-(3-methoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-fluoro-4-phenoxyphenyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one, N-(3-(3-(3-(3-chloro-2-fluorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-(3-chloro-2-fluorophenoxy)phenyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one, N-(3-(3-(4-(2,3-dichlorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(2,3-dichlorophenoxy)phenyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(2,3-dichlorophenoxy)phenyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-chloro-2-fluorophenoxy)-3-fluorophenyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(2-chloro-3-fluorophenoxy)phenyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(2-chloro-3-fluorophenoxy)phenyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(pyridin-2-yloxy)phenyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one, (R)-1-(1-acryloylpiperidin-3-yl)-3- (3-fluoro-4-(m-tolyloxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(3-chlorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3- (3-chloro-4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3- (3-chloro-4-(m-tolyloxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(2-oxo-3-(4-phenoxyphenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)cinnamamide, N-(3-(2-oxo-3-(4-phenoxyphenyl)-2,3-

dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)methacrylamide, N-(3-(3-(3-chloro-4-(4-(trifluoromethyl)phenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-(trifluoromethoxy)phenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(3-(4-(3-ethoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(3-isopropylphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, 4-(4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)phenoxy)-N-methylpicolinamide, N-(3-(2-oxo-1-(4-phenoxyphenyl)-1H-imidazo[4,5-b]pyridin-3(2H)-yl)phenyl)acrylamide, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(3-fluorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(3-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(2-oxo-3-(4-phenoxyphenyl)-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)phenyl)acrylamide, (R)-3-(1-acryloylpyrrolidin-3-yl)-1-(4-phenoxyphenyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one, N-(3-(2-oxo-1-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-3(2H)-yl)phenyl)acrylamide, (R)-3-(1-acryloylpiperidin-3-yl)-1-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(2-oxo-3-(4-(4-(trifluoromethyl)phenoxy)phenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(4-methoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(2,3-difluorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(3,4-difluorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(3,5-difluorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(3-chloro-2-fluorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(3-chloro-5-fluorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(3,5-dichlorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(3,4-dimethoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(3-fluoro-4-phenoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-chloro-2-fluorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(3-chloro-2-methylphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(2-chloro-3-methoxyphenoxy)phenyl)-1H-

imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(3-(4-(3-fluoro-2-methoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-fluoro-2-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(2-fluoro-3-methylphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-chloro-2-methylphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(3-fluoro-2-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(2-fluoro-3-methylphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(3-methoxy-2-methylphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-methoxy-2-methylphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(3-(3-chloro-4-(m-tolyloxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(3-chloro-4-(3-isopropoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(3-fluorophenoxy)-3-methylphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(2,3-dimethylphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(3-chloro-4-(2,3-dimethylphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-chlorophenoxy)-3-fluorophenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(3-(4-(3-chloro-2-methylphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (R)-1-(1-acryloylpyrrolidin-3-yl)-7-chloro-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(2-oxo-3-(3-(m-tolyloxy)phenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-isopropylphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(3-(4-(3-chlorophenoxy)-3-methylphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-methacryloylpyrrolidin-3-yl)-3-(3-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(2-oxo-3-(4-(phenylthio)phenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(3-methoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(3,4-dichlorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(4-chloro-3-fluorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-

yl)phenyl)acrylamide, N-(3-(3-(4-(3-fluoro-4-methoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(4-cyanophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(4-methoxy-3-methylphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, 1-(1-acryloylpyrrolidin-3-yl)-3-(4- (pyridin-4-yloxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, 1-(1-acryloylpyrrolidin-3-yl)-3-(4- (pyridazin-3-yloxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(2-oxo-3-(4-((2,4,5-trifluorobenzyl)oxy) phenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(2-oxo-3-(4-(pyridin-2-ylmethoxy)phenyl)-2,3-dihydro-1H-imidazo[4,5-c] pyridin-1-yl)phenyl)acrylamide, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(benzyloxy)-3-chlorophenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-((3,4-dichlorobenzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-((2,4-difluorobenzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-((3-(trifluoromethyl)benzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-((3,4-difluorobenzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-((2,4-difluorobenzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-((2-(trifluoromethyl)benzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-(pyridin-2-ylmethoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-((4-(trifluoromethyl)benzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-((4-(trifluoromethyl)benzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-((3,5-difluorobenzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-((2,4-dichlorobenzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-((2,5-difluorobenzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-((2-(trifluoromethyl)benzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-((3-(trifluoromethyl)benzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-((4-(trifluoromethyl)benzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(pyridin-2-ylmethoxy)phenyl)-

1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-((3,4-difluorobenzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-((3,4-dichlorobenzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-((2-fluorobenzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(3-(3-fluoro-4-((2-fluorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-((3,4-dichlorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-((3,5-difluorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-((2,5-difluorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-((4-chlorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-((3-fluorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(3-chloro-4-((4-(trifluoromethyl)benzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(benzyloxy)-3-chlorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-((2-methylbenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-((2,6-difluorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-((2,6-difluorobenzyl)oxy)-3-fluorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-((2-fluorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-((2,4-dichlorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-((3-chlorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-((2-chlorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(2-oxo-3-(4-((2-(trifluoromethyl)benzyl)oxy)phenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(3-(benzyloxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(benzyloxy)-3-fluorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(3-chloro-4-((2-fluorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (S)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-((2-fluorobenzyl)oxy)phenyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one, (S)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(benzyloxy)-3-fluorophenyl)-1,3-dihydro-2H-imidazo[4,5-

c]pyridin-2-one, N-(3-(3-(4-((3-chloro-2-fluorobenzyl)oxy)-3-fluorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (N-(3-(3-(4-(benzyloxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(2-oxo-3-(4-((3-(trifluoromethyl)benzyl)oxy)phenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-((3,4-difluorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(2-oxo-3-(4-((4-(trifluoromethyl)benzyl)oxy)phenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(3-chloro-4-((3-(trifluoromethyl)benzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-((4-chloro-2-fluorobenzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(3-(4-((4-chloro-2-fluorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, ((R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(benzyloxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(3-(4-((4-fluorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-((2,4-difluorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, 4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)-N-(4-fluorobenzyl)benzamide, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(morpholine-4-carbonyl)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, 4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)-N-(3-(trifluoromethyl)phenyl)benzamide, 4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)-N-(3-methoxybenzyl)benzamide, N-(3-(3-(4-(morpholine-4-carbonyl)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, 4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)-N-phenylbenzamide, 4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)-N-(m-tolyl)benzamide, (R)-4-(1-(1-acryloylpyrrolidin-3-yl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)-N-(3-methoxybenzyl)benzamide, N-(4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)phenyl)benzamide, N-(4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)phenyl)-2-methoxybenzamide, N-(4-(1-(3-acrylamidophenyl) -2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)phenyl)-3-chlorobenzamide, N-(3-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)phenyl)-4-(tert-butyl)benzamide, N-(4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)phenyl)benzamide, N-(4-(1-(3-acrylamidophenyl)-2-oxo-1,2-dihydro-3H-imidazo[4,5-c]pyridin-3-yl)phenyl)-2-(trifluoromethyl)benzamide, N-(4-(1-(3-acrylamidophenyl)-2-oxo-1,2-dihydro-3H-

imidazo[4,5-c]pyridin-3-yl)phenyl)-4-(trifluoromethyl)benzamide, N-(4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)phenyl)-4-methoxybenzamidee, N-(4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)phenyl)-3-fluorobenzamide, N-(4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)phenyl)-3-methoxybenzamide, N-(4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)phenyl)-3-methylbenzamide, N-(3-(3-(3'-methyl-[1,1'-biphenyl]-4-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-([1,1'-biphenyl]-4-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c] pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4'-methyl-[1,1'-biphenyl]-3-yl) -2-oxo-2,3-dihydro-1H-imidazo [4,5-c]pyridin-1-yl)phenyl)acrylamide, (R)1-(1-acryloylpyrrolidin-3-yl)-3-(2'-methyl-[1,1'-biphenyl]-3-yl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(2'-fluoro-4'-methoxy-[1,1'-biphenyl]-4-yl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-4-yl)-3-(2',4'-dichloro-[1,1'-biphenyl]-4-yl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(3-(4'-methyl-[1,1'-biphenyl]-4-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (R)-3-([1,1'-biphenyl]-3-yl)-1-(1-acryloylpyrrolidin-3-yl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, and N-(3-(3-(4-cyclopropylphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(2-fluoro-3-methoxyphenoxy)phenyl)-7-methoxy-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-7-ethoxy-3-(4-(2-fluoro-3-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(2-fluoro-3-methoxyphenoxy)phenyl)-7-methyl-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-((1-(but-2-ynoyl)pyrrolidin-2-yl)methyl)-3-(4-(2-fluoro-3-methoxyphenoxy)phenyl)-7-methyl-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-((1-acryloylpyrrolidin-2-yl)methyl)-3-(4-(2-fluoro-3-methoxyphenoxy)phenyl)-7-methyl-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-(but-2-ynoyl)piperidin-3-yl)-3-(4-(2-fluoro-3-methoxyphenoxy)phenyl)-7-methyl-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(2-fluoro-3-methoxyphenoxy)phenyl)-7-methyl-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-(but-2-ynoyl)pyrrolidin-3-yl)-3-(4-(2-fluoro-3-methoxyphenoxy)phenyl)-7-methyl-1H-imidazo[4,5-c]pyridin-2(3H)-one, (E)-N-(3-(6-amino-8-oxo-7-(4-phenoxyphenyl)-7H-purin-9(8H)-yl)phenyl)-4-(cyclopropyl(methyl)amino)-N-methylbut-2-enamide, (R)-1-(1-(but-2-ynoyl)piperidin-3-yl)-3-(4-(2-fluoro-3-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-7-methyl-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-

one, (S,Z)-9-(1-acryloylpyrrolidin-3-yl)-6-(hydroxyimino)-7-(4-phenoxyphenyl)-7,9-dihydro-1H-purin-8(6H)-one, 1-(1-Acryloyl-pyrrolidin-2-ylmethyl)-3-(4-phenoxy-phenyl)-1,3-dihydro-imidazo[4,5-c]pyridin-2-one, (S,Z)-1-(1-acryloylpyrrolidin-3-yl)-N'-hydroxy-2-oxo-3-(4-phenoxyphenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridine-4-carboximidamide, 4,4-Dimethyl-2-{2-[2-oxo-3-(4-phenoxy-phenyl)-2,3-dihydro-imidazo[4,5-c]pyridin-1-ylmethyl]-pyrrolidine-1-carbonyl}-pent-2-enenitrile, (R)-1-(1-acryloylpyrrolidin-3-yl)-2-oxo-3-(4-phenoxyphenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridine-7-carbonitrile. (R)-1-(1-acryloylpyrrolidin-3-yl)-4-methoxy-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-4-hydroxy-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-7-chloro-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(2-chloro-3-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(2-fluoro-3-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R,E)-1-(1-(4-(cyclopropyl(methyl)amino)but-2-enoyl)pyrrolidin-3-yl)-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R,E)-1-(1-(4-(cyclopropyl(methyl)amino)but-2-enoyl)piperidin-3-yl)-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-4-nitro-3-(4-phenoxyphenyl)-1H-benzo[d]imidazol-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-4-amino-3-(4-phenoxyphenyl)-1H-benzo[d]imidazol-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(2-fluoro-3-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, 2-oxo-2-(3-(2-oxo-3-(4-phenoxyphenyl) -2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)piperidin-1-yl)acetic acid, 3-(2-oxo-3-(4-phenoxyphenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl) cyclohexanecarboxylic acid, and 2-oxo-2-(3-(2-oxo-3-(4-phenoxyphenyl)-2,3-dihydro-1H-imidazo[4,5-c] pyridin-1-yl)piperidin-1-yl)acetamide.

DETAILED DESCRIPTION OF THE INVENTION

The methods described herein include administering to a subject in need a composition containing a therapeutically effective amount of one or more Btk inhibitor compounds described herein.

Prodrugs means any compound which releases an active parent drug according to Formula I *in vivo* when such prodrug is administered to a mammalian subject. Prodrugs of a compound of Formula I are prepared by modifying functional groups present in the compound of Formula I in such a way that the modifications may be cleaved in vivo to release the parent compound. Prodrugs may be prepared by modifying functional groups

present in the compounds in such a way that the modifications are cleaved, either in routine manipulation or *in vivo*, to the parent compounds.

Tautomers mean compounds produced by the phenomenon wherein a proton of one atom of a molecule shifts to another atom. Tautomers also refer to one of two or more structural isomers that exist in equilibrium and are readily converted from one isomeric form to another. One of ordinary skill in the art would recognize that other tautomeric ring atom arrangements are possible. All such isomeric forms of these compounds are expressly included in the present disclosure.

Isomers mean compounds having identical molecular formulae but differ in the nature or sequence of bonding of their atoms or in the arrangement of their atoms in space. Isomers that differ in the arrangement of their atoms in space are termed stereoisomers. Stereoisomers that are not mirror images of one another are termed diastereomers, and those that are non-superimposable mirror images of each other are termed enantiomers. When a compound has an asymmetric center, for example, it is bonded to four different groups, a pair of enantiomers is possible. A chiral compound can exist as either individual enantiomer or as a mixture thereof. Unless otherwise indicated, the description is intended to include individual stereoisomers as well as mixtures.

Certain compounds of the present disclosure can exist in unsolvated forms as well as solvated forms, including hydrated forms. Solvates refer to a complex formed by combination of solvent molecules with the compound of Formula I. The solvent can be an organic compound, an inorganic compound, or a mixture thereof.

Pharmaceutically acceptable salts represent those salts which are, within the scope of medical judgement, suitable for use in contact for the tissues of humans and lower animals without undue toxicity, irritation, allergic response and the like, and are commensurate with a reasonable benefit/risk ratio. They may be obtained during the final isolation and purification of the compounds of the invention, or separately by reacting the free base function with a suitable mineral acid such as hydrochloric acid, phosphoric acid, or sulfuric acid, or with an organic acid such as for example ascorbic acid, citric acid, tartaric acid, lactic acid, maleic acid, malonic acid, fumaric acid, glycolic acid, succinic acid, propionic acid, acetic acid, methanesulfonic acid, and the like. The acid function can be reacted with an organic or a mineral base, like sodium hydroxide, potassium hydroxide or lithium hydroxide.

Therapeutically effective amount means an amount of compound or a composition of the present invention effective in inhibiting Bruton's tyrosine kinase and thus producing the desired therapeutic effect.

As used herein, the term alkyl refers to a monovalent straight or branched chain, saturated aliphatic hydrocarbon radical having a number of carbon atoms in the specified range. For example, C_{1-6} alkyl refers to any of the hexyl alkyl and pentyl alkyl isomers as well as n-, iso-, sec- and t-butyl, n- and iso-propyl, ethyl and methyl. Alkyl also includes saturated aliphatic hydrocarbon radicals wherein one or more hydrogens are replaced with deuterium, for example, CD_3.

The term branched alkyl refers to an alkyl group as defined above except that straight chain alkyl groups in the specified range are excluded. As defined herein, branched alkyl includes alkyl groups in which the alkyl is attached to the rest of the compound via a secondary or tertiary carbon. For example, isopropyl is a branched alkyl group.

The term cycloalkyl refers to any monocyclic ring of an alkane having a number of carbon atoms in the specified range. For example, C_{3-6}cycloalkyl refers to cyclopropyl, cyclobutyl,cyclopentyl, and cyclohexyl.

The term halogen refers to fluorine, chlorine, bromine and iodine (alternatively referred to as fluoro, chloro, bromo, and iodo).

The term haloalkyl refers to an alkyl group as defined above in which one or more of the hydrogen atoms have been replaced with a halogen (i.e., F, Cl, Br and/or I). For example, C_{1-6} haloalkyl refers to a C_1 to C_6 linear or branched alkyl group as defined above with one or more halogen substituents. The term fluoroalkyl has an analogous meaning except that the halogen substituents are restricted to fluoro. Suitable fluoroalkyls include the series $(CH_2)_{0-4}CF_3$.

The term C(O) or CO refers to carbonyl. The terms $S(O)_2$or SO_2 refers to sulfonyl. The term S(O) or SO refers to sulfinyl.

The term aryl refers to phenyl, naphthyl, tetrahydronaphthyl, idenyl, dihydroindenyl and the like. An aryl of particular interest is phenyl.

The term heteroaryl refers to (i) a 5- or 6-membered heteroaromatic ring containing from 1 to 4 heteroatoms independently selected from N, O and S, or (ii) is a heterobicyclic ring selected from quinolinyl, isoquinolinyl, and quinoxalinyl. Suitable 5- and 6-membered heteroaromatic rings include, for example, pyridyl (also referred to as pyridinyl), pyrrolyl, pyrazinyl, pyrimidinyl, pyridazinyl, triazinyl, thienyl, furanyl, imidazolyl, pyrazolyl,

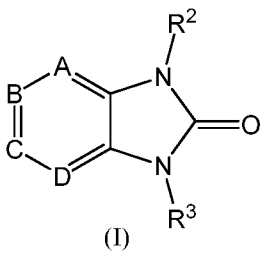
triazolyl, tetrazolyl, oxazolyl, isooxazolyl, oxadiazolyl, oxatriazolyl, thiazolyl, isothiazolyl, and thiadiazolyl. A class of heteroaryls of interest consists of (i) 5- and 6-membered heteroaromatic rings containing from 1 to 3 heteroatoms independently selected from N, O and S, and (ii) heterobicyclic rings selected from quinolinyl, isoquinolinyl, and quinoxalinyl. Heteroaryls of particular interest are pyrrolyl, imidazolyl, pyridyl, pyrazinyl, quinolinyl (or quinolyl), isoquinolinyl (or isoquinolyl), and quinoxalinyl.

Examples of 4- to 7-membered, saturated heterocyclic rings within the scope of this invention include, for example, azetidinyl, piperidinyl, morpholinyl, thiomorpholinyl, thiazolidinyl, isothiazolidinyl, oxazolidinyl, isoxazolidinyl, pyrrolidinyl, imidazolidinyl, piperazinyl, tetrahydrofuranyl, tetrahydrothienyl, pyrazolidinyl, hexahydropyrimidinyl, thiazinanyl, thiazepanyl, azepanyl, diazepanyl, tetrahydropyranyl, tetrahydrothiopyranyl, and dioxanyl. Examples of 4- to 7-membered, unsaturated heterocyclic rings within the scope of this invention include mono-unsaturated heterocyclic rings corresponding to the saturated heterocyclic rings listed in the preceding sentence in which a single bond is replaced with a double bond (e.g., a carbon-carbon single bond is replaced with a carbon-carbon double bond).

It is understood that the specific rings listed above are not a limitation on the rings which can be used in the present invention. These rings are merely representative.

Synthetic methods for preparing the compounds of the present invention are illustrated in the following Schemes, Methods, and Examples. Starting materials are commercially available or may be prepared according to procedures known in the art or as described herein. The compounds of the invention are illustrated by means of the specific examples shown below. However, these specific examples are not to be construed as forming the only genus that is considered as the invention. These examples further illustrate details for the preparation of the compounds of the present invention. Those skilled in the art will readily appreciate that known variations in the conditions and processes can be used to prepare such compounds.

Formula (I)



(I)

The Btk inhibitor compounds of Formula I can be prepared by methods well known in the art of organic chemistry. The starting material used for the synthesis of these compounds can be either synthesized or obtained from commercial sources, such as, but not limited to, China chemical companies or Sigma-Aldrich Chemical Co. (St. Louis, Mo.) at China. The compounds described herein, and other related compounds having different substituents are optionally synthesized using techniques and materials, such as described, for example, in March, ADVANCED ORGANIC CHEMISTRY 4th Ed., (Wiley 1992); Carey and Sundberg, ADVANCED ORGANIC CHEMISTRY 4th Ed., Vols. A and B (Plenum 2000, 2001); Fieser and Fieser's Reagents for Organic Synthesis, Volumes 1-17 (John Wiley and Sons, 1991); Rodd's Chemistry of Carbon Compounds, Volumes 1-5 and Supplementals (Elsevier Science Publishers, 1989); Organic Reactions, Volumes 1-40 (John Wiley and Sons, 1991); and Larock's Comprehensive Organic Transformations (VCH Publishers Inc., 1989). Other methods for the synthesis of compounds described herein may be found in United States Patent Application Publication No. US 2011/0130429 A1, Burgey*et al. Bioorganic& Medicinal* Chemisty Letters 10 (2006) 5052-5056. The definitions of chemistry terms used in this application may be found in these reference (if not otherwise defined herein). As a guide the following synthetic methods may be utilized.

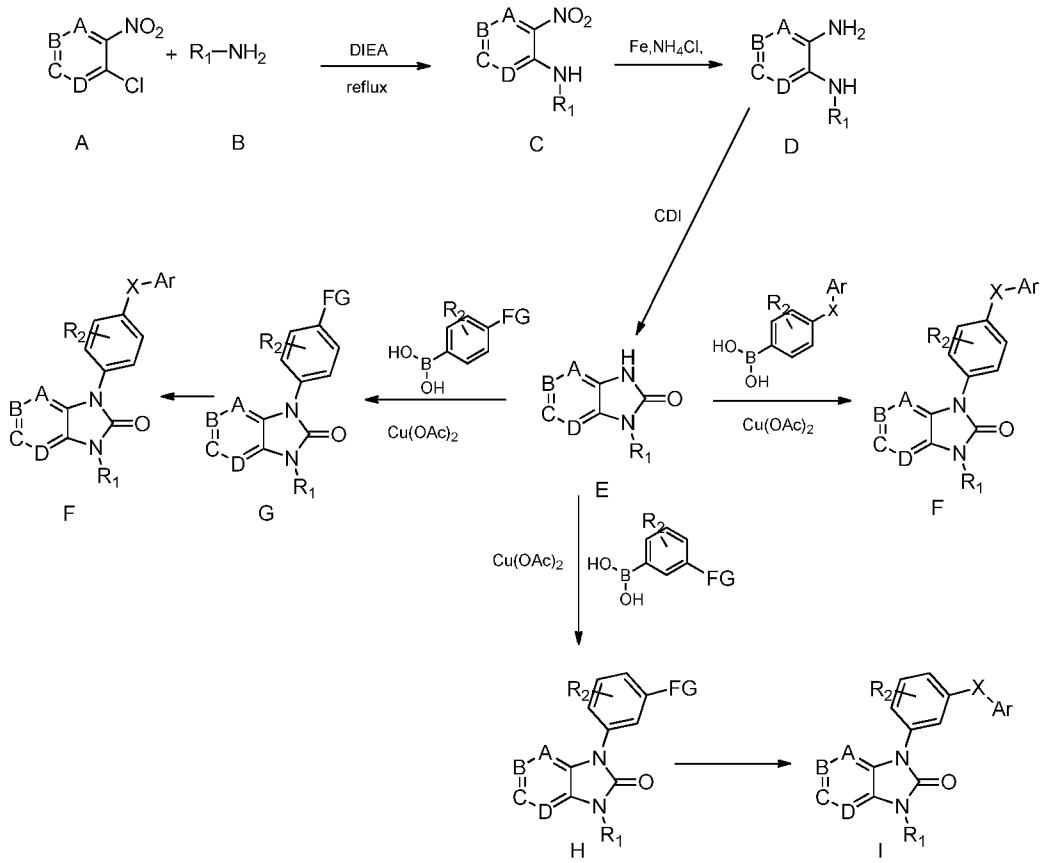
During the synthetic sequences it may be necessary and/or desirable to protect sensitive or reactive groups on any of the molecules concerned. This is achieved by means of conventional protecting groups, such as those described in T.W Greene and P.G.M. Wutts "Protective groups in Organic Synthesis" 3rd Edition, John Wiley and Sons, 1999. The protective groups are optionally removed at a convenient subsequent stage using methods well known in the art. The products of the reactions are optionally isolated and purified. If desired, using conventional techniques, but not limited to, filtration, distillation crystallization, chromatography and the like. Such materials are optionally characterized using conventional means, including physical constant and spectra data.

Compounds described herein may possess one or more sterocenters and each center may exist in the R or S configuration. The compounds presented herein include all diasterometic, enantiomeric, and epimeric forms as well as the appropriate mixtures thereof.

The Btk inhibitor compounds of Formula I can be, for example, 1H-imidazo[4,5-c]pyridin-2(3H)-one derivatives. Specifically, the Btk inhibitor compounds of Formula I can be, for example, compounds F, wherein R_1-R_2 have the previously defined meanings. A non-

limiting example of a synthetic approach towards the preparation of compounds F can be prepared by the general synthetic route shown in Scheme I.

Scheme I

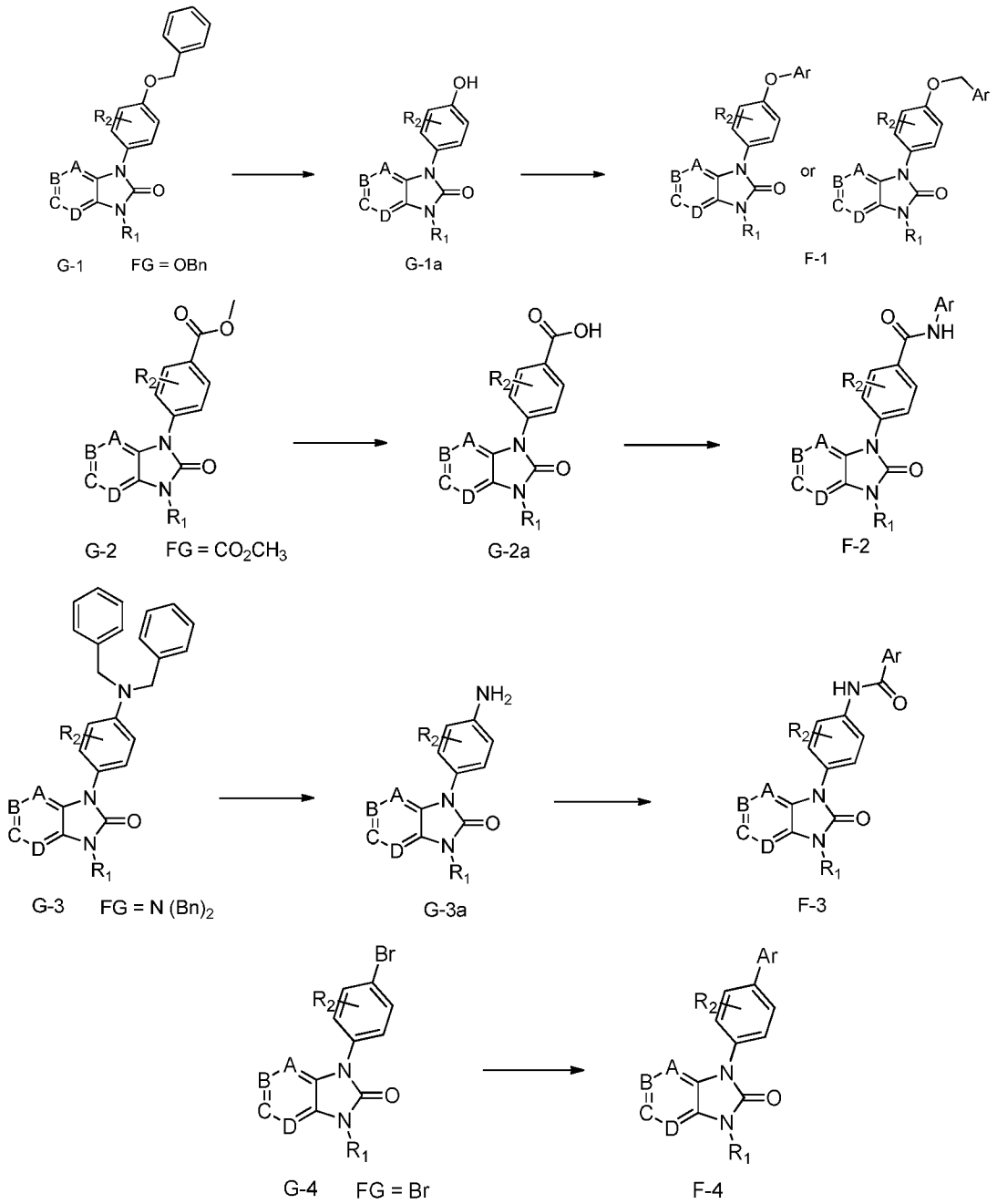


Referring to Scheme I, amine (B) could be added to a range of substituted o-halonitroaromatics A, followed by nitro group reduction of the product C with Fe metal in NH_4Cl in acidic methanol to deliver the o-amino anilines D. Ring closure with carbonyldiimidazole to obtain the key intermediates E, which then are derivatized by copper catalyst coupling reaction using appropriately substituted phenylboronic acid (corresponding boronic esters may also be used) directly affords the desired compounds F. In a typical procedure, a mixture of intermediates E, a copper catalyst (e.g. $Cu(OAc)_2$), base (e.g. TEA, DIPEA or the like) and an aryl boronic acid or aryl boronic ester in a suitable solvent such as DCM, or toluene to form compounds F.

Alternatively, compounds F or I may be obtained from compounds G or H, in which FG is a functional group (e.g. ester, protected anilines, protected phenols, bromide) that can be easily converted to groups defined for XAr. Non-limiting examples of suitable functional groups in compounds G are a benzyl ether, dibenzyl anime, or methyl ester, which can be

treated with base or Pd/C/H_2 to form the key intermediates G-1a, G-2a, G-3a, then form corresponding compounds F-1, F-2, F-3, F-4 at Scheme II.

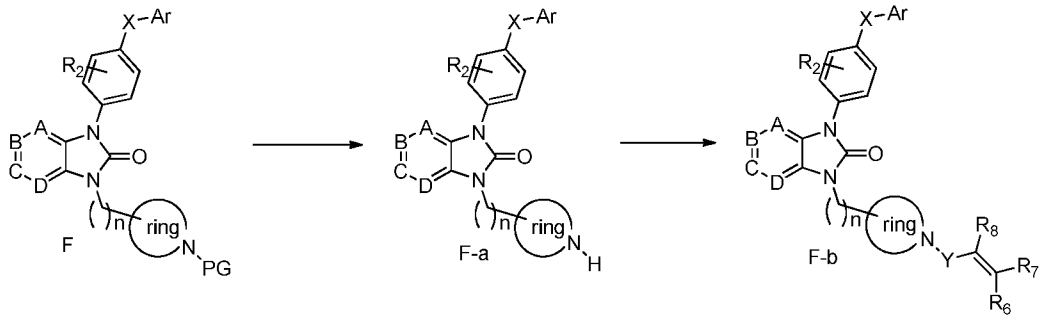
Scheme II



The deprotection reactions for the protective groups of compound F in Scheme III are known and can be run by the methods described below. Examples here are (a) deprotection reaction under acidic conditions for Boc protecting group and (b) deprotection reactions based on hydrogenolysis for benzyl protecting group. After deprotection with these conditions,

coupling with, but not limited to, an acid chloride, such as, but not limited to, aryloyl chloride, completes the synthesis to provide compound F-b.

