(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
13 January 2022 (13.01.2022)

WIPO | PCT

(10) International Publication Number
WO 2022/011337 A1

(51) International Patent Classification:
A61K 31/506 (2006.01) *A61K 31/519* (2006.01)
A61K 31/517 (2006.01)

(21) International Application Number:
PCT/US2021/041270

(22) International Filing Date:
12 July 2021 (12.07.2021)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
63/050,382 10 July 2020 (10.07.2020) US
63/137,814 15 January 2021 (15.01.2021) US

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, IT, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report (Art. 21(3))*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

WO 2022/011337 A1

(54) Title: KINASE MODULATORS AND METHODS OF USE THEREOF

(57) Abstract: The present invention relates to novel compounds that modulate the activity of one or more kinases, such as TYK2 or mutants thereof. The compounds, which may be kinase inhibitors or activators, are useful for treating autoimmune diseases, such as, such as psoriasis, lupus, multiple sclerosis, and inflammatory bowel disease.

KINASE MODULATORS AND METHODS OF USE THEREOF

Cross-Reference to Related Applications

This application claims the benefit of, and priority to, U.S. Provisional Patent Application No. 63/137,814, filed January 15, 2021, and U.S. Provisional Patent Application No. 63/050,382, filed July 10, 2020, the contents of each of which are incorporated by reference.

Field of the Invention

The invention provided compounds that modulate the activity of kinases, such as Tyrosine Kinase 2 (TYK2).

Background

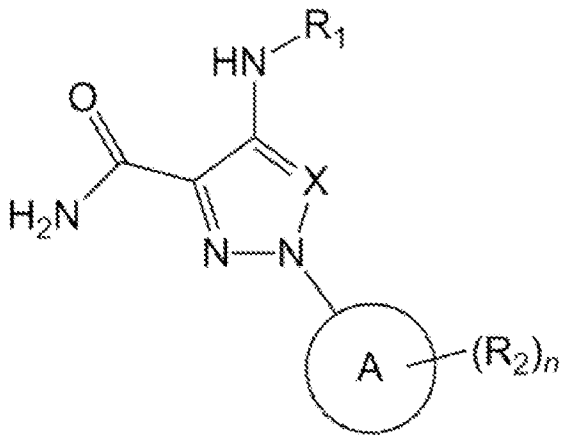
A variety of medical conditions that affect millions of people are caused or exacerbated by unregulated activity of protein kinases. For example, aberrant kinase activity is associated with autoimmune diseases, inflammatory diseases, bone diseases, metabolic diseases, neurological and neurodegenerative diseases, cancer, cardiovascular diseases, allergies, asthma, Alzheimer's disease, Parkinson's disease, skin disorders, eye diseases, infectious diseases and hormone-related diseases. For many such disorders, however, no effective inhibitor or activator exists for the particular kinase that causes the disorder or its symptoms. Consequently, patients continue to suffer from an array of disorders due to the lack of suitable medicaments for their conditions.

Summary

The invention provides compounds that modulate the activity of protein kinases that are associated with human diseases, disorders, and conditions. In particular, compounds of the invention inhibit TYK2, a member of the Janus Kinase (JAK) family of non-receptor protein kinases. Altered or unregulated activity of TYK2 promotes inflammation and is implicated in autoimmune diseases, such as psoriasis, lupus, multiple sclerosis, and inflammatory bowel disease. Thus, embodiments of the invention are useful as pharmaceutical compositions for treatment of such autoimmune conditions. The invention also provides methods of using the

compounds to modulate kinase activity in cells and to treat conditions, such as autoimmune conditions, for which modulation of kinase activity provides a therapeutic benefit.

In an aspect, the invention provides compounds of Formula (II):



(II),

wherein:

X is N or CH;

R_1 is $C(O)CH_2R_3$, optionally substituted cycloalkyl, optionally substituted cycloheteroalkyl, optionally substituted cycloalkenyl, optionally substituted cycloheteroalkenyl, optionally substituted aryl, or optionally substituted heteroaryl;

each instance of R_2 is independently halo, haloalkyl, cyano, optionally substituted alkoxyl, optionally substituted alkyl, optionally substituted heteroalkyl, optionally substituted alkenyl, optionally substituted heteroalkenyl;

R_3 is optionally substituted cycloalkyl, optionally substituted cycloheteroalkyl, optionally substituted cycloalkenyl, optionally substituted cycloheteroalkenyl, optionally substituted aryl, or optionally substituted heteroaryl;

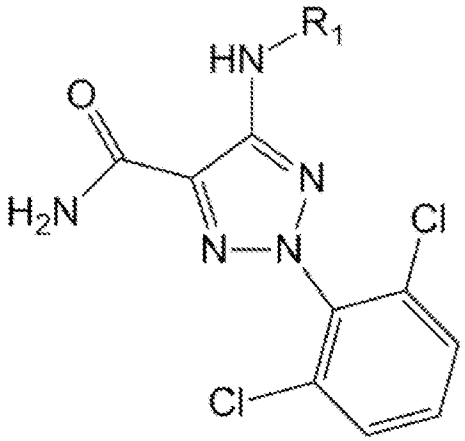
A is cycloalkyl, cycloheteroalkyl, cycloalkenyl, cycloheteroalkenyl, aryl, or heteroaryl; and

n is 0-5.

The optionally substituted aryl in R_1 may be other than a phenyl.

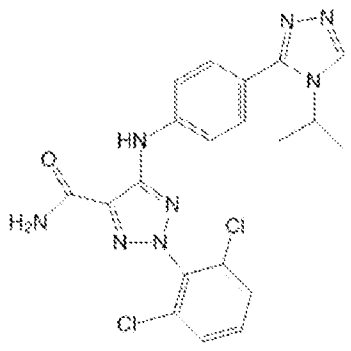
A may be an aryl substituted with 2 or 3 instances of R_2. A may be a phenyl substituted with 2 or 3 instances of R_2. A may be a heteroaryl substituted with 2 or 3 instances of R_2. A may be a six-membered heteroaryl substituted with 2 or 3 instances of R_2.

The compound of Formula (II) may be represented by Formula (IIa):

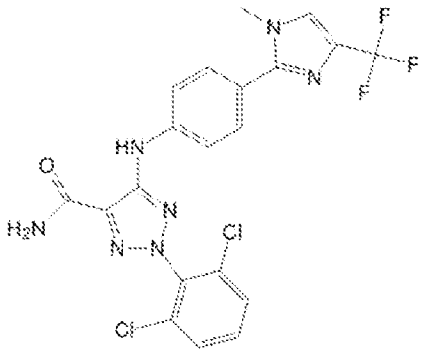


(IIa).

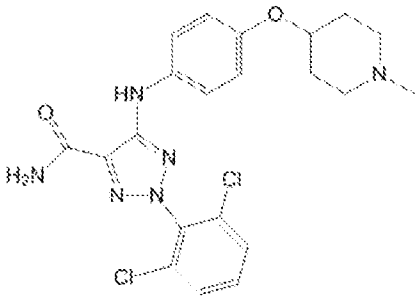
The compound of Formula (IIa) may be represented by one of Formulas (IIa-1), (IIa-2), (IIa-3), (IIa-4), (IIa-5), (IIa-6), (IIa-7), (IIa-8), (IIa-9), (IIa-10), (IIa-11), (IIa-12), (IIa-13), (IIa-14), (IIa-15), (IIa-16), and (IIa-17):



(IIa-1),



(IIa-2),



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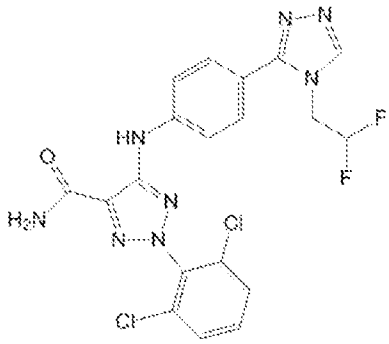
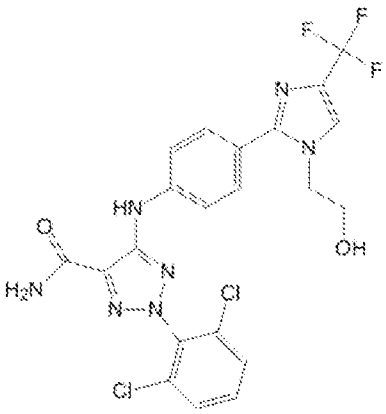
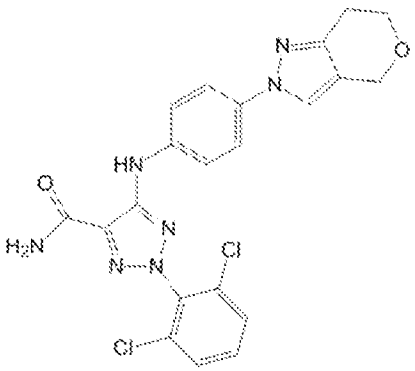


(IIa-4),



(IIa-5),



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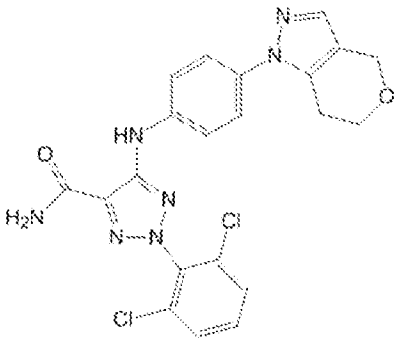
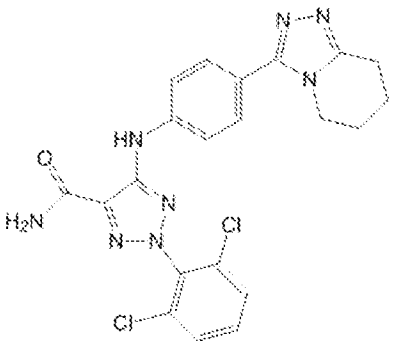
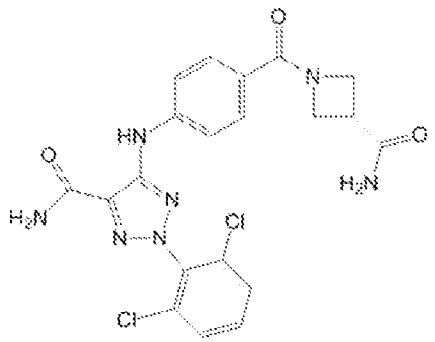


(IIa-7),



(IIa-8),



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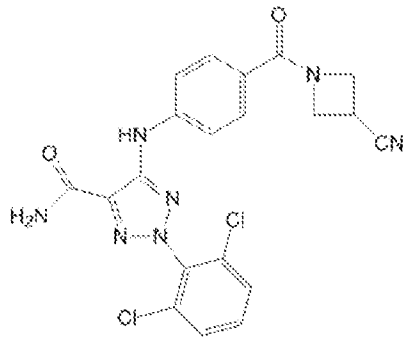

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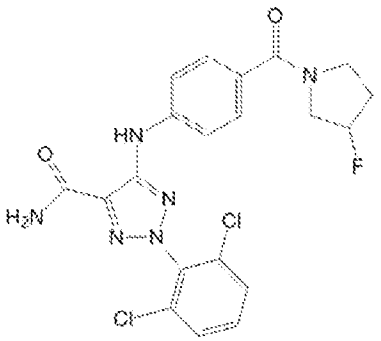
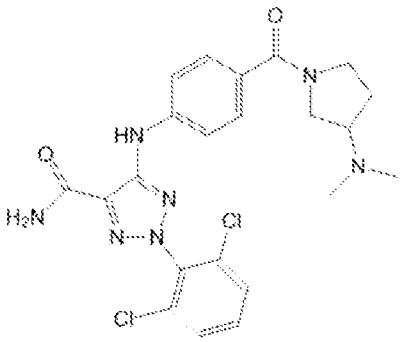
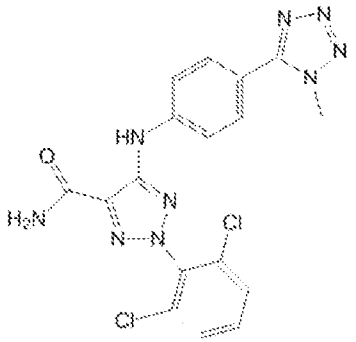


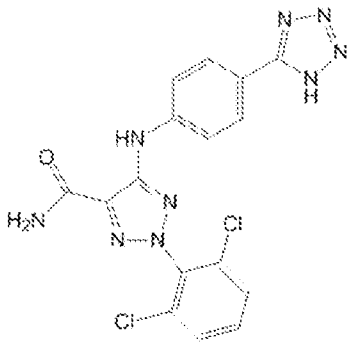
(IIa-11),



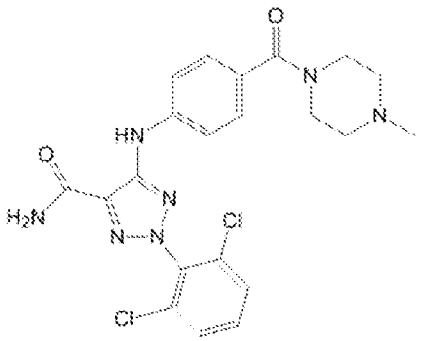
(IIa-12),



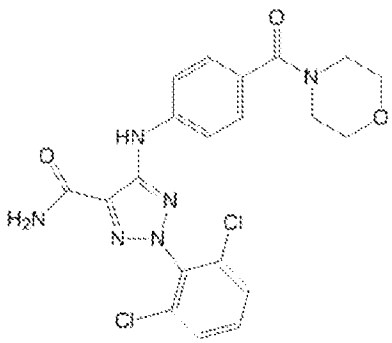
(IIa-13),



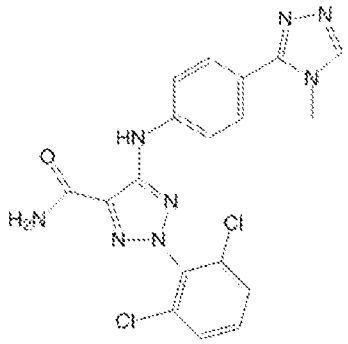
(IIa-14),



(IIa-15),

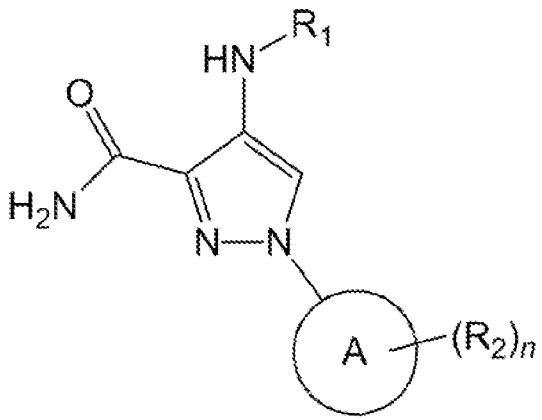


(IIa-16), and



(IIa-17).