Scheme III



General experimental conditions: Preparative thin layer chromatography (PTLC) was performed on 20 x 20 cm plates (500 micron thick silica gel). Silica gel chromatography was performed on a Biotage Horizon flash chromatography system. 1H NMR spectra were recorded on a Bruker Ascend TM 400 spectrometer at 400 MHz at 298 °K, and the chemical shifts are given in parts per million (ppm) referenced to the residual proton signal of the deuterated solvents: $CHCl_3$ at $\delta = 7.26$ ppm and CH_3OH or CH_3OD at $\delta = 3.30$ ppm. LCMS spectra were taken on an Agilent Technologies 1260 Infinity or 6120 Quadrupole spectrometer. The mobile phase for the LC was acetontrile (A) and water (B) with 0.01% formic acid, and the eluent gradient was from 5-95% A in 6.0 min, 60-95% A in 5.0 min, 80-100% A in 5.0 min and 85-100% A in 10 min using a SBC18 50 mm×4.6 mm× 2.7 µm capillary column. Mass spectra (MS) were measured by electrospray ion-mass spectroscopy (ESI). All temperatures are in degrees Celsius unless otherwise noted.

Analytical HPLC mass spectrometry conditions:

LC1: Column: SB-C18 50 mm×4.6 mm× 2.7 µm

Temperature: 50 °C

Eluent: 5:95 v/v acetonitrile/water + 0.01% formic acid in 6 min.

Flow Rate: 1.5 mL/min, Injection 5 µL

Detection: PDA, 200-600 nm

MS: mass range 150-750 amu; positive ion electrospray ionization

LC2: Column: SB-C18 50 mm×4.6 mm× 2.7 µm

Temperature: 50 °C

Eluent: 5:95 to 95:5 v/v acetonitrile/water + 0.05% TFA over 3.00 min.

Flow Rate: 1.5 mL/min, Injection 5µL

Detection: PDA, 200-600 nm

MS: mass range 150-750 amu; positive ion electrospray ionization

LC3: Column: SB-C18 50 mm×4.6 mm× 2.7 μm

Temperature: 50 ºC

Eluent: 10:90 to 98:2 v/v acetonitrile/water + 0.05% TFA over 3.75 min.

Flow Rate: 1.0 mL/min, Injection 10 μL

Detection: PDA, 200-600 nm

MS: mass range 150-750 amu; positive ion electrospray ionization

List of Abbreviations:

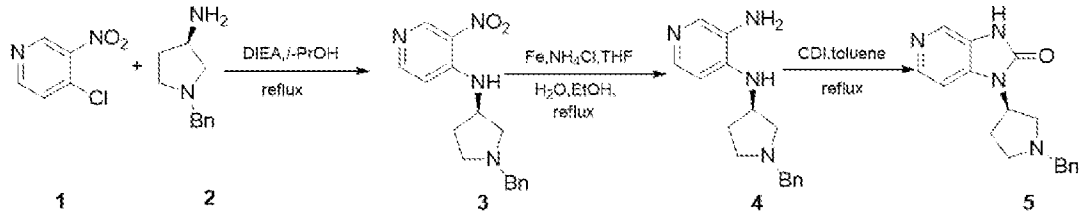
AcOH	=	acetic acid
Alk	=	alkyl
Ar	=	aryl
Boc	=	*tert*-butyloxycarbonyl
bs	=	broad singlet
CH_2Cl_2	=	dichloromethane
d	=	doublet
dd	=	doublet of doublets
DBU	=	1,8-diazabicyclo[5.4.0]undec-7-ene
DCM	=	dichloromethane
DEAD	=	diethyl azodicarboxylate
DMF	=	*N,N*-dimethylformamide
DMSO	=	dimethyl sulfoxide
EA	=	ethyl acetate
ESI	=	electrospray ionization
Et	=	ethyl
EtOAc	=	ethyl acetate
EtOH	=	ethyl alcohol
h	=	hours
HOAc	=	acetic acid
LiOH	=	lithium hydroxide
m	=	multiplet
Me	=	methyl
MeCN	=	acetonitrile
MeOH	=	methyl alcohol

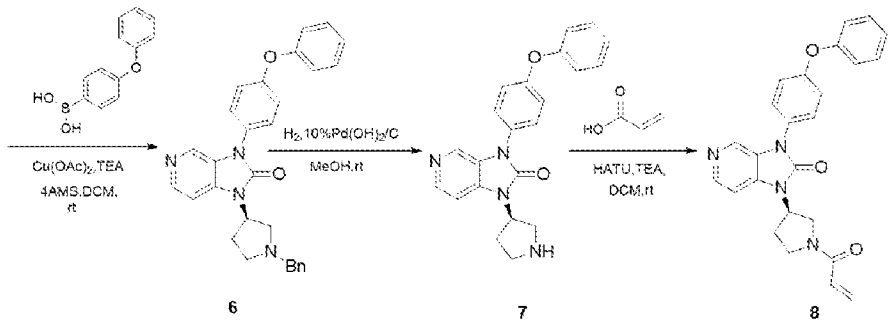
$MgSO_4$	=	magnesium sulfate
min	=	minutes
MS	=	mass spectroscopy
NaCl	=	sodium chloride
NaOH	=	sodium hydroxide
Na_2SO_4	=	sodium sulfate
NMR	=	nuclear magnetic resonance spectroscopy
PE	=	petroleum ether
PG	=	protecting group
Ph	=	phenyl
rt	=	room temperature
s	=	singlet
t	=	triplet
TFA	=	trifluoroacetic acid
THF	=	tetrahydrofuran
Ts	=	p-toluenesulfonyl (tosyl)

The compounds of the present invention can be prepared following general methods detailed below. In certain embodiments, provided herein are methods of making the tyrosine kinase inhibitor compounds described herein. In certain embodiments, compounds described herein are synthesized using the following synthetic schemes. In other embodiments, compounds are synthesized using methodologies analogous to those described below by the use of appropriate alterative starting materials. All key intermediates were prepared according to the following methods.

Example 1

(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one





6 7 8

Step 1: (R)-N-(1-benzylpyrrolidin-3-yl)-3-nitropyridin-4-amine (3)

A mixture of4-chloro-3-nitropyridine (12.2 g, 77.4 mmol), (R)-1-benzylpyrrolidin-3-amine (15 g, 85.2 mmol), and N,N-diisopropylethylamine (47 mL, 271.1 mmol) in 2-propanol (309 mL) was heated at reflux for 4 h. Volatile components were removed under vacuum and the residue was purified by column chromatography on silica gel (gradient: PE/EA=10/1) to provide the title product 22.1 g, yield 96%.

^{1}H NMR (400 MHz, DMSO-d_6): δ 9.03 (s,1H), 8.27 (d, J = 6 Hz,1H), 8.22 (d, J = 7.2 Hz,1H), 7.34-7.26 (m, 4H), 7.25 (d, J = 4 Hz,1H), δ 7.02 (d, J = 6.4 Hz,1H), δ 4.31-4.29 (m, 1H), δ 3.65 (s, 2H), δ 2.80-2.73 (m, 2H), δ 2.65-2.61 (m, 1H), δ 2.41-2.33 (m, 2H), δ 1.74-1.73 (m, 1H).

Step 2: (R)-N4-(1-benzylpyrrolidin-3-yl)pyridine-3,4-diamine (4)

To a solution of (3) 22.1 g (74.1 mmol) in EtOH (504 mL) was added. Fe (22.55 g, 400 mmol), NH_4Cl (127 mL), THF (257 mL), and H_2O (127 mL). Then the reaction mixture was stirred at 85 degree for 2 h. The precipitate was filtered off. Solvent was removed. The reaction mixture was extracted with EA. Organic phase was purified by column chromatography on silica gel gradient: (DCM/MeOH =100/1-50/1) to give the title product 17 g, yield 85.5%.

^{1}H NMR (400 MHz, DMSO-d_6): δ 7.62 (s,1H), 7.55 (d, J = 5.2Hz,1H), 7.34-7.31(m,5H), 7.25-7.23 (m, 1H), 6.28 (d, J = 5.2 Hz,1H), 5.30 (d, J = 6.4 Hz,1H), 4.64 (s, 2H), 3.95-3.94 (m, 1H), 3.59 (d, J = 4.4 Hz, 2H), 2.83-2.80 (m, 1H), 2.79-2.62 (m, 1H), 2.46-2.41 (m, 2H), 2.27-2.22 (m,1H), 1.69-1.65 (m, 1H). LC-MS: m/z = 268 $[M+H]^+$.

Step 3: (R)-1-(1-benzylpyrrolidin-3-yl)-1H-imidazo[4,5-c]pyridin-2(3H)-one (5)

A mixture of (4) (9.5 g, 35.4 mmol) and carbonyldiimodazole (11.48 g , 70.8 mmol) in toluene (200 mL) was reflux for 3 h. Volatile components were removed under vacuum, before being poured into H_2O. The reaction mixture was extracted with EA, Organic phase was purified by column chromatography on silica gel (gradient: DCM/MeOH = 100/1-50/1) to give the title product (7 g, yield 67.3%).

^{1}H NMR (400 MHz, DMSO-d_6): δ 7.62 (s,1H), 7.55 (d, J = 5.2Hz,1H), 7.34-7.31 (m, 5H), 7.25-7.23 (m, 1H), 6.28 (d, J = 5.2 Hz,1H), 5.30 (d, J = 6.4 Hz,1H), 4.64 (s, 2H), 3.95-3.94 (m, 1H), 3.59 (d, J = 4.4 Hz, 2H), 2.83-2.80 (m, 1H), 2.79-2.62 (m, 1H), 2.46-2.41 (m,2H), 2.27-2.22 (m,1H), 1.69-1.65 (m, 1H). LC-MS: m/z = 295 $[M+H]^+$.

Step 4: (R)-1-(1-benzylpyrrolidin-3-yl)-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one (6)

Intermediate 5 (0.1 g, 0.34 mmol), (4-phenoxyphenyl)boronic acid (0.145 g, 0.68 mmol), TEA (68 mg, 0.68 mmol) and 4 A molecular sieves (130 mg) were added to DCM (3 mL) in a vial Copper (II) acetate (67 mg, 0.34 mmol) was added in one portion. The mixture was stirred for about 22 h at rt. Volatile components were removed under vacuum , before being poured into H_2O, The reaction mixture was extracted with EA, Organic phase was purified by column chromatography on silica gel (gradient: DCM/MeOH=100/1-50/1) to give the title product (63 mg, yield 40.1%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.29 (s, 1H), 8.23 (s, 1H), 7.80 (s, 1H), 7.39-7.37 (m, 2H), 7.36-7.31 (m, 5H), 7.27 (s, 2H), 7.07-7.01 (m, 5H), 5.19 (s, 1H), 3.72 (d, J = 12.8 Hz, 1H), 3.57 (d, J = 12.8 Hz, 1H), 3.15 (s, 1H), 3.30-2.98 (m, 1H), 2.64-2.59 (m, 1H), 2.35-2.29 (m, 2H), 2.118 (s, 1H).LC-MS: m/z = 462 $[M+H]^+$.

Step 5: (R)-3-(4-phenoxyphenyl)-1-(pyrrolidin-3-yl)-1H-imidazo[4,5-c]pyridin-2(3H)-one (7)

A suspension of 6 (50 mg, 0.1 mmol) and 10% $Pd(OH)_2$/C (20 mg) in MeOH (10 mL) was hydrogenated at 50 psi H_2 for 8 h. The suspension was filtered through Celite and concentrated. The residue was dried in vacuo to provide the title product (35 mg). LC-MS: m/z = 373 $[M+H]^+$.

Step 6: (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one (8)

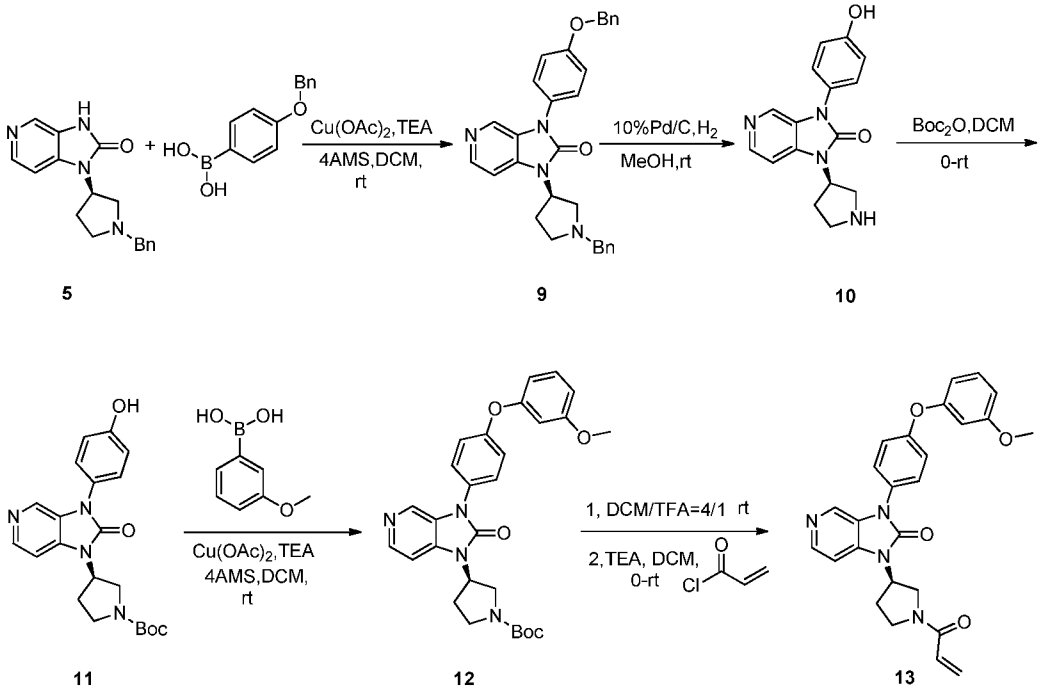
Intermediates 7 (35 mg, 0.094 mmol), HATU (39.3 mg, 0.10 mmol), TEA (19 mg, 0.18 mmol) and acrylic acid (7.4 mg, 0.10mmol) were added to DCM (3 mL) was added in one portion. The mixture was stirred for about 2 h at rt. Volatile components were removed under vacuum , before being poured into H_2O, The reaction mixture was extracted with EA, Organic phase was purified by P-TLC to give the title product (10 mg).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.35 (s, 2H), 7.47-7.45 (m, 2H), 7.41-7.37 (m, 2H), 7.17 (d, J = 8.4 Hz, 3H), 7.10 (d, J = 7.6 Hz, 2H), 7.03 (d, J = 8.4 Hz, 1H), 6.51-6.41 (m, 2H), 5.78-

5.73 (m, 1H), 5.22-5.13 (m, 1H), 4.11-3.99 (m, 3H), 3.76-3.64 (m, 1H), 2.73-2.65 (m, 1H), 2.47-2.39 (m, 1H). LC-MS-8: m/z = 427 $[M+H]^+$.

Example 2

(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one



5 9 10

11 12 13

Step 1: (R)-3-(4-(benzyloxy)phenyl)-1-(1-benzylpyrrolidin-3-yl)-1H-imidazo[4,5-c]pyridin-2(3H)-one (9)

To a solution of intermediate 5 (2 g, 6.8 mmol), (4-(benzyloxy)phenyl)boronic acid (3.1 g, 13.6 mmol), TEA (1.57 g, 13.6 mmol) and 4 A molecular sieves (3 g) were added to DCM (50 mL) in a vial Copper (II) acetate (1.23 g, 6.8 mmol) was added in one portion. The mixture was stirred for about 15 h at rt. Volatile components were removed under vacuum, before being poured into H_2O. The reaction mixture was extracted with EA, Organic phase was purified by column chromatography on silica gel (gradient: DCM/MeOH=100/1-50/1), give the title product (0.8 mg, yield 25 %).

^1H NMR (400 MHz, $CDCl_3$): δ 8.36-8.28 (m, 2H), 7.87 (s, 1H), 7.46-7.31 (m, 12H), 7.11 (d, J = 4.4 Hz, 2H), 5.26-5.23 (m, 1H), 5.09 (s, 2H), 3.78 (d, J = 6.4 Hz, 1H), 3.63 (d, J = 6.4 Hz, 1H), 3.23-3.19 (m, 1H), 3.06-3.03 (m, 1H), 2.69-2.64 (m, 1H), 2.44-2.36 (m, 2H), 2.17-2.14 (m, 1H).LCMS: m/z = 477 $[M+H]^+$.

Step 2: (R)-3-(4-hydroxyphenyl)-1-(pyrrolidin-3-yl)-1H-imidazo[4,5-c]pyridin-2(3H)-one (10)

A suspension of 9 (0.8 g, 1.68 mmol) and 10% Pd/C (0.1 g) in MeOH (15 mL) was hydrogenated at 50 psi H_2 for 20h. The suspension was filtered through Celite and concentrated. The residue was dried in vacuo to provide the title crude product 0.49 g. LCMS: m/z = 297 $[M+H]^+$.

Step 3: (R)-tert-butyl 3-(3-(4-hydroxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)pyrrolidine-1-carboxylate (11)

To a suspension of 10 (0.49 g ; 1.68 mmol) and TEA (0.17 g, 1.68 mmol) in CH_2Cl_2 (15 mL) at 0°C was added di-tert-butylcarbonate (0.31 g, 1.68 mmol). The solution was then stirred to room temperature for 1 h. before being poured into H_2O, The reaction mixture was extracted with DCM, Organic phase was purified by column chromatography on silica gel (gradient: DCM/MeOH=100/1-50/1) to give the title product (0.58 g, yield 87.8%).

^1H NMR (400 MHz, $CDCl_3$): δ 9.29 (br, 1H), 8.35 (d, J = 2.8 Hz 1H), 8.23 (s, 1H), 7.27 (d, J = 4 Hz, 2H), 7.11 (d, J = 2.8 Hz 1H), 6.96 (d, J = 5.2 Hz 2H), 5.19-5.13 (m, 1H), 3.85 (br, 3H), 3.54-3.48 (m, 1H), 2.60-2.54 (m, 1H), 2.38-2.30 (m, 1H), 1.50 (s, 9H).LCMS: m/z = 397 $[M+H]^+$.

Step 4: (R)-tert-butyl 3-(3-(4-(3-methoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)pyrrolidine-1-carboxylate (12)

To a solution of 11 (30 mg, 0.075 mmol), (3-methoxyphenyl)boronic acid (23 mg, 0.15 mmol), TEA (15.3 mg, 0.15 mmol) and 4 A molecular sieves (0.1 g) were added to DCM (5 mL) in a vial Copper (II) acetate (13.7 mg, 0.075 mmol) was added in one portion. The mixture was stirred for about 20 h at rt. Volatile components were removed under vacuum , before being poured into H_2O, The reaction mixture was extracted with EA, Organic phase was purified by column chromatography on silica gel (gradient: DCM/MeOH=100/1-50/1), give the title product (32 mg, yield 86.4 %).

^1H NMR (400 MHz, $CDCl_3$): δ 8.36 (br, 2H), 7.46 (d, J = 4.4 Hz 2H), 7.30-7.26 (m, 1H), 7.16 (d, J = 4.4 Hz, 2H), 7.08 (br, 1H), 6.73-6.65 (m, 3H), 5.19-5.15 (m, 1H), 3.81 (s, 3H), 3.75-3.76 (m, 3H), 3.51-3.4 (m, 1H), 2.59-2.54 (m, 1H), 2.37-2.30 (m, 1H), 1.49 (s, 9H).LCMS: m/z = 503 $[M+H]^+$.

Step 5: (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one(13)

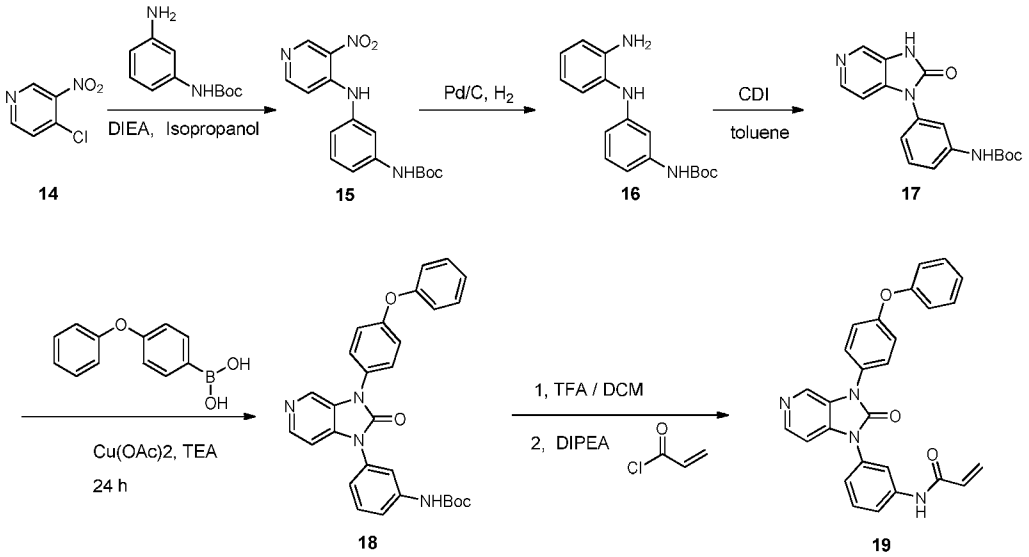
Intermediate 12 (32 mg, 0.063 mmol) were added to CF_3COOH/DCM=4/1 (5 mL) in one portion. The mixture was stirred for about 1 h at rt. Volatile components were removed under vacuum to give a crude title product, and directly used in next step without further purification. LCMS: m/z = 403 $[M+H]^+$.

To a solution of Acryloyl chloride (5.7 mg, 0.068 mmol) in DCM (1 mL) was added to a stirred solution of a crude product (25.3 mg, 0.063 mmol) and TEA (12.7mg, 0.126 mmol) in DCM (5 mL) at 0° C. The reaction mixture was stirred for 1 h, poured onto brine and extracted with DCM. The organic layer was dried, concentrated and recrystallized from DCM/MeOH=100/1 to give the title product (5 mg, yield 17.4 %).

^1H NMR (400 MHz, $CDCl_3$): δ 8.38-8.34 (m, 2H), 7.46 (d, J = 3.6 Hz, 2H), 7.30-7.26 (m, 1H), 7.17 (d, J = 4.2 Hz, 2H), 7.05-7.01 (m, 1H), 6.73-6.65 (m, 3H), 6.51-6.41 (m, 2H), 5.79-5.72 (m, 1H), 5.22-5.15 (m, 1H), 4.11-3.98 (m, 3H), 3.81 (s, 3H), 3.78-3.71 (m, 1H), 2.79-2.60-2.39 (m, 1H), 2.50-2.37 (m, 1H). LCMS: m/z = 457 $[M+H]^+$.

Example 3

N-(3-(2-oxo-3-(4-phenoxyphenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl) (19)



Step 1: tert-butyl (3-((3-nitropyridin-4-yl)amino)phenyl)carbamate (15):

4-chloro-3-nitropyridine (1.614 g, 10.18 mmol, 1.0 eq) was dissolved in isopropanol (30 mL), added tert-butyl (3-aminophenyl)carbamate (2.12 g, 10.18 mmol, 1.0 eq) and DIPEA (2.63 g, 20.36 mmol, 2.0 eq), the mixture solution was stirred reflux for 5 h. Then stopped and removed the solution under reduce pressure, the residue was added EA and saturated $NaHCO_3$, extracted with EA and dried with Na_2SO_4, filtered and concentrated, purified with silica column (PE:EA = 5:1～2:1) to obtain the title product (2.9 g), yellow solid, Yield: 2.9 g, 86.3%. ^1H

NMR (400 MHz, $CDCl_3$): δ = 9.62 (s, 1H), 9.28 (s, 1H), 8.26 (d, *J* = 6.0 Hz, 1H), 7.57 (s, 1H), 7.38-7.34 (m, 1H), 7.15 (d, *J* = 8.0 Hz, 1H), 7.01-6.95 (m, 2H), 6.61 (s, 1H), 1.52 (s, 9H).

Step 2: tert-butyl (3-((2-aminophenyl)amino)phenyl)carbamate (16):

Intermediate 15 (2.9 g) was dissolved in Mathanol (50.0 mL), added Pd/C (200 mg), under H_2atmospherethe mixture was stirred for 3 h at RT, stopped the reaction, filtered and concentrated under reduce pressure to obtain the title product used next step without purification, tan solid, Yield: 2.6 g, 98.9%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.05 (s, 1H), 7.97 (d, *J* = 5.6 Hz, 1H), 7.29 (s, 1H), 7.24-7.20 (m, 1H), 7.04 (d, *J* = 5.2 Hz, 1H), 6.89 (d, *J* = 8.0 Hz, 1H), 6.78-6.76 (m, 1H), 6.55 (s, 1H), 5.83 (s, 1H), 3.34 (s, 2H), 1.51 (s, 9H). LCMS (ESI) m /z = 301$[M+H]^+$.

Step 3: tert-butyl (3-(2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)carbamate (17):

Intermediate 16 (740 mg, 1.0 eq) was dissolved in toluene (30 mL), added CDI (800 mg, 2.0 eq), the mixture solution were stirred under reflux for 4 h. Then allowed the reaction was cooled to room temperature, added water and extracted with EA, dried with Na_2SO_4, filtered and concentrated, purified with silica column (DCM :MeOH = 50:1～20:1) to obtain the title product, yellow solid, Yield: 700 mg, 86.8%. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.41 (s, 1H), 9.58 (s, 1H), 8.30 (s, 1H), 8.20 (d, *J* = 5.2 Hz, 1H), 7.68 (s, 1H), 7.50-7.42 (m, 2H), 7.14 (d, *J* = 7.6 Hz, 1H), 7.04-7.01 (m, 2H), 1.48 (s, 9H). LCMS (ESI) m /z = 327 $[M+H]^+$.

Step 4: tert-butyl (3-(2-oxo-3-(4-phenoxyphenyl)-2,3-dihydro-1H-imidazo [4,5-c]pyridin-1-yl)phenyl)carbamate(18):

Intermediate 17 (101 mg, 0.308 mmol, 1.0 eq) was dissolved in DCM (3.0 mL), added Cupric acetate (56 mg, 0.308 mmol, 1.0 eq), (4-phenoxyphenyl)boronic acid (132 mg, 0.617 mmol, 2.0 eq), 4A molecular sieve (131 mg) and TEA (62 mg, 0.617 mmol, 2.0 eq), the mixture solution were stirred under for 30 h at RT. Then filtered the solution and removed the solution under reduce pressure, added water and extracted with EA, dried with Na_2SO_4, filtered and concentrated, purified with silica column (PE:EA = 4:1～1:1) to obtain the title product, brown solid, Yield: 50 mg, 32.7%. ^{1}H NMR (400 MHz, $CDCl_3$):δ = 8.40 (s, 1H), 8.37 (d, *J* = 5.6 Hz, 1H), 7.78 (s, 1H), 7.55 (d, *J* = 8.8 Hz, 2H), 7.48-7.44 (m, 1H), 7.42-7.38 (m, 2H), 7.32 (d, *J* = 8.8 Hz, 1H), 7.24 (d, *J* = 7.6 Hz, 1H), 7.19-7.10 (m, 6H), 6.69 (s, 1H), 1.52 (s, 9H). LCMS (ESI) m /z = 495 $[M+H]^+$.

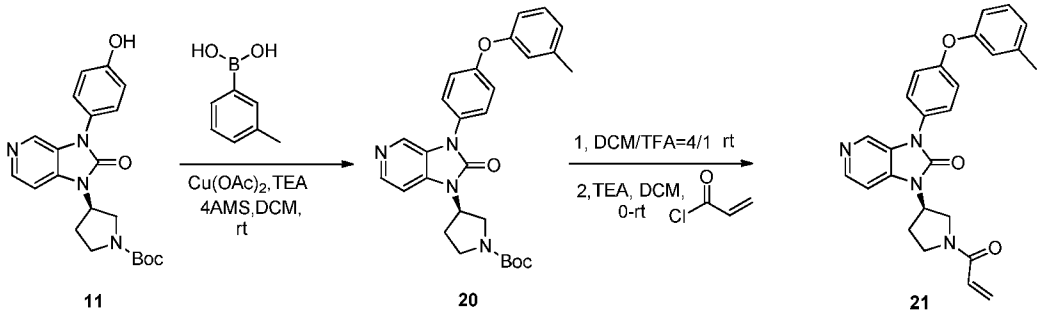
Step 5: N-(3-(2-oxo-3-(4-phenoxyphenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl) (19)

Intermediate 18 (50 mg) was dissolved in DCM (5.0 mL), added TFA (2.0 mL), the mixture was stirred for 1 h at RT, stopped and removed the solution under reduce pressure, the residue was added saturated $NaHCO_3$, extracted with EA and dried with Na_2SO_4, filtered and concentrated, obtained crude product (tan solid, 45 mg) used next step without purification. ^1H NMR (400 MHz, $CDCl_3$):δ = 8.39 (s, 1H), 8.35 (d, J = 5.2 Hz, 1H), 7.55 (d, J = 8.8 Hz, 2H), 7.42-7.38 (m, 2H), 7.34-7.30 (m, 1H), 7.19-7.16 (m, 3H), 7.12-7.10 (m, 3H), 6.91-6.87 (m, 2H), 6.77-6.74 (m, 1H), 3.87 (s, 2H). LCMS (ESI) m /z = 395 $[M+H]^+$.