In another aspect, the invention provides compounds of Formula (I):



(I),

wherein:

R_1 is $C(O)CH_2R_3$, optionally substituted cycloalkyl, optionally substituted cycloheteroalkyl, optionally substituted cycloalkenyl, optionally substituted cycloheteroalkenyl, optionally substituted aryl, or optionally substituted heteroaryl;

each instance of R_2 is independently halo, haloalkyl, cyano, optionally substituted alkoxyl, optionally substituted alkyl, optionally substituted heteroalkyl, optionally substituted alkenyl, optionally substituted heteroalkenyl;

R_3 is optionally substituted cycloalkyl, optionally substituted cycloheteroalkyl, optionally substituted cycloalkenyl, optionally substituted cycloheteroalkenyl, optionally substituted aryl, or optionally substituted heteroaryl;

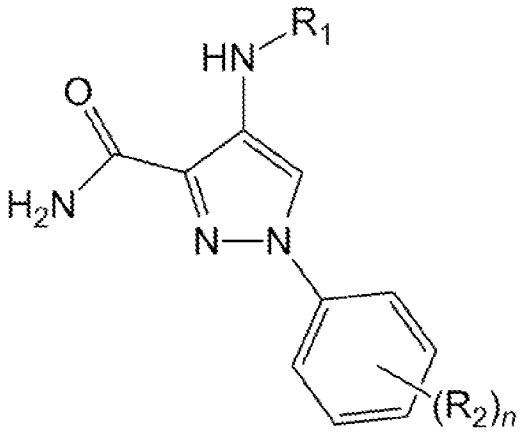
A is cycloalkyl, cycloheteroalkyl, cycloalkenyl, cycloheteroalkenyl, aryl, or heteroaryl; and

n is 0-5.

The optionally substituted aryl in R_1 may be other than a phenyl.

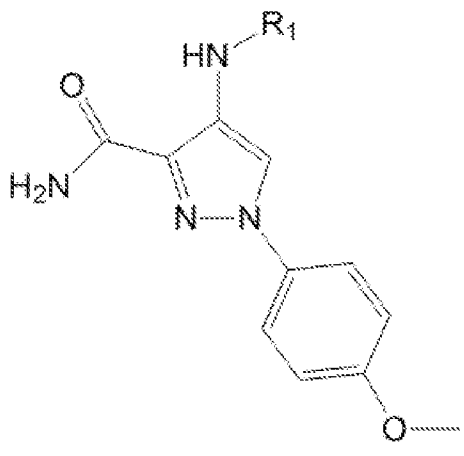
A may be an aryl substituted with 2 or 3 instances of R_2. A may be a phenyl substituted with 2 or 3 instances of R_2. A may be a heteroaryl substituted with 2 or 3 instances of R_2. A may be a six-membered heteroaryl substituted with 2 or 3 instances of R_2.

The compound of Formula (I) may be represented by Formula (Ia):

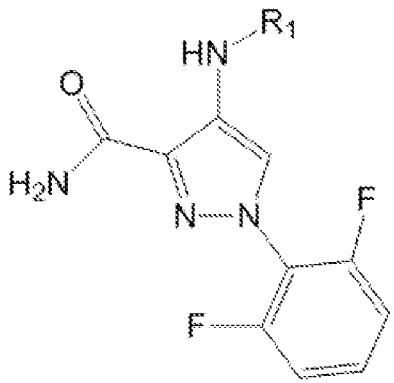


(Ia).

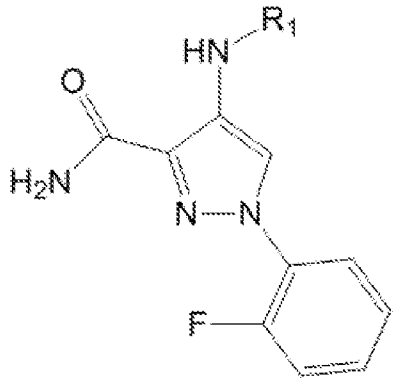
The compound of Formula (Ia) may be represented by one of Formulas (Ia-1), (Ia-2), (Ia-3), (Ia-4), (Ia-5), (Ia-6), and (Ia-7):



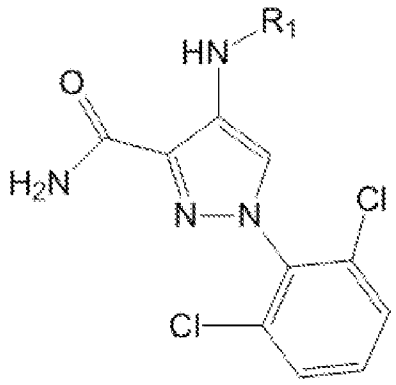
(Ia-1),



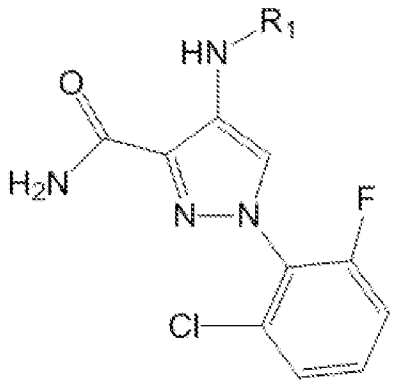
(Ia-2),



(Ia-3),



(Ia-4),



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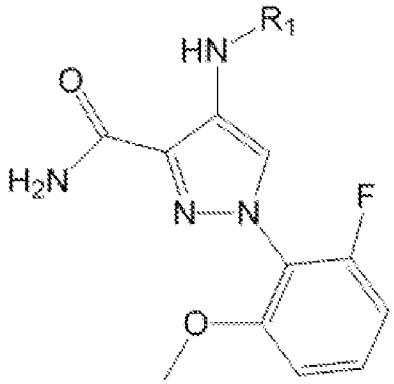
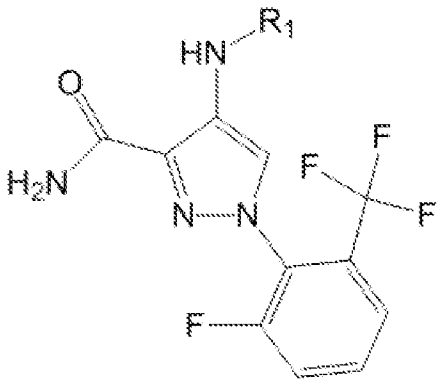
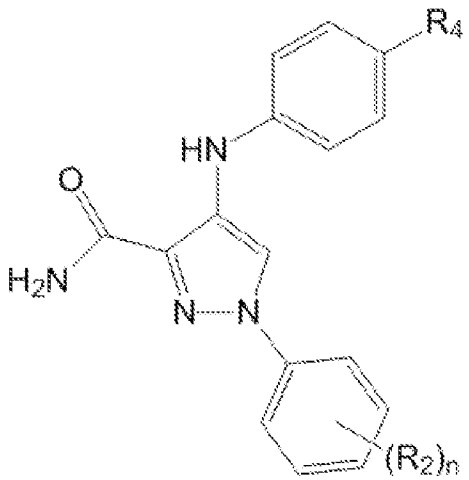


(Ia-6), and



(Ia-7).

The compound of Formula (I) may be represented by Formula (Ib):



(Ib),

wherein:

R_4 is H, $C(O)NR_5R_6$, $C(O)R_5$, $S(O)_2R_5$, $S(O)_2NR_5R_6$, $P(O)R_7R_8$, OR_5, optionally substituted cycloalkyl, optionally substituted cycloheteroalkyl, optionally substituted cycloalkenyl, optionally substituted cycloheteroalkenyl, optionally substituted aryl, or optionally substituted heteroaryl;

either:

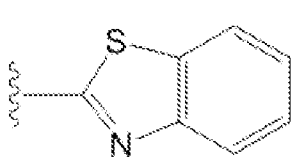
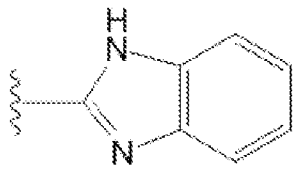
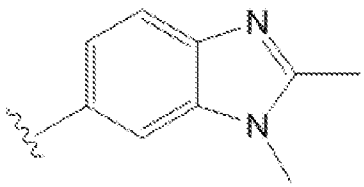
R_5 is H, optionally substituted alkyl, optionally substituted heteroalkyl, optionally substituted cycloalkyl, optionally substituted cycloheteroalkyl, optionally substituted cycloalkenyl, optionally substituted cycloheteroalkenyl, optionally substituted aryl, or optionally substituted heteroaryl, and R_6, if present, is H, optionally substituted alkyl, or optionally substituted heteroalkyl; or

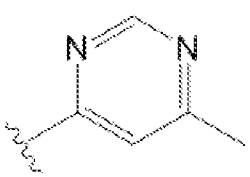
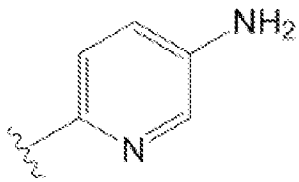
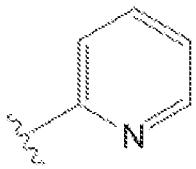
R_5 and R_6 together form an optionally substituted cycloalkyl or optionally substituted cycloheteroalkyl;

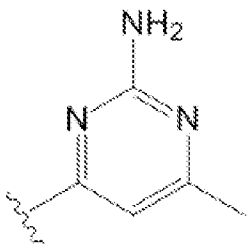
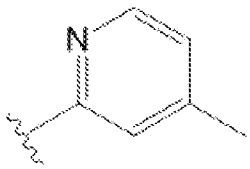
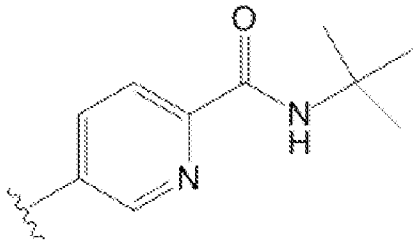
R_7 is optionally substituted alkyl or optionally substituted heteroalkyl; and

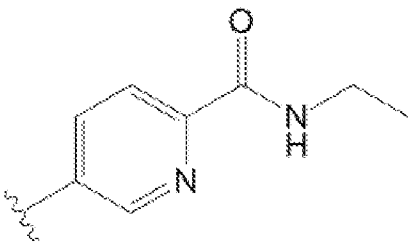
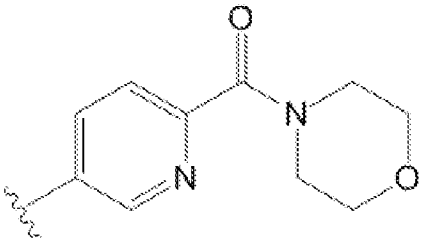
R_8 is optionally substituted alkyl or optionally substituted heteroalkyl.

R_1 may be a heteroaryl having one of the following structures:

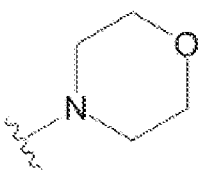




, and .

R_3 may have the following structure:



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In another aspect, the invention provides pharmaceutical compositions containing one or more compounds of the invention, such as any of the compounds described above.

In another aspect, the invention provides methods of modulating the activity of a kinase by contacting cells containing a kinase with one or more compounds of the invention, such as any of those described above.

The compound may inhibit activity of the kinase. The compound may increase activity of the kinase.

The kinase may be a JAK family kinase. The kinase may be, LRRK2, NUAK1, JAK1, JAK2, or TYK2.

In another aspect, the invention provides methods of treating a condition in a subject by administering to the subject a compound of the invention, such as any of those described above.

The condition may be characterized by elevated activity of a kinase. The condition may be characterized by altered activity of a kinase.

The kinase may be a JAK family kinase. The kinase may be LRRK2, NUAK1, JAK1, JAK2, or TYK2.

The condition may be an autoimmune disease, inflammatory disease, bone disease, metabolic disease, neurological or neurodegenerative disease, cancer, cardiovascular disease, allergies, asthma, Alzheimer's disease, Parkinson's disease, skin disorder, eye disease, infectious disease, or hormone-related disease.

In another aspect, the invention provides use of a compound of the invention, such as any of those described above, for making a medicament. In embodiments of the use, the medicament is useful for treating a condition in a subject.

In embodiments of the use the condition is characterize by elevated activity or altered activity of a kinase. In embodiments of the use, the kinase is a JAK family kinase. In embodiments of the use, the kinase is LRRK2, NUAK1, JAK1, JAK2, or TYK2.

In embodiments of the use, the condition is an autoimmune disease, inflammatory disease, bone disease, metabolic disease, neurological or neurodegenerative disease, cancer, cardiovascular disease, allergies, asthma, Alzheimer's disease, Parkinson's disease, skin disorder, eye disease, infectious disease, or hormone-related disease.

Detailed Description

Chemical definitions

The expression alkyl refers to a radical of a straight-chain or branched saturated hydrocarbon group having from 1 to 20 carbon atoms ("$C_{1–20}$ alkyl"). In some embodiments, an alkyl group has 1 to 12 carbon atoms ("$C_{1–12}$ alkyl"). In some embodiments, an alkyl group has 1 to 10 carbon atoms ("$C_{1–10}$ alkyl"). In some embodiments, an alkyl group has 1 to 9 carbon atoms ("$C_{1–9}$ alkyl"). In some embodiments, an alkyl group has 1 to 8 carbon atoms ("$C_{1–8}$ alkyl"). In some embodiments, an alkyl group has 1 to 7 carbon atoms ("$C_{1–7}$ alkyl"). In some embodiments, an alkyl group has 1 to 6 carbon atoms ("$C_{1–6}$ alkyl", also referred to herein as "lower alkyl"). In some embodiments, an alkyl group has 1 to 5 carbon atoms ("$C_{1–5}$ alkyl"). In some embodiments, an alkyl group has 1 to 4 carbon atoms ("$C_{1–4}$ alkyl"). In some embodiments, an alkyl group has 1 to 3 carbon atoms ("$C_{1–3}$ alkyl"). In some embodiments, an alkyl group has 1 to 2 carbon atoms ("$C_{1–2}$ alkyl"). In some embodiments, an alkyl group has 1 carbon atom ("C_1 alkyl"). In some embodiments, an alkyl group has 2 to 6 carbon atoms ("$C_{2–6}$ alkyl"). Examples of C_{1-6} alkyl groups include methyl (C_1), ethyl (C_2), n-propyl (C_3), isopropyl (C_3), n-butyl (C_4), tert-butyl (C_4), sec-butyl (C_4), isobutyl (C_4), n-pentyl (C_5), 3-pentanyl (C_5), amyl (C_5), neopentyl (C_5), 3-methyl-2-butanyl (C_5), tertiary amyl (C_5), and n-hexyl (C_6). Additional examples of alkyl groups include n-heptyl (C_7), n-octyl (C_8) and the like. Unless otherwise specified, each instance of an alkyl group is independently optionally substituted, i.e., unsubstituted (an "unsubstituted alkyl") or substituted (a "substituted alkyl") with one or more substituents; e.g., from 1 to 5 substituents, 1 to 3 substituents, or 1 substituent. In certain embodiments, the alkyl group is unsubstituted C_{1-10} alkyl (e.g., $-CH_3$). In certain embodiments, the alkyl group is substituted C_{1-10} alkyl. Common alkyl abbreviations include Me ($-CH_3$), Et ($-CH_2CH_3$), iPr ($-CH(CH_3)_2$), nPr ($-CH_2CH_2CH_3$), n-Bu ($-CH_2CH_2CH_2CH_3$), or i-Bu ($-CH_2CH(CH_3)_2$).

The expression heteroalkyl refers to an alkyl group, as defined herein, which further comprises 1 or more (e.g., 1, 2, 3, or 4) heteroatoms (e.g., oxygen, sulfur, nitrogen, boron, silicon, phosphorus) within the parent chain, wherein the one or more heteroatoms is inserted between adjacent carbon atoms within the parent carbon chain and/or one or more heteroatoms is inserted between a carbon atom and the parent molecule, i.e., between the point of attachment. In certain embodiments, a heteroalkyl group refers to a saturated group having from 1 to 10 carbon atoms and 1, 2, 3, or 4 heteroatoms ("heteroC_{1-10} alkyl"). In some embodiments, a heteroalkyl

group is a saturated group having 1 to 9 carbon atoms and 1, 2, 3, or 4 heteroatoms ("heteroC_{1-9} alkyl"). In some embodiments, a heteroalkyl group is a saturated group having 1 to 8 carbon atoms and 1, 2, 3, or 4 heteroatoms ("heteroC_{1-8} alkyl"). In some embodiments, a heteroalkyl group is a saturated group having 1 to 7 carbon atoms and 1, 2, 3, or 4 heteroatoms ("heteroC_{1-7} alkyl"). In some embodiments, a heteroalkyl group is a group having 1 to 6 carbon atoms and 1, 2, or 3 heteroatoms ("heteroC_{1-6} alkyl"). In some embodiments, a heteroalkyl group is a saturated group having 1 to 5 carbon atoms and 1 or 2 heteroatoms ("heteroC_{1-10} alkyl"). In some embodiments, a heteroalkyl group is a saturated group having 1 to 4 carbon atoms and 1 or 2 heteroatoms ("heteroC_{1-4} alkyl"). In some embodiments, a heteroalkyl group is a saturated group having 1 to 3 carbon atoms and 1 heteroatom ("heteroC_{1-3} alkyl"). In some embodiments, a heteroalkyl group is a saturated group having 1 to 2 carbon atoms and 1 heteroatom ("heteroC_{1-2} alkyl"). In some embodiments, a heteroalkyl group is a saturated group having 1 carbon atom and 1 heteroatom ("heteroC_1 alkyl").In some embodiments, a heteroalkyl group is a saturated group having 2 to 6 carbon atoms and 1 or 2 heteroatoms ("heteroC_{2-6} alkyl").

The expression alkenyl refers to a radical of a straight-chain or branched hydrocarbon group having from 2 to 20 carbon atoms, one or more carbon-carbon double bonds (e.g., 1, 2, 3, or 4 carbon-carbon double bonds) ("C_{2-20} alkenyl"). In some embodiments, an alkenyl group has 2 to 10 carbon atoms ("C_{2-10} alkenyl"). In some embodiments, an alkenyl group has 2 to 9 carbon atoms ("C_{2-9} alkenyl"). In some embodiments, an alkenyl group has 2 to 8 carbon atoms ("C_{2-8} alkenyl"). In some embodiments, an alkenyl group has 2 to 7 carbon atoms ("C_{2-7} alkenyl"). In some embodiments, an alkenyl group has 2 to 6 carbon atoms ("C_{2-6} alkenyl"). In some embodiments, an alkenyl group has 2 to 5 carbon atoms ("C_{2-5} alkenyl"). In some embodiments, an alkenyl group has 2 to 4 carbon atoms ("C_{2-4} alkenyl"). In some embodiments, an alkenyl group has 2 to 3 carbon atoms ("C_{2-3} alkenyl"). In some embodiments, an alkenyl group has 2 carbon atoms ("C_2 alkenyl"). The one or more carbon-carbon double bonds can be internal (such as in 2-butenyl) or terminal (such as in 1- butenyl). Examples of C_{2-4} alkenyl groups include ethenyl (C_2), 1-propenyl (C_3), 2-propenyl (C_3), 1-butenyl (C_4), 2-butenyl (C_4), butadienyl (C_4), and the like. Examples of C_{2-6} alkenyl groups include the aforementioned C_{2-4} alkenyl groups as well as pentenyl (C_5), pentadienyl (C_5), hexenyl (C_6), and the like. Additional examples of alkenyl include heptenyl (C_7), octenyl (C_8), octatrienyl (C_8), and the like. Unless otherwise specified, each instance of an alkenyl group is independently optionally substituted, i.e.,

unsubstituted (an "unsubstituted alkenyl") or substituted (a "substituted alkenyl") with one or more substituents e.g., from 1 to 5 substituents, 1 to 3 substituents, or 1 substituent. In certain embodiments, the alkenyl group is unsubstituted C_{2-10} alkenyl. In certain embodiments, the alkenyl group is substituted C_{2-10} alkenyl.

The term "heteroalkenyl," as used herein, refers to an alkenyl group, as defined herein, which further comprises one or more (e.g., 1, 2, 3, or 4) heteroatoms (e.g., oxygen, sulfur, nitrogen, boron, silicon, phosphorus) wherein the one or more heteroatoms is inserted between adjacent carbon atoms within the parent carbon chain and/or one or more heteroatoms is inserted between a carbon atom and the parent molecule, i.e., between the point of attachment. In certain embodiments, a heteroalkenyl group refers to a group having from 2 to 10 carbon atoms, at least one double bond, and 1, 2, 3, or 4 heteroatoms ("heteroC_{2-10} alkenyl"). In some embodiments, a heteroalkenyl group has 2 to 9 carbon atoms at least one double bond, and 1, 2, 3, or 4 heteroatoms ("heteroC_{2-9} alkenyl"). In some embodiments, a heteroalkenyl group has 2 to 8 carbon atoms, at least one double bond, and 1, 2, 3, or 4 heteroatoms ("heteroC_{2-8} alkenyl"). In some embodiments, a heteroalkenyl group has 2 to 7 carbon atoms, at least one double bond, and 1, 2, 3, or 4 heteroatoms ("heteroC_{2-7} alkenyl"). In some embodiments, a heteroalkenyl group has 2 to 6 carbon atoms, at least one double bond, and 1, 2, or 3 heteroatoms ("heteroC_{2-6} alkenyl"). In some embodiments, a heteroalkenyl group has 2 to 5 carbon atoms, at least one double bond, and 1 or 2 heteroatoms ("heteroC_{2-5} alkenyl"). In some embodiments, a heteroalkenyl group has 2 to 4 carbon atoms, at least one double bond, and l or 2 heteroatoms ("heteroC_{2-4} alkenyl"). In some embodiments, a heteroalkenyl group has 2 to 3 carbon atoms, at least one double bond, and 1 heteroatom ("heteroC_{2-3} alkenyl"). In some embodiments, a heteroalkenyl group has 2 to 6 carbon atoms, at least one double bond, and 1 or 2 heteroatoms ("heteroCC_{2-6} alkenyl").

The expression cycloalkyl refers to a saturated or partially unsaturated (for example, a cycloalkenyl group) cyclic group that contains one or more rings, e.g., 2 or 3 rings, and contains from 3 to 14 ring carbon atoms, such as from 3 to 10 (e.g., 3, 4, 5, 6 or 7) ring carbon atoms. The expression cycloalkyl refers furthermore to groups in which one or more hydrogen atoms have been replaced by fluorine, chlorine, bromine or iodine atoms or by OH, =O, SH, =S, NH_2, =NH, N_3 or NO_2 groups, thus, for example, cyclic ketones such as, for example, cyclohexanone, 2-cyclohexenone or cyclopentanone. Further specific examples of cycloalkyl groups are a cyclopropyl, cyclobutyl, cyclopentyl, spiro[4,5]decanyl, norbornyl, cyclohexyl, cyclopentenyl,

cyclohexadienyl, decalinyl, bicyclo[4.3.0]nonyl, tetraline, cyclopentylcyclohexyl, fluorocyclohexyl or cyclohex-2-enyl group.

The expression cycloheteroalkyl or heterocycloalkyl refers to a cycloalkyl group as defined above in which one or more (e.g., 1, 2, or 3) ring carbon atoms have been replaced by an oxygen, nitrogen, silicon, selenium, phosphorus or sulfur atom or a SO group or a SO_2 group. A cycloheteroalkyl or heterocycloalkyl group may have 1 or 2 rings containing from 3 to 10 (e.g., 3, 4, 5, 6 or 7) ring atoms (e.g., C, O, N or S). Cycloheteroalkyl or heterocycloalkyl groups include cycloheteroalkenyl or heterocycloalkenyl groups. The expression cycloheteroalkyl or heterocycloalkyl refers furthermore to groups that are substituted by fluorine, chlorine, bromine or iodine atoms or by OH, =O, SH, =S, NH_2, =NH, N_3 or NO_2 groups. Examples are a piperidinyl, prolinyl, imidazolidinyl, piperazinyl, morpholinyl, urotro pinyl, pyrrolidinyl, tetrahydrothiophenyl, tetrahydropyranyl, tetrahydrofuryl or 2-pyrazolinyl group and also lactams, lactones, cyclic imides and cyclic anhydrides.

The expression alkylcycloalkyl refers to groups that contain both cycloalkyl and also alkyl, alkenyl or alkynyl groups in accordance with the above definitions, for example alkylcycloalkyl, cycloalkylalkyl, alkylcycloalkenyl, alkenylcycloalkyl and alkynylcycloalkyl groups. An alkylcycloalkyl group preferably contains a cycloalkyl group that contains one or two rings having from 3 to 10 (e.g., 3, 4, 5, 6 or 7) ring carbon atoms, and one or two alkyl or alkynyl groups having 1 or 2 to 6 carbon atoms.

The expression heteroalkylcycloalkyl refers to alkylcycloalkyl groups as defined above in which one or more (e.g., 1, 2 or 3) carbon atoms have been replaced by an oxygen, nitrogen, silicon, selenium, phosphorus or sulfur atom or a SO group or a SO_2 group. A heteroalkylcycloalkyl group preferably contains 1 or 2 rings having from 3 to 10 (e.g., 3, 4, 5, 6 or 7) ring atoms, and one or two alkyl, alkenyl, alkynyl or heteroalkyl groups having from 1 or 2 to 6 carbon atoms. Examples of such groups are alkylheterocycloalkyl, alkylheterocycloalkenyl, alkenylheterocycloalkyl, alkynylheterocycloalkyl, heteroalkylcycloalkyl, heteroalkylheterocycloalkyl and heteroalkylheterocycloalkenyl, the cyclic groups being saturated or mono-, di- or tri-unsaturated.

The expression aryl refers to an aromatic group that contains one or more rings, e.g., 2 or 3 rings, containing from 6 to 14 ring carbon atoms, such as from 6 to 10 ring carbon atoms. The expression aryl refers furthermore to groups that are substituted by fluorine, chlorine, bromine or

iodine atoms or by CH_3, OH, SH, NH_2, N_3 or NO_2 groups. Examples are the phenyl, naphthyl, biphenyl, 2-fluorophenyl, anilinyl, 3-nitrophenyl or 4-hydroxyphenyl group.

The expression heteroaryl refers to an aromatic group that contains one or more rings, e.g., 2 or 3 rings, containing from 5 to 14 ring atoms, such as from 5 to 10 ring atoms, and contains one or more (e.g., 1, 2, 3 or 4) oxygen, nitrogen, phosphorus or sulfur ring atoms. The expression heteroaryl refers furthermore to groups that are substituted by fluorine, chlorine, bromine or iodine atoms or by CH_3, OH, SH, N_3, NH_2 or NO_2 groups. Examples are pyridyl (e.g. 4-pyridyl), imidazolyl (e.g. 2-imidazolyl), phenylpyrrolyl (e.g. 3-phenylpyrrolyl), thiazolyl, isothiazolyl, 1,2,3-triazolyl, 1,2,4-triazolyl, oxadiazolyl,thiadiazolyl, indolyl, indazolyl, tetrazolyl, pyrazinyl, pyrimidinyl, pyridazinyl, oxazolyl, isoxazolyl, triazolyl, tetrazolyl, isoxazolyl, indazolyl, indolyl, benzimidazolyl, benzoxazolyl, benzisoxazolyl, benzthiazolyl, pyridazinyl, quinolinyl, isoquinolinyl, pyrrolyl, purinyl, carbazolyl, acridinyl, pyrimidyl, 2,3'-bifuryl, pyrazolyl (e.g. 3-pyrazolyl) and isoquinolinyl groups.

The expression aralkyl refers to groups containing both aryl and also alkyl, alkenyl, alkynyl and/or cycloalkyl groups in accordance with the above definitions, such as, for example, aryl- alkyl, arylalkenyl, arylalkynyl, arylcycloalkyl, arylcycloalkenyl, alkylarylcycloalkyl and alkylarylcycloalkenyl groups. Specific examples of aralkyls are toluene, xylene, mesitylene, styrene, benzyl chloride, o-fluorotoluene, lH-indene, tetraline, dihydronaphthalene, indanone, phenylcyclopentyl, cumene, cyclohexylphenyl, fluorene and indane. An aralkyl group preferably contains one or two aromatic ring systems containing from 6 to 10 carbon atoms and one or two alkyl, alkenyl and/or alkynyl groups containing from 1 or 2 to 6 carbon atoms and/or a cycloalkyl group containing 5 or 6 ring carbon atoms.