Crude intermediate (23 mg, 0.058 mmol, 1.0 eq) and DIEA (9 mg, 0.070 mmol, 1.2 eq) were dissolved in THF (2.0 mL), added acryloyl chloride (5.6 mg, 0.061 mmol, 1.05 eq) slowed at 0°C, the mixture solution was stirred for 0.5 h at RT, followed the reaction with LCMS, stopped the reaction added water and extracted with EA, dried with Na_2SO_4, filtered and concentrated, the residue was purification with silica gel plate (PE:EA=20:80) obtain the title product (8 mg) colorless oil, Yield: 8 mg, 30.6%. ^1H NMR (400 MHz, $CDCl_3$):δ = 8.40 (s, 1H), 8.38 (d, J = 5.2 Hz, 1H), 8.01 (s, 1H),7.76 (s, 1H), 7.55 (d, J = 8.8 Hz, 2H), 7.49 (d, J = 5.6 Hz, 2H), 7.42-7.38 (m, 2H), 7.34-7.32 (m, 1H), 7.20-7.17 (m, 4H), 7.12 (d, J = 7.6 Hz, 2H), 6.44 (d, J = 16.8 Hz, 1H), 6.27-6.20 (m, 1H), 5.78 (d, J = 10.4 Hz, 1H). LCMS (ESI) m /z = 449 $[M+H]^+$.

Example 4

(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(m-tolyloxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one



11 20 21

Step 1: (R)-tert-butyl 3-(2-oxo-3-(4-(m-tolyloxy)phenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)pyrrolidine-1-carboxylate (20)

To a solution of intermediate 11 (100 mg, 0.25 mmol), m-tolylboronic acid (68 mg, 0.5 mmol), TEA (45 mg, 0.5 mmol) and 4 A molecular sieves (0.1 g) were added to DCM (5 mL) in a vial Copper (II) acetate (45 mg, 0.25 mmol) was added in one portion. The mixture was stirred for about 20 h at rt. Volatile components were removed under vacuum , before being poured into H_2O, The reaction mixture was extracted with EA, organic phase was purified by

column chromatography on silica gel (gradient: DCM/MeOH=100/1-50/1) to give the title product (68 mg, yield 56.2 %). LCMS: m/z = 487 $[M+H]^+$.

Step 2: (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(m-tolyloxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one (21)

Intermediate 20 (68 mg, 0.13 mmol) were added to CF_3COOH/DCM=4/1 (10 mL) in one portion. The mixture was stirred for about 1 h at rt. Volatile components were removed under vacuum to give a crude title product and directly used in next step without further purification. LCMS: m/z = 387 $[M+H]^+$.

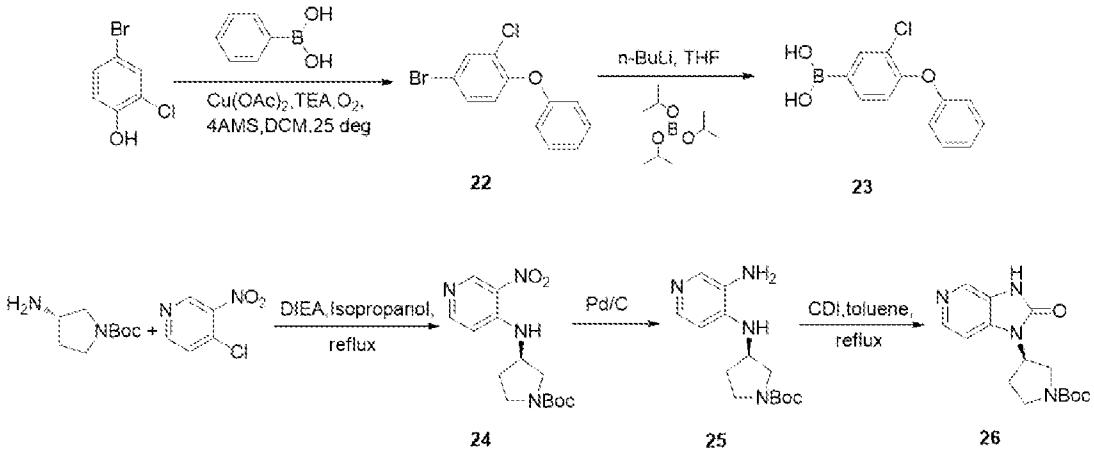
A solution of Acryloyl chloride (11.8 mg, 0.13 mmol) in DCM (5 mL) was added to a stirred solution of crude intermediate (54 mg, 0.13 mmol) and TEA (131mg, 1.3 mmol) in DCM (5 mL) at 0° C. The reaction mixture was stirred for 1 h, poured onto brine and extracted with DCM. The organic layer was dried, concentrated and recrystallized from DCM/MeOH = 100/1 to give the title product (29 mg, yield 53.7 %).

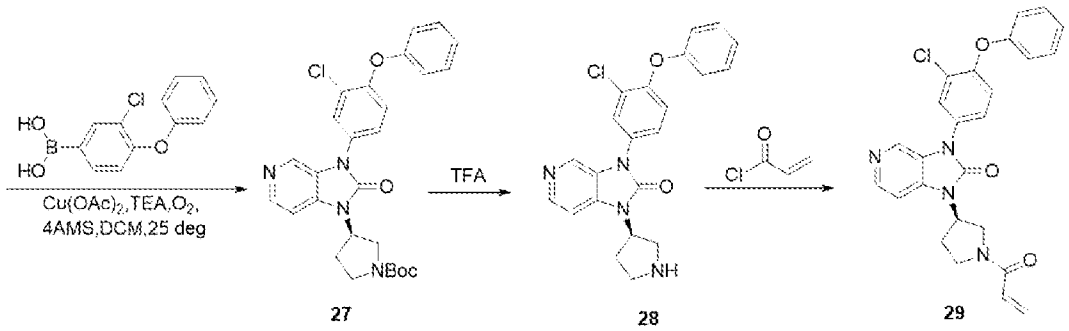
^1H NMR (400 MHz, $CDCl_3$): δ 8.36 (br, 2H), 7.47-7.44 (m, 2H), 7.29-7.25 (m, 1H), 7.14 (d, J = 8 Hz, 2H), 7.06-6.98 (m, 2H), 6.90 (d, J = 8 Hz, 2H), 6.52-6.41 (m, 2H), 5.79-5.72 (m, 1H), 5.22-5.16 (m, 1H), 4.12-4.00 (m, 3H), 3.76-3.74 (m, 1H), 2.74-2.61 (m, 1H), 2.47-2.39(m, 1H), 2.36 (s, 3H).

LCMS: m/z = 441 $[M+H]^+$.

Example 5

(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-phenoxyphenyl)-1H-imidazo[4,5-c] pyridin-2(3H)-one





Step 1: 4-bromo-2-chloro-1-phenoxybenzene (22):

4-bromo-2-chlorophenol (10 g, 48.2 mmol, 1.0 eq) was dissolved in DCM (120.0 mL), added Cupric acetate (4.38 g, 24.1 mmol, 0.5 eq), phenylboronic acid (8.82 g, 72.3 mmol, 1.5 eq), 4A molecular sieve (15 g) and TEA (13.4 mL, 96.4 mmol, 2.0 eq), the mixture solution was stirred for overnight at RT under Oxygen atmosphere. Then filtered the solution and removed the solution under reduce pressure, added water and extracted with EA, dried with Na_2SO_4, filtered and concentrated, purified with silica column (PE:EA = 100:1～10:1) to provide title product as colorless oil, Yield: 5.5 g, 40.2%. ^{1}H NMR (400 MHz, $CDCl_3$):δ = 7.61 (d, J = 1.6 Hz, 1H), 7.32-7.37 (m, 3H), 7.12-7.15 (m, 1H), 6.95-7.02 (m, 2H), 6.84 (d, J = 8.4 Hz, 1H).

Step 2: (3-chloro-4-phenoxyphenyl)boronic acid (23)

n-BuLi (2.45 M in hexane, 5.4 mL, 13.3 mmol) at - 78°C under nitrogen was added to a solution of 22 (2.9 g, 10.23 mmol) in THF (15 mL). After stirring for 15 min at - 78°C, triisopropy borate(2.5 g, 13.3 mmol) was added in one portion. The mixture was warmed to 25 °C, stirred for 30 min, and quenched with dilute HCl solution. The mixture was extracted with EtOAc (150 mL), washed with water, dried (Na_2SO_4) and evaporated to obtain a crude title product used directly for the step 6 without further purification.

Step 3: (R)-tert-butyl 3-((3-nitropyridin-4-yl)amino)pyrrolidine-1-carboxylate (24)

4-chloro-3-nitropyridine (10.145 g, 63.99 mmol, 1.0 eq) was dissolved in isopropanol (1200 mL), added (S)-tert-butyl 3-aminopyrrolidine-1-carboxylate (11.92 g, 63.99 mmol, 1.0 eq) and DIPEA (16.5 g, 127.98 mmol, 2.0 eq), the mixture solution was stirred reflux for 3.5 h. Then stopped and removed the solution under reduce pressure, added water, extracted with EA and dried with Na_2SO_4, filtered and concentrated to obtain a crude title product as yellow oil: 20 g. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.24 (s, 1H), 8.35 (d, J = 4.8 Hz, 1H), 8.23 (d, J = 4.8 Hz, 1H), 6.73 (d, J = 6.4 Hz, 1H), 4.23 (s, 1H), 3.78-3.83 (m, 1H), 3.56 (s, 2H), 3.35-3.44 (m, 1H), 2.32-2.36 (m, 1H), 2.05 (s, 1H), 1.48 (s, 9H). LCMS (ESI) m /z = 309 $[M+H]^+$.

Step 4: (R)-tert-butyl 3-((3-aminopyridin-4-yl)amino)pyrrolidine-1-carboxylate (25)

Intermediate 25 (20 g, 64.94 mmol, 1.0 eq) was dissolved in MeOH (150.0 mL), added Pd/C (4.0 g), the mixture solution was stirred for 6 h at room temperature under Hydrogenatmosphere. Then filtered the solution and removed the solution under reduce pressure to obtain a crude title product as yellow solid, Yield: 17 g, 94.2%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00 (s, 1H), 7.94 (s, 1H), 6.48 (d, *J* = 5.2 Hz, 1H), 4.19 (s, 1H), 4.07 (s, 1H), 3.74 (s, 1H), 3.49 (s, 3H), 3.25-3.36 (m, 1H), 3.09 (s, 2H), 2.21-2.26 (m, 1H), 1.95 (s, 1H), 1.72 (s, 1H), 1.47 (s, 9H). LCMS (ESI) m /z = 279 $[M+H]^+$.

Step 5: (R)-tert-butyl 3-(2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)pyrrolidine-1 -carboxylate (26):

Intermediate 25 (17 g, 61.15 mmol, 1.0 eq) was dissolved in toluene (200 mL), added CDI (19.8 g, 122.3 mmol, 2.0 eq), the mixture solution were stirred under reflux for 4 h. Then allowed the reaction was cooled to room temperature, added water and extracted with EA, dried with Na_2SO_4, filtered and concentrated, purified with silica column (DCM :MeOH = 200:1～50:1) to obtain the title product as canary yellow solid, Yield: 13 g, 59.4%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.35 (s, 1H), 8.43 (s, 1H), 8.33 (s, 1H), 7.03 (d, *J* = 3.6 Hz, 1H), 5.12 (s, 1H), 3.71-3.80 (m, 3H), 3.50 (s, 1H), 2.50-2.56 (m, 1H), 2.30-2.32 (m, 1H), 1.50 (s, 9H). LCMS (ESI) m /z = 305 $[M+H]^+$.

Step 6: (R)-tert-butyl 3-(3-(3-chloro-4-phenoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c] pyridin-1-yl)pyrrolidine-1-carboxylate (27):

Intermediate 26 (2.17 g, 7.1 mmol, 1.0 eq) was dissolved in DCM (100.0 mL), added Cupric acetate (646 mg, 3.55 mmol, 0.5 eq), Boronic acid 23 (3.53 g, 14.2 mmol, 2.0 eq), 4A molecular sieve (3.0 g) and TEA (2.0 mL, 14.2 mmol, 2.0 eq), the mixture solution was stirred for overnight at RT under Oxygen atmosphere. Then filtered the solution and removed the solution under reduce pressure, added water and extracted with EA, dried with Na_2SO_4, filtered and concentrated, purified with silica column (DCM:MeOH = 200:1～50:1) to obtain the title product 27 as gray solid, Yield: 1.7 g, 47.0%. ^{1}H NMR (400 MHz, $CDCl_3$):δ = 8.40 (s, 2H), 7.68 (s, 1H), 7.36-7.42 (m, 3H), 7.17-7.21 (m, 1H), 7.07-7.10 (m, 4H), 5.14-5.18 (m, 1H), 3.83 (s, 3H), 3.51 (d, *J* = 8.4 Hz, 1H), 2.54-2.59 (m, 1H), 2.33-2.36 (m, 1H), 1.50 (s, 9H). LCMS (ESI) m /z = 507 $[M+H]^+$.

Step 7: (R)-3-(3-chloro-4-phenoxyphenyl)-1-(pyrrolidin-3-yl)-1H-imidazo[4,5-c]pyridin-2(3H)-one (28):

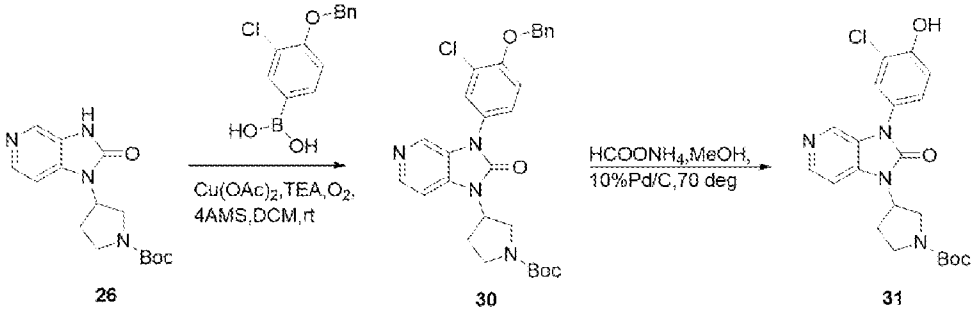
Intermediate 27(920 mg) was dissolved in DCM (20.0 mL), added TFA (4.0 mL), the mixture was stirred for 2.5 h at RT, and the solvent was removed under reduce pressure, the residue was added saturated $NaHCO_3$, extracted with EA and dried with Na_2SO_4, filtered and concentrated to provide a crude product 28 used next step without further purification. LCMS (ESI) m /z = 407 $[M+H]^+$.

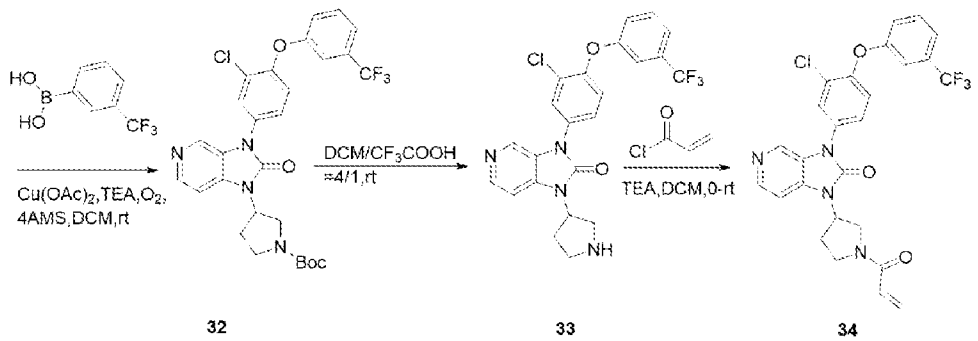
Step 8: (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-phenoxyphenyl)-1H-imidazo[4,5-c] pyridin-2(3H)-one (29):

Intermediate 28 (738 mg, 1.82 mmol, 1.0 eq) was dissolved in THF (10.0 mL), added TEA (368 mg, 3.64 mmol, 2.0 eq), acryloyl chloride (197 mg, 2.18 mmol, 1.2 eq) slowly at 0°C, the mixture solution was stirred for 0.5 h at RT, followed the reaction with LCMS, water was added to the reaction mixture and extracted with EA, dried with Na_2SO_4, filtered and concentrated, the residue was purification with silica column (DCM : MeOH = 200:1～30:1) to obtain the title product as canary yellow solid, Yield: 489 mg, 58.3%. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.40 (s, 1H), 7.68 (s, 1H), 7.36-7.42 (m, 3H), 7.17-7.21 (m, 1H), 7.04-7.10 (m, 4H), 6.41-6.52 (m, 2H), 5.74-5.80 (m, 1H), 5.13-5.24 (m, 1H), 3.97-4.14 (m, 3H), 3.65-3.77 (m, 1H), 2.62-2.77 (m, 1H), 2.38-2.49 (m, 1H). LCMS (ESI) m /z = 461 $[M+H]^+$.

Example 6

1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-(3-(trifluoromethyl)phenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one





Step 1: tert-butyl 3-(3-(4-(benzyloxy)-3-chlorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)pyrrolidine-1-carboxylate (30)

To a solution of 26 (1 g, 3.28 mmol), (4-(benzyloxy)-3-chlorophenyl)boronic acid (1.72 g, 3.57 mmol), TEA (0.66 g, 6.57 mmol) and 4 A molecular sieves (1 g) were added to DCM (30 mL) in a vial Copper (II) acetate (0.59 g, 6.57 mmol) was added in one portion. The mixture was stirred for about 21 h at rt. Volatile components were removed under vacuum, before being poured into H_2O, The reaction mixture was extracted with EA, Organic phase was purified by column chromatography on silica gel (gradient: DCM/MeOH = 100/1-50/1) to give the title product (0.83 g, yield 48.8 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.7 (br, 2H), 7.58 (d, J = 4.0 Hz, 1H), 7.49 (d, J = 4.0 Hz, 2H), 7.45-7.28 (m, 5H), 7.12-7.08(m, 2H), 5.23 (s, 2H), 5.18-5.12 (m, 1H), 3.82-3.76 (m, 3H), 3.53-3.48 (m, 1H), 2.57-2.52 (m, 1H), 2.36-2.30 (m, 1H), 1.49(s, 9H).LCMS: m/z 521, 523 $[M+H]^+$.

Step 2: tert-butyl 3-(3-(3-chloro-4-hydroxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)pyrrolidine-1-carboxylate (31)

To a solution of 30 (0.83 g, 1.59 mmol), $HCOONH_4$ (1 g, 15.9 mmol) and 10% Pd/C (0.35 g) in MeOH (30 mL) was added in one portion. The mixture was stirred for about 10 min at 70 deg. The suspension was filtered through Celite and concentrated. before being poured into H_2O, The reaction mixture was extracted with EA, Organic phase was purified by column chromatography on silica gel (gradient: DCM/MeOH=100/1-50/1) to give the title product (0.4 g, yield 58.8 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.39 (br, 1H), 8.31 (br, 1H), 7.51 (s, 1H), 7.30 (d, J = 8.0 Hz, 1H), 7.15 (d, J = 8.0 Hz, 1H), 7.09 (br, 1H), 5.17-5.13 (m, 1H), 3.83 (br, 3H), 3.53-3.47 (m, 1H), 2.60-2.50 (m, 1H), 2.35-2.32 (m, 1H), 1.50 (s, 9H).LCMS: m/z = 431,433 $[M+H]^+$.

Step 3: tert-butyl 3-(3-(3-chloro-4-(3-(trifluoromethyl)phenoxy) phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)pyrrolidine-1-carboxylate (32)

To a solution of 31 (30 mg, 0.069 mmol), (3-(trifluoromethyl)phenyl)boronic acid (26.5 mg, 0.139 mmol), TEA (14 mg, 0.139 mmol) and 4 A molecular sieves (0.2 g) were added to DCM (4 mL) in a vial Copper (II) acetate (12.6 mg, 0.069 mmol) was added in one portion. The mixture was stirred for about 14 h at rt. Volatile components were removed under vacuum, before being poured into H_2O, The reaction mixture was extracted with EA, Organic phase

was purified by column chromatography on silica gel (gradient: DCM/MeOH=100/1-50/1) to give the title product (20 mg, yield 50.5 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (s, 1H), 7.71 (d, J = 2.0 Hz, 1H), 7.64 (d, J = 8.0 Hz, 1H), 7.53-7.47 (m, 2H), 7.45-7.40 (m, 2H), 7.34 (s, 1H), 7.21-7.09 (m, 2H), 5.18-5.14 (m, 1H), 3.84-3.69 (m, 3H), 3.55-3.48 (m, 1H), 2.59-2.50 (m, 1H), 2.39-2.31 (m, 1H), 1.49 (s, 9H).LCMS: m/z = 575,576 $[M+H]^+$.

Step 4:3-(3-chloro-4-(3-(trifluoromethyl)phenoxy)phenyl)-1-(pyrrolidin-3-yl)-1H-imidazo[4,5-c]pyridin-2(3H)-one (33)

22 (20 mg, 0.034 mmol) were added to CF_3COOH/DCM=4/1 (5 mL) in one portion. The mixture was stirred for about 1 h at rt. Volatile components were removed under vacuum to give a crude title product, and directly used in next step without further purification. LCMS: m/z = 475,476 $[M+H]^+$.

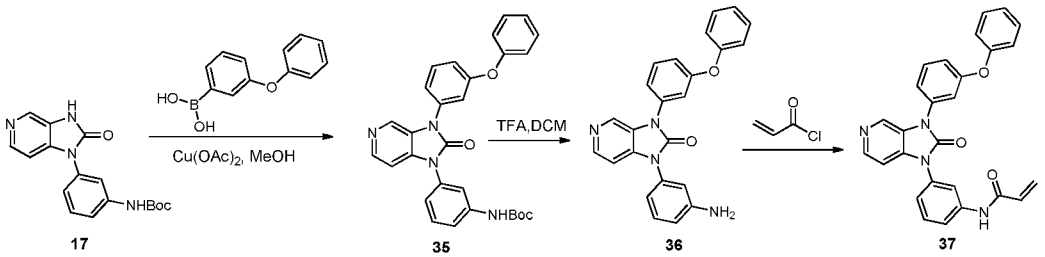
Step 5:1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-(3-(trifluoromethyl)phenoxy)-phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one (34)

A solution of Acryloyl chloride (3.0 mg, 0.034 mmol) in DCM (1 mL) was added to a stirred solution of 33 (16 mg, 0.034 mmol) and TEA (13.7mg, 0.136 mmol) in DCM (3 mL) at 0° C.The reaction mixture was stirred for 1 h, poured onto brine and extracted with DCM. The organic layer was dried, concentrated and recrystallized from DCM/MeOH=100/1 to give the title product (8 mg, yield 44.69 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.42 (br, 2H), 7.72 (s, 1H), 7.52-7.41 (m, 3H), 7.32 (s, 1H), 7.20-7.16 (m, 2H), 7.08-7.03 (m, 1H), 6.52-6.41 (m, 2H), 5.80-5.73 (m, 1H), 5.21-5.12 (m, 1H), 4.12-3.97 (m, 3H), 3.77-3.68 (m, 1H), 2.77-2.64 (m, 1H), 2.49-2.40 (m, 1H). LCMS: m/z = 529,531 $[M+H]^+$.

Example 7

N-(3-(2-oxo-3-(3-phenoxyphenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide



Step 1: tert-butyl (3-(2-oxo-3-(3-phenoxyphenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridine -1-yl)phenyl)carbamate (35):

Intermediate 17 (1.25 g, 3.83 mmol, 1.0 eq) was dissolved in MeOH (20.0 mL), added Cupric acetate (70 mg, 0.38 mmol, 0.1 eq), (3-phenoxyphenyl)boronic acid (0.9 g, 4.21 mmol, 1.1 eq), the mixture solution was stirred for 5 h under reflux. Then filtered the solution and removed the solution under reduce pressure, added water and extracted with EA, dried with Na_2SO_4, filtered and concentrated, purified with silica column (DCM: MeOH = 100:1～50:1) to obtain the title product as gray solid, Yield: 430 mg, 22.7%. ^1H NMR (400 MHz, $CDCl_3$, 298 K):δ = 8.38-8.40 (m, 2H), 7.75 (s, 1H), 7.44-7.52 (m, 2H), 7.33-7.40 (m, 4H), 7.20-7.25 (m, *2*H), 7.08-7.17 (m, 5H), 6.67 (s, 1H), 1.51 (s, 9H). LCMS (ESI) m /z = 495 $[M+H]^+$.

Step 2: 1-(3-aminophenyl)-3-(3-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one (36):

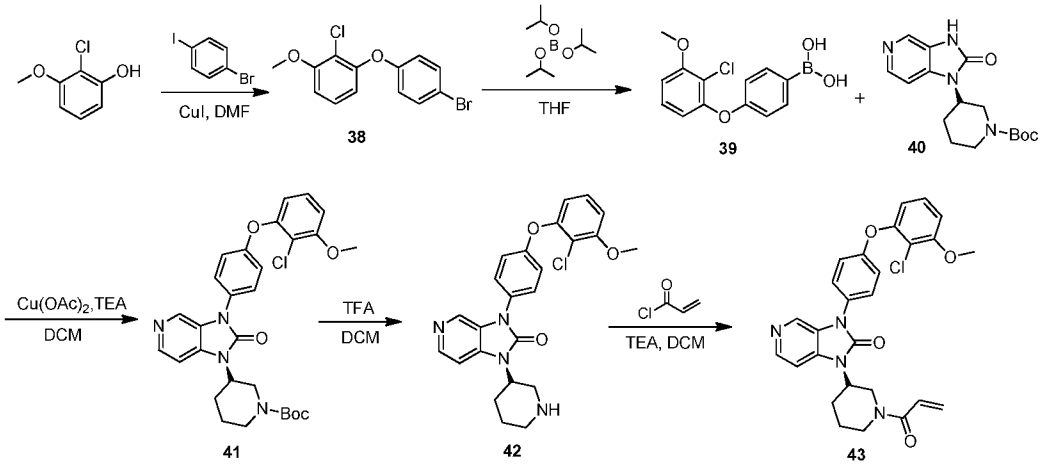
Intermediate 35 (420 mg) was dissolved in DCM (8.0 mL), added TFA (2.0 mL), the mixture was stirred for 1 h at RT. The solvent was removed under reduce pressure, the residue was added saturated $NaHCO_3$, extracted with EA and dried with Na_2SO_4, filtered and concentrated, obtained crude product 13 used next step without purification, colorless oil, Yield: 28 mg, 72.7%. ^1H NMR (400 MHz, $CDCl_3$):δ = 8.44 (s, 1H), 8.35 (s, 1H), 7.49-7.54 (m, 1H), 7.29-7.40 (m, 4H), 7.25 (s, 1H), 7.08-7.17 (m, 5H), 6.85-6.88 (m, 2H), 6.74-6.76 (m, 1H), 3.86 (s, 2H). LCMS (ESI) m /z = 395 $[M+H]^+$.

Step 3: N-(3-(2-oxo-3-(3-phenoxyphenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide (37):

Intermediate 36 (35 mg, 0.089 mmol, 1.0 eq) was dissolved in THF (4.0 mL), added acryloyl chloride (9 mg, 0.098 mmol, 1.1 eq) slowly at 0°C, the mixture solution was stirred for 0.5 h at RT, the reaction was added water and extracted with EA, dried with Na_2SO_4, filtered and concentrated, the residue was purification with silica gel plate (DCM : MeOH = 40:1) to obtain product 14, colorless oil, Yield: 21 mg, 52.7%. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.45 (s, 1H), δ = 8.37 (d, *J* = 5.2 Hz, 1H), 7.98 (s, 1H), 7.75 (s, 1H), 7.47-7.55 (m, 3H), 7.34-7.40 (m, 3H), 7.28-7.30 (m, 1H), 7.09-7.17 (m, 5H), 6.43 (d, *J* = 16.8 Hz, 1H), 6.19-6.25 (m, 1H), 5.77 (d, *J* = 10.4 Hz, 1H). LCMS (ESI) m /z = 449 $[M+H]^+$.

Example 8

(S)-1-(1-acryloylpiperidin-3-yl)-3-(4-(2-chloro-3-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one



Step 1: 1-(4-bromophenoxy)-2-chloro-3-methoxybenzene (38)

To a solution of 1-bromo-4-iodobenzene (2g, 7.04mmol) in dioxane (30 ml), was added 2-chloro-3-methoxyphenol (1g, 7.04mmol), CuI (0.134 g, 0.704mmol), Cs_2CO_3 (4.59 g, 14.08mmol), 3-(dimethylamino)propanoic acid hydrochloride (0.294 g, 0.212mmol). The mixture was stirred at 105 °C for 18 h, the mixture was filtered, before being poured into H_2O, The reaction mixture was extracted with DCM, Organic phase was purified by column chromatography on silica gel (PE) to give title product (1.2 g, yield 49.5 %).

^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.59 (d, J = 8.0 Hz, 1 H), 7.41 (d, J = 8.0 Hz, 1 H), 7.20-7.16 (m, 1H), 6.83 (d, J = 8.0 Hz, 1 H), 6.77 (d, J = 8.0 Hz, 1 H), 6.71 (d, J = 8.0 Hz, 1 H), 6.62 (d, J = 8.0 Hz, 1 H), 3.93 (s, 3H).

Step 2: (4-(2-chloro-3-methoxyphenoxy)phenyl)boronic acid (39)

To a solution of 1-(4-bromophenoxy)-2-chloro-3-methoxybenzene (38) (1.2 g, 3.08 mmol) in THF was cooled to -78 deg under N_2, n-BuLi(1.82mL, 4.61mmol) was added dropwise under same condition. The mixture was stirred for 30 min at -78 deg. triisopropyl borate (0.868g, 4.61 mmol) was added dropwise at -68 deg. After 15 min, the mixture warm to 8 deg and stirred for 2 h, then 2N HCl was added to adjust to pH=3 and stirred for 30 min, was added H_2O(15 mL), the mixture was extracted three times with EA and dried Na_2SO_4, to give title product for crude (0.4 g).

Step 3: (S)-tert-butyl 3-(3-(4-(2-chloro-3-methoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)piperidine-1-carboxylate (41)

(R)-tert-butyl 3-(2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)piperidine-1-carboxylate (40, prepared as described in Example 1, Step 1, 2 and 3), 0.1 g, 0.314 mmol), (4-(2-chloro-3-methoxyphenoxy) phenyl) boronic acid (39) (0.174 g, 0.628 mmol), TEA (63 mg, 0.628 mmol) and 4 A molecular sieves (0.1 g) were added to DCM (10 mL) in a vial

Copper (II) acetate (57 mg, 0.314 mmol) was added in one portion. The mixture was stirred for about 22 h at 25 deg. Volatile components were removed under vacuum , before being poured into H_2O, The reaction mixture was extracted with EA, Organic phase was purified by column chromatography on silica gel (gradient: DCM/MeOH=100/1-50/1) to give the title product (25 mg, yield 14.4 %). LCMS: m/z = 552 $[M+H]^+$.