The expression heteroaralkyl refers to an aralkyl group as defined above in which one or more (e.g., 1, 2, 3 or 4) carbon atoms have been replaced by an oxygen, nitrogen, silicon, selenium, phosphorus, boron or sulfur atom, that is to say to groups containing both aryl or heteroaryl, respectively, and also alkyl, alkenyl, alkynyl and/or heteroalkyl and/or cycloalkyl and/or heterocycloalkyl groups in accordance with the above definitions. A heteroaralkyl group preferably contains one or two aromatic ring systems containing from 5 or 6 to 10 ring carbon atoms and one or two alkyl, alkenyl and/or alkynyl groups containing 1 or 2 to 6 carbon atoms and/or a cycloalkyl group containing 5 or 6 ring carbon atoms, wherein 1, 2, 3 or 4 of these carbon atoms have been replaced by oxygen, sulfur or nitrogen atoms.

Examples are arylheteroalkyl, arylheterocycloalkyl, arylheterocycloalkenyl, arylalkyl heterocycloalkyl, arylalkenylheterocycloalkyl, arylalkynylheterocycloalkyl, arylalkylhetero cycloalkenyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, heteroarylheteroalkyl, heteroarylcycloalkyl, heteroarylcycloalkenyl, heteroarylheterocycloalkyl, hetero arylheterocycloalkenyl, heteroarylalkylcycloalkyl, heteroarylalkylheterocycloalkenyl, hetero arylheteroalkylcycloalkyl, heteroarylheteroalkylcycloalkenyl and heteroarylheteroalkylhetero cycloalkyl groups, the cyclic groups being saturated or mono-, di- or tri-unsaturated. Specific examples are a tetrahydroisoquinolinyl, benzoyl, 2- or 3-ethylindolyl, 4-methylpyridino, 2-, 3- or 4-methoxyphenyl, 4-ethoxyphenyl, 2-, 3- or 4-carboxyphenylalkyl group.

As stated above, the expressions cycloalkyl, cycloheteroalkyl, heterocycloalkyl, alkylcycloalkyl, heteroalkylcycloalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl also refer to groups that are substituted by fluorine, chlorine, bromine or iodine atoms or by CH_3, OH, =O, SH, =S, NH_2, =NH, N_3 or NO_2 groups.

The expression carbocyclyl or carbocyclic refers to a radical of a non-aromatic cyclic hydrocarbon group having from 3 to 10 ring carbon atoms ("C_{3-10} carbocyclyl") and zero heteroatoms in the nonaromatic ring system. In some embodiments, a carbocyclyl group has 3 to 8 ring carbon atoms 10 ("C_{3-8} carbocyclyl"). In some embodiments, a carbocyclyl group has 3 to 7 ring carbon atoms ("C_{3-7} carbocyclyl"). In some embodiments, a carbocyclyl group has 3 to 6 ring carbon atoms ("C_{3-6} carbocyclyl"). In some embodiments, a carbocyclyl group has 5 to 10 ring carbon atoms ("C_{5-10} carbocyclyl"). Exemplary C_{3-6} carbocyclyl groups include, without limitation, cyclopropyl (C_3), cyclopropenyl (C_3), cyclobutyl (C_4), cyclobutenyl (C_4), cyclopentyl (C_5), cyclopentenyl (C_5), cyclohexyl (C_6), cyclohexenyl (C_6), cyclohexadienyl (C_6), and the like. Exemplary C_{3-8} carbocyclyl groups include, without limitation, the aforementioned C_{3-6} carbocyclyl groups as well as cycloheptyl (C_7), cycloheptenyl (C_7), cycloheptadienyl (C_7), cycloheptatrienyl (C_7), cyclooctyl (G), cyclooctenyl (G), bicyclo[2.2.1]heptanyl (C_7), bicyclo[2.2.2]octanyl (G), and the like. Exemplary C_{3-10} carbocyclyl groups include, without 20 limitation, the aforementioned G-s carbocyclyl groups as well as cyclononyl (C_9), cyclononenyl (C_9), cyclodecyl (C_{10}), cyclodecenyl (C_{10}), octahydro-1H-indenvl (C_9), decahydronaphthalenyl (C_{10}), spiro[4.5]decanyl (C_{10}), and the like. As the foregoing examples illustrate, in certain embodiments, the carbocyclyl group is either monocyclic ("monocyclic carbocyclyl") or contain a fused, bridged or spiro ring system such as a bicyclic system ("bicyclic carbocyclyl") and can

be saturated or can be partially unsaturated. "Carbocyclyl" also includes ring systems wherein the carbocyclyl ring, as defined above, is fused with one or more aryl or heteroaryl groups wherein the point of attachment is on the carbocyclyl ring, and in such instances, the number of carbons continue to designate the number of carbons in the carbocyclic ring system. Unless otherwise specified, each instance of a carbocyclyl group is independently optionally substituted, *i.e.*, unsubstituted (an "unsubstituted carbocyclyl") or substituted (a "substituted carbocyclyl") with one or more substituents. In certain embodiments, the carbocyclyl group is unsubstituted C_{3-10} carbocyclyl. In certain embodiments, the carbocyclyl group is a substituted C_{3-10} carbocyclyl.

In some embodiments, "carbocyclyl" is a monocyclic, saturated carbocyclyl group having from 3 to 10 ring carbon atoms ("C_{3-10} cycloalkyl"). In some embodiments, a cycloalkyl group has 3 to 8 ring carbon atoms ("C_{3-8} cycloalkyl"). In some embodiments, a cycloalkyl group has 3 to 6 ring carbon atoms ("C_{3-6} cycloalkyl"). In some embodiments, a cycloalkyl group has 5 to 6 ring carbon atoms ("C_{5-6} cycloalkyl"). In some embodiments, a cycloalkyl group has 5 to 10 ring carbon atoms ("C_{5-10} cycloalkyl"). Examples of C_{5-6} cycloalkyl groups include cyclopentyl (C_5) and cyclohexyl (C_5). Examples of C_{3-6} cycloalkyl groups include the aforementioned C_{5-6} cycloalkyl groups as well as cyclopropyl (C_3) and cyclobutyl (C_4). Examples of C_{3-8} cycloalkyl groups include the aforementioned C_{3-6} cycloalkyl groups as well as cycloheptyl (C_7) and cyclooctyl (C_8). Unless otherwise specified, each instance of a cycloalkyl group is independently unsubstituted (an "unsubstituted cycloalkyl") or substituted (a "substituted cycloalkyl") with one or more substituents. In certain embodiments, the cycloalkyl group is unsubstituted C_{3-10} cycloalkyl. In certain embodiments, the cycloalkyl group is substituted C_{3-10} cycloalkyl.

The expression heterocyclyl or heterocyclic refers to a radical of a 3- to 14-membered non-aromatic ring system having ring carbon atoms and 1 to 4 ring heteroatoms, wherein each heteroatom is independently selected from nitrogen, oxygen, sulfur, boron, phosphorus, and silicon ("3-14 membered heterocyclyl"). In heterocyclyl groups that contain one or more nitrogen atoms, the point of attachment can be a carbon or nitrogen atom, as valency permits. A heterocyclyl group can either be monocyclic ("monocyclic heterocyclyl") or a fused, bridged or spiro ring system such as a bicyclic system ("bicyclic heterocyclyl"), and can be saturated or can be partially unsaturated. Heterocyclyl bicyclic ring systems can include one or more heteroatoms in one or both rings. "Heterocyclyl" also includes ring systems wherein the heterocyclyl ring, as defined above, is fused with one or more carbocyclyl groups wherein the point of attachment is

either on the carbocyclyl or heterocyclyl ring, or ring systems wherein the heterocyclyl ring, as defined above, is fused with one or more aryl or heteroaryl groups, wherein the point of attachment is on the heterocyclyl ring, and in such instances, the number of ring members continue to designate the number of ring members in the heterocyclyl ring system. Unless otherwise specified, each instance of heterocyclyl is independently optionally substituted, i.e., unsubstituted (an "unsubstituted heterocyclyl") or substituted (a "substituted heterocyclyl") with one or more substituents. In certain embodiments, the heterocyclyl group is unsubstituted 3-10 membered heterocyclyl. In certain embodiments, the heterocyclyl group is substituted 3-10 membered heterocyclyl.

In some embodiments, a heterocyclyl group is a 5-10 membered non-aromatic ring system having ring carbon atoms and 1-4 ring heteroatoms, wherein each heteroatom is independently selected from nitrogen, oxygen, sulfur, boron, phosphorus, and silicon ("5-10 membered heterocyclyl"). In some embodiments, a heterocyclyl group is a 5-8 membered non-aromatic ring system having ring carbon atoms and 1-4 ring heteroatoms, wherein each heteroatom is independently selected from nitrogen, oxygen, and sulfur ("5-8 membered heterocyclyl"). In some embodiments, a heterocyclyl group is a 5-6 membered non-aromatic ring system having ring carbon atoms and 1¬4 ring heteroatoms, wherein each heteroatom is independently selected from nitrogen, oxygen, and sulfur ("5-6 membered heterocyclyl"). In some embodiments, the 5-6 membered heterocyclyl has 1-3 ring heteroatoms selected from nitrogen, oxygen, and sulfur. In some embodiments, the 5-6 membered heterocyclyl has 1-2 ring heteroatoms selected from nitrogen, oxygen, and sulfur. In some embodiments, the 5-6 membered heterocyclyl has one ring heteroatom selected from nitrogen, oxygen, and sulfur.

Exemplary 3-membered heterocyclyl groups containing one heteroatom include, without limitation, azirdinyl, oxiranyl, thiorenyl. Exemplary 4-membered heterocyclyl groups containing one heteroatom include, without limitation, azetidinyl, oxetanyl and thietanyl. Exemplary 5-membered heterocyclyl groups containing one heteroatom include, without limitation, tetrahydrofuranyl, dihydrofuranyl, tetrahydrothiophenyl, dihydrothiophenyl, pyrrolidinyl, dihydropyrrolyl and pyrrolyl-2,5-dione. Exemplary 5-membered heterocyclyl groups containing two heteroatoms include, without limitation, dioxolanyl, oxasulfuranyl, disulfuranyl, and oxazolidin-2-one. Exemplary 5-membered heterocyclyl groups containing three heteroatoms include, without limitation, triazolinyl, oxadiazolinyl, and thiadiazolinyl. Exemplary 6-

membered heterocyclyl groups containing one heteroatom include, without limitation, piperidinyl, tetrahydropyranyl, dihydropyridinyl, and thianyl. Exemplary 6-membered heterocyclyl groups 5 containing two heteroatoms include, without limitation, piperazinyl, morpholinyl, dithianyl, dioxanyl. Exemplary 6-membered heterocyclyl groups containing two heteroatoms include, without limitation, triazinanyl. Exemplary 7-membered heterocyclyl groups containing one heteroatom include, without limitation, azepanyl, oxepanyl and thiepanyl. Exemplary 8- membered heterocyclyl groups containing one heteroatom include, without limitation, azocanyl, oxecanyl and thiocanyl. Exemplary 5-membered heterocyclyl groups fused to a C_6 aryl ring (also referred to herein as a 5,6-bicyclic heterocyclic ring) include, without limitation, indolinyl, isoindolinyl, dihydrobenzofuranyl, dihydrobenzothienyl, benzoxazolinonyl, and the like. Exemplary 6-membered heterocyclyl groups fused to an aryl ring (also referred to herein as a 6,6- bicyclic heterocyclic ring) include, without limitation, tetrahydroquinolinyl, tetrahydroisoquinolinyl, and the like.

The expression optionally substituted means that at least one hydrogen present on a group (e.g., a carbon or nitrogen atom) is replaced with a permissible substituent, e.g., a substituent which upon substitution results in a stable compound, e.g., a compound which does not spontaneously undergo transformation such as by rearrangement, cyclization, elimination, or other reaction. Heteroatoms, such as nitrogen, may have substituents, such as any suitable substituent described herein which satisfies the valencies of the heteroatoms and results in the formation of a stable moiety.

For example and without limitation, optional substituents include fluorine, chlorine, bromine, and iodine atoms and CF_3, CN, OH, =O, SH, =S, NH_2, =NH, N_3 and NO_2 groups. Optional substituents also include C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_1-C_{10} heteroalkyl, C_3-C_{16} cycloalkyl, C_2-C_{17} heterocycloalkyl, C_4-C_{20} alkylcycloalkyl, C_2-C_{19} heteroalkylcycloalkyl, C_6-C_{18} aryl, C_{1-17} heteroaryl, C_7-C_{20} aralkyl or C_2-C_{19} heteroaralkyl, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_1-C_6 heteroalkyl, C_3-C_{10} cycloalkyl, C_2-C_9 heterocycloalkyl, C_7-C_{12} alkylcycloalkyl, C_2-C_{11} heteroalkylcycloalkyl, C_6-C_{10} aryl, C_1-C_9 heteroaryl, C_7-C_{12} aralkyl, C_2-C_{11} heteroaralkyl, and C_1-C_{10} haloalkyl groups.

Exemplary substituents are F, Cl, Br, OH, SH, =O, NH_2, amino, C_{1-4} alkyl, C_{1-4} heteroalkyl cyclopropyl, SF_5, NO, NO_2.

Other exemplary substituents are F, Cl, Br, OH, SH, =O, NH_2, C_{1-4} alkyl (e.g. methyl, ethyl, t-butyl), NMe_2, $CONH_2$, CH_2NMe_2, $NHSO_2Me$, $C(CH_3)2CN$, COMe, OMe, SMe, COOMe, COOEt, CH_2COOH, OCH_2COOH, COOH, SOMe, SO_2Me, cyclopropyl, SO_2NH_2, SO_2NHMe, $SO_2CH_2CH_2OH$, $NHCH_2CH_2OH$, $CH_2CH_2OCH_3$, SF_5, SO_2NMe_2, NO, NO_2, OCF_3, SO_2CF_3, CN or CF_3.

Other exemplary substituents are F, Cl, Br, Me, OMe, CN or CF_3.

The term halogen preferably refers to F, Cl, Br or I.

According to certain embodiments, all alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, alkylcycloalkyl, heteroalkylcycloalkyl, aralkyl and heteroaralkyl groups described herein may optionally be substituted.

When an aryl, heteroaryl, cycloalkyl, alkylcycloalkyl, heteroalkylcycloalkyl, heterocycloalkyl, aralkyl or heteroaralkyl group contains more than one ring, these rings may be bonded to each other via a single or double bond or these rings may be annulated.

Other optional substituents include, but are not limited to, halogen, -CN, $-NO_2$, $-N_3$, $-SO_2H$, $-SO_3H$, -OH, $-OR^{aa}$, $-ON(R^{bb})_2$, $-N(R^{bb})_2$, $-N(R^{bb})_3^+X^-$, $-N(OR^{cc})R^{bb}$, -SH, $-SR^{aa}$, $-SSR^{CC}$, $-C(O)R^{aa}$, $-CO_2H$, -CHO, $-C(OR^{cc})_2$, $-CO_2R^{aa}$, $-OC(O)R^{aa}$, $-OCO_2R^{aa}$, $-C(O)N(R^{bb})_2$, $-C(O)N(R^{aa})(R^{bb})$, $-OC(O)N(R^{bb})_2$, $-NR^{bb}C(O)R^{aa}$, $-NR^{bb}CO_2R^{aa}$, $-NR^{bb}C(O)N(R^{bb})_2$, $-C(NR^{bb})R^{aa}$, $-C(NR^{bb})OR^{aa}$, $-OC(NR^{bb})R^{aa}$, $-OC(NR^{bb})OR^{aa}$, $-C(NR^{bb})N(R^{bb})_2$, $-OC(NR^{bb})N(R^{bb})_2$, $-NR^{bb}C(NR^{bb})N(R^{bb})_2$, $-C(O)NR^{bb}SO_2R^{aa}$, $-NR^{bb}SO_2R^{aa}$, $-SO_2N(R^{bb})_2$, $-SO_2R^{aa}$, $-SO_2OR^{aa}$, $-OSO_2R^{aa}$, -S(O)R^{aa}, e.g.,-S(O)R^{aa}, $-OS(O)R^{aa}$, $-Si(R^{aa})_3$, $-OSi(R^{aa})_3$ $-C(S)N(R^{bb})_2$, $-C(O)SR^{aa}$, $-C(S)SR^{aa}$, $-SC(S)SR^{aa}$, $-SC(O)SR^{aa}$, $-OC(O)SR^{aa}$, $-SC(O)OR^{aa}$, $-SC(O)R^{aa}$, $-P(O)_2R^{aa}$, $-OP(O)_2R^{aa}$, $-P(O)(R^{aa})_2$, $-OP(O)(R^{aa})_2$, $-OP(O)(OR^{cc})_2$, $-P(O)_2N(R^{bb})_2$, $-OP(O)_2N(R^{bb})_2$, $-P(O)(NR^{bb})_2$, $-OP(O)(NR^{bb})_2$, $-NR^{bb}P(O)(OR^{cc})_2$, $-NR^{bb}P(O)(NR^{bb})_2$, $-P(R^{cc})_2$, $-P(R^{cc})_3$, $-OP(R^{cc})_2$, $-OP(R^{cc})_3$, $-B(R^{aa})_2$, $-B(OR^{cc})_2$, $-BR^{aa}(OR^{cc})$, C_{1-10} alkyl, C_{1-10} haloalkyl, C_{2-10} alkenyl, C_{3-10} carbocyclyl, 3-14 membered heterocyclyl, C_{6-14} aryl, and 5-14 membered heteroaryl, wherein each alkyl, alkenyl, carbocyclyl, heterocyclyl, aryl, and heteroaryl is independently substituted with 0, 1, 2, 3, 4, or 5 R^{dd} groups; or two geminal hydrogens on a carbon atom are replaced with the group =O, =S, $=NN(R^{bb})_2$, $=NNR^{bb}C(O)R^{aa}$, $=NNR^{bb}C(O)OR^{aa}$, $=NNR^{bb}S(O)_2R^{aa}$, $=NR^{bb}$, or $=NOR^{cc}$; in which:

each instance of R^{aa} is, independently, selected from C_{1-10} alkyl, C_{1-10} heteroalkyl, C_{1-10} haloalkyl, C_{2-10} alkenyl, C_{3-10} cycloalkyl, C_{3-10} cycloheteroalkyl, C_{3-10} cycloalkenyl, C_{3-10}

cycloheteroalkenyl, C_{3-10} carbocyclyl, 3-14 membered heterocyclyl, C_{6-14} aryl, and 5-14 membered heteroaryl, or two R^{aa} groups are joined to form a 3-14 membered cycloalkyl, 3-14 membered cycloheteroalkyl, 3-14 membered heterocyclyl or 5-14 membered heteroaryl ring, wherein each alkyl, heteroalkyl, alkenyl, cycloalkyl, cycloheteroalkyl, cycloalkenyl, cycloheteroalkenyl, carbocyclyl, heterocyclyl, aryl, and heteroaryl is independently substituted with 0, 1,2, 3, 4, or 5 R^{dd} groups;

each instance of R^{bb} is, independently, selected from hydrogen, -OH, $-OR^{aa}$, $-N(R^{cc})_2$, -CN, $-C(O)R^{aa}$, $-C(O)N(R^{cc})_2$, $-CO_2R^{aa}$, $-SO_2R^{aa}$, $-C(NR^{cc})OR^{aa}$, $-C(NR^{cc})N(R^{cc})_2$, $-SO_2N(R^{cc})_2$, $-SO_2R^{cc}$, $-SO_2OR^{cc}$, $-SOR^{aa}$, $-C(S)N(R^{cc})_2$, $-C(O)SR^{cc}$, $-C(S)SR^{cc}$, $-P(O)_2R^{aa}$, $-P(O)(R^{aa})_2$, $-P(O)_2N(R^{cc})_2$, $-P(O)(NR^{cc})_2$, C_{1-10} alkyl, C_{1-10} heteroalkyl, C_{1-10} haloalkyl, C_{2-10} alkenyl, C_{3-10} cycloalkyl, C_{3-10} cycloheteroalkyl, C_{3-10} cycloalkenyl, C_{3-10} cycloheteroalkenyl, C_{3-10} carbocyclyl, 3-14 membered heterocyclyl, C_{6-14} aryl, and 5-14 membered heteroaryl, or two R^{aa} groups are joined to form a 3-14 membered heterocyclyl or 5-14 membered heteroaryl ring, wherein each alkyl, heteroalkyl, alkenyl, cycloalkyl, cycloheteroalkyl, cycloalkenyl, cycloheteroalkenyl, carbocyclyl, heterocyclyl, aryl, and heteroaryl is independently substituted with 0, 1,2, 3, 4, or 5 R^{dd} groups;

each instance of R^{cc} is, independently, selected from hydrogen, C_{1-10} alkyl, C_{1-10} haloalkyl, C_{2-10} alkenyl, C_{3-10} carbocyclyl, 3-14 membered heterocyclyl, C_{6-14} aryl, and 5-14 membered heteroaryl, or two R^{aa} groups are joined to form a 3-14 membered heterocyclyl or 5-14 membered heteroaryl ring, wherein each alkyl, alkenyl, carbocyclyl, heterocyclyl, aryl, and heteroaryl is independently substituted with 0, 1, 2, 3, 4, or 5 R^{dd} groups;

each instance of R^{dd} is, independently, selected from halogen, -CN, $-NO_2$, $-N_3$, $-SO_2H$, $-SO_3H$, -OH, $-OR^{ee}$, $-ON(R^{ff})_2$, $-N(R^{ff})_2$, -N(Rn);CX~, $-N(OR^{ee})R^{ff}$, -SH, $-SR^{ee}$, $-SSR^{ee}$, $-C(O)R^{ee}$, $-CO_2H$, $-CO_2R^{ee}$, $-OC(O)R^{ee}$, $-OCO_2R^{ee}$, $-C(O)N(R^{ff})_2$, $-OC(O)N(R^{ff})_2$, $-NR^{ff}C(O)R^{ee}$, $-NR^{ff}CO_2R^{ee}$, $-NR^{ff}C(O)N(R^{ff})_2$, $-C(NR^{ff})OR^{ee}$, $-OC(NR^{ff})R^{ee}$, $-OC(NR^{ff})OR^{ee}$, $-C(NR^{ff})N(R^{ff})_2$, $-OC(NR^{ff})N(R^{ff})_2$, $-NR^{ff}C(NR^{ff})N(R^{ff})_2$,- $NR^{ff}SO_2R^{ee}$, $-SO_2N(R^{ff})_2$, $-SO_2R^{ee}$, $-SO_2OR^{ee}$, $-OSO_2R^{ee}$, $-S(O)R^{ee}$, e.g.,$-S(O)R^{cc}$, $-Si(R^{ee})_3$, $-OSi(R^{ee})_3$, $-C(S)N(R^{ff})_2$, $-C(O)SR^{ee}$, $-C(S)SR^{ee}$, $-SC(S)SR^{ee}$, $-P(O)_2R^{ee}$, $-P(O)(R^{ee})_2$, $-OP(O)(R^{ee})_2$, $-OP(O)(OR^{ee})_2$, C_{1-6} alkyl, C_{1-6} heteroalkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{3-10} carbocyclyl, 3-10 membered heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, wherein each alkyl, alkenyl, carbocyclyl, heterocyclyl, aryl, and heteroaryl

is independently substituted with 0, 1, 2, 3, 4, or 5 R^{gg} groups, or two geminal R^{dd} substituents can be joined to form =O or =S;

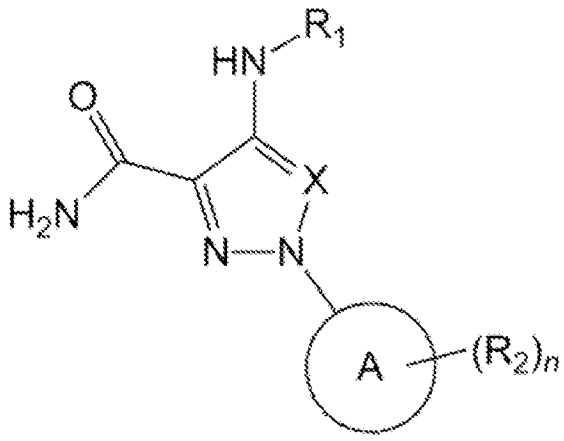
each instance of R^{ee} is, independently, selected from C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{3-10} carbocyclyl, 3-10 membered heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, wherein each alkyl, alkenyl, carbocyclyl, heterocyclyl, aryl, and heteroaryl is independently substituted with 0, 1,2, 3, 4, or 5 R^{gg} groups;

each instance of R^{ff} is, independently, selected from hydrogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{3-10} carbocyclyl, 3-10 membered heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, or two R^{ff} groups are joined to form a 3-14 membered heterocyclyl or 5-14 membered heteroaryl ring, wherein each alkyl, alkenyl, carbocyclyl, heterocyclyl, aryl, and heteroaryl is independently substituted with 0, 1,2, 3, 4, or 5 R^{gg} groups; and

each instance of R^{gg} is, independently, halogen, -CN, $-NO_2$, $-N_3$, $-SO_2H$, $-SO_3H$, -OH, $-OC_{1-6}$ alkyl, $-ON(C_{1-6}$ alkyl$)_2$, $-N(C_{1-6}$ alkyl$)_2$, $-N(C_{1-6}$ alkyl$)_3^+X^-$, $-NH(C_{1-6}$ alkyl$)_2^+X^-$, $-NH_2(C_{1-6}$ alkyl$)^+X^-$-MR^+X^-, $-N(OC_{1-6}$ alkyl$)(C_{1-6}$ alkyl), -N(OH)(C_{1-6} alkyl), - NH(OH), -SH, $-SC_{1-6}$ alkyl, $-SS(C_{1-6}$ alkyl), $-C(O)(C_{1-6}$ alkyl), $-CO_2H$, $-CO_2(C_{1-6}$ alkyl), $-OC(O)(C_{1-6}$ alkyl), $-OCO_2(C_{1-6}$ alkyl), $-C(O)NH_2$, $-C(O)N(C_{1-6}$ alkyl$)_2$, - $OC(O)NH(C_{1-6}$ alkyl), $-NHC(O)(C_{1-6}$ alkyl), $-N(C_{1-6}$ alkyl)$C(O)(C_{1-6}$ alkyl), - $NHCO_2(C_{1-6}$ alkyl), $-NHC(O)N(C_{1-6}$ alkyl$)_2$, $-NHC(O)NH(C_{1-6}$ alkyl), $-NHC(O)NH_2$, $-C(NH)O(C_{1-6}$ alkyl),$-OC(NH)(C_{1-6}$ alkyl), $-OC(NH)OC_{1-6}$ alkyl, $-C(NH)N(C_{1-6}$ alkyl$)_2$, $-C(NH)NH(C_{1-6}$ alkyl), $-C(NH)NH_2$, $-OC(NH)N(C_{1-6}$ alkyl$)_2$, - $OC(NH)NH(C_{1-6}$ alkyl), $-OC(NH)NH_2$, $-NHC(NH)N(C_{1-6}$ alkyl$)_2$, $-NHC(NH)NH_2$, - $NHSO_2(C_{1-6}$ alkyl), $-SO_2N(C_{1-6}$ alkyl$)_2$, $-SO_2NH(C_{1-6}$ alkyl), $-SO_2NH_2$,$-SO_2C_{1-6}$ alkyl, - SO_2OC_{1-6} alkyl, $-OSO_2C_{1-6}$ alkyl, $-SOC_{1-6}$ alkyl, $-Si(C_{1-6}$ alkyl$)_3$, $-OSi(C_{1-6}$ alkyl$)_3$ - $C(S)N(C_{1-6}$ alkyl$)_2$, $C(S)NH(C_{1-6}$ alkyl), $C(S)NH_2$, $-C(O)S(C_{1-6}$ alkyl), $-C(S)SC_{1-6}$ alkyl, $-SC(S)SC_{1-6}$ alkyl, $-P(O)_2(C_{1-6}$ alkyl), $-P(O)(C_{1-6}$ alkyl$)_2$, $-OP(O)(C_{1-6}$ alkyl$)_2$, $-OP(O)(OC_{1-6}$ alkyl$)_2$, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{3-10} carbocyclyl, C_{3-10} aryl, 3-10 membered heterocyclyl, 5-10 membered heteroaryl; or two geminal R^{gg} substituents can be joined to form =O or =S; wherein X^- is a counterion.