Step 4: (S)-3-(4-(2-chloro-3-methoxyphenoxy)phenyl)-1-(piperidin-3-yl)-1H-imidazo[4,5-c]pyridin-2(3H)-one (42)

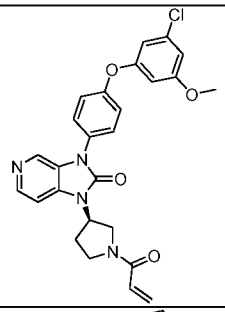
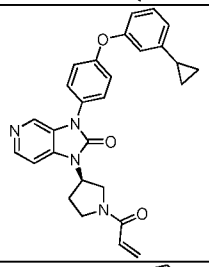
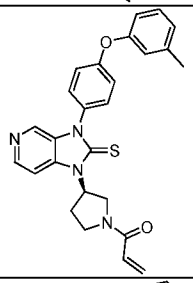
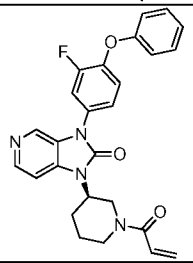
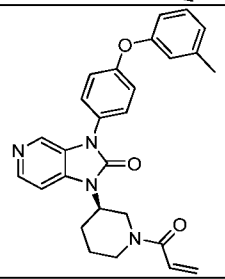
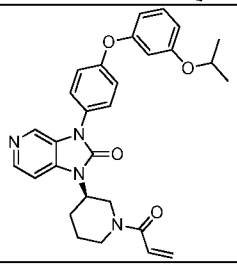
To a solution of (R)-tert-butyl-3-(3-(4-(2-chloro-3-methoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)piperidine-1-carboxylate (5) (25 mg, 0.045 mmol) were added to CF_3COOH/DCM = 4/1 (5 mL) in one portion. The mixture was stirred for about 1 h at rt. Volatile components were removed under vacuum to give the title product of crude product (20 mg), and directly used in next step without further purification. LCMS: m/z = 451 $[M+H]^+$.

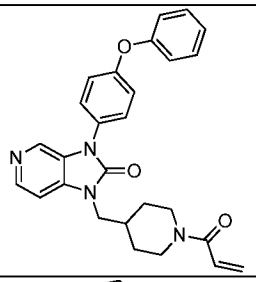
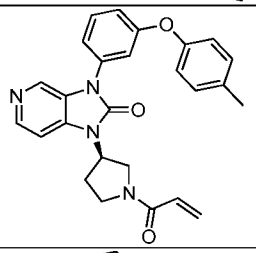
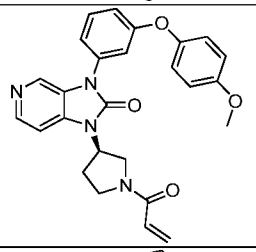
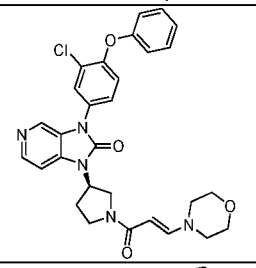
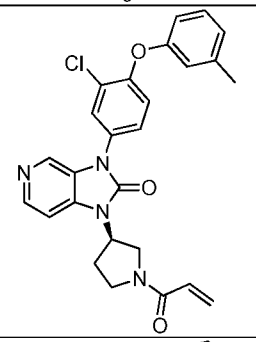
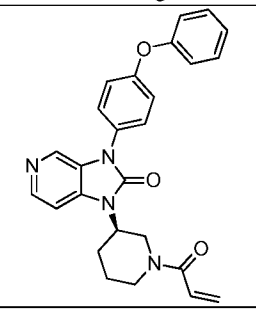
Step 5: (S)-1-(1-acryloylpiperidin-3-yl)-3-(4-(2-chloro-3-methoxyphenoxy)- phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one (43)

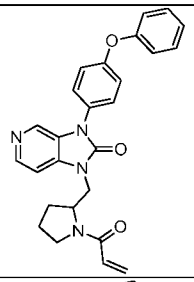
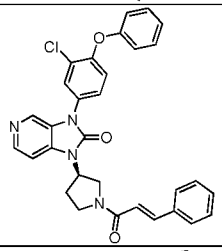
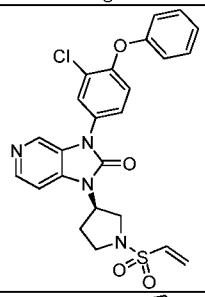
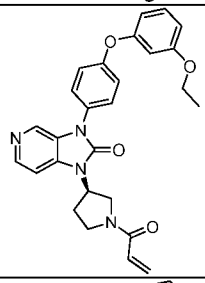
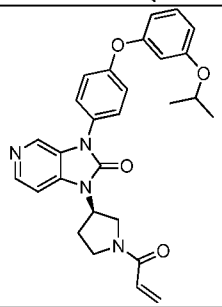
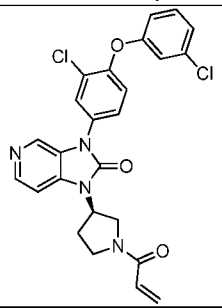
To a solution of Acryloyl chloride (4 mg, 0.044 mmol) in DCM (1 mL) was added to a stirred solution of (R)-3-(4-(2-chloro-3-methoxyphenoxy)phenyl)-1-(piperidin-3-yl)-1H-imidazo[4,5-c]pyridin-2(3H)-one (6)(20 mg, 0.044 mmol) and TEA (9mg, 0.88 mmol) in DCM (5 mL) at 0° C. The reaction mixture was stirred for 1 h, poured onto brine and extracted with DCM. The organic layer was dried, concentrated and recrystallized from DCM/MeOH=100/1 to give the title product (3.5 mg, yield 15.7 %).

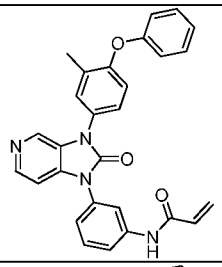
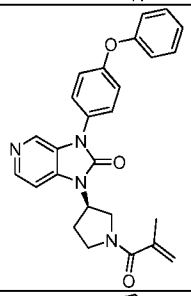
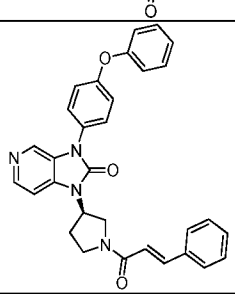
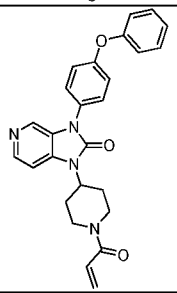
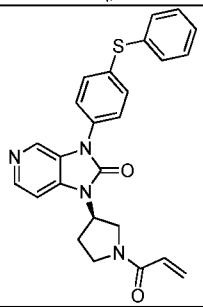
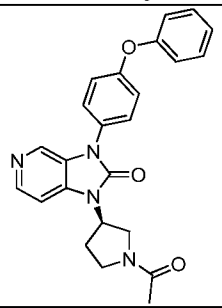
^{1}H-NMR(400 MHz, $CDCl_3$): δ 8.41 (br, 1H), 8.34 (br, 1H), 7.44 (d, J = 8.0 Hz, 2H), 7.30-7.23 (m, 2H), 7.11 (d, J = 8.0 Hz, 2H), 6.82(d, J = 8.0 Hz, 1H), 6.74 (d, J = 8.0 Hz, 1H), 6.61-6.58 (m, 1H), 6.43-6.14 (m, 1H), 5.74 (br, 1H), 4.84 (br, 1H), 4.22-4.09 (m, 2H), 3.96 (s, 3H), 3.48 (br, 0.6H), 3.18 (br, 0.6H), 2.64-2.54 (m, 1H), 2.16-2.13 (m, 1H), 2.02-2.00 (m, 1H), 1.68 (br, 1H). LCMS: m/z = 506 $[M+H]^+$.

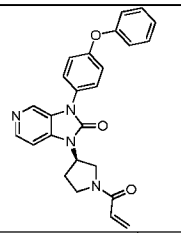
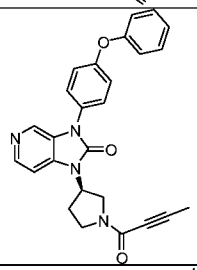
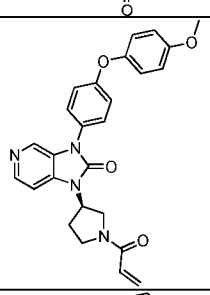
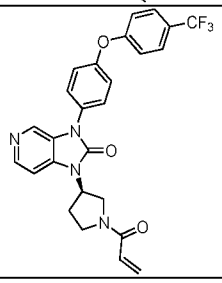
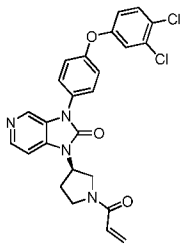
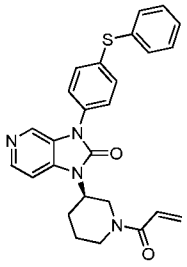
The following additional Examples 9-165 shown in the Table below were prepared following the procedures outlined in the general methods above and detailed in Examples 1-8.

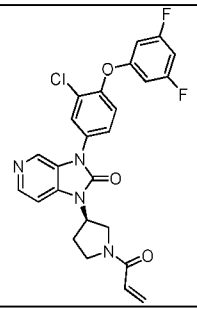
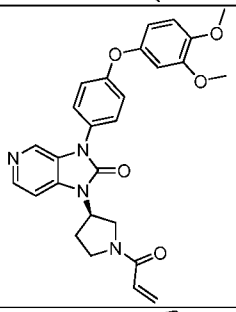
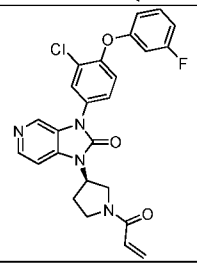
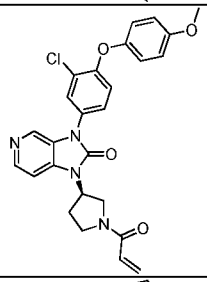
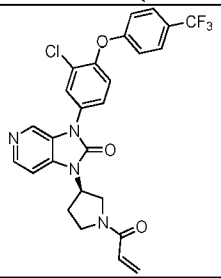
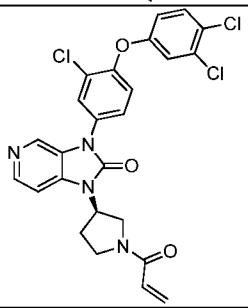
Entry	Structure	MS(cald) $[M+H]^+$ / MS (found)	Name
9		491.14 / 491.1, 492.1	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-chloro-5-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
10		467.20/ 467.2	(R)-1-(1-acryloylpyrrolidin-3-yl) -3-(4-(3-cyclopropylphenoxy)phenyl) -1H-imidazo[4,5-c]pyridin-2(3H)-one
11		457.16/ 457.1	(R)-1-(3-(2-thioxo-3-(4-(m-tolyloxy)phenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin -1-yl)pyrrolidin-1-yl)prop-2-en-1-one
12		459.18/ 459.2	(R)-1-(1-acryloylpiperidin-3-yl)-3-(3-fluoro-4-phenoxyphenyl) -1H-imidazo[4,5-c]pyridin-2(3H)-one
13		455.20/ 455.2	(R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(m-tolyloxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
14		499.23/ 499.2	(R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(3-isopropoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one

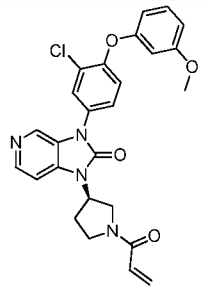
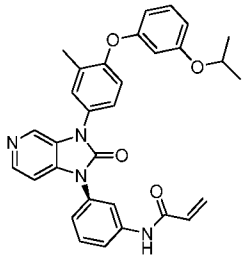
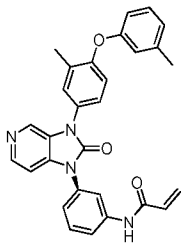
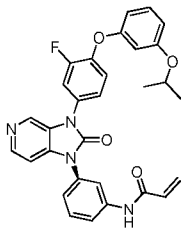
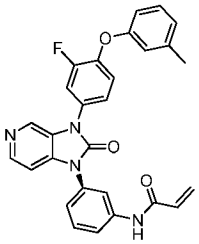
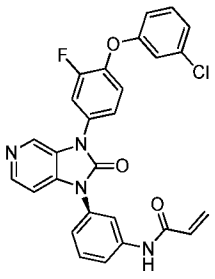
15		456.20/ 456.2	1-((1-acryloylpiperidin-4-yl)methyl)-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
16		441.18/ 441.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-(p-tolyloxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
17		457.18/ 457.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-(4-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
18		546.18/ 560.1,561.1,280.7, 281.4	(R,E)-3-(3-chloro-4-phenoxyphenyl)-1-(1-(3-morpholinoacryloyl)pyrolidin-3-yl)-1H-imidazo[4,5-c]-pyridin-2(3H)-one
19		475.15/ 475.2,477.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-(m-tolyloxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
20		441.18/ 441.2	(R)-1-(1-acryloylpiperidin-3-yl)-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one

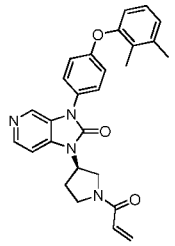
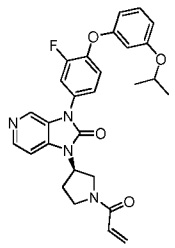
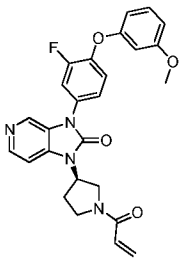
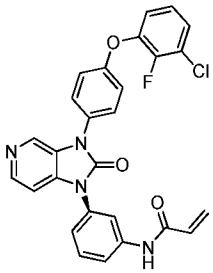
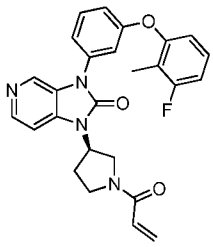
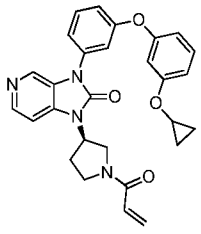
21		441.18/ 441.2	1-((1-acryloylpyrrolidin-2-yl)methyl)-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
22		537.16/ 537.1, 538.1	(R,E)-3-(3-chloro-4-phenoxyphenyl)-1-(1-cinnamoylpyrrolidin-3-yl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
23		497.10/ 497.1, 498.1	(R)-3-(3-chloro-4-phenoxyphenyl)-1-(1-(vinylsulfonyl)pyrrolidin-3-yl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
24		471.20/ 471.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-ethoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
25		485.21/ 485.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-isopropoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
26		495.09 / 495.0, 497.1	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-(3-chlorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one

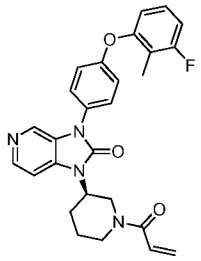
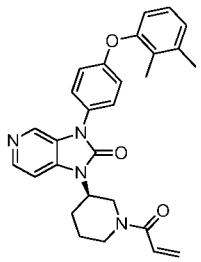
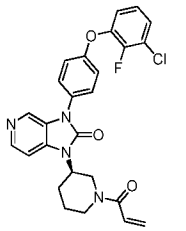
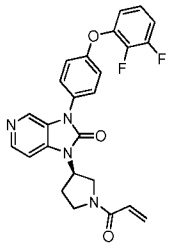
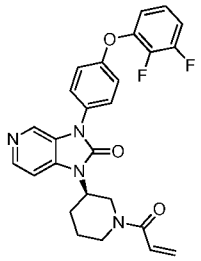
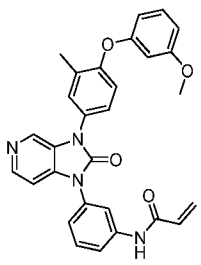
27		463.17 / 463.2	N-(3-(3-(3-methyl-4-phenoxyphenyl) -2-oxo-2,3-dihydro-1H-imidazo [4,5-c]pyridin-1-yl)phenyl)acrylamide
28		441.18/441.1	(R)-1-(1-methacryloylpyrrolidin-3-yl)-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
29		503.20/503.2	(R,E)-1-(1-cinnamoylpyrrolidin-3-yl)-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
30		441.08/441.0	1-(1-acryloylpiperidin-4-yl)-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
31		442.14/442.1	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(phenylthio)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
32		415.17 / 415.1	(R)-1-(1-acetylpyrrolidin-3-yl)-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one

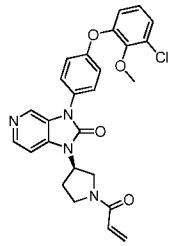
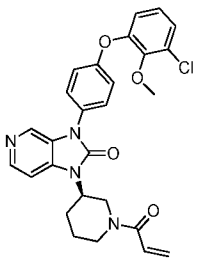
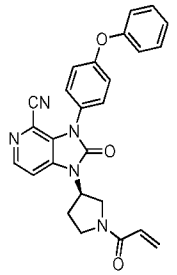
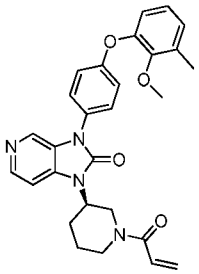
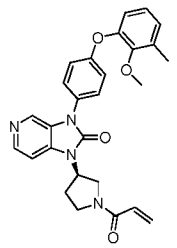
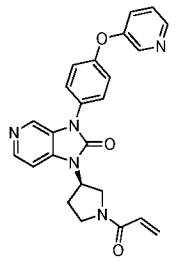
33		427.17 / 427.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
34		439.17 / 439.2	(R)-1-(1-(but-2-ynoyl)pyrrolidin-3-yl)-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
35		457.18 / 457.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(4-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
36		495.16 / 495.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(4-(trifluoromethyl)phenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
37		495.09 / 495.1, 496.1, 497.1, 498.1	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3,4-dichlorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
38		456.16	(R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(phenylthio)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one

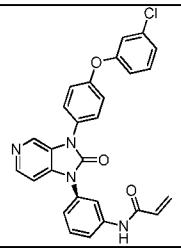
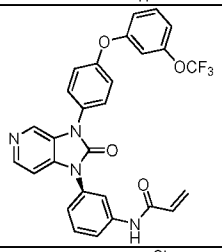
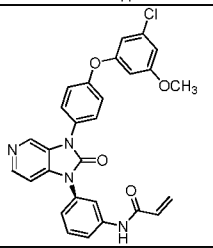
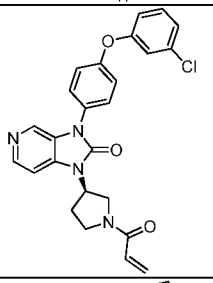
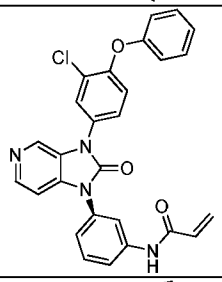
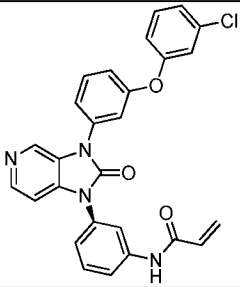
39		497.11 / 497.1, 498.1	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-(3,5-difluorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
40		487.19 / 487.1	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3,4-dimethoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
41		479.12 / 479.1,481.1	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-(3-fluorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
42		491.14 / 491.1,492.1	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-(4-methoxyphenoxy) phenyl)-1H-imidazo[4,5-c]pyridine-2(3H)-one
43		529.12 / 529.1, 530.1	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-(4-(trifluoromethyl)phenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
44		529.05 / 529.0, 530.1, 531.0, 532.0	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-(3,4-dichlorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one

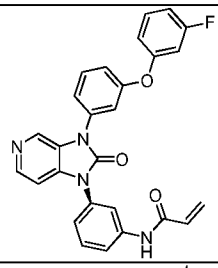
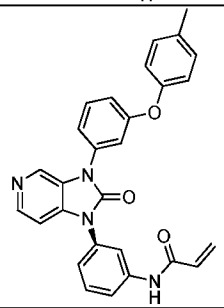
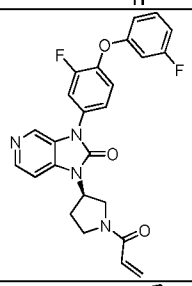
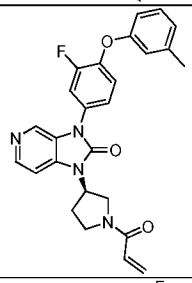
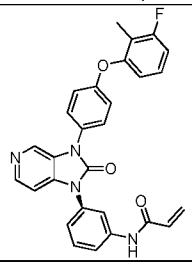
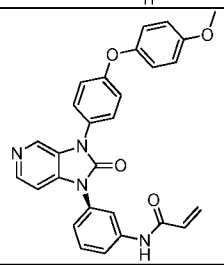
45		491.14 / 491.1, 493.1	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro -4-(3-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
46		521.21/ 521.2	N-(3-(3-(4-(3-isopropoxyphenoxy)-3-methylphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c] pyridin-1-yl)phenyl)acrylamide
47		477.18 / 477.2	N-(3-(3-(3-methyl-4-(m-tolyloxy)phenyl) -2-oxo-2,3-dihydro-1H-imidazo [4,5-c]pyridin-1-yl)phenyl)acrylamide
48		525.19 / 525.2	N-(3-(3-(3-fluoro-4-(3-isopropoxy phenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl) phenyl)acrylamide
49		481.16 / 481.2	N-(3-(3-(3-fluoro-4-(m-tolyloxy) phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl) phenyl)acrylamide
50		501.11 / 501.1	(N-(3-(3-(4-(3-chlorophenoxy)-3-fluorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl) acrylamide

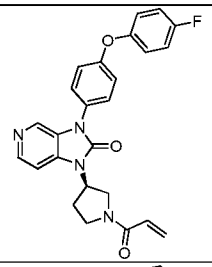
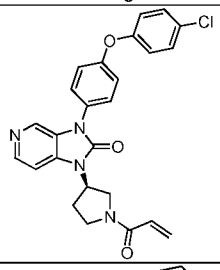
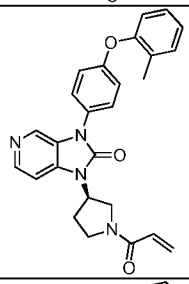
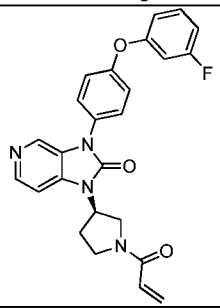
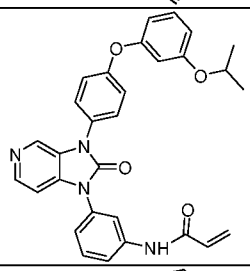
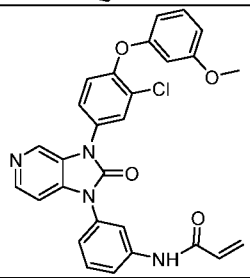
51		455.20 / 455.2	(R)-1-(1-acryloylpyrrolidin-3-yl) -3-(4-(2,3-dimethylphenoxy) phenyl)-1H-imidazo[4,5-c] pyridin-2(3H)-one
52		503.20 / 503.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-fluoro-4-(3-isopropoxyphenoxy)phenyl) -1H-imidazo[4,5-c]pyridin-2(3H)-one
53		475.17 / 475.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-fluoro-4-(3-methoxyphenoxy)phenyl) -1H-imidazo[4,5-c]pyridin-2(3H)-one
54		501.11 / 501.1	N-(3-(3-(4-(3-chloro-2-fluoro phenoxy)phenyl)-2-oxo-2,3-dihydro -1H-imidazo[4,5-c]pyridin-1-yl) phenyl)acrylamide
55		459.18 / 459.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-(3-fluoro-2-methylphenoxy) phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
56		483.20 / 483.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3 -(3-(3-cyclopropoxyphenoxy)phenyl) -1H-imidazo[4,5-c]pyridin-2(3H)-one

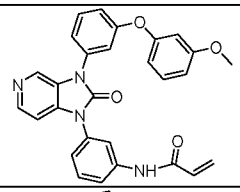
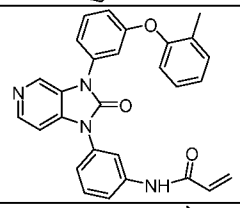
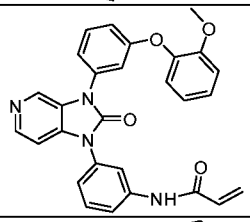
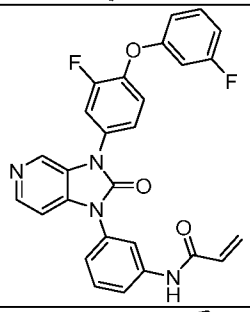
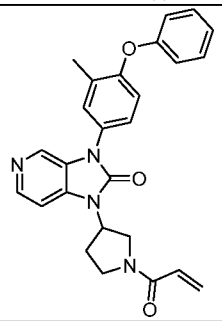
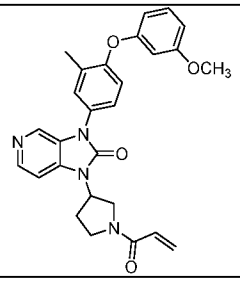
57		473.19 / 473.2	(R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(3-fluoro-2-methylphenoxy)phenyl) -1H-imidazo[4,5-c]pyridin-2(3H)-one
58		469.22 / 469.2	(R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(2,3-dimethylphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
59		493.14 / 493.2	(R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(3-chloro-2-fluorophenoxy)phenyl) -1H-imidazo[4,5-c]pyridin-2(3H)-one
60		463.15 / 463.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(2,3-difluorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
61		477.17 / 477.2	(R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(2,3-difluorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
62		493.18 / 493.2	N-(3-(3-(4-(3-methoxyphenoxy)-3-methylphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl) phenyl)acrylamide

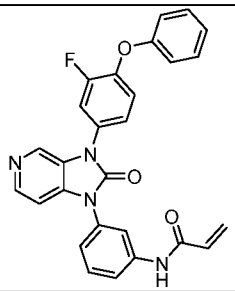
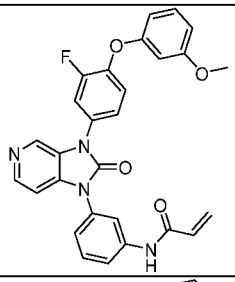
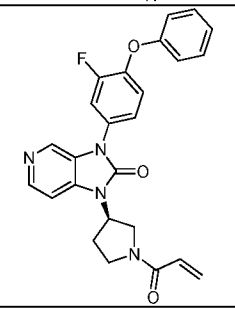
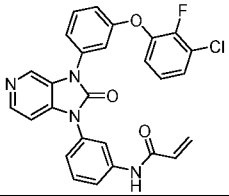
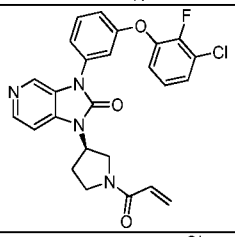
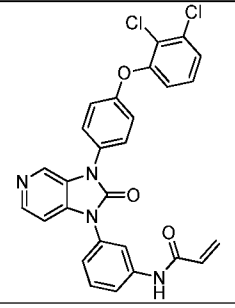
63		491.14 / 491.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-chloro-2-methoxyphenoxy) phenyl)-1H-imidazo[4,5-c]pyridine -2(3H)-one
64		505.16 / 505.2	(R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(3-chloro-2-methoxyphenoxy)phenyl) -1H-imidazo[4,5-c]pyridin-2(3H)-one
65		452.16 / 452.2	((R)-1-(1-acryloylpyrrolidin-3-yl)-2-oxo-3-(4-phenoxyphenyl)-2,3-di hydro-1H-imidazo[4,5-c]pyridine-4-carbonitrile
66		485.21 / 485.2	(R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(2-methoxy-3-methylphenoxy) phenyl)-1H-imidazo[4,5-c] pyridin-2(3H)-one
67		471.20 / 471.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(2-methoxy-3-methylphenoxy)phenyl) -1H-imidazo[4,5-c]pyridin-2(3H)-one
68		428.16 / 428.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(pyridin-3-yloxy)phenyl)-1H -imidazo[4,5-c]pyridin-2(3H)-one

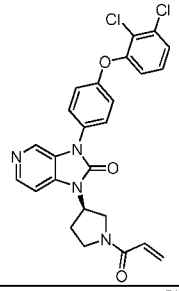
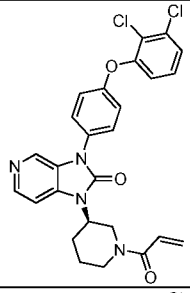
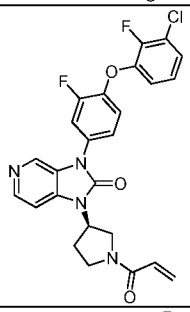
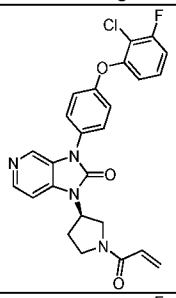
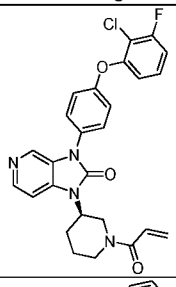
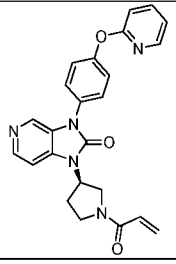
69		484.11/ 484.1	N-(3-(3-(4-(3-chlorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
70		533.14 / 533.1	N-(3-(2-oxo-3-(4-(3-(trifluoromethoxy)phenoxy)phenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
71		514.12 / 514.1	N-(3-(3-(4-(3-chloro-5-methoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
72		462.13 / 462.1	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-chlorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
73		484.11 / 484.1	N-(3-(3-(3-chloro-4-phenoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
74		484.11 / 484.1	N-(3-(3-(3-(3-chlorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide

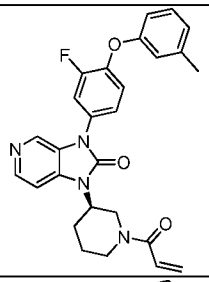
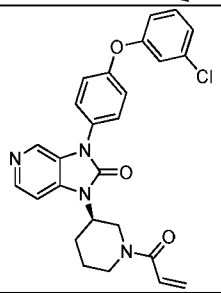
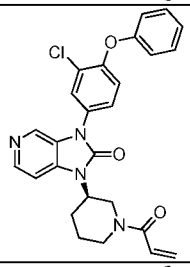
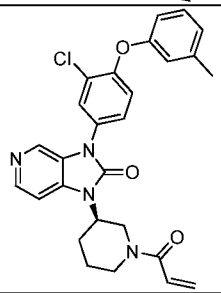
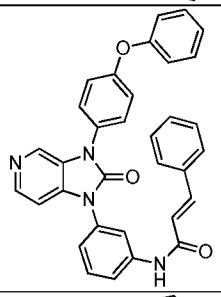
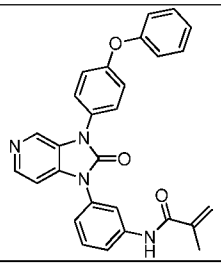
75		467.15 / 467.2	N-(3-(3-(3-(3-fluorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
76		463.17 / 463.2	N-(3-(2-oxo-3-(3-(p-tolyloxy)phenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
77		463.15 / 463.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-fluoro-4-(3-fluorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
78		459.18 / 459.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-fluoro-4-(m-tolyloxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
79		481.16 / 481.2	N-(3-(3-(4-(3-fluoro-2-methylphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
80		479.17 / 479.2	N-(3-(3-(4-(4-methoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide

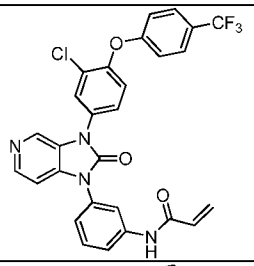
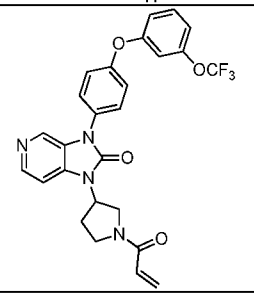
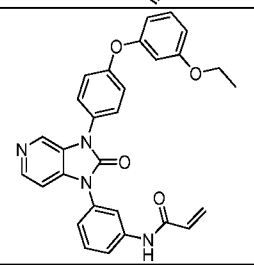
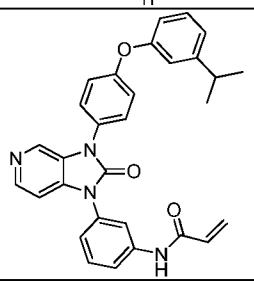
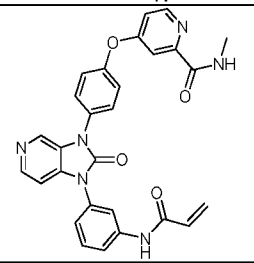
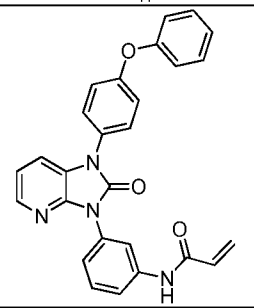
81		445.16 / 445.1	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(4-fluorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
82		461.13 / 461.1	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(4-chlorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
83		441.18 / 441.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(o-tolyloxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
84		445.16/ 445.1	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-fluorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
85		506.20 / 507.2	N-(3-(3-(4-(3-isopropoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
86		512.13 / 513.1	N-(3-(3-(3-chloro-4-(3-methoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide

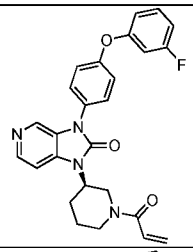
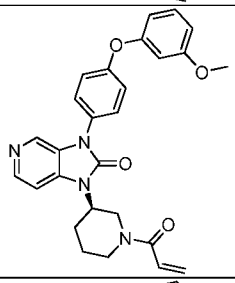
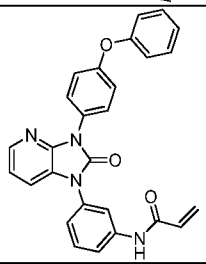
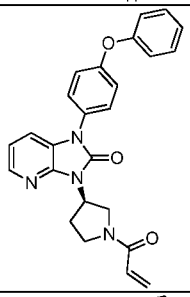
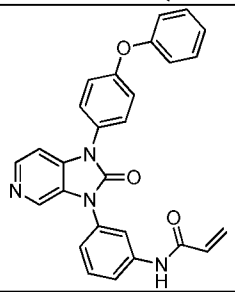
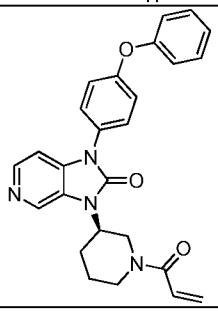
87		478.16 / 479.2	N-(3-(3-(3-(3-methoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
88		462.17 / 463.2	N-(3-(2-oxo-3-(3-(o-tolyloxy)phenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
89		478.16 / 479.2	N-(3-(3-(3-(2-methoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
90		484.13 / 485.0	N-(3-(3-(3-fluoro-4-(3-fluorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
91		440.18 / 441.2	1-(1-acryloylpyrrolidin-3-yl)-3-(3-methyl-4-phenoxyphenyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one
92		470.20 / 471.2	1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-methoxyphenoxy)-3-methylphenyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one

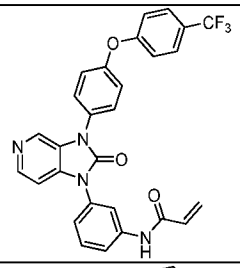
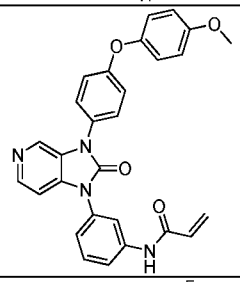
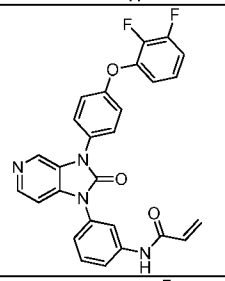
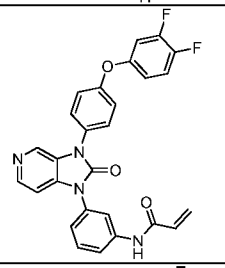
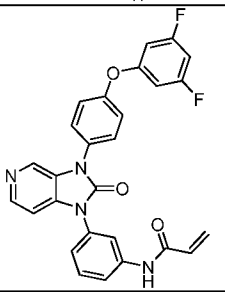
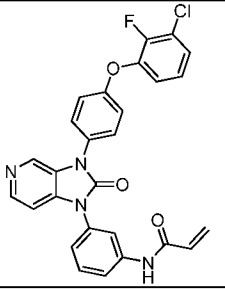
93		466.14 / 467.1	N-(3-(3-(3-fluoro-4-phenoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
94		496.15 / 497.2	N-(3-(3-(3-fluoro-4-(3-methoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
95		444.16 / 445.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-fluoro-4-phenoxyphenyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one
96		500.11 / 501.1	N-(3-(3-(3-(3-chloro-2-fluorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
97		478.12 / 479.1	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-(3-chloro-2-fluorophenoxy)phenyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one
98		516.08 / 517.1	N-(3-(3-(4-(2,3-dichlorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide

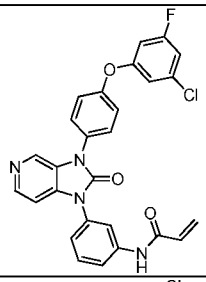
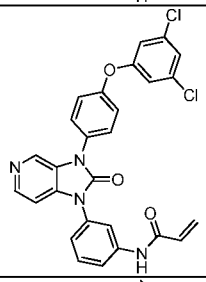
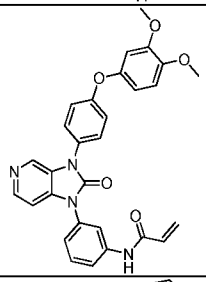
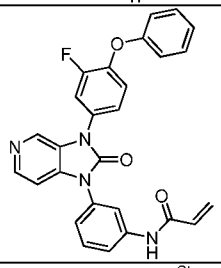
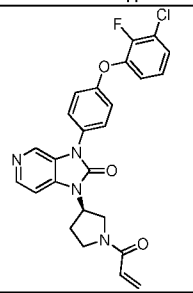
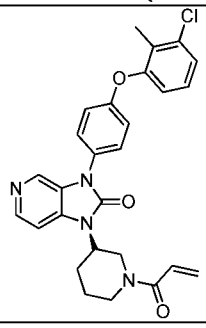
99		494.09 / 495.1	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(2,3-dichlorophenoxy)phenyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one
100		508.11 / 509.1	(R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(2,3-dichlorophenoxy)phenyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one
101		496.11 / 497.1	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-chloro-2-fluorophenoxy)-3-fluorophenyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one
102		478.12 / 479.1	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(2-chloro-3-fluorophenoxy)phenyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one
103		492.14 / 493.2	(R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(2-chloro-3-fluorophenoxy)phenyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one
104		427.16 / 428.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(pyridin-2-yloxy)phenyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one

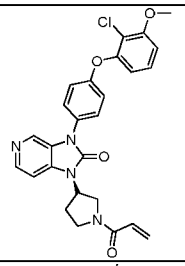
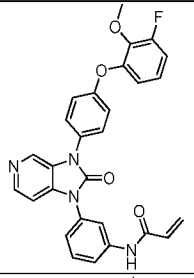
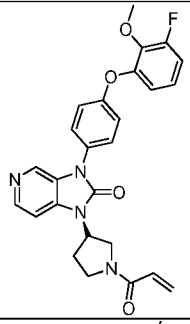
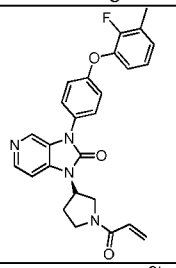
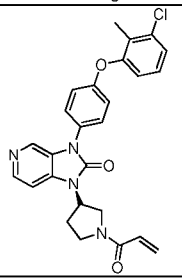
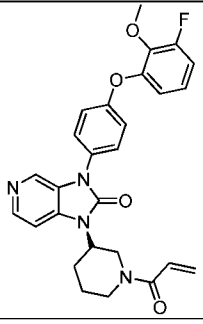
105		473.19 / 473.2	(R)-1-(1-acryloylpiperidin-3-yl)-3-(3-fluoro-4-(m-tolyloxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
106		475.15 / 475.2	(R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(3-chlorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
107		475.15 / 475.2	(R)-1-(1-acryloylpiperidin-3-yl)-3-(3-chloro-4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
108		488.16 / 488.1	(R)-1-(1-acryloylpiperidin-3-yl)-3-(3-chloro-4-(m-tolyloxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
109		525.18 / 525.2	N-(3-(2-oxo-3-(4-phenoxyphenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)cinnamamide
110		463.17 / 463.2	N-(3-(2-oxo-3-(4-phenoxyphenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)methacrylamide

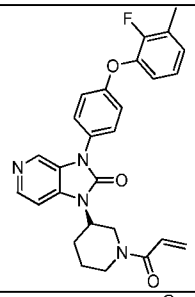
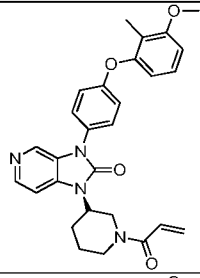
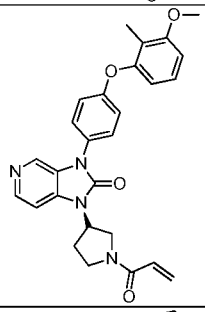
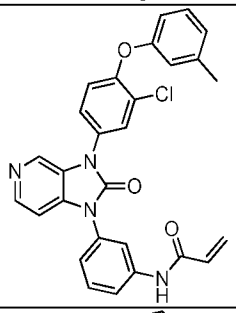
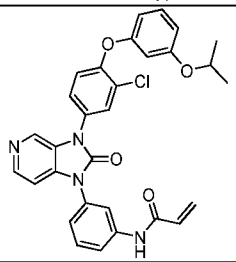
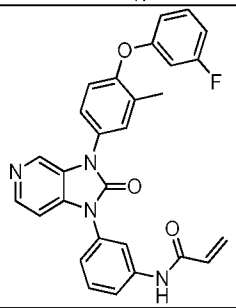
111		551.10 / 551.1	N-(3-(3-(3-chloro-4-(4-(trifluoromethyl)phenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
112		511.15 / 511.2	1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-(trifluoromethoxy)phenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
113		493.18 / 493.2	N-(3-(3-(4-(3-ethoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
114		491.20 / 491.2	N-(3-(3-(4-(3-isopropylphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
115		507.17 / 507.2	4-(4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)phenoxy)-N-methylpicolinamide
116		449.15 / 449.2	N-(3-(2-oxo-1-(4-phenoxyphenyl)-1H-imidazo[4,5-b]pyridin-3(2H)-yl)phenyl)acrylamide

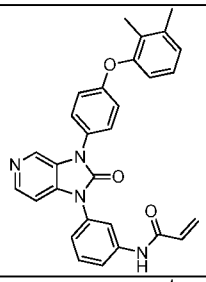
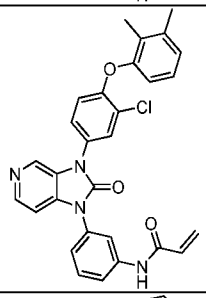
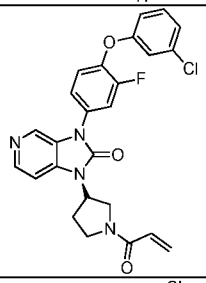
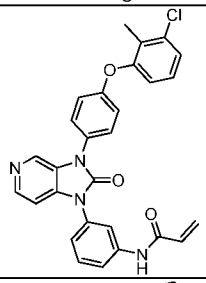
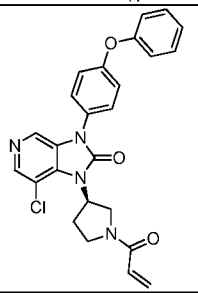
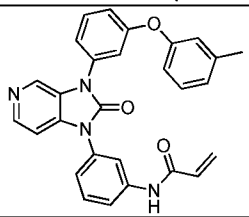
117		459.18 / 459.2	(R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(3-fluorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
118		471.20 / 471.2	(R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(3-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
119		449.15 / 449.2	N-(3-(2-oxo-3-(4-phenoxyphenyl)-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)phenyl)acrylamide
120		427.17 / 427.2	(R)-3-(1-acryloylpyrrolidin-3-yl)-1-(4-phenoxyphenyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one
121		449.15 / 449.2	N-(3-(2-oxo-1-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-3(2H)-yl)phenyl)acrylamide
122		441.18 / 441.2	(R)-3-(1-acryloylpiperidin-3-yl)-1-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one

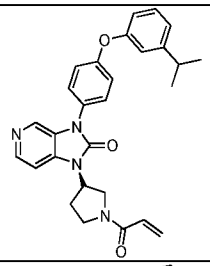
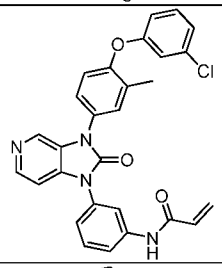
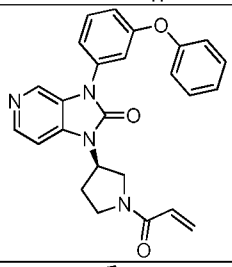
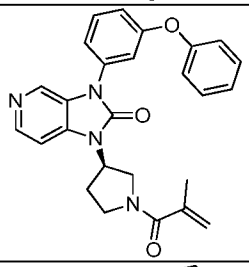
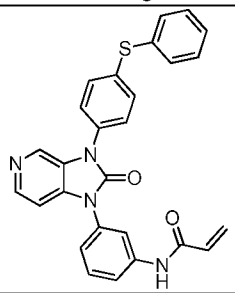
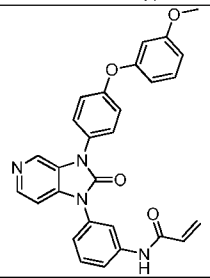
123		517.14 / 517.1	N-(3-(2-oxo-3-(4-(4-(trifluoromethyl)phenoxy)phenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
124		479.16 / 479.2	N-(3-(3-(4-(4-methoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
125		485.13 / 485.1	N-(3-(3-(4-(2,3-difluorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
126		485.13 / 485.1	N-(3-(3-(4-(3,4-difluorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
127		485.13 / 485.1	N-(3-(3-(4-(3,5-difluorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
128		501.11 / 501.1 503.1	N-(3-(3-(4-(3-chloro-2-fluorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide

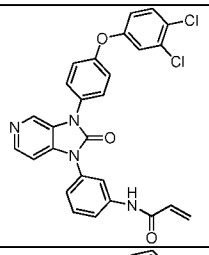
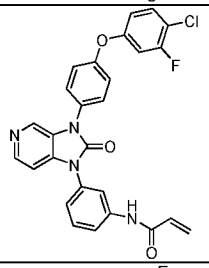
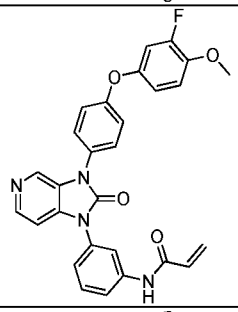
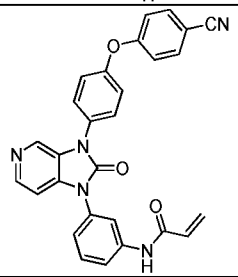
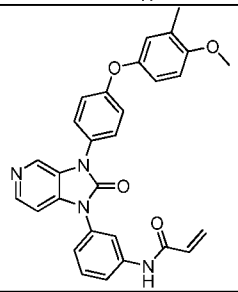
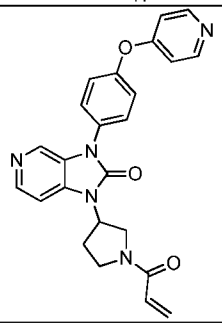
129		501.11 / 501.1 503.1	N-(3-(3-(4-(3-chloro-5-fluorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
130		517.08 / 517.1 519.1	N-(3-(3-(4-(3,5-dichlorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
131		509.17 / 509.2	N-(3-(3-(4-(3,4-dimethoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
132		467.14 / 467.1	N-(3-(3-(3-fluoro-4-phenoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
133		479.12 / 479.1	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-chloro-2-fluorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
134		489.16 / 489.1,490.1	(R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(3-chloro-2-methylphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one

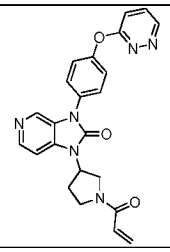
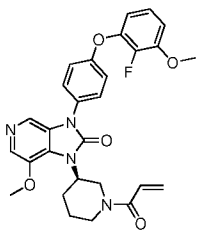
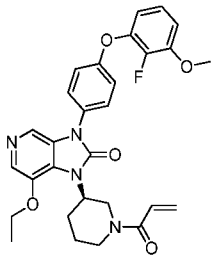
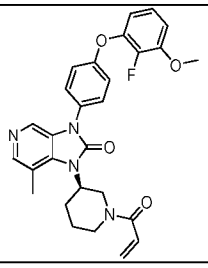
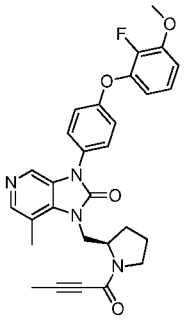
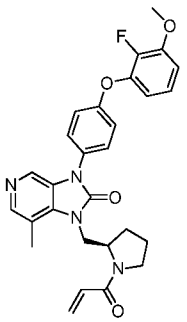
135		491.14 / 491.1 492.1	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(2-chloro-3-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
136		497.15 / 497.2	N-(3-(3-(4-(3-fluoro-2-methoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
137		475.17 / 475.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-fluoro-2-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
138		459.18 / 459.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(2-fluoro-3-methylphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
139		475.15 / 475.2 476.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-chloro-2-methylphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
140		489.19 / 489.2	(R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(3-fluoro-2-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one

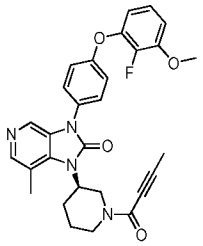
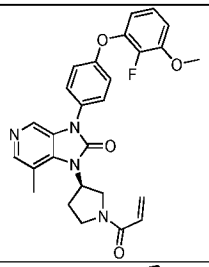
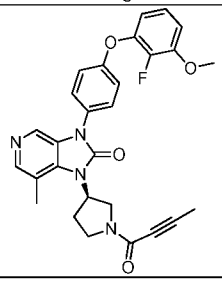
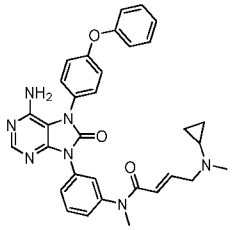
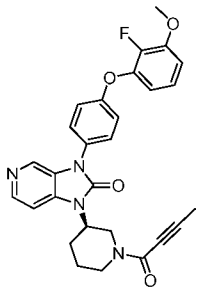
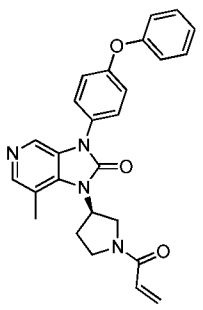
141		473.19 / 473.2	(R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(2-fluoro-3-methylphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
142		485.21 / 485.2	(R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(3-methoxy-2-methylphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
143		471.2 / 471.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-methoxy-2-methylphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
144		497.13 / 497.1 498.1	N-(3-(3-(3-chloro-4-(m-tolyloxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
145		541.16 / 541.2 542.2	N-(3-(3-(3-chloro-4-(3-isopropoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
146		481.16 / 481.1	N-(3-(3-(4-(3-fluorophenoxy)-3-methylphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide

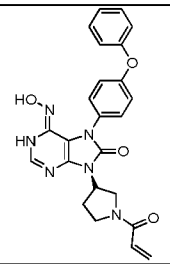
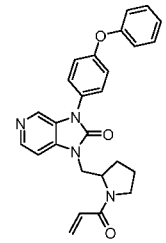
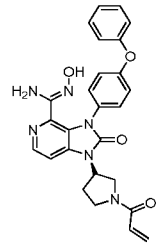
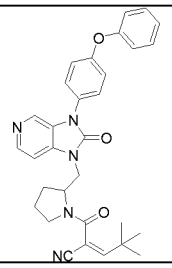
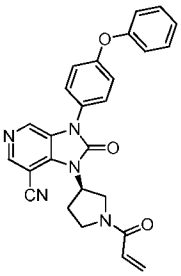
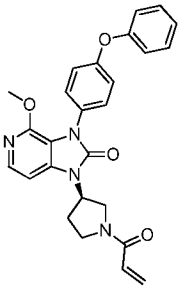
147		477.18 / 477.2	N-(3-(3-(4-(2,3-dimethylphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
148		511.15 / 511.2	N-(3-(3-(3-chloro-4-(2,3-dimethylphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
149		479.12 / 479.1 480.1	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-chlorophenoxy)-3-fluorophenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
150		497.13 / 497.1 480.1	N-(3-(3-(4-(3-chloro-2-methylphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
151		461.13/ 461.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-7-chloro-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
152		463.17 / 463.2	N-(3-(2-oxo-3-(3-(m-tolyloxy)phenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide

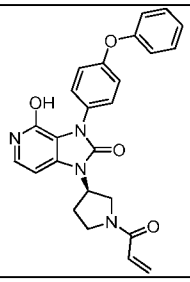
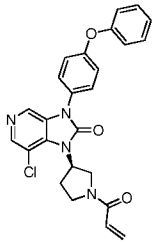
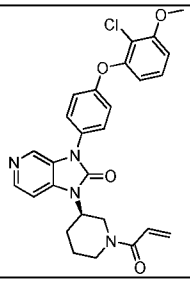
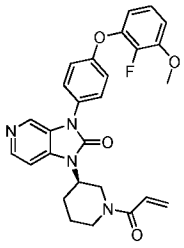
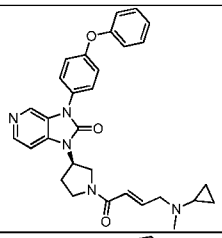
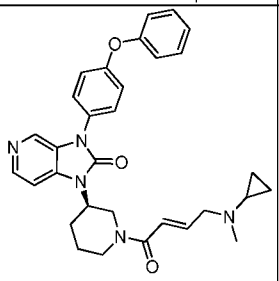
153		469.22 / 469.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-isopropylphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
154		497.13 / 497.1 498.1	N-(3-(3-(4-(3-chlorophenoxy)-3-methylphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
155		427.17 / 427.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
156		441.18 / 441.2	(R)-1-(1-methacryloylpyrrolidin-3-yl)-3-(3-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
157		464.13	N-(3-(2-oxo-3-(4-(phenylthio)phenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
158		479.16 / 479.2	N-(3-(3-(4-(3-methoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide

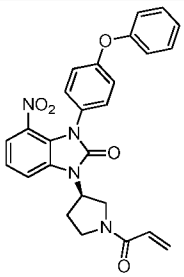
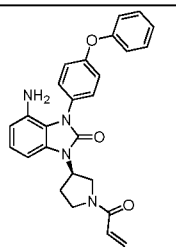
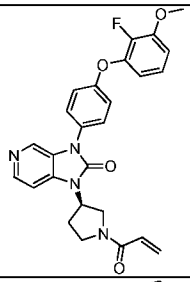
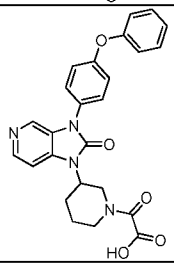
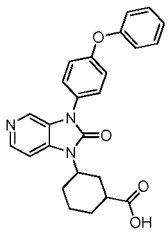
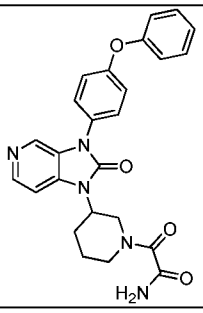
159		517.08 / 517.1	N-(3-(3-(4-(3,4-dichlorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
160		501.11 / 501.1	N-(3-(3-(4-(4-chloro-3-fluorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
161		497.15 / 497.2	N-(3-(3-(4-(3-fluoro-4-methoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
162		474.15 / 474.2	N-(3-(3-(4-(4-cyanophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
163		493.18 / 493.2	N-(3-(3-(4-(4-methoxy-3-methylphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
164		427.16 / 428.2	1-(1-acryloylpyrrolidin-3-yl)-3-(4-(pyridin-4-yloxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one

165		428.16 / 429.1	1-(1-acryloylpyrrolidin-3-yl)-3-(4-(pyridazin-3-yloxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
166		519.20 / 519.2	(R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(2-fluoro-3-methoxyphenoxy)phenyl)-7-methoxy-1H-imidazo[4,5-c]pyridin-2(3H)-one
167		533.21/ 533.2	(R)-1-(1-acryloylpiperidin-3-yl)-7-ethoxy-3-(4-(2-fluoro-3-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
168		503.20/ 503.2	(R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(2-fluoro-3-methoxyphenoxy)phenyl)-7-methyl-1H-imidazo[4,5-c]pyridin-2(3H)-one
169		515.20/ 515.2	(R)-1-((1-(but-2-ynoyl)pyrrolidin-2-yl)methyl)-3-(4-(2-fluoro-3-methoxyphenoxy)phenyl)-7-methyl-1H-imidazo[4,5-c]pyridin-2(3H)-one
170		503.20/ 503.2	(R)-1-((1-acryloylpyrrolidin-2-yl)methyl)-3-(4-(2-fluoro-3-methoxyphenoxy)phenyl)-7-methyl-1H-imidazo[4,5-c]pyridin-2(3H)-one

171		515.20/ 515.2	(R)-1-(1-(but-2-ynoyl)piperidin-3-yl)-3-(4-(2-fluoro-3-methoxyphenoxy)phenyl)-7-methyl-1H-imidazo[4,5-c]pyridin-2(3H)-one
172		489.19/ 489.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(2-fluoro-3-methoxyphenoxy)phenyl)-7-methyl-1H-imidazo[4,5-c]pyridin-2(3H)-one
173		501.19/ 501.2	(R)-1-(1-(but-2-ynoyl)pyrrolidin-3-yl)-3-(4-(2-fluoro-3-methoxyphenoxy)phenyl)-7-methyl-1H-imidazo[4,5-c]pyridin-2(3H)-one
174		562.25/ 562.2	(E)-N-(3-(6-amino-8-oxo-7-(4-phenoxyphenyl)-7H-purin-9(8H)-yl)phenyl)-4-(cyclopropyl(methyl)amino)-N-methylbut-2-enamide
175		501.19/ 501.2	(R)-1-(1-(but-2-ynoyl)piperidin-3-yl)-3-(4-(2-fluoro-3-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
176		441.18/ 441.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-7-methyl-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one

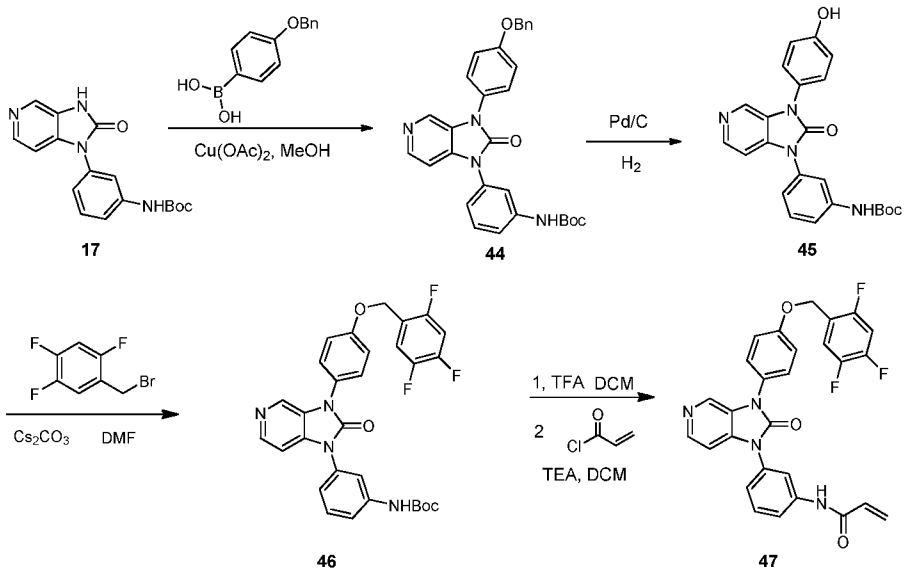
177		459.17/ 459.2	(S,Z)-9-(1-acryloylpyrrolidin-3-yl)-6-(hydroxyimino)-7-(4-phenoxyphenyl)-7,9-dihydro-1H-purin-8(6H)-one
178		440.52 440.5	1-(1-Acryloyl-pyrrolidin-2-ylmethyl)-3-(4-phenoxy-phenyl)-1,3-dihydro-imidazo[4,5-c]pyridin-2-one
179		485.19/ 485.2	(S,Z)-1-(1-acryloylpyrrolidin-3-yl)-N'-hydroxy-2-oxo-3-(4-phenoxyphenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridine-4-carboximidamide
180		521.62 521.6	4,4-Dimethyl-2-{2-[2-oxo-3-(4-phenoxy-phenyl)-2,3-dihydro-imidazo[4,5-c]pyridin-1-ylmethyl]-pyrrolidine-1-carbonyl}-pent-2-enenitrile
181		452.16/ 452.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-2-oxo-3-(4-phenoxyphenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridine-7-carbonitrile
182		457.18/ 457.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-4-methoxy-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one

183		443.16/ 443.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-4-hydroxy-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
184		461.13/ 461.1	(R)-1-(1-acryloylpyrrolidin-3-yl)-7-chloro-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
185		505.16/ 505.2	(R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(2-chloro-3-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
186		489.19/ 489.2	(R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(2-fluoro-3-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
187		510.24/ 501.2	(R,E)-1-(1-(4-(cyclopropyl(methyl)amino)but-2-enoyl)pyrrolidin-3-yl)-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
188		524.26/ 524.3	(R,E)-1-(1-(4-(cyclopropyl(methyl)amino)but-2-enoyl)piperidin-3-yl)-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one

189		471.16/ 471.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-4-nitro-3-(4-phenoxyphenyl)-1H-benzo[d]imidazol-2(3H)-one
190		441.18/ 441.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-4-amino-3-(4-phenoxyphenyl)-1H-benzo[d]imidazol-2(3H)-one
191		475.17/ 475.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(2-fluoro-3-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
192		459.16/ 459.1	2-oxo-2-(3-(2-oxo-3-(4-phenoxyphenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)piperidin-1-yl)acetic acid
193		430.17/ 430.1	3-(2-oxo-3-(4-phenoxyphenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl) cyclohexanecarboxylic acid
194		458.18/ 458.2	2-oxo-2-(3-(2-oxo-3-(4-phenoxyphenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)piperidin-1-yl)acetamide

Example 195

N-(3-(2-oxo-3-(4-((2,4,5-trifluorobenzyl)oxy) phenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide



Step1: tert-butyl (3-(3-(4-(benzyloxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)carbamate (44)

Intermediate 17 (0.914 g, 2.80 mmol, 1.0 eq) was dissolved in MeOH (20.0 mL), addedCupric acetate (59 mg, 0.28 mmol, 0.1 eq), (4-(benzyloxy)phenyl)boronic acid (0.83 g, 3.64 mmol, 1.3 eq), the mixture solution was stirred for 5 h under reflux. Then filtered the solution and removed the solution under reduce pressure, added water and extracted with EA, dried with Na_2SO_4, filtered and concentrated, purified with silica column (DCM: MeOH = 100:1～50:1) to obtain the title product as gray solid, Yield: 160 mg, 11.2%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.37-8.43 (m, 1H), 7.77 (s, 1H), 7.31-7.51 (m, 10H), 7.24 (d, *J* = 8.0 Hz, 1H), 7.15 (d, *J* = 8.8 Hz, 2H), 6.66 (s, 1H), 5.14 (s, 2H), 1.52 (s, 9H). LCMS (ESI) m /z = 509 $[M+H]^+$.