Compounds

In an aspect, the invention provides compounds of Formula (II):



(II),

wherein:

X is N or CH;

R_1 is $C(O)CH_2R_3$, optionally substituted cycloalkyl, optionally substituted cycloheteroalkyl, optionally substituted cycloalkenyl, optionally substituted cycloheteroalkenyl, optionally substituted aryl, or optionally substituted heteroaryl;

each instance of R_2 is independently halo, haloalkyl, cyano, optionally substituted alkoxyl, optionally substituted alkyl, optionally substituted heteroalkyl, optionally substituted alkenyl, optionally substituted heteroalkenyl;

R_3 is optionally substituted cycloalkyl, optionally substituted cycloheteroalkyl, optionally substituted cycloalkenyl, optionally substituted cycloheteroalkenyl, optionally substituted aryl, or optionally substituted heteroaryl;

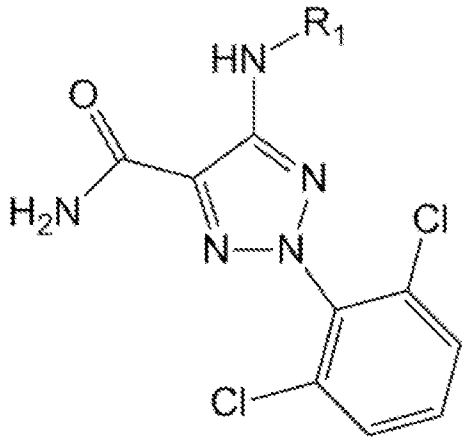
A is cycloalkyl, cycloheteroalkyl, cycloalkenyl, cycloheteroalkenyl, aryl, or heteroaryl; and

n is 0-5.

The optionally substituted aryl in R_1 may be other than a phenyl.

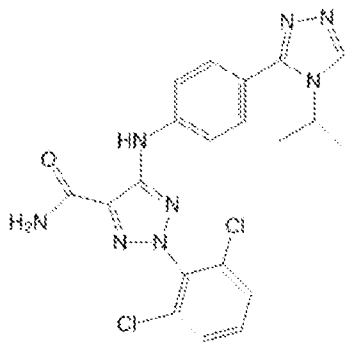
A may be an aryl substituted with 2 or 3 instances of R_2. A may be a phenyl substituted with 2 or 3 instances of R_2. A may be a heteroaryl substituted with 2 or 3 instances of R_2. A may be a six-membered heteroaryl substituted with 2 or 3 instances of R_2.

The compound of Formula (II) may be represented by Formula (IIa):

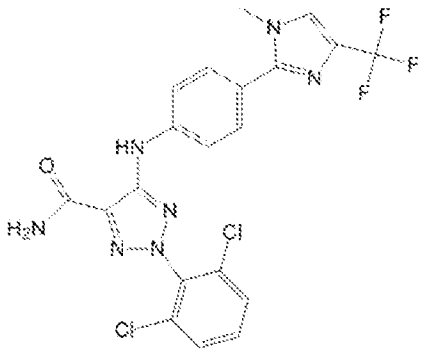


(IIa).

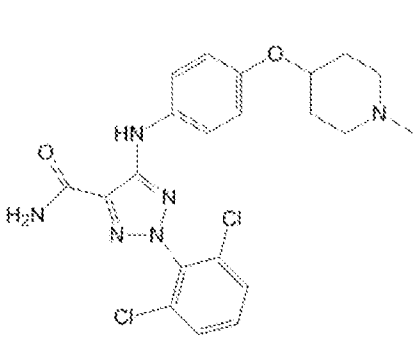
The compound of Formula (IIa) may be represented by one of Formulas (IIa-1), (IIa-2), (IIa-3), (IIa-4), (IIa-5), (IIa-6), (IIa-7), (IIa-8), (IIa-9), (IIa-10), (IIa-11), (IIa-12), (IIa-13), (IIa-14), (IIa-15), (IIa-16), and (IIa-17):



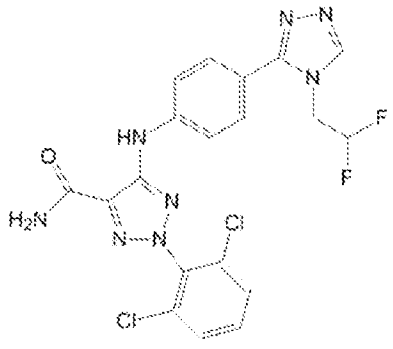
(IIa-1),



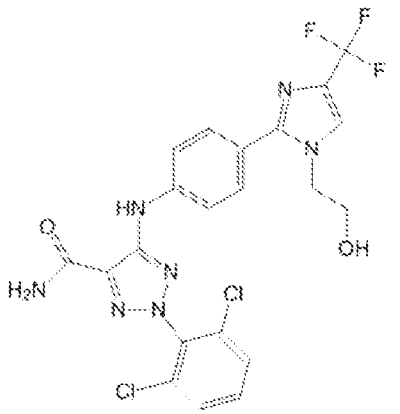
(IIa-2),



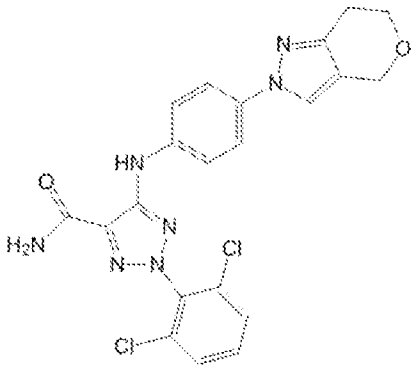
(IIa-3),



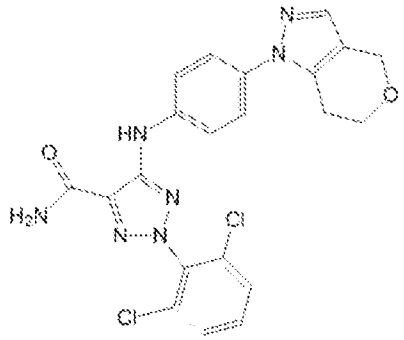
(IIa-4),



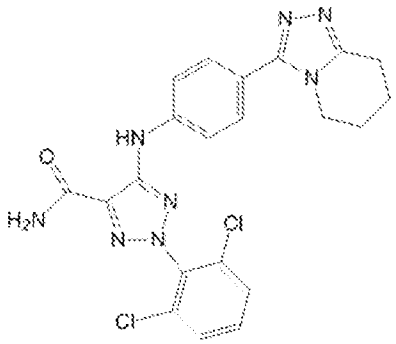
(IIa-5),



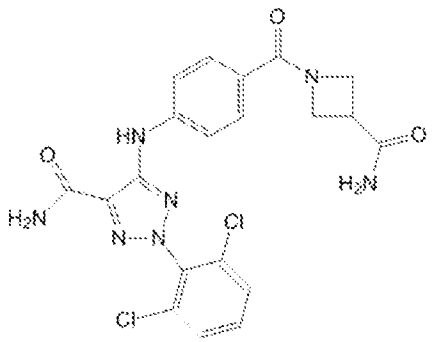
(IIa-6),



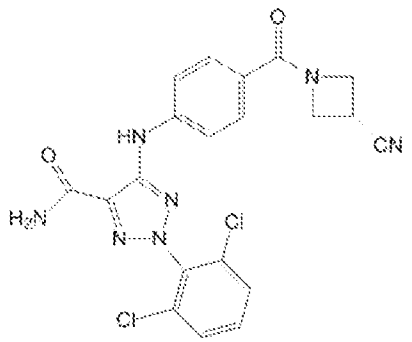
(IIa-7),



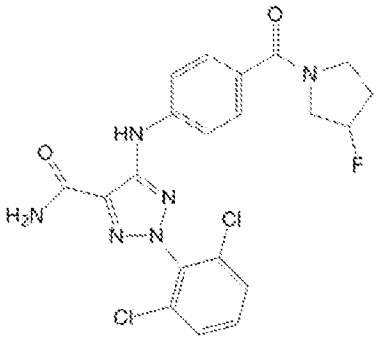
(IIa-8),



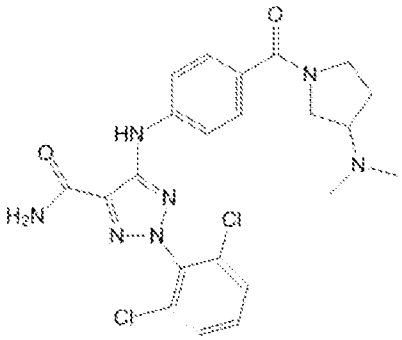
(IIa-9),



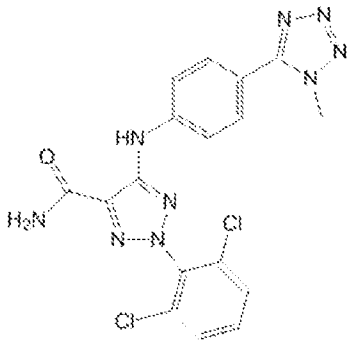
(IIa-10),



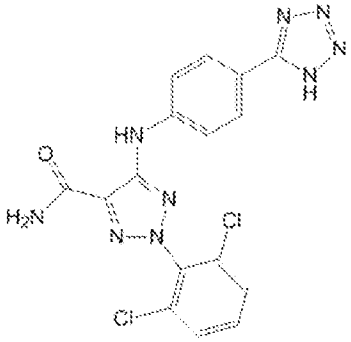
(IIa-11),



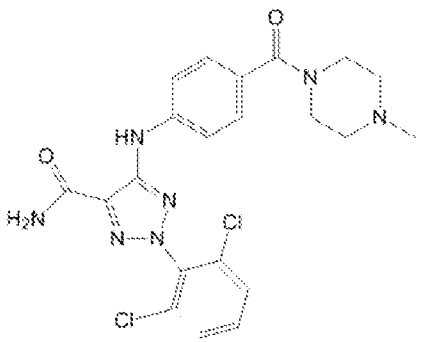
(IIa-12),



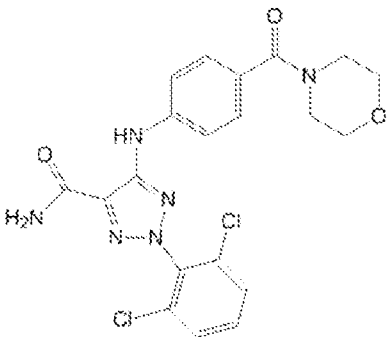
(IIa-13),



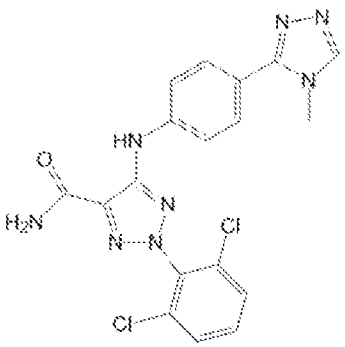
(IIa-14),



(IIa-15),



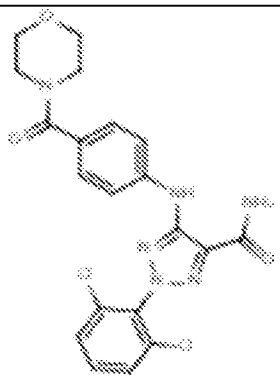
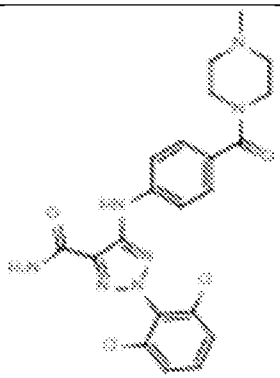
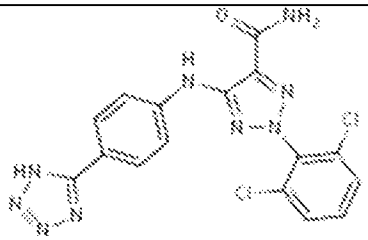
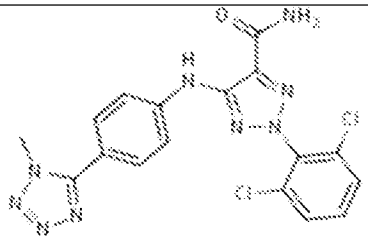
(IIa-16), and

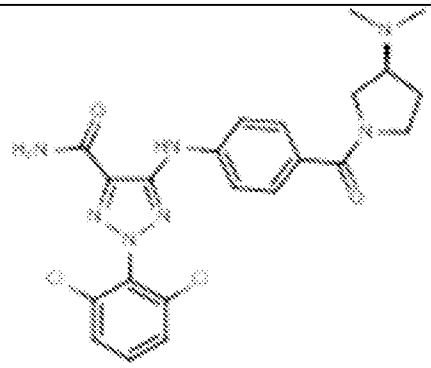
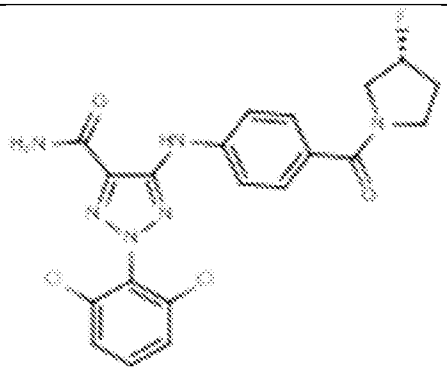
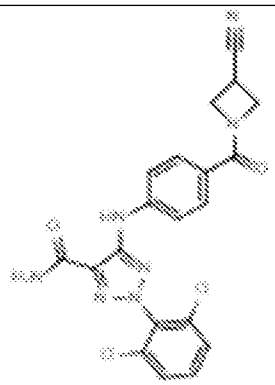
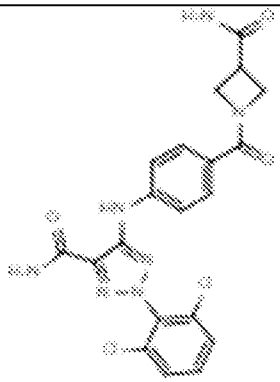


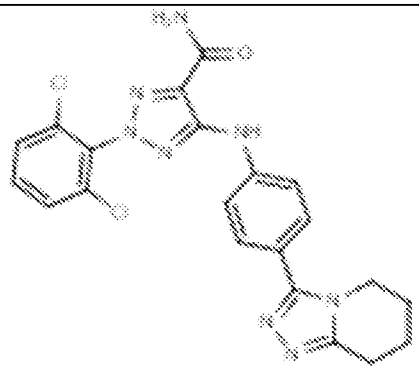
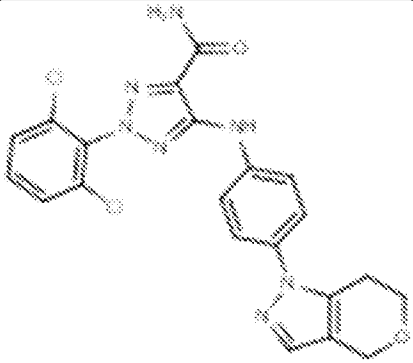
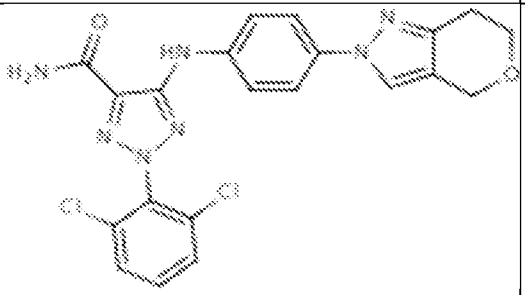
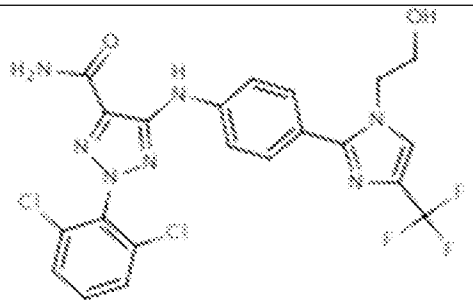
(IIa-17).