Step 2: tert-butyl (3-(3-(4-hydroxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c] pyridin-1-yl)phenyl)carbamate (45):

Intermediate 44 (120 mg, 0.24 mmol, 1.0 eq) was dissolved in MeOH (10.0 mL), added Pd/C (40 mg), the mixture solution was stirred for 3 h under H_2 atmosphere. Then filtered the solution and the solvent was removed under reduce pressure to obtain the title product as gray solid, Yield: 83 mg, 84.1%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.36 (d, *J* = 4.4 Hz, 1H), 8.30 (s, 1H), 7.79 (s, 1H), 7.45-7.49 (m, 1H), 7.37 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.8 Hz, 1H), 7.23

(s, 1H), 7.16 (d, J = 5.6 Hz, 1H), 6.97 (d, J = 8.4 Hz, 2H), 6.71 (s, 1H), 1.52 (s, 9H). LCMS (ESI) m /z = 419 $[M+H]^+$.

Step 3: tert-butyl (3-(3-(4-hydroxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)carbamate (46)

To a solution of intermediate 45 (0.05 g, 0.12 mmol) in DMF (5 mL) was added 2,4,5-trifluorobenzyl bromide (0.027 g, 0.12 mmol) and Cs_2CO_3 (0.078 g, 0.24 mmol). The mixture was stirred at 25°C, after 2hrs, the reaction mixture was partitioned between H_2O and DCM, the organic layer was washed by brine, dried over Na_2SO_4, filtered, concentrated to give the title product as a crude product (0.04 g). LCMS (ESI) m /z = 563 $[M+H]^+$.

Step 4: N-(3-(2-oxo-3-(4-((2,4,5-trifluorobenzyl)oxy)phenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide (47)

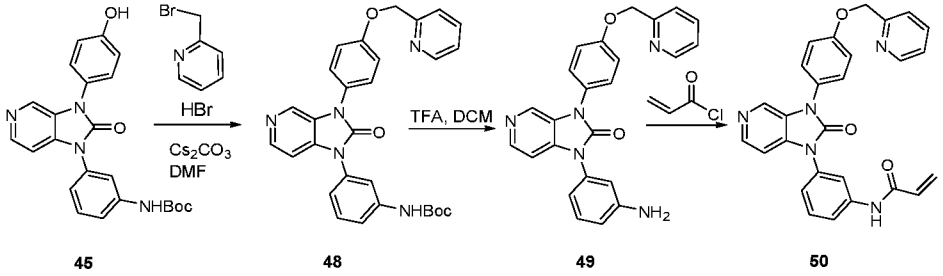
To a solution of intermediate 46 (0.04 g, crude) in DCM (4 mL) was added TFA (1.5 mL) at 0°C, the mixture was allowed to warm to 25°C, after 1h, the mixture was adjusted to pH=7 with $NaHCO_3$ solution, the residue was partitioned between H_2O and DCM, the organic layer was washed by brine, dried over Na_2SO_4, filtered, concentrated to give a crude title product (0.02 g). LCMS (ESI) m /z = 463 $[M+H]^+$.

To a stirred solution of crude product (0.02 g, 0.043 mmol) in DCM (10 mL) was added acryloyl chloride (0.004 g, 0.043 mmol) and TEA (0.009 g, 0.086 mmol). The mixture was stirred at 15°C, after 0.5h, the mixture was partitioned between H_2O and DCM, the organic layer was washed by brine, dried over Na_2SO_4, filtered, concentrated and purified by Pre-TLC to give the title product (5 mg, 22.4%).

^1H NMR (400 MHz, $CDCl_3$): δ 5.06(s, 1H), 5.67-5.70 (d, 1H), 6.13-6.16 (d, 1H), 6.29-6.33(d, 1H), 6.91-6.93(m, 1H), 7.04-7.09(m, 3H), 7.16-7.19(m, 1H), 7.31-7.34(m, 3H), 7.45-7.47(m, 2H), 7.94(s, 1H), 8.28-8.34(m, 3H). LCMS (ESI) m /z = 517 $[M+H]^+$.

Example 196

N-(3-(2-oxo-3-(4-(pyridin-2-ylmethoxy)phenyl)-2,3-dihydro-1H-imidazo[4,5-c] pyridin-1-yl)phenyl)acrylamide



45 48 49 50

Step 1: tert-butyl (3-(2-oxo-3-(4-(pyridin-2-ylmethoxy)phenyl)-2,3-dihydro-1H-imidazo [4,5-c]pyridin-1-yl)phenyl)carbamate (48):

Intermediate 39 (76 mg, 0.183 mmol, 1.0 eq) was dissolved in DMF (2.0 mL), addedCesium carbonate (178 mg, 0.548 mmol, 3.0 eq), 2-(bromomethyl)pyridine hydrobromide salt (51 mg, 0.201 mmol, 1.1 eq), the mixture solution was stirred for 2 h at room temperature. Then added water and extracted with EA, washed with brine, dried with Na_2SO_4, filtered and concentrated, purified with silica column (DCM: MeOH = 100:1～50:1) to obtain the title product, Yield: 48 mg, 51.9%. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.63 (d, *J* = 4.4 Hz, 1H), 8.36 (s, 1H), 8.35 (s, 1H), 7.75-7.77 (m, 2H), 7.55 (d, *J* = 7.6 Hz, 1H), 7.50 (d, *J* = 8.8 Hz, 2H), 7.44-7.48 (m, 1H), 7.32 (d, *J* = 8.0 Hz, 1H), 7.23 (d, *J* = 7.2 Hz, 1H), 7.17 (d, *J* = 9.2 Hz, 2H), 7.13 (d, *J* = 5.6 Hz, 1H), 6.67 (s, 1H), 5.29 (s, 2H), 1.52 (s, 9H). LCMS (ESI) m /z = 510 $[M+H]^+$.

Step 2: 1-(3-aminophenyl)-3-(4-(pyridin-2-ylmethoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one (49):

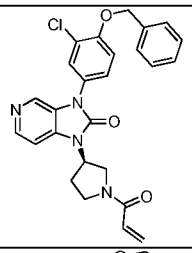
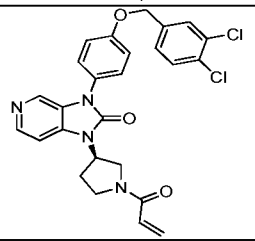
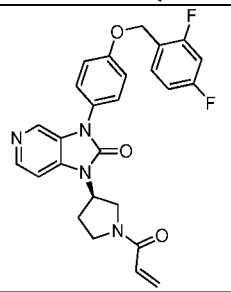
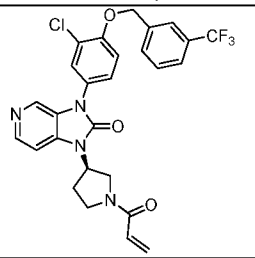
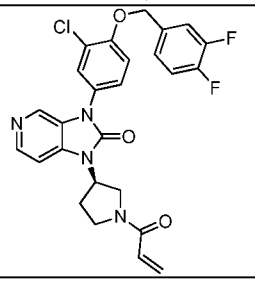
Intermediate 48 (48 mg) was dissolved in DCM (5.0 mL), added TFA (2.0 mL), the mixture was stirred for 1.5 h at RT, stopped and removed the solution under reduce pressure, the residue was added saturated $NaHCO_3$, extracted with EA and dried with Na_2SO_4, filtered and concentrated to obtain crude title product used next step without purification, yellow oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.63 (d, *J* = 4.4 Hz, 1H), 8.35 (s, 2H), 7.73-7.77 (m, 1H), 7.55 (d, *J* = 7.6 Hz, 1H), 7.50 (d, *J* = 9.2 Hz, 2H), 7.30-7.34 (m, 1H), 7.24 (s, 1H), 7.16 (d, *J* = 9.2 Hz, 2H), 7.11 (d, *J* = 4.8 Hz, 1H), 6.90 (d, *J* = 8.0 Hz, 1H), 6.87 (s, 1H), 6.74-6.76 (m, 1H), 5.29 (s, 2H), 3.87 (s, 2H). LCMS (ESI) m /z = 410 $[M+H]^+$.

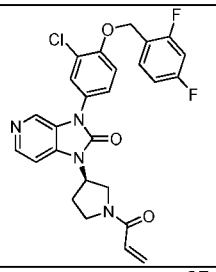
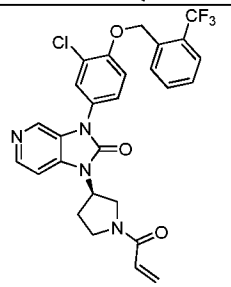
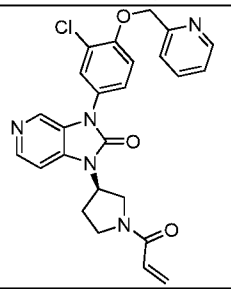
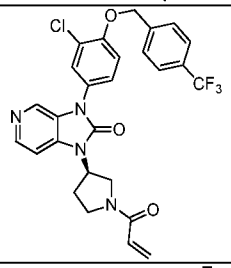
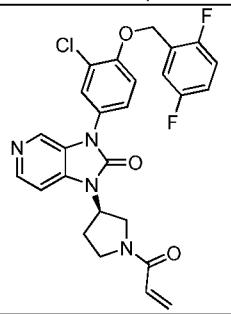
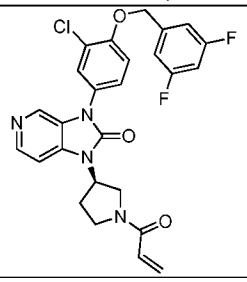
Step 3: N-(3-(2-oxo-3-(4-(pyridin-2-ylmethoxy)phenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide (50):

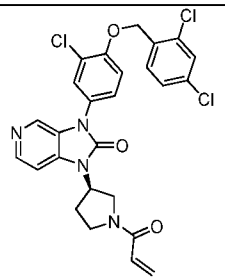
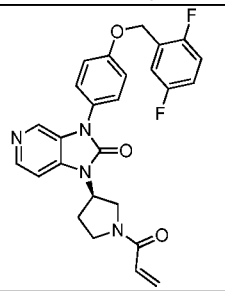
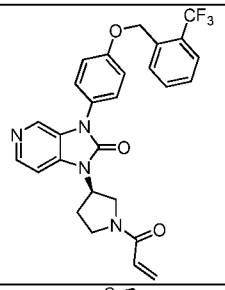
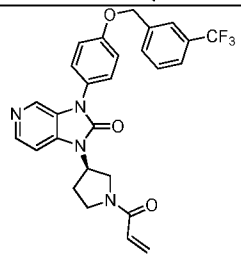
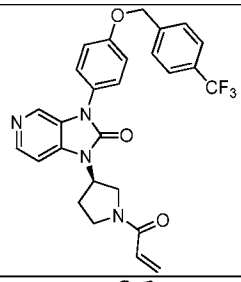
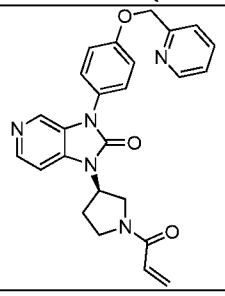
Crude intermediate 49 (42 mg, 0.103 mmol, 1.0 eq) was dissolved in THF (4.0 mL), added DIEA (20 mg, 0.154 mmol, 1.5 eq), acryloyl chloride (10.2 mg, 0.113 mmol, 1.1 eq) slowly at 0°C, the mixture solution was stirred for 0.5 h at RT, followed the reaction with LCMS, stopped the reaction added water and extracted with EA, dried with Na_2SO_4, filtered and concentrated, the residue was purification with silica gel plate (DCM : MeOH = 30:1) to obtain the title product, colorless oil, Yield: 8.0 mg, 16.8%. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.63 (d, *J* = 4.4 Hz, 1H), 8.36 (s, 1H), 8.35 (s, 1H), 8.32 (s, 1H), 7.99 (s, 1H), 7.73-7.77 (m, 1H), 7.56 (d, *J* = 7.6 Hz, 1H), 7.51 (d, *J* = 8.8 Hz, 2H), 7.41 (d, *J* = 7.2 Hz, 2H), 7.24-7.28 (m,

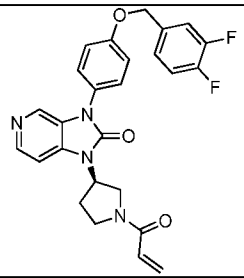
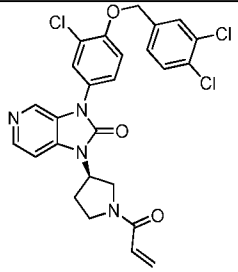
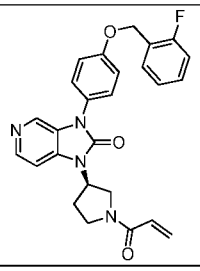
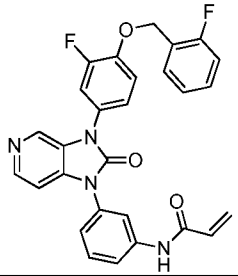
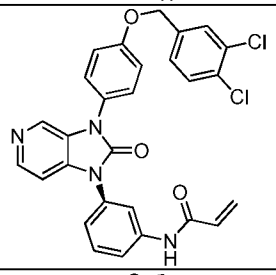
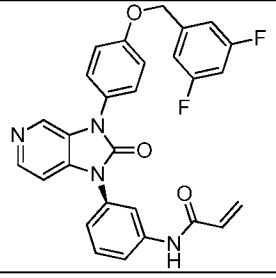
1H), 7.48 (d, J = 8.8 Hz, 2H), 7.11 (d, J = 5.2 Hz, 1H), 6.39 (d, J = 16.4 Hz, 1H), 6.16-6.23 (m, 1H), 5.71 (d, J = 10.4 Hz, 1H), 5.29 (s, 2H). LCMS (ESI) m /z = 464 $[M+H]^+$.

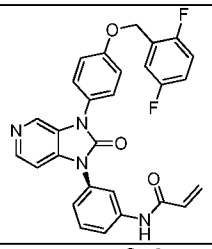
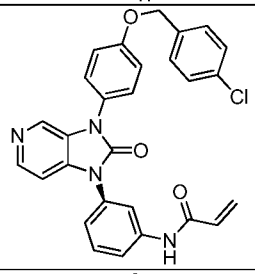
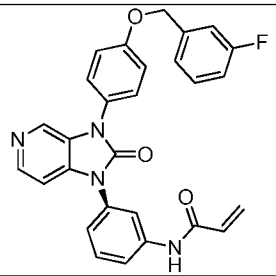
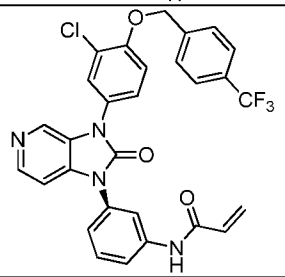
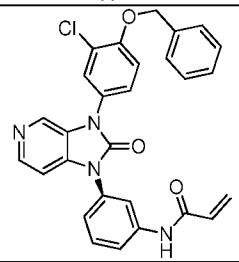
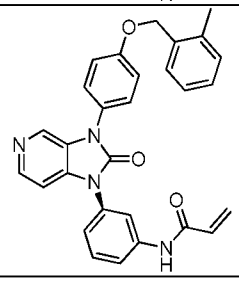
The following additional Examples 197-248 shown in the Table below were prepared following the procedures outlined in the general methods above and detailed in Examples 195-196.

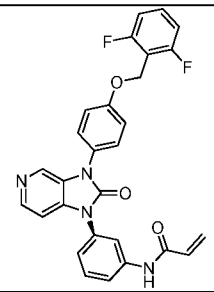
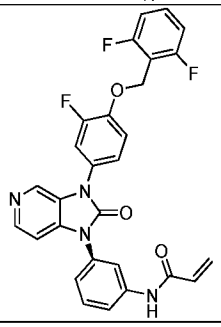
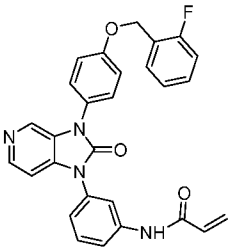
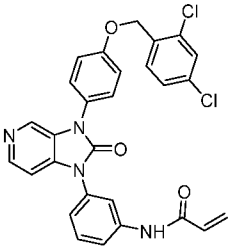
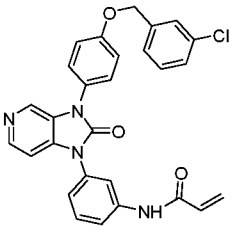
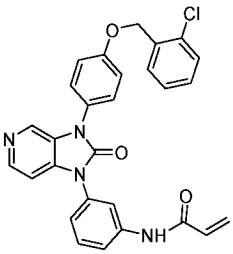
Entry	Structure	MS(cald) $[M+H]^+$ / MS (found)	Name
197		475.15 / 475.1,477.1	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(benzyloxy)-3-chlorophenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
198		509.11 / 509.1,511.1,510.1, 513.1	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-((3,4-dichlorobenzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
199		477.17 / 477.1	(R)-1-(1-acryloylpyrrolidin-3-yl)-3 -(4-((2,4-difluorobenzyl)oxy)phenyl) -1H-imidazo[4,5-c]pyridin-2(3H)-one
200		543.13 / 543.1,545.1,544.1, 546.1	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-((3-(trifluoromethyl)benzyl) oxy)phenyl)-1H-imidazo[4,5-c]pyridine -2(3H)-one
201		511.13 / 511.1,512.1	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-((3,4-difluorobenzyl) oxy)phenyl)-1H-imidazo[4,5-c]pyridine -2(3H)-one

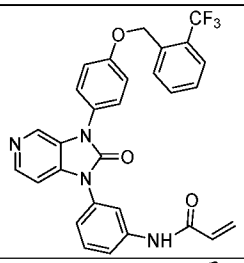
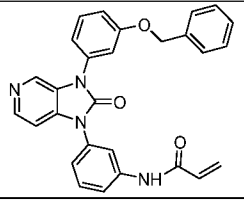
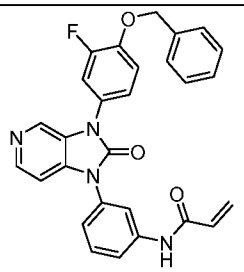
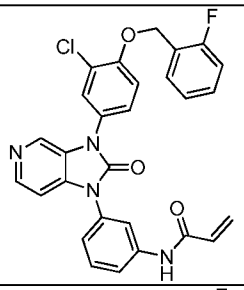
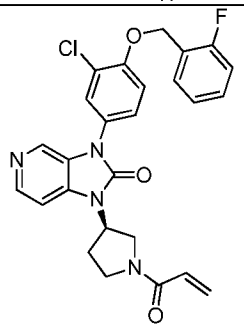
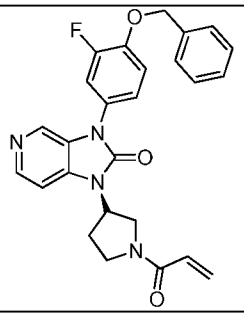
202		511.13 / 511.1,512.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro -4-((2,4-difluorobenzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
203		543.13 / 543.1,544.1	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro -4-((2-(trifluoromethyl)benzyl)oxy)phenyl) -1H-imidazo[4,5-c]pyridin-2(3H)-one
204		476.14 / 476.1,477.1,238.6, 239.3	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro -4-(pyridin-2-ylmethoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
205		543.13 / 543.2,544.1	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro -4-((4-(trifluoromethyl)benzyl)oxy)phenyl) -1H-imidazo[4,5-c]pyridin-2(3H)-one
206		511.13 / 511.1,512.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro -4-((2,5-difluorobenzyl)oxy)phenyl) -1H-imidazo[4,5-c]pyridin-2(3H)-one
207		511.13 / 511.1,513.1	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro -4-((3,5-difluorobenzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one

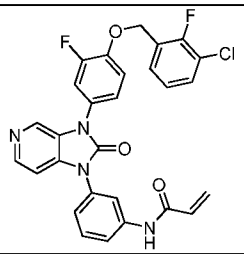
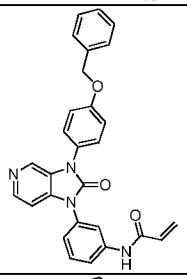
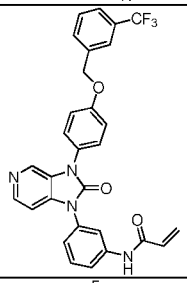
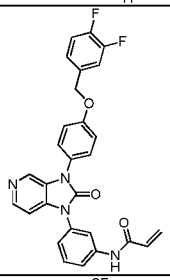
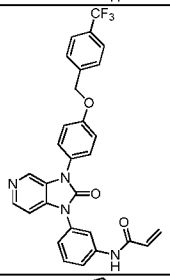
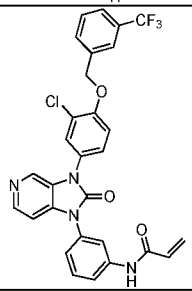
208		543.07 / 543.1,544.1	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-((2,4-dichlorobenzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
209		477.17 / 477.1	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-((2,5-difluorobenzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
210		509.17 / 509.1	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-((2-(trifluoromethyl)benzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridine-2(3H)-one
211		509.17 / 509.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-((3-(trifluoromethyl)benzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
212		509.17 / 509.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-((4-(trifluoromethyl)benzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
213		442.18 / 442.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(pyridin-2-ylmethoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one

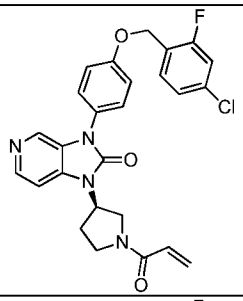
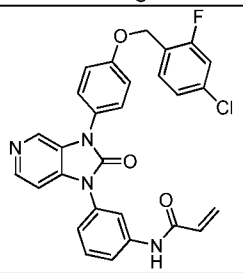
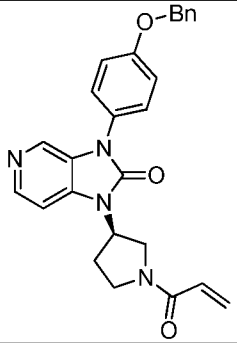
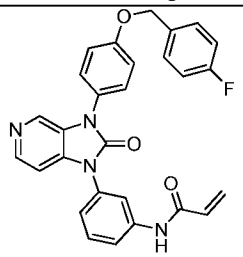
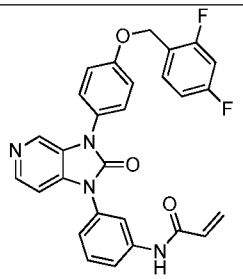
214		477.17 / 477.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-((3,4-difluorobenzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
215		543.07 / 543.1,544.1,545.0, 546.1	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-((3,4-dichlorobenzyl)oxy) phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
216		459.18 / 459.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-((2-fluorobenzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
217		499.15 / 499.2	N-(3-(3-(3-fluoro-4-((2-fluorobenzyl)oxy)phenyl) -2-oxo-2,3-dihydro-1H-imidazo[4,5-c] pyridin-1-yl)phenyl)acrylamide
218		532.09 / 532.1	N-(3-(3-(4-((3,4-dichlorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
219		499.15 / 499.2	N-(3-(3-(4-((3,5-difluorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide

220		499.15 / 499.2	N-(3-(3-(4-((2,5-difluorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
221		498.13 / 498.1	N-(3-(3-(4-((4-chlorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
222		481.16 / 481.2	N-(3-(3-(4-((3-fluorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
223		566.11 / 566.1	N-(3-(3-(3-chloro-4-((4-(trifluoromethyl)benzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
224		498.13 / 498.1	N-(3-(3-(4-(benzyloxy)-3-chlorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
225		477.19 / 477.2	N-(3-(3-(4-((2-methylbenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide

226		499.15 / 499.2	N-(3-(3-(4-((2,6-difluorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
227		517.14 / 517.1	N-(3-(3-(4-((2,6-difluorobenzyl)oxy)-3-fluorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
228		481.16 / 481.2	N-(3-(3-(4-((2-fluorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
229		531.09 / 531.1	N-(3-(3-(4-((2,4-dichlorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
230		497.13 / 497.1	N-(3-(3-(4-((3-chlorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
231		497.13 / 497.1	N-(3-(3-(4-((2-chlorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide

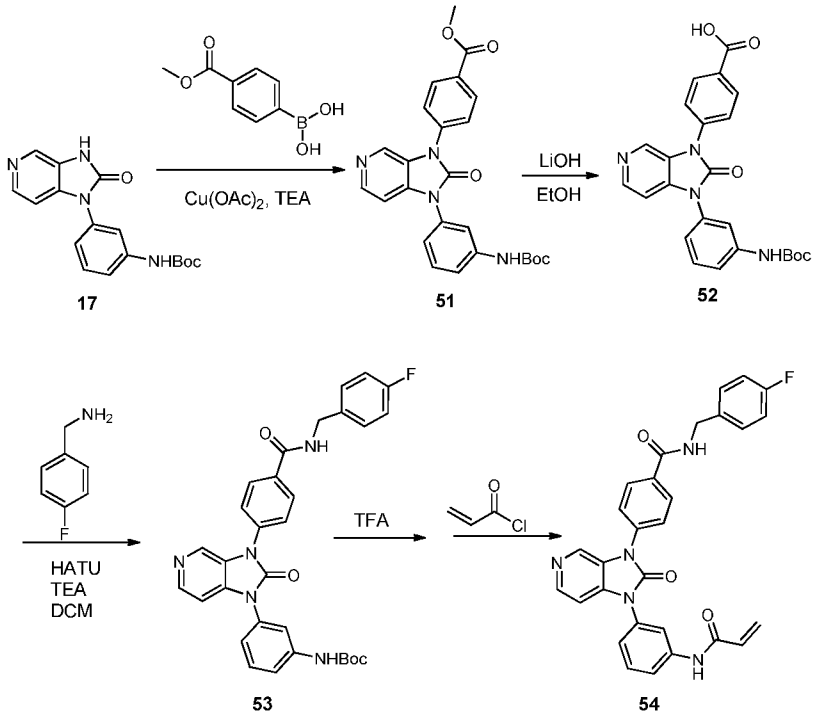
232		531.16 / 531.2	N-(3-(2-oxo-3-(4-((2-(trifluoromethyl)benzyl)oxy)phenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
233		463.17 / 463.2	N-(3-(3-(3-(benzyloxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
234		481.16 / 481.2	N-(3-(3-(4-(benzyloxy)-3-fluorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
235		515.12 / 515.1	N-(3-(3-(3-chloro-4-((2-fluorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
236		493.14 / 493.1	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-((2-fluorobenzyl)oxy)phenyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one
237		459.18 / 459.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(benzyloxy)-3-fluorophenyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one

238		533.11 / 533.1	N-(3-(3-(4-((3-chloro-2-fluorobenzyl)oxy)-3-fluorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
239		463.17 / 463.2	(N-(3-(3-(4-(benzyloxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
240		531.16 / 531.2	N-(3-(2-oxo-3-(4-((3-(trifluoromethyl)benzyl)oxy)phenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
241		499.15 / 499.1	N-(3-(3-(4-((3,4-difluorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
242		531.16 / 531.2	N-(3-(2-oxo-3-(4-((4-(trifluoromethyl)benzyl)oxy)phenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
243		565.12 / 565.1	N-(3-(3-(3-chloro-4-((3-(trifluoromethyl)benzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide

244		493.12 / 493.1	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-((4-chloro-2-fluorobenzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
245		515.14 / 515.1	N-(3-(3-(4-((4-chloro-2-fluorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
246		441.18 / 441.2	((R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(benzyloxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
247		481.16 / 481.2	N-(3-(3-(4-((4-fluorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
248		499.15 / 499.2	N-(3-(3-(4-((2,4-difluorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide

Example 249

4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)-N-(4-fluorobenzyl)benzamide



Step 1: methyl 4-(1-(3-((tert-butoxycarbonyl)amino)phenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)benzoate (51)

Intermediate 17 (0.96 g, 2.94 mmol, 1.0 eq) was dissolved in DCM (30.0 mL), added Cupric acetate (530 mg, 2.94 mmol, 1.0 eq), (4-(methoxycarbonyl)phenyl)boronic acid (1.06 g, 5.88 mmol, 2.0 eq), 4A molecular sieve (1.3 g) and TEA (1.23 mL, 0.617 mmol, 2.0 eq), the mixture solution was stirred for 20 h at RT. Then filtered the solution and removed the solution under reduce pressure, added water and extracted with EA, dried with Na_2SO_4, filtered and concentrated, purified with silica column (PE:EA = 4:1～1:1) to obtain the title product, brown solid, Yield: 420 mg, 33.2%. ^{1}H NMR (400 MHz, $CDCl_3$):δ = 8.25 (d, J = 8.0 Hz, 2H), 7.80 (s, 1H), 7.85 (d, J = 7.6 Hz, 2H), 7.45-7.49 (m, 1H), 7.31 (d, J = 7.6 Hz, 1H), 7.22 (d, J = 7.2 Hz, 2H), 6.74 (s, 1H), 3.97 (s, 3H), 1.52 (s, 9H). LCMS (ESI) m /z = 461[M+H]$^+$.

Step 2: 4-(1-(3-((tert-butoxycarbonyl)amino)phenyl)-2-oxo-1H-imidazo[4,5-c]pyridine-3(2H)-yl)benzoic acid(52)

Intermediate 51 (420 mg, 1.0 eq) was dissolved in EtOH(10 mL), added lithium hydroxide (192 mg, 5.0 eq), the mixture solution were stirred for 2 h at 50 °C. Then added 1 M HCl to PH= 6-5, extracted with EA, dried with Na_2SO_4, filtered and concentrated to obtain product used next step without in purification, gray solid, Yield: 338 mg, 83.0%. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.60 (s, 1H), 9.67 (s, 1H), 8.17 (d, J = 8.4 Hz, 2H),7.82-7.86 (m, 3H), 7.50 (d, J = 6.0 Hz, 2H), 7.22-7.23 (m, 1H), 1.49 (s, 9H). LCMS (ESI) m /z = 447 [M+H]$^+$.

Step 3: tert-butyl (3-(3-(4-((4-fluorobenzyl)carbamoyl)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)carbamate (53)

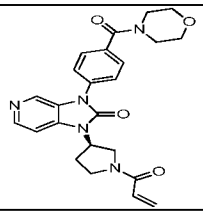
Intermediate 52 (66 mg, 0.148 mmol, 1.0 eq) was dissolved in DCM (30 mL), added (4-fluorophenyl)methanamine(22.2 mg, 0.178 mmol, 1.2 eq), TEA (45 mg, 0.444 mmol, 3.0 eq), HATU (67.5 mg, 0.178 mmol, 1.2 eq), the mixture solution were stirred for 2 h at room temperature. Then stopped and removed the solution under reduce pressure, the residue was added saturated $NaHCO_3$, extracted with EA washed with brine, dried with Na_2SO_4, filtered and concentrated, purified with silica column (DCM:MeOH = 100:1～50:1) to obtain the title product as colorless oil, Yield: 47 mg, 57.4%. LCMS (ESI) m /z = 554 $[M+H]^+$.

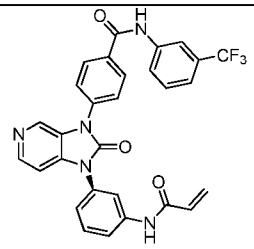
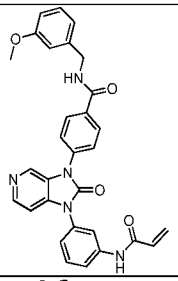
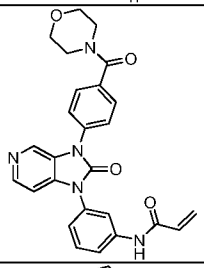
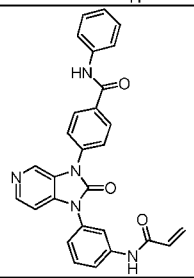
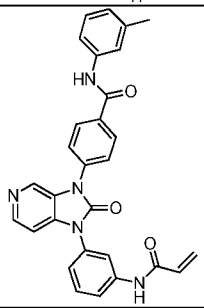
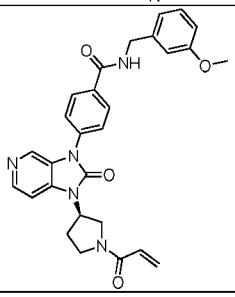
Step 4: 4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)-N-(4-fluorobenzyl)benzamide(54)

Intermediate 53 (47 mg) was dissolved in DCM (5.0 mL), added TFA (2.0 mL), the mixture was stirred for 1 h at RT, stopped and removed the solution under reduce pressure, the residue was added saturated $NaHCO_3$, extracted with EA and dried with Na_2SO_4, then filtered and concentrated to provide a crude product used next step without purification, colorless oil, Yield: 28 mg, 72.7%. LCMS (ESI) m /z = 454 $[M+H]^+$..

Crude product (28 mg, 0.062 mmol, 1.0 eq) and DIEA (9 mg, 0.070 mmol, 1.1 eq) were dissolved in THF (2.0 mL), added acryloyl chloride (6 mg, 0.065 mmol, 1.05 eq) slowly at 0°C, the mixture solution was stirred for 0.5 h at RT, followed the reaction with LCMS, stopped the reaction added water and extracted with EA, dried with Na_2SO_4, filtered and concentrated, the residue was purification with silica gel plate (DCM : MeOH = 20:1) to obtain the title product, colorless oil, Yield: 2 mg, 6.4%. ^1H NMR (400 MHz, CD_3OD): δ = 8.60 (s, 1H), δ = 8.23 (s, 1H), 8.13 (d, *J* = 8.0 Hz, 2H), 7.83 (d, *J* = 8.4 Hz, 2H), 7.63-7.66 (m, 3H), 7.39-7.44 (m, 3H), 7.05-7.10 (m, 2H), 6.41-6.50 (m, 2H), 5.81-5.84 (m, 1H), 4.61 (d, *J* = 4.4 Hz, 2H). LCMS (ESI) m /z = 507 $[M+H]^+$.

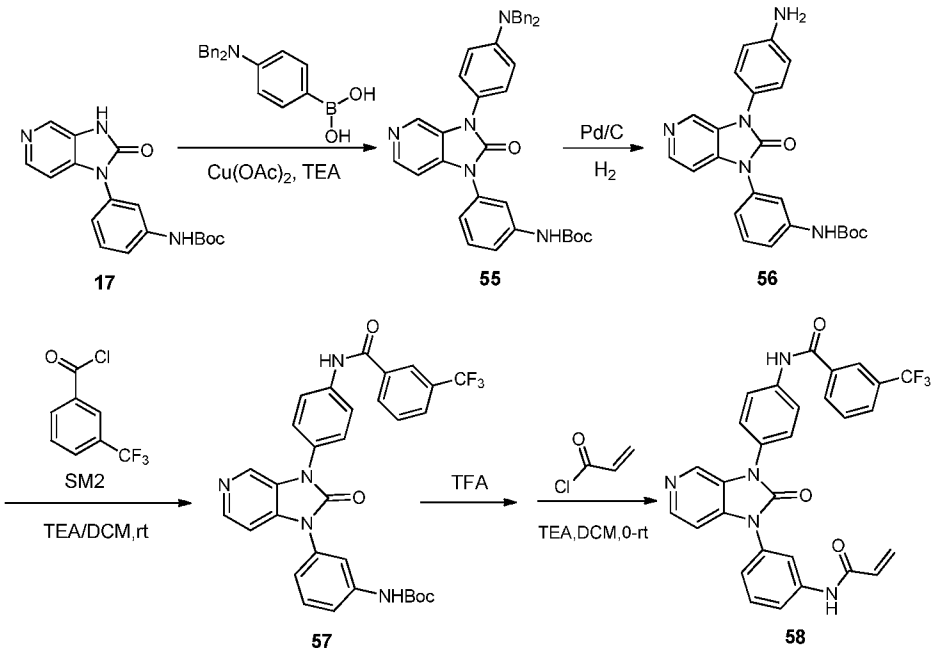
The following additional Examples 250-256 shown in the Table below were prepared following the procedures outlined in the general methods above and detailed in Example 249.

Entry	Structure	MS(cald) [M+H] $^+$/ MS (found)	Name
250		448.19 / 448.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(morpholine-4-carbonyl)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one

251		544.16 / 544.2	4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)-N-(3-(trifluoromethyl)phenyl)benzamide
252		520.19 / 520.2	4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)-N-(3-methoxybenzyl)benzamide
253		470.18 / 470.2	N-(3-(3-(4-(morpholine-4-carbonyl)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
254		476.16 / 476.2	4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)-N-phenylbenzamide
255		490.18 / 490.2	4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)-N-(m-tolyl)benzamide
256		498.21 / 498.2	(R)-4-(1-(1-acryloylpyrrolidin-3-yl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)-N-(3-methoxybenzyl)benzamide

Example 257

N-(4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)phenyl)benzamide



Step 1: tert-butyl (3-(3-(4-(dibenzylamino)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)carbamate(55)

The mixture of intermediate 17 (2 g, 6.1 mmol), (4-(dibenzylamino)phenyl)-boronic acid (3.8 g, 12.2 mmol), TEA (1.23 g, 12.2 mmol) and 4 A molecular sieves (1 g) were added to DCM (40 mL) in a vial Copper (II) acetate (1.1 g, 6.1 mmol) was added in one portion. The mixture was stirred for about 22 h at rt. Volatile components were removed under vacuum , before being poured into H_2O, The reaction mixture was extracted with EA, Organic phase was purified by column chromatography on silica gel (gradient: DCM/MeOH = 100/1-50/1), give the title product (1.2 g, yield 33.3%).

^{1}HNMR (400MHz, CD_3OD): δ 8.33 (br, 2H), 7.73 (s, 1H), 7.46-7.11 (m, 16H), 6.85 (d, J = 8.0 Hz, 2H), 6.67 (s, 1H), 4.72 (s, 4H), 1.50(s, 9H). LCMS: m/z = 598 $[M+H]^+$.

Step 2: tert-butyl (3-(3-(4-aminophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)carbamate(56)

A suspension of 55 (1.2 g, 1.68 mmol) and 10% Pd/C (0.3 g) in MeOH (20 mL) was hydrogenated at 50 psi H_2 for 20h. The suspension was filtered through Celite and concentrated. The residue was dried in vacuo to provide the title product (0.2 g crude). LCMS: m/z = 372 $[M+H]^+$.

Step 3: tert-butyl (3-(2-oxo-3-(4-(3-(trifluoromethyl)benzamido)phenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)carbamate (57)

To a stirred solution of 56 (60 mg, 0.14 mmol) in DCM (6 mL) was added SM2 (33 mg, 0.16 mmol) and TEA (17.4 mg, 0.17 mmol). The mixture was stirred at 15°C, after 1.0 h, the mixture was washed with H_2O ,extracted with DCM, dried over Na_2SO_4, filtered, concentrated to give a crude title product which was used for the next step without further purification. LCMS (ESI) m /z = 590 $[M+H]^+$.

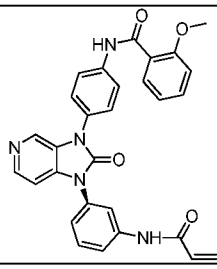
Step 4: N-(4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)phenyl)benzamide (58)

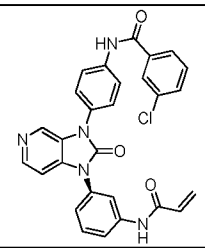
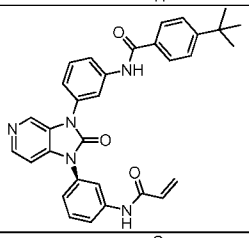
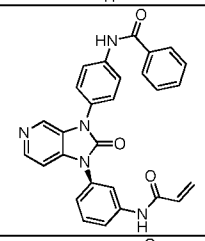
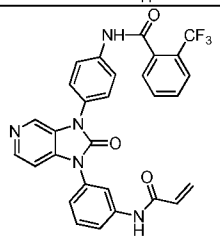
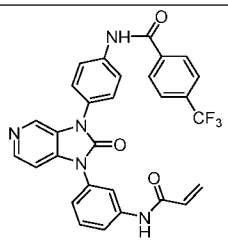
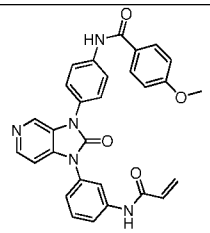
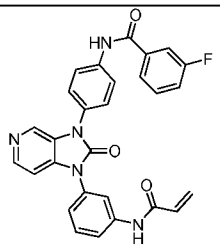
To a stirred solution of 57 in DCM (4 mL) was added CF_3COOH (1 mL),The mixture was stirred at 15°C, after 1.0 h, the mixture was added $NaHCO_3$ to adjust the Ph=8 ,extracted with DCM, dried over Na_2SO_4, filtered, concentrated and purified by Pre-TLC to give the product (42 mg). LCMS (ESI) m /z = 490 $[M+H]^+$.

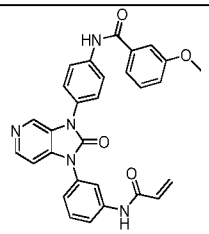
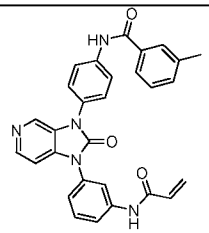
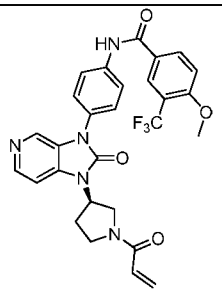
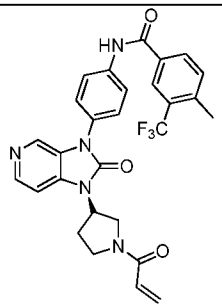
To a stirred solution of de-Boc intermediate (42 mg, 0.086 mmol) in DCM (6 mL) was added acryloyl chloride (8.5 mg, 0.09 mmol) and TEA (17.3 mg, 0.17 mmol). The mixture was stirred at 15 °C, after 1.0 h, the mixture was washed with H_2O, extracted with DCM, dried over Na_2SO_4, filtered, concentrated and purified by Pre-TLC to give the title product (21 mg, 51.4%).

^{1}HNMR (CD_3OD, 400MHz) 5.79-5.82(d, 1H), 6.41-6.45 (m, 2H), 7.39-7.41 (d, 1H), 7.56-7.58(q, 1H), 7.70-7.73(m, 2H), 7.74-7.76(m, 2H), 7.77-7.79(m, 2H), 7.90-7.92(d, 1H), 7.92-8.01(m, 3H), 8.03(s, 1H), 8.08-8.11(d, 1H), 8.24 (s, 1H). LCMS (ESI) m /z = 544 $[M+H]^+$.

The following additional Examples 258-269 shown in the Table below were prepared following the procedures outlined in the general methods above and detailed in Example 257.

Entry	Structure	MS(cald) $[M+H]^+$ / MS (found)	Name
258		506.18 / 506.2	N-(4-(1-(3-acrylamidophenyl)-2-oxo -1H-imidazo[4,5-c]pyridin -3(2H)-yl)phenyl)-2-methoxybenzamide

259		510.13 / 510.1	N-(4-(1-(3-acrylamidophenyl) -2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)phenyl)-3-chlorobenzamide
260		532.23 / 532.2	N-(3-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)phenyl)-4-(tert-butyl)benzamide
261		576.17 / 576.2	N-(4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)phenyl)benzamide
262		544.15 / 544.2	N-(4-(1-(3-acrylamidophenyl)-2-oxo-1,2-dihydro-3H-imidazo[4,5-c]pyridin-3-yl)phenyl)-2-(trifluoromethyl)benzamide
263		544.15 / 544.2	N-(4-(1-(3-acrylamidophenyl)-2-oxo-1,2-dihydro-3H-imidazo[4,5-c]pyridin-3-yl)phenyl)-4-(trifluoromethyl)benzamide
264		506.18 / 506.2	N-(4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)phenyl)-4-methoxybenzamidee
265		494.16 / 494.2	N-(4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)phenyl)-3-fluorobenzamide

266		506.18 / 506.2	N-(4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)phenyl)-3-methoxybenzamide
267		490.18 / 490.2	N-(4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)phenyl)-3-methylbenzamide
268		552.18/ 552.2	(R)-N-(4-(1-(1-acryloylpyrrolidin-3-yl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)phenyl)-4-methoxy-3-(trifluoromethyl)benzamide
269		536.18/ 536.2	(S)-N-(4-(1-(1-acryloylpyrrolidin-3-yl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)phenyl)-4-methyl-3-(trifluoromethyl)benzamide

Example 270

Step 1: tert-butyl (3-(3-(4-bromophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)carbamate(59)

Intermediate 17 (0.5 g, 1.53 mmol), (4-bromophenyl)boronic acid (0.61 g, 3.0 mmol), TEA (0.3 g, 3.0 mmol) and 4 A molecular sieves (0.1 g) were added to DCM (15 mL) in a vial Copper (II) acetate (0.27 g, 1.53 mmol) was added in one portion. The mixture was stirred for about 22 h at rt. Volatile components were removed under vacuum , before being poured into H_2O. The reaction mixture was extracted with EA, Organic phase was purified by column chromatography on silica gel (gradient: DCM/MeOH=100/1-50/1) to give the title product (0.26 g, yield = 33.3%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.83-7.80 (m, 2H), 7.71 (d, *J* = 8.0 Hz, 2H), 7.51-7.44 (m, 3H), 7.30-7.26 (m, 1H), 7.21 (d, *J* = 8.0 Hz, 1H), 6.68 (s, 1H), 1.51 (s, 9H). LCMS: m/z = 481.1,483.1 $[M+H]^+$.

Step 2: tert-butyl (3-(3-(3'-methyl-[1,1'-biphenyl]-4-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)carbamate (60)

To a solution of 59 (50 mg, 0.1 mmol) and m-tolylboronic acid (28 mg , 0.2mmol) in dioxane (5 mL) and water 1 mL) was added K_2CO_3 (28 mg,0.2 mmol) followed by $(Ph_3P)_4Pd$ (10 mg, 0.05mmol) under N_2 with stirring. The mixture was refluxed for 8 h until the material was disappeared. The reaction mixture was cooled to room temperature. The dioxane was removed by rotary evaporation. The residue was poured into water and extracted with EA. The organic layer was dried over Na_2SO_4, filtered and the solvent was removed by rotary evaporation. The product was isolated by flash chromatography on silica gel using 100:1-50:1 DCM:MeOH to give the title product (20 mg, yield 39.1 %). LCMS: m/z = 493$[M+H]^+$.

Step 3: 1-(3-aminophenyl)-3-(3'-methyl-[1,1'-biphenyl]-4-yl)-1H-imidazo[4,5-c]pyridin-2(3H)-one (61)

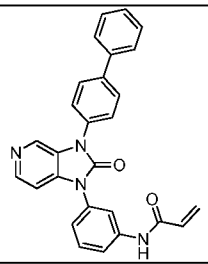
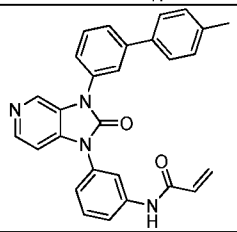
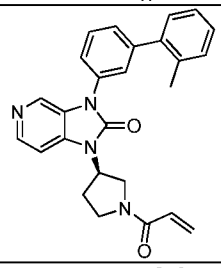
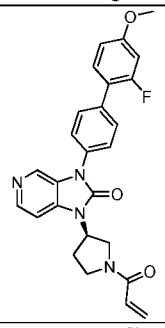
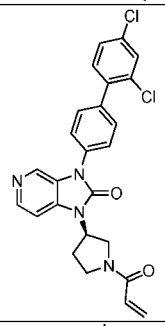
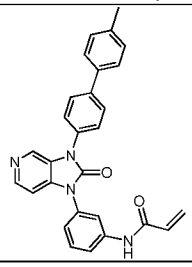
Intermediate 60 (20 mg, 0.040 mmol) were added to CF_3COOH/DCM=4/1 (5 mL) in one portion. The mixture was stirred for about 1 h at rt. Volatile components were removed under vacuum, give a crude title product, and directly used in next step without further purification. LCMS: m/z = 393$[M+H]^+$.

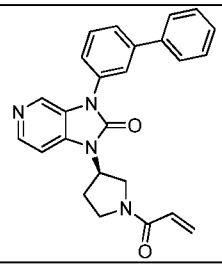
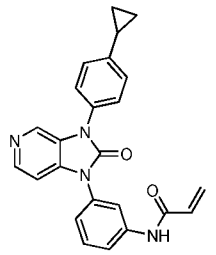
Step 4: N-(3-(3-(3'-methyl-[1,1'-biphenyl]-4-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide (62)

To a solution of Acryloyl chloride (3.6 mg, 0.04 mmol) in DCM (1 mL) was added to a stirred solution of 61 (16 mg, 0.04 mmol) and TEA (41mg, 0.4 mmol) in DCM (5 mL) at 0° C.The reaction mixture was stirred for 1 h, poured onto brine and extracted with DCM. The organic layer was dried, concentrated and recrystallized from DCM/MeOH=100/1 to give the title product (3 mg, yield 6.5 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.45 (br, 1H), 8.37 (br, 1H), 7.98(br, 1H), 7.81 (br,1H), 7.54-7.45 (m, 3H), 7.34-7.23(m, 3H), 7.13 (d, *J* = 4.0 Hz, 1H), 7.10 (d, *J* = 4.0 Hz, 1H), 6.97-6.90 (m, 3H), 6.45-6.40 (m, 1H), 6.24-6.18 (m, 1H), 5.77-5.75 (m, 1H), 2.35 (s, 3H).LCMS: m/z = 447 $[M+H]^+$.

The following additional Examples 271-278 shown in the Table below were prepared following the procedures in Examples 270.

Entry	Structure	MS(cald) $[M+H]^+$ / MS (found)	Name
271		433.16 / 433.1	N-(3-(3-([1,1'-biphenyl]-4-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
272		447.17 / 447.2	N-(3-(3-(4'-methyl-[1,1'-biphenyl]-3-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide
273		425.19 / 425.2	(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(2'-methyl-[1,1'-biphenyl]-3-yl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
274		459.18 / 459.2	(R)-1-(1-acryloylpiperidin-4-yl)-3-(2'-fluoro-4'-methoxy-[1,1'-biphenyl]-4-yl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
275		479.10 / 479.1,480.2,481.1, 483.1	(R)-1-(1-acryloylpiperidin-4-yl)-3-(2',4'-dichloro-[1,1'-biphenyl]-4-yl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
276		447.17 / 447.2	N-(3-(3-(4'-methyl-[1,1'-biphenyl]-4-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide

277		411.17 / 411.2	(R)-3-([1,1'-biphenyl]-3-yl)-1-(1-acryloylpyrrolidin-3-yl)-1H-imidazo[4,5-c]pyridin-2(3H)-one
278		397/397	N-(3-(3-(4-cyclopropylphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide

Btk kinase assay and other kinases assay

Btk kinase activity was determined using a homogenous time resolved fluorescence (HTRF) methodology. Measurements were performed in a reaction volume of 15μL using 384-well assay plates. Kinase enzyme, inhibitor, ATP and 1μM peptide substrate were incubated in a reaction buffer compose of Hepes50mM (pH7.0), NaN3 0.02%, BSA 0.01%, Orthocanadate0.1mM. After one hour, the kinase reaction was quenched by the addition of Eμ-labeled antibody and XL-665 in 1 x Detection buffer containing 60mM EDTA (Cisbio), and the mixture was allowed to incubate for one hour. The HTRF signal was measured on a multimode plate reader (EnVision® Multilabel Reader, Perkin Elmer) with an excitation wavelength (λ_{Ex}) of 330 nm and detection wavelengths (λ_{Em}) of 615 and 665 nm. Activity was determined by the ratio of the fluorescence at 665nm to that at 615nm. For each compound, enzyme activity as measured at various concentrations of compound, Negative control reactions were performed in the absence of inhibitor in two replicates and eight no enzyme controls were used to determine baseline fluorescence levels. IC_{50}s were obtained according to the equation:

Y=100/(1+10^((LogIC50-X)*HillSlope)). For BTK assay, [ATP] = 80μM, BTK = 3.4 nM.

For LYN assay, [ATP] = 20μM , LYN = 0.12 n M. For LCK assay, [ATP] = 20μM, LCK = 0.2 nM. For BLK assay, [ATP] = 20μM, BLK = 0.6 n M.

Example 279

The following Table shows the activity of selected compounds of this invention in the BTK inhibition assay. The compound numbers correspond to the compound numbers in previous Tables. Compounds having an activity designated as "A" provided an IC 50 ≤ 10

nM; Compounds having an activity designated as "B" provided an IC_{50} 10 -100 nM; Compounds having an activity designated as "C" provided an IC_{50} 100-1000 nM; Compounds having an activity designated as "D" provided an IC_{50} 1000-10000 nM; Compounds having an activity designated as "E" provided an $IC_{50} \geq 10000$ nM.

5

BTK Inhibition Data							
Compound #	BTK Inhibition	Compound #	BTK Inhibition	Compound #	BTK Inhibition	Compound #	BTK Inhibition
1	B	2	A	3	B	4	A
5	A	6	B	7	B	8	A
9	B	10	C	11	C	12	B
13	B	14	B	15	C	16	B
17	C	18	C	19	B	20	B
21	B	22	E	23	B	24	B
25	A	26	A	27	D	28	D
29	E	30	E	31	A	32	E
33	B	34	E	35	B	36	C
37	C	38	A	39	B	40	B
41	A	42	B	43	C	44	B
45	B	46	D	47	D	48	B
49	B	50	C	51	A	52	C
53	B	54	B	55	B	56	B
57	B	58	B	59	B	60	A
61	B	62	B	63	B	64	C
65	D	66	B	67	B	68	C
69	B	70	D	71	C	72	B
73	B	74	B	75	B	76	B
77	B	78	B	79	B	80	C
81	C	82	C	83	B	84	B
85	B	86	C	87	B	88	B
89	B	90	B	91	B	92	B
93	A	94	B	95	B	96	B
97	B	98	B	99	B	100	B
101	B	102	B	103	B	104	C
105	B	106	B	107	B	108	B
109	E	110	C	111	D	112	B
113	B	114	B	115	C	116	C
117	B	118	B	119	D	120	D
121	C	122	D	123	E	124	C
125	B	126	C	127	C	128	A
129	C	130	C	131	B	132	A
133	A	134	B	135	B	136	B
137	C	138	B	139	B	140	C
141	B	142	B	143	B	144	B
145	C	146	B	147	B	148	B

BTK Inhibition Data							
Compound #	BTK Inhibition	Compound #	BTK Inhibition	Compound #	BTK Inhibition	Compound #	BTK Inhibition
149	B	150	B	151	A	152	B
153	B	154	D	155	B	156	D
157	A	158	B	159	B	160	C
161	C	162	C	163	C	164	D
165	C	166	A	167	A	168	A
169	C	170	C	171	C	172	A
173	B	174	B	175	C	176	A
177	C	178	B	179	E	180	C
181	B	182	E	183	E	184	A
185	A	186	A	187	C	188	C
189	E	190	C	191	A	192	D
193	D	194	E	195	B	196	C
197	C	198	C	199	C	200	C
201	B	202	C	203	C	204	C
205	C	206	C	207	C	208	C
209	C	210	B	211	C	212	C
213	D	214	D	215	D	216	C
217	C	218	C	219	C	220	C
221	B	222	B	223	C	224	C
225	C	226	C	227	C	228	C
229	B	230	B	231	B	232	B
233	B	234	C	235	B	236	C
237	B	238	C	239	C	240	B
241	C	242	C	243	C	244	C
245	C	246	C	247	B	248	C
249	B	250	D	251	D	252	C
253	D	254	D	255	D	256	D
257	D	258	B	259	C	260	B
261	C	262	C	263	C	264	C
265	C	266	C	267	E	268	C
269	C	270	E	271	B	272	C
273	C	274	C	275	E	276	D
277	C	278	B				

Example 280

The following Table shows the activity of selected compounds of this invention in the BTK, BLK, LYN, LCK inhibition assay. The compound numbers correspond to the compound numbers in previous Tables. Compounds having an activity designated as "A" provided an $IC_{50} \leq 10$ nM; Compounds having an activity designated as "B" provided an IC_{50} 10 -100 nM; Compounds having an activity designated as "C" provided an IC_{50} 100-1000 nM; Compounds having an activity designated as "D" provided an IC_{50} 1000-10000 nM;

Compounds having an activity designated as "E" provided an $IC_{50} \geq 10000$ nM; N/A is not available.

Table 2

Compound	BTK IC_{50}	BLK IC_{50}	LYN IC_{50}	LCK IC_{50}
1	B	B	E	E
2	A	B	E	E
3	B	C	E	N/A
4	A	B	D	D
5	A	B	E	E
8	A	C	D	E
20	B	B	E	D
26	A	C	D	E
31	A	C	D	E
38	A	B	E	E
51	A	B	E	E
60	A	B	E	E
103	B	C	D	E
128	B	C	E	E
132	A	C	E	E
133	A	B	E	E
138	B	C	E	E

Calcium FluxAssay

Calcium flux fluorescence-based assays were performed in aFDSS7000EX (Hamamatsu Photonics) fluorometric imaging plate reader according to manufacturer instructions. Compounds to be assayed were dissolved in DMSO, diluted to appropriate concentrations in Ca^{2+} buffer ranging from 0 to 10 μM (at a dilution factor of 0.1), added 5 μl (6 X) to each well (the final DMSO concentration was 0.1% in each well). Then 12.5 μL 2X dye loading solution (Fluo-4 NW Calcium Assay Kits, Invitrogen) was added per well of a 384-well plate. Afterwards, actively growing Ramos cells (ATCC) in RPM1640 medium supplemented with 10% FBS (Invitrogen) were washed and re-plated in assay buffer (from Fluo-4 NW Calcium Assay Kits, Invitrogen) to approximately 6.4×10^6/ml(80000 cells/12.5 μL in 384-well plates). The plates were incubated at 37°C for 30 minutes, then at room temperature for an additional 30 minutes. The plates were now ready to be used in an experiment. Immediately after the transfer and a 10-s recording of baseline fluorescence, the compound treated cells were stimulated with a goat anti-human IgM antibody (10μg/ml; Jackson Immuno Research) and read in a FDSS for 240 seconds. Difference between the signal and that at baseline, designated adjusted relative fluorescence unit, was calculated by

using a custom Excel (Microsoft, Redmond, WA) template to determine IgM-induced calcium influx and its inhibition by compounds. The table belows show the result. Compounds having an activity designated as " A" provided an IC 50 ≤ 10 nM; Compounds having an activity designated as " B" provided an IC $_{50}$ 10 -100 nM; Compounds having an activity designated as " C" provided an IC_{50} 100-1000 nM;.

Table3

Cmpd.	Ramos Ca Flux (nM)
Example 4	B
Example 5	B

Btk occupancy in cellular assays

For PCI-33380 labeling of human B cells, 10^6 Jeko-1 cells were pre-incubated with compound for 1.5 h before labeling. Then cells were treated with PCI-33380 at 5 μM for 1 h. Washed, lysed in Ripa buffer containing sample reducing agent, and analyzed by SDS/PAGE and fluorescent gel scanning using a Typhoon scanner 9500 (GE Healthcare) (Ex, 532nm; Em,555nm). The gel was then blotted and total Btk levels detected by standard Western blot with Btk antibody (CST).

By using the fluorescently tagged derivative PCI-33380, we found that 100nM of Compound 4 and 5 were sufficient to fully occupy the active site of Btk in human mantle cell lymphoma cell lines Jeko-1 cells in culture.

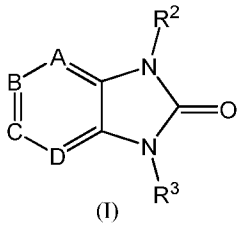
Btk occupancy *in vivo*

For analysis of Btk occupancy in Babc/L mice following oral dosing of compounds after 4 hours. Isolating peripheral blood mononuclear cells (PBMCs) with mouse peripheral blood separation kit (Hao Yang Biological Manufacture CO., LTD, Tianjin) were collected from Babc/L mice (1ml blood from two mice). Spleens were processed to splenocytes followed by 5 min incubation in red blood cell lysing buffer (from mouse peripheral blood separation kit). PBMCs or splenocytes were then PCI-33380–labeled and lysates analyzed by fluorescent gel scanning as described in cellular assays. Compound 5was achieved full occupancy at 25mg/kg single oral dose in all Babc/L mice.

What is claimed is:

1. A compound of Formula (I) having the following structure:

Formula (I)



(I)

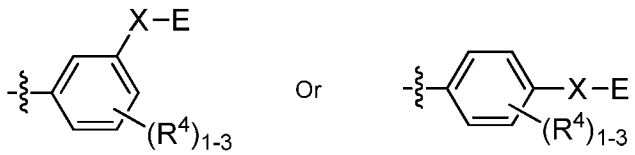
wherein:

A is N or CR^1;

B, C, and D are each N or C-H, with the proviso that only one or two of A, B, C, and D can be N;

R^1 is hydrogen, amino, OH, CN, NHOH or $CONH_2$;

R^2 is



-X-E is one of the followings:

(1) X is O, OCR^aR^b, S(O), $S(O)_2$, CR^aR^b, $NR^c(C=O)$, $C=ONR^c$ or a bond; and E is a hydrogen, an aryl or a heteroaryl substituted with one to three R^5 substituents; or a 3-7 membered saturated or partially unsaturated carbocyclic ring, an 8-10 membered bicyclic saturated, partially unsaturated or aryl ring, a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, a 7-10 membered bicyclic saturated or partially unsaturated heterocyclic ring having 1-5 heteroatoms independently selected from nitrogen, oxygen , or sulfur, or an 8-10 membered bicyclic heteroaryl ring having 1-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; or

(2) -X-E is hydrogen, halogen , $-OR^a$, $-O(CH_2)_{1-4}R^a$, -CN, $-NO_2$;

R^4 and R^5 are each independently selected from the group consisting of hydrogen, halogen, hydroxy, cyano, OCF_3, OCF_2H, C_{1-6} alkyl, optionally substituted with one to five fluorines, C_{3-6} cycloalkyl, optionally substituted with one to five fluorines, C_{1-4} alkoxy, optionally substituted with one to five fluorines, C_{1-4} alkylthio, optionally substituted with one to five fluorines, C_{1-4} alkylsulfonyl, optionally substituted with one to five fluorines, carboxy, C_{1-4} alkyloxycarbonyl, and C_{1-4} alkylcarbonyl;

R^a and $R^b$are each independently hydrogen, fluorine, or C_{1-3} alkyl, optionally substituted with one to five fluorines;

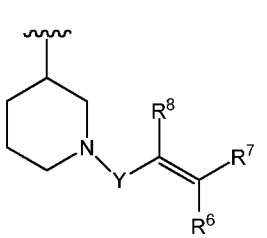
$R^c$is hydrogen or C_{1-3} alkyl, optionally substituted with one to five fluorines;

R^3 is a group having a double bond,

an isomer thereof, a tautomer thereof, a pharmaceutical acceptable solvate thereof, or a pharmaceutical acceptable prodrug thereof.

2. The compound of claim 1, E is selected from aryl, heteroaryl, carbocyclyl , heterocyclyl, any of which is optionally substituted with one to three R^5 substituents.

3. The compound of claim 1, wherein R^3 is selected from the group consisting of: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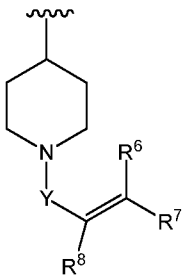
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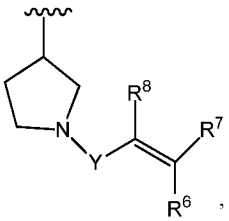
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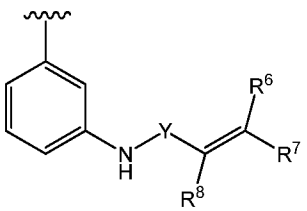
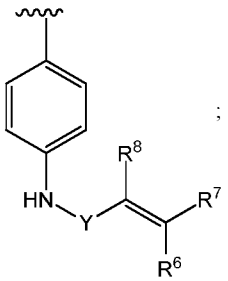
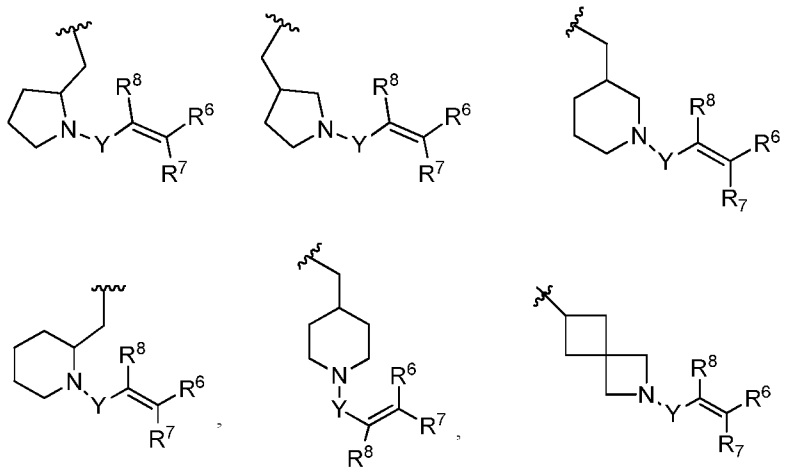

and

;

Y is C(=O); OC(=O), NHC(=O),S=O, $S(=O)_2$, or $NHS(=O)_2$;

R^6, R^7, R^8 are each independently hydrogen, halogen, CN, C_{1-4} alkyl, C_{1-6} alkoxyalkyl, C_{1-8} alkylaminoalkyl, or C_{1-4} alkylphenyl;

or R^7 and R^8 taken together form a bond.

4. The compound of claim 3, wherein R^3 is selected from the group consisting of:



Y is C(=O); OC(=O), NHC(=O),S=O, $S(=O)_2$, or $NHS(=O)_2$;

R^6, R^7, R^8 are each independently hydrogen, halogen, CN, C_{1-4} alkyl, C_{1-6} alkoxyalkyl, C_{1-8} alkylaminoalkyl, or C_{1-4} alkylphenyl;

or R^7 and R^8 taken together form a bond.

5. The compound of claim 1, wherein A is CR^1, and one of B, C, and D is N.

6. The compound of claim 1, wherein A is CR^1, B is N, and C and D are CR^1.

7. A pharmaceutical composition comprising a therapeutically effective amount of the compound of claim 1, and a pharmaceutically acceptable excipient.

8. A method for treating an autoimmune disease comprising administering to a subject in need thereof a composition containing a therapeutically effective amount of the compound of claim 1.

9. A compound selected from the group consisting of (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-methoxyphenoxy)phenyl)-1H-imidazo[4,5-

c]pyridin-2(3H)-one, N-(3-(2-oxo-3-(4-phenoxyphenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl), (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(m-tolyloxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one,(R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-phenoxyphenyl)-1H-imidazo[4,5-c] pyridin-2(3H)-one, 1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-(3-(trifluoromethyl)phenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(2-oxo-3-(3-phenoxyphenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (S)-1-(1-acryloylpiperidin-3-yl)-3-(4-(2-chloro-3-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-chloro-5-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-cyclopropylphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(3-(2-thioxo-3-(4-(m-tolyloxy)phenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)pyrrolidin-1-yl)prop-2-en-1-one, (R)-1-(1-acryloylpiperidin-3-yl)-3-(3-fluoro-4-phenoxyphenyl) -1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(m-tolyloxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, 1-((1-acryloylpiperidin-4-yl)methyl)-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, 1-((1-acryloylpiperidin-4-yl)methyl)-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-(p-tolyloxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3- (3-(4-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R,E)-3-(3-chloro-4-phenoxyphenyl)-1- (1-(3-morpholinoacryloyl)pyrrolidin-3-yl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3- (3-chloro-4-(m-tolyloxy)phenyl)- 1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, 1-((1-acryloylpyrrolidin-2-yl)methyl) -3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R,E)-3-(3-chloro-4-phenoxyphenyl)-1- (1-cinnamoylpyrrolidin-3-yl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-3-(3-chloro-4-phenoxyphenyl)-1- (1-(vinylsulfonyl)pyrrolidin-3-yl)- 1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3- (4-(3-ethoxyphenoxy)phenyl)- 1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3- (4-(3-isopropoxyphenoxy)phenyl)- 1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-(3-chlorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(3-(3-methyl-4-phenoxyphenyl) -2-oxo-2,3-dihydro-1H-imidazo [4,5-c]pyridin-1-yl)phenyl)acrylamide, (R)-1-(1-methacryloylpyrrolidin-3-yl)- 3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R,E)-1-(1-cinnamoylpyrrolidin-3-yl)-3- (4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, 1-(1-acryloylpiperidin-4-yl)-3-

(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(phenylthio)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acetylpyrrolidin-3-yl)-3- (4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3- (4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-(but-2-ynoyl)pyrrolidin-3-yl) -3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4- (4-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4- (4-(trifluoromethyl)phenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3,4-dichlorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(phenylthio)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4- (3,5-difluorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4- (3,4-dimethoxyphenoxy)phenyl)- 1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3- (3-chloro-4-(3-fluorophenoxy)phenyl) -1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-(4-methoxyphenoxy)phenyl)- 1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-(4-(trifluoromethyl)phenoxy)phenyl) -1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4- (3,4-dichlorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-(3-methoxyphenoxy)phenyl)- 1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(3-(4-(3-isopropoxyphenoxy)- 3-methylphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c] pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(3-methyl-4-(m-tolyloxy)phenyl) -2-oxo-2,3-dihydro-1H-imidazo [4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(3-fluoro-4-(3-isopropoxyphenoxy) phenyl)-2-oxo-2,3-dihydro-1H-imidazo [4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(3-fluoro-4-(m-tolyloxy) phenyl)-2-oxo-2,3-dihydro-1H-imidazo [4,5-c]pyridin-1-yl)phenyl)acrylamide, (N-(3-(3-(4-(3-chlorophenoxy)-3-fluorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl) acrylamide, (R)-1-(1-acryloylpyrrolidin-3-yl) -3-(4-(2,3-dimethylphenoxy) phenyl)-1H-imidazo[4,5-c] pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3- (3-fluoro-4-(3-isopropoxyphenoxy)phenyl) -1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3- (3-fluoro-4-(3-methoxyphenoxy)phenyl) -1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3- (3-fluoro-4-(3-methoxyphenoxy)phenyl) -1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-

3-yl)-3- (3-(3-fluoro-2-methylphenoxy) phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-(3-cyclopropoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3- (4-(3-fluoro-2-methylphenoxy)phenyl) -1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3- (4-(2,3-dimethylphenoxy)phenyl)- 1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3- (4-(3-chloro-2-fluorophenoxy)phenyl) -1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3- (4-(2,3-difluorophenoxy)phenyl)- 1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(2,3-difluorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(3-(4-(3-methoxyphenoxy)- 3-methylphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl) phenyl)acrylamide, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-chloro-2-methoxyphenoxy)phenyl)- 1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4- (3-chloro-2-methoxyphenoxy)phenyl) -1H-imidazo[4,5-c]pyridin-2(3H)-one, ((R)-1-(1-acryloylpyrrolidin-3-yl)-2-oxo-3-(4-phenoxyphenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridine-4-carbonitrile, (R)-1-(1-acryloylpiperidin-3-yl)-3- (4-(2-methoxy-3-methylphenoxy) phenyl)-1H-imidazo[4,5-c] pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3- (4-(2-methoxy-3-methylphenoxy)phenyl) -1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3- (4-(2-methoxy-3-methylphenoxy)phenyl) -1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(3-(4-(3-chlorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(2-oxo-3-(4-(3-(trifluoromethoxy)phenoxy)phenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(3-chloro-5-methoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-chlorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(3-(3-chloro-4-phenoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(3-(3-chlorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(3-(3-fluorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(2-oxo-3-(3-(p-tolyloxy)phenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-fluoro-4-(3-fluorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-fluoro-4-(m-tolyloxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(3-(4-(3-fluoro-2-methylphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(4-methoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-

imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (R)-1-(1-acryloylpyrrolidin-3-yl)-3- (4-(4-fluorophenoxy)phenyl)-1H- imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3- (4-(4-chlorophenoxy)phenyl)-1H-imidazo[4,5- c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)- 3-(4-(o-tolyloxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3- (4-(3-fluorophenoxy)phenyl)-1H-imidazo[4,5- c]pyridin-2(3H)-one, N-(3-(3-(4-(3-isopropoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(3-chloro-4-(3-methoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(3-(3-methoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(2-oxo-3-(3-(o-tolyloxy)phenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1- yl)phenyl)acrylamide, N-(3-(3-(3-(2-methoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(3-fluoro-4-(3-fluorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, 1-(1-acryloylpyrrolidin-3-yl)-3-(3-methyl-4-phenoxyphenyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one, 1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-methoxyphenoxy)-3-methylphenyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one, N-(3-(3-(3-fluoro-4-phenoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(3-fluoro-4-(3-methoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-fluoro-4-phenoxyphenyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one, N-(3-(3-(3-(3-chloro-2-fluorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-(3-chloro-2-fluorophenoxy)phenyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one, N-(3-(3-(4-(2,3-dichlorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(2,3-dichlorophenoxy)phenyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(2,3-dichlorophenoxy)phenyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-chloro-2-fluorophenoxy)-3-fluorophenyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(2-chloro-3-fluorophenoxy)phenyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(2-chloro-3-fluorophenoxy)phenyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(pyridin-2-yloxy)phenyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one, (R)-1-(1-acryloylpiperidin-3-

yl)-3- (3-fluoro-4-(m-tolyloxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3- (4-(3-chlorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3- (3-chloro-4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3- (3-chloro-4-(m-tolyloxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(2-oxo-3-(4-phenoxyphenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)cinnamamide, N-(3-(2-oxo-3-(4-phenoxyphenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)methacrylamide, N-(3-(3-(3-chloro-4-(4-(trifluoromethyl)phenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-(trifluoromethoxy)phenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(3-(4-(3-ethoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(3-isopropylphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, 4-(4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)phenoxy)-N-methylpicolinamide, N-(3-(2-oxo-1-(4-phenoxyphenyl)-1H-imidazo[4,5-b]pyridin-3(2H)-yl)phenyl)acrylamide, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(3-fluorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(3-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(2-oxo-3-(4-phenoxyphenyl)-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)phenyl)acrylamide, (R)-3-(1-acryloylpyrrolidin-3-yl)-1-(4-phenoxyphenyl)-1H-imidazo[4,5-b]pyridin-2(3H)-one, N-(3-(2-oxo-1-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-3(2H)-yl)phenyl)acrylamide, (R)-3-(1-acryloylpiperidin-3-yl)-1-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(2-oxo-3-(4-(4-(trifluoromethyl)phenoxy)phenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(4-methoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(2,3-difluorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(3,4-difluorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(3,5-difluorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(3-chloro-2-fluorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(3-chloro-5-fluorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(3,5-dichlorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(3,4-

dimethoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(3-fluoro-4-phenoxyphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-chloro-2-fluorophenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(3-chloro-2-methylphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(2-chloro-3-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(3-(4-(3-fluoro-2-methoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-fluoro-2-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(2-fluoro-3-methylphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-chloro-2-methylphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(3-fluoro-2-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(2-fluoro-3-methylphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(3-methoxy-2-methylphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-methoxy-2-methylphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(3-(3-chloro-4-(m-tolyloxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(3-chloro-4-(3-isopropoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(3-fluorophenoxy)-3-methylphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(2,3-dimethylphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(3-chloro-4-(2,3-dimethylphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-chlorophenoxy)-3-fluorophenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(3-(4-(3-chloro-2-methylphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (R)-1-(1-acryloylpyrrolidin-3-yl)-7-chloro-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(2-oxo-3-(3-(m-tolyloxy)phenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(3-isopropylphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(3-(4-(3-chlorophenoxy)-3-methylphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-methacryloylpyrrolidin-3-yl)-3-(3-

phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(2-oxo-3-(4-(phenylthio)phenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(3-methoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(3,4-dichlorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(4-chloro-3-fluorophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(3-fluoro-4-methoxyphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(4-cyanophenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(4-methoxy-3-methylphenoxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, 1-(1-acryloylpyrrolidin-3-yl)-3-(4- (pyridin-4-yloxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, 1-(1-acryloylpyrrolidin-3-yl)-3-(4- (pyridazin-3-yloxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(2-oxo-3-(4-((2,4,5-trifluorobenzyl)oxy) phenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(2-oxo-3-(4-(pyridin-2-ylmethoxy)phenyl)-2,3-dihydro-1H-imidazo[4,5-c] pyridin-1-yl)phenyl)acrylamide, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(benzyloxy)-3-chlorophenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-((3,4-dichlorobenzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-((2,4-difluorobenzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-((3-(trifluoromethyl)benzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-((3,4-difluorobenzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-((2,4-difluorobenzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-((2-(trifluoromethyl)benzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-(pyridin-2-ylmethoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-((4-(trifluoromethyl)benzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-((4-(trifluoromethyl)benzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-((3,5-difluorobenzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-((2,4-dichlorobenzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-((2,5-

difluorobenzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-((2-(trifluoromethyl)benzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-((3-(trifluoromethyl)benzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-((4-(trifluoromethyl)benzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(pyridin-2-ylmethoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-((3,4-difluorobenzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-((3,4-dichlorobenzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-((2-fluorobenzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(3-(3-fluoro-4-((2-fluorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-((3,4-dichlorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-((3,5-difluorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-((2,5-difluorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-((4-chlorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-((3-fluorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(3-chloro-4-((4-(trifluoromethyl)benzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(benzyloxy)-3-chlorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-((2-methylbenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-((2,6-difluorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-((2,6-difluorobenzyl)oxy)-3-fluorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-((2-fluorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-((2,4-dichlorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-((3-chlorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-((2-chlorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(2-oxo-3-(4-((2-(trifluoromethyl)benzyl)oxy)phenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(3-(benzyloxy)phenyl)-

2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-(benzyloxy)-3-fluorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(3-chloro-4-((2-fluorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (S)-1-(1-acryloylpyrrolidin-3-yl)-3-(3-chloro-4-((2-fluorobenzyl)oxy)phenyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one, (S)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(benzyloxy)-3-fluorophenyl)-1,3-dihydro-2H-imidazo[4,5-c]pyridin-2-one, N-(3-(3-(4-((3-chloro-2-fluorobenzyl)oxy)-3-fluorophenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (N-(3-(3-(4-(benzyloxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(2-oxo-3-(4-((3-(trifluoromethyl)benzyl)oxy)phenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-((3,4-difluorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(2-oxo-3-(4-((4-(trifluoromethyl)benzyl)oxy)phenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(3-chloro-4-((3-(trifluoromethyl)benzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-((4-chloro-2-fluorobenzyl)oxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(3-(4-((4-chloro-2-fluorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, ((R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(benzyloxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(3-(4-((4-fluorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4-((2,4-difluorobenzyl)oxy)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, 4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)-N-(4-fluorobenzyl)benzamide, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(morpholine-4-carbonyl)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, 4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)-N-(3-(trifluoromethyl)phenyl)benzamide, 4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)-N-(3-methoxybenzyl)benzamide, N-(3-(3-(4-(morpholine-4-carbonyl)phenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, 4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)-N-phenylbenzamide, 4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)-N-(m-tolyl)benzamide, (R)-4-(1-(1-acryloylpyrrolidin-3-yl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)-N-(3-methoxybenzyl)benzamide, N-(4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)phenyl)benzamide, N-(4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-

3(2H)-yl)phenyl)-2-methoxybenzamide, N-(4-(1-(3-acrylamidophenyl) -2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)phenyl)-3-chlorobenzamide, N-(3-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)phenyl)-4-(tert-butyl)benzamide, N-(4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)phenyl)benzamide, N-(4-(1-(3-acrylamidophenyl)-2-oxo-1,2-dihydro-3H-imidazo[4,5-c]pyridin-3-yl)phenyl)-2-(trifluoromethyl)benzamide, N-(4-(1-(3-acrylamidophenyl)-2-oxo-1,2-dihydro-3H-imidazo[4,5-c]pyridin-3-yl)phenyl)-4-(trifluoromethyl)benzamide, N-(4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)phenyl)-4-methoxybenzamidee, N-(4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)phenyl)-3-fluorobenzamide, N-(4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)phenyl)-3-methoxybenzamide, N-(4-(1-(3-acrylamidophenyl)-2-oxo-1H-imidazo[4,5-c]pyridin-3(2H)-yl)phenyl)-3-methylbenzamide, N-(3-(3-(3'-methyl-[1,1'-biphenyl]-4-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, N-(3-(3-([1,1'-biphenyl]-4-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c] pyridin-1-yl)phenyl)acrylamide, N-(3-(3-(4'-methyl-[1,1'-biphenyl]-3-yl) -2-oxo-2,3-dihydro-1H-imidazo [4,5-c]pyridin-1-yl)phenyl)acrylamide, (R)1-(1-acryloylpyrrolidin-3-yl)-3-(2'-methyl-[1,1'-biphenyl]-3-yl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(2'-fluoro-4'-methoxy-[1,1'-biphenyl]-4-yl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-4-yl)-3-(2',4'-dichloro-[1,1'-biphenyl]-4-yl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(3-(4'-methyl-[1,1'-biphenyl]-4-yl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (R)-3-([1,1'-biphenyl]-3-yl)-1-(1-acryloylpyrrolidin-3-yl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, N-(3-(3-(4-cyclopropylphenyl)-2-oxo-2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)phenyl)acrylamide, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(2-fluoro-3-methoxyphenoxy)phenyl)-7-methoxy-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-7-ethoxy-3-(4-(2-fluoro-3-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(2-fluoro-3-methoxyphenoxy)phenyl)-7-methyl-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-((1-(but-2-ynoyl)pyrrolidin-2-yl)methyl)-3-(4-(2-fluoro-3-methoxyphenoxy)phenyl)-7-methyl-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-((1-acryloylpyrrolidin-2-yl)methyl)-3-(4-(2-fluoro-3-methoxyphenoxy)phenyl)-7-methyl-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-(but-2-ynoyl)piperidin-3-yl)-3-(4-(2-fluoro-3-methoxyphenoxy)phenyl)-7-methyl-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(2-fluoro-3-methoxyphenoxy)phenyl)-7-methyl-1H-

imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-(but-2-ynoyl)pyrrolidin-3-yl)-3-(4-(2-fluoro-3-methoxyphenoxy)phenyl)-7-methyl-1H-imidazo[4,5-c]pyridin-2(3H)-one, (E)-N-(3-(6-amino-8-oxo-7-(4-phenoxyphenyl)-7H-purin-9(8H)-yl)phenyl)-4-(cyclopropyl(methyl)amino)-N-methylbut-2-enamide, (R)-1-(1-(but-2-ynoyl)piperidin-3-yl)-3-(4-(2-fluoro-3-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-7-methyl-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (S,Z)-9-(1-acryloylpyrrolidin-3-yl)-6-(hydroxyimino)-7-(4-phenoxyphenyl)-7,9-dihydro-1H-purin-8(6H)-one, 1-(1-Acryloyl-pyrrolidin-2-ylmethyl)-3-(4-phenoxy-phenyl)-1,3-dihydro-imidazo[4,5-c]pyridin-2-one, (S,Z)-1-(1-acryloylpyrrolidin-3-yl)-N'-hydroxy-2-oxo-3-(4-phenoxyphenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridine-4-carboximidamide, 4,4-dimethyl-2-{2-[2-oxo-3-(4-phenoxy-phenyl)-2,3-dihydro-imidazo[4,5-c]pyridin-1-ylmethyl]-pyrrolidine-1-carbonyl}-pent-2-enenitrile, (R)-1-(1-acryloylpyrrolidin-3-yl)-2-oxo-3-(4-phenoxyphenyl)-2,3-dihydro-1H-imidazo[4,5-c]pyridine-7-carbonitrile, (R)-1-(1-acryloylpyrrolidin-3-yl)-4-methoxy-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-4-hydroxy-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-7-chloro-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(2-chloro-3-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpiperidin-3-yl)-3-(4-(2-fluoro-3-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R,E)-1-(1-(4-(cyclopropyl(methyl)amino)but-2-enoyl)pyrrolidin-3-yl)-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R,E)-1-(1-(4-(cyclopropyl(methyl)amino)but-2-enoyl)piperidin-3-yl)-3-(4-phenoxyphenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-4-nitro-3-(4-phenoxyphenyl)-1H-benzo[d]imidazol-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-4-amino-3-(4-phenoxyphenyl)-1H-benzo[d]imidazol-2(3H)-one, (R)-1-(1-acryloylpyrrolidin-3-yl)-3-(4-(2-fluoro-3-methoxyphenoxy)phenyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, 2-oxo-2-(3-(2-oxo-3-(4-phenoxyphenyl) -2,3-dihydro-1H-imidazo[4,5-c]pyridin-1-yl)piperidin-1-yl)acetic acid, 3-(2-oxo-3-(4-phenoxyphenyl)-2,3-dihydro -1H-imidazo[4,5-c]pyridin-1-yl) cyclohexanecarboxylic acid, and 2-oxo-2-(3-(2-oxo-3-(4-phenoxyphenyl)-2,3-dihydro-1H-imidazo[4,5-c] pyridin-1-yl)piperidin-1-yl)acetamide.

10. The use of claim 9, which is administered in combination with a therapeutic agent selected from the group consisting of: anticancer drugs, steroid drugs, methotrexates,

leflunomides, anti-TNFa agents, calcineurin inhibitors, antihistaminic drugs, and a mixture thereof.

11. A pharmaceutical composition for preventing or treating cancers, tumors, inflammatory diseases, autoimmune diseases, or immunologically mediated disease comprising a therapeutically effective amount of the compound of claim 9, and a pharmaceutically acceptable excipient.

12. A method for treating an autoimmune disease, cancers, tumors, inflammatory diseases, or immunologically mediated diseases comprising administering to a subject in need thereof a composition containing a therapeutically effective amount of the compound of claim 9 and other therapeutic agents.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 16/55096

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - C07D 401/14; A61K 31/506 (2016.01)
CPC - C07B 2200/13, C07D 401/14
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC(8): C07D 401/14; A61K 31/506 (2016.01)
CPC: C07B 2200/13, C07D 401/14

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
None

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PatBase; Keyword limited: BRUTON'S TYROSINE KINASE/BRUTON/BRUTONS TYROSINE KINASE/BTK; inhibitor/inactivation/mechanism-based/suicide; indole acrylamide/purin acrylamide

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2015/0094299 A1 (YAMAMOTO et al.) 02 April 2015 (02.04.2015), entire document, especially: para [0039]; para [0041]; para [0042]; para [0045]; para [0138]; para [0142]; para [0205], Example 8, 9-(1-acryloyl-3-azetidinyl)-6-amino-7-(4-phenoxyphenyl)-7,9-dihydro-8H-purin-8-one; para [0215], Example 8(4), 9-[(3R)-1-acryloyl-3-pyrrolidinyl]-6-amino-7-(4-phenoxyphenyl)-7,9-dihydro-8H-purin-8-one; para [0215], Example 8(3), 9-(1-acryloyl-4-piperidinyl)-6-amino-7-(4-phenoxyphenyl)-7,9-dihydro-8H-purin-8-one.	1-12
A	WO 2011/152351 A1 (ONO PHARMACEUTICAL CO) 08 December 2011 (08.12.2011), entire document.	1-12
A	SINGH et al. "The resurgence of covalent drugs", Nature Reviews Drug Discovery. 2011. Vol. 10, pp 307-317, entire document, especially: pg 315, Table 1, Ibrutinib.	1-12
A	US 6,489,338 B2 (YU et al.) 03 December 2002 (03.12.2002), entire document.	1-12

☐ Further documents are listed in the continuation of Box C. ☐

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
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"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
26 November 2016	27 DEC 2016
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774