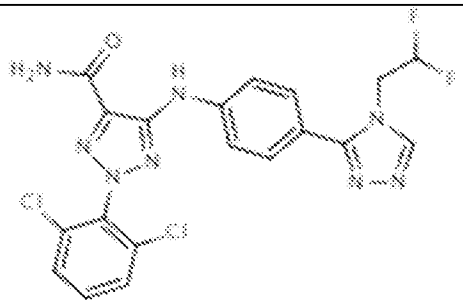
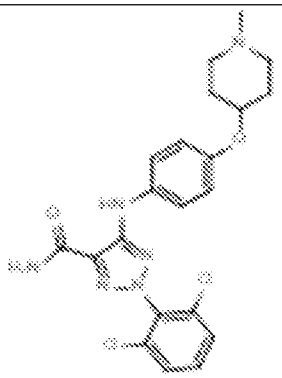
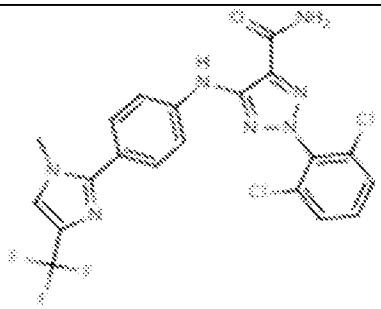
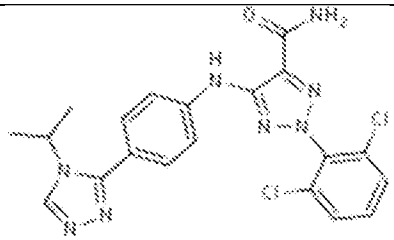
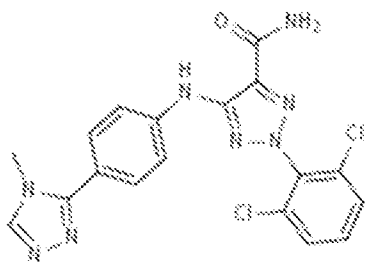
The compound of Formula (II) may have one of the structures shown in Table 1a.

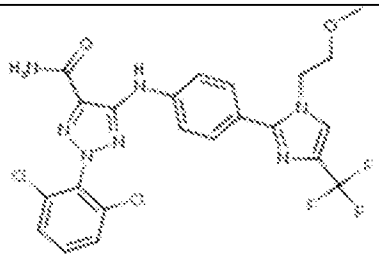
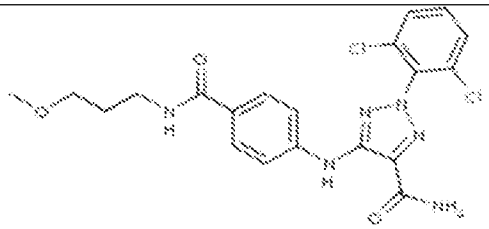
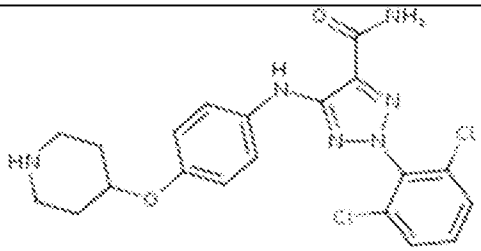
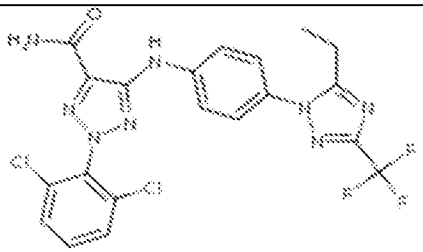
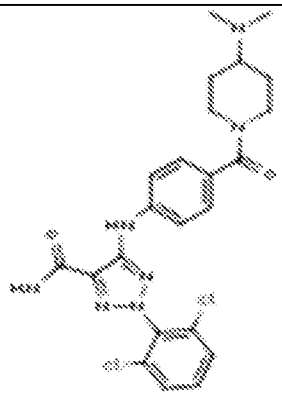
Table 1a.

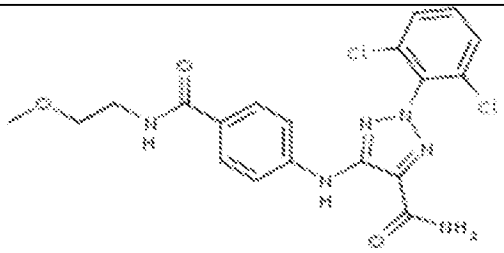
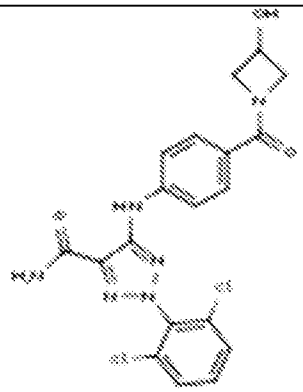
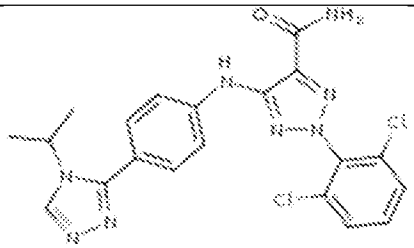
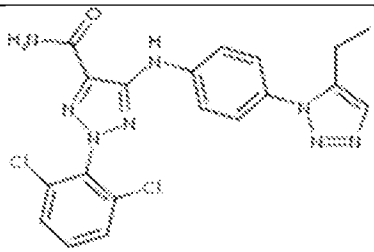
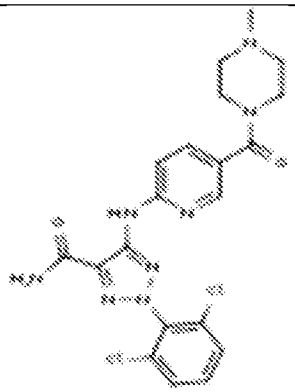
Compound No.	Structure	IUPAC-Name
101		2-(2,6-Dichloro-phenyl)-5-[4-(morpholine-4-carbonyl)-phenylamino]-2H-[1,2,3]triazole-4-carboxylic acid amide
102		2-(2,6-Dichloro-phenyl)-5-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-2H-[1,2,3]triazole-4-carboxylic acid amide
103		2-(2,6-Dichloro-phenyl)-5-[4-(1H-tetrazol-5-yl)-phenylamino]-2H-[1,2,3]triazole-4-carboxylic acid amide
104		2-(2,6-Dichloro-phenyl)-5-[4-(1-methyl-1H-tetrazol-5-yl)-phenylamino]-2H-[1,2,3]triazole-4-carboxylic acid amide

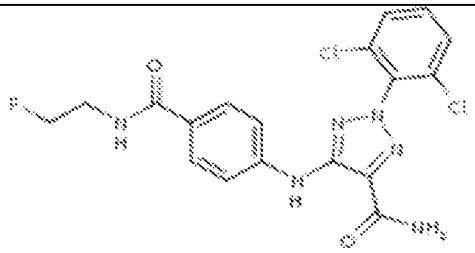
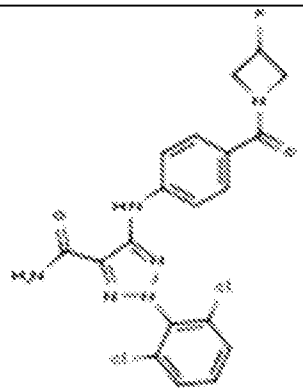
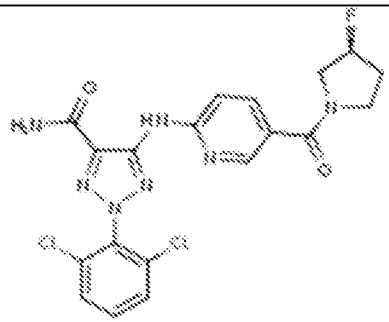
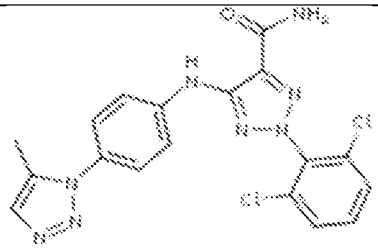
Compound No.	Structure	IUPAC-Name
105		2-(2,6-Dichloro-phenyl)-5-[4-((S)-3-dimethylamino-pyrrolidine-1-carbonyl)-phenylamino]-2H-[1,2,3]triazole-4-carboxylic acid amide
106		2-(2,6-Dichloro-phenyl)-5-[4-((R)-3-fluoro-pyrrolidine-1-carbonyl)-phenylamino]-2H-[1,2,3]triazole-4-carboxylic acid amide
107		5-[4-(3-Cyano-azetidine-1-carbonyl)-phenylamino]-2-(2,6-dichloro-phenyl)-2H-[1,2,3]triazole-4-carboxylic acid amide
108		2-(2,6-dichlorophenyl)-5-((4-(1-(2-hydroxyethyl)-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide

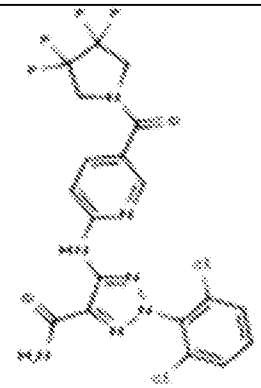
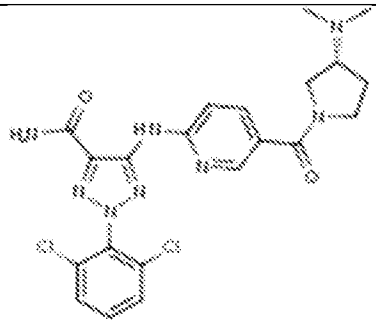
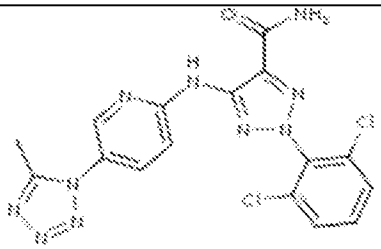
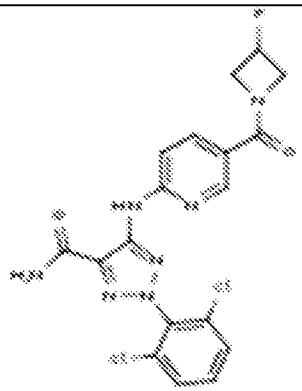
Compound No.	Structure	IUPAC-Name
109		2-(2,6-Dichloro-phenyl)-5-[4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-3-yl)-phenylamino]-2H-[1,2,3]triazole-4-carboxylic acid amide
110		2-(2,6-Dichloro-phenyl)-5-[4-(6,7-dihydro-4H-pyrano[4,3-c]pyrazol-1-yl)-phenylamino]-2H-[1,2,3]triazole-4-carboxylic acid amide
111		2-(2,6-Dichloro-phenyl)-5-[4-(6,7-dihydro-4H-pyrano[4,3-c]pyrazol-2-yl)-phenylamino]-2H-[1,2,3]triazole-4-carboxylic acid amide
112		2-(2,6-dichlorophenyl)-5-((4-(1-(2-hydroxyethyl)-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide

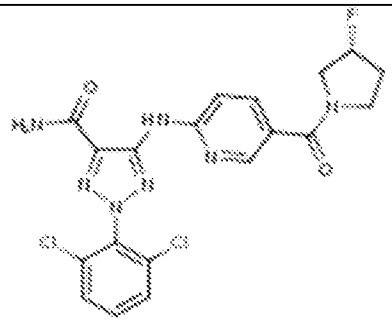
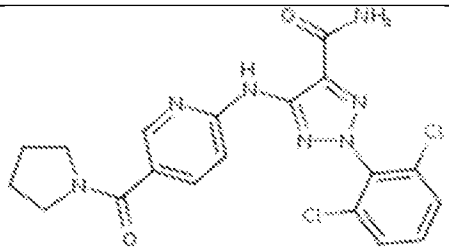
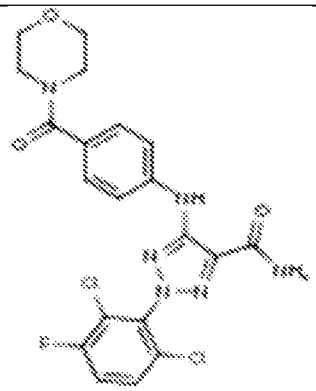
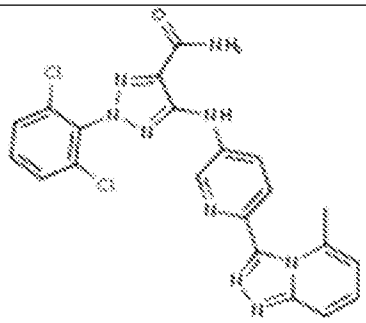
Compound No.	Structure	IUPAC-Name
113		2-(2,6-dichlorophenyl)-5-((4-(4-(2,2-difluoroethyl)-4H-1,2,4-triazol-3-yl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide
114		2-(2,6-dichlorophenyl)-5-((4-((1-methylpiperidin-4-yl)oxy)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide
115		2-(2,6-dichlorophenyl)-5-((4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide
116		2-(2,6-dichlorophenyl)-5-((4-(4-isopropyl-4H-1,2,4-triazol-3-yl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide
117		2-(2,6-dichlorophenyl)-5-((4-(4-methyl-4H-1,2,4-triazol-3-yl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide

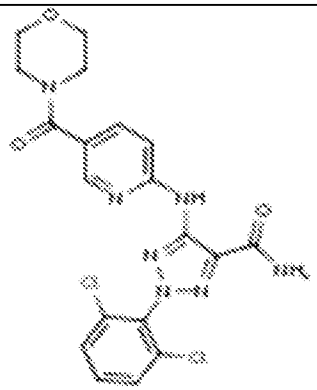
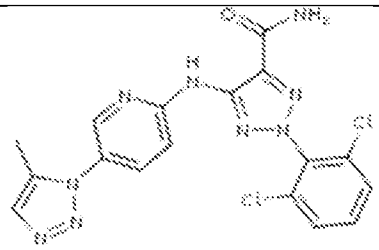
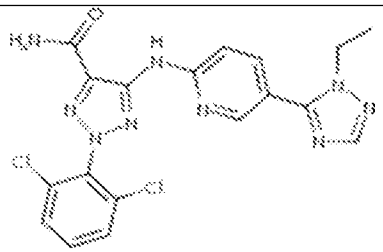
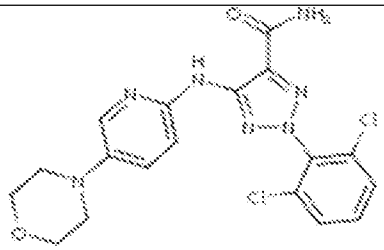
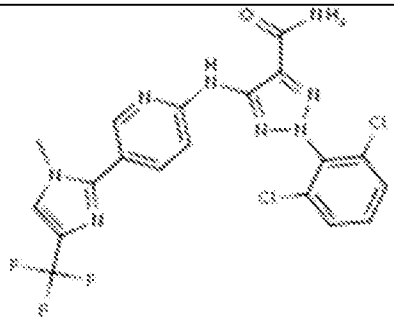
Compound No.	Structure	IUPAC-Name
118		2-(2,6-dichlorophenyl)-5-((4-(1-(2-methoxyethyl)-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide
119		2-(2,6-dichlorophenyl)-5-((4-((3-methoxypropyl)carbamoyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide
120		2-(2,6-dichlorophenyl)-5-((4-(piperidin-4-yloxy)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide
121		2-(2,6-dichlorophenyl)-5-((4-(5-ethyl-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide
122		2-(2,6-dichlorophenyl)-5-((4-(4-(dimethylamino)piperidine-1-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide

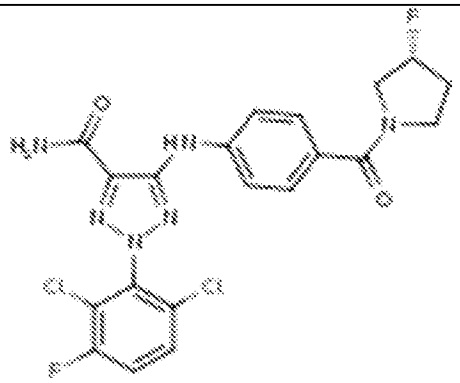
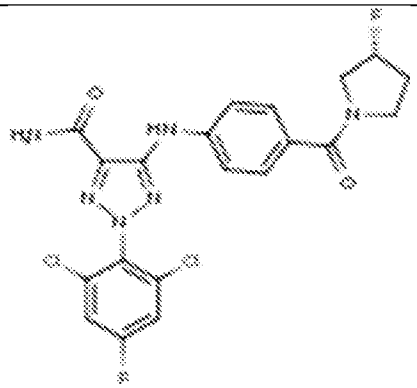
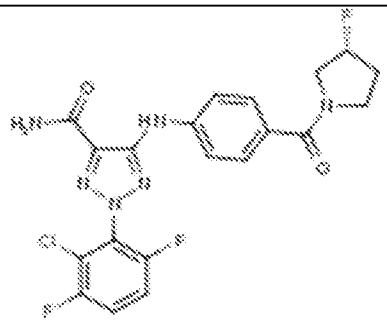
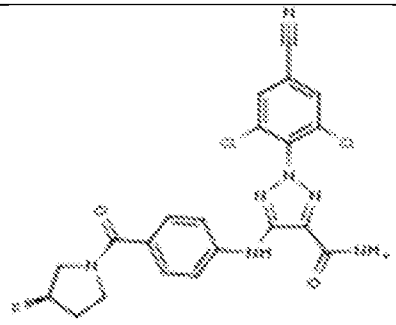
Compound No.	Structure	IUPAC-Name
123		2-(2,6-dichlorophenyl)-5-((4-((2-methoxyethyl)carbamoyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide
124		2-(2,6-dichlorophenyl)-5-((4-(3-hydroxyazetidine-1-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide
125		2-(2,6-dichlorophenyl)-5-((4-(4-isopropyl-4H-1,2,4-triazol-3-yl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide
126		2-(2,6-dichlorophenyl)-5-((4-(5-ethyl-1H-1,2,3-triazol-1-yl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide
127		2-(2,6-dichlorophenyl)-5-((5-(4-methylpiperazine-1-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide

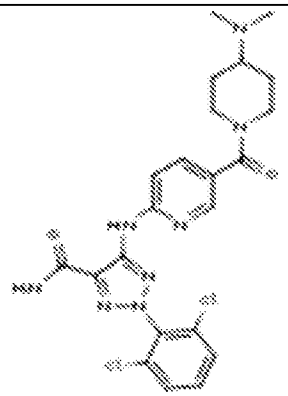
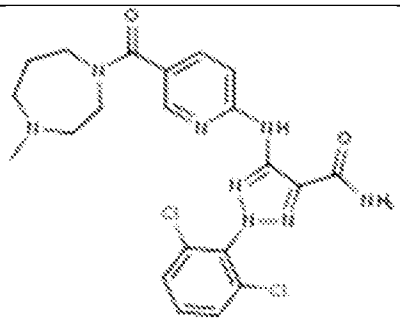
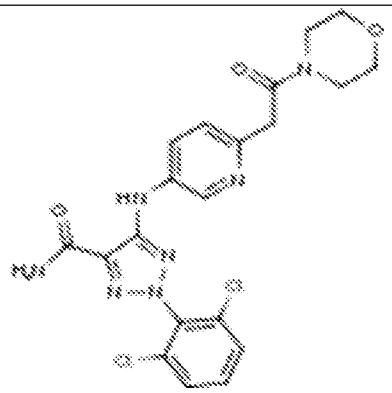
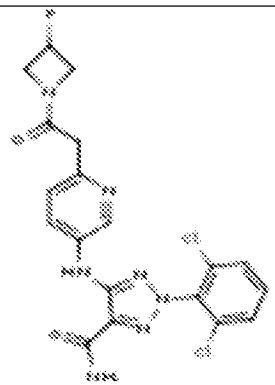
Compound No.	Structure	IUPAC-Name
128		2-(2,6-dichlorophenyl)-5-((4-((2-fluoroethyl)carbamoyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide
129		2-(2,6-dichlorophenyl)-5-((4-(3-fluoroazetidine-1-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide
130		(S)-2-(2,6-dichlorophenyl)-5-((5-(3-fluoropyrrolidine-1-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide
131		2-(2,6-dichlorophenyl)-5-((4-(5-methyl-1H-1,2,3-triazol-1-yl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide

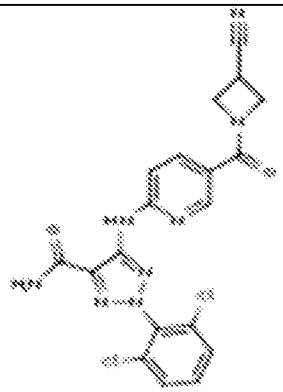
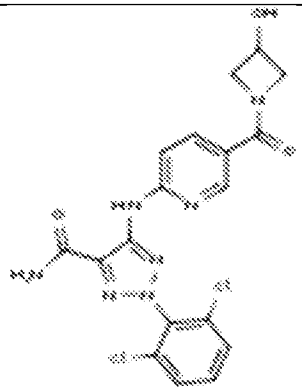
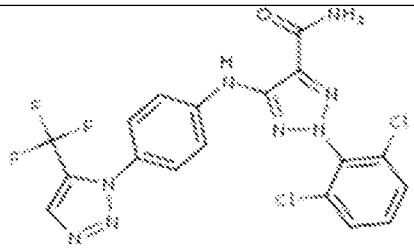
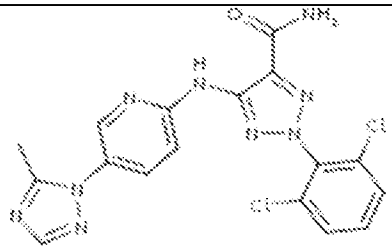
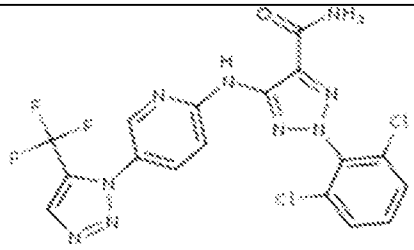
Compound No.	Structure	IUPAC-Name
132		2-(2,6-dichlorophenyl)-5-((5-(3,3,4,4-tetrafluoropyrrolidine-1-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide
133		(R)-2-(2,6-dichlorophenyl)-5-((5-(3-(dimethylamino)pyrrolidine-1-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide
134		2-(2,6-dichlorophenyl)-5-((5-(5-methyl-1H-tetrazol-1-yl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide
135		2-(2,6-dichlorophenyl)-5-((5-(3-fluoroazetidine-1-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide

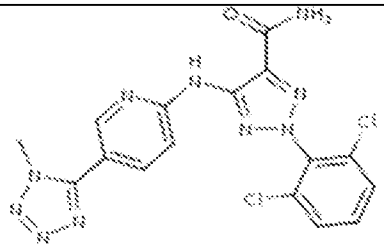
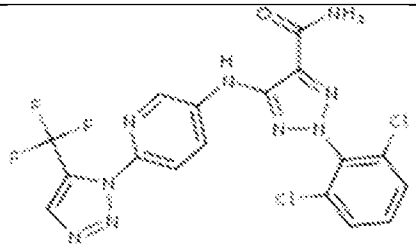
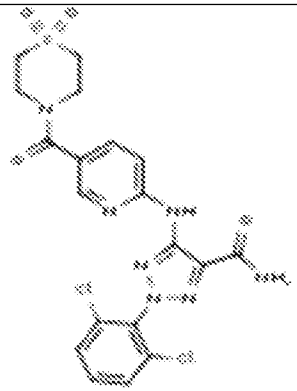
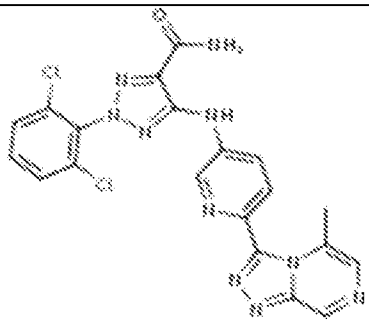
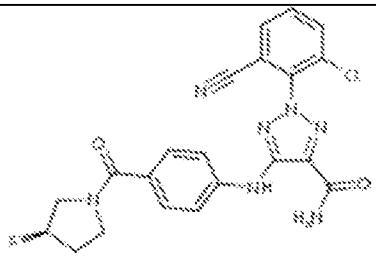
Compound No.	Structure	IUPAC-Name
136		(R)-2-(2,6-dichlorophenyl)-5-((5-(3-fluoropyrrolidine-1-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide
137		2-(2,6-dichlorophenyl)-5-((5-(pyrrolidine-1-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide
138		2-(2,6-dichloro-3-fluorophenyl)-5-((4-(morpholine-4-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide
139		2-(2,6-dichlorophenyl)-5-((6-(5-methyl-[1,2,4]triazolo[4,3-a]pyridin-3-yl)pyridin-3-yl)amino)-2H-1,2,3-triazole-4-carboxamide

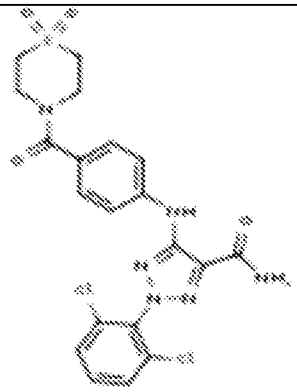
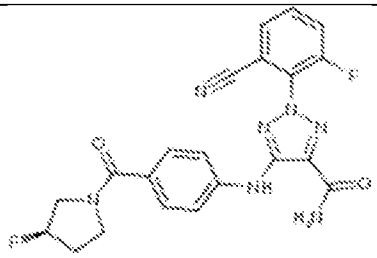
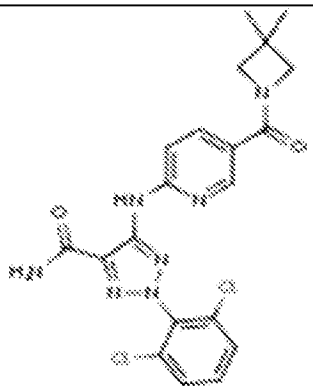
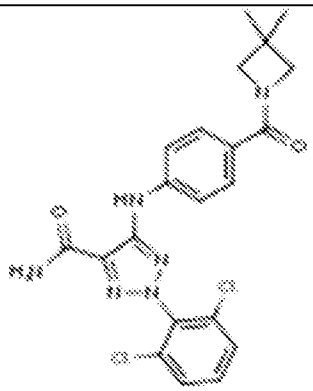
Compound No.	Structure	IUPAC-Name
140		2-(2,6-dichlorophenyl)-5-((5-(morpholine-4-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide
141		2-(2,6-dichlorophenyl)-5-((5-(5-methyl-1H-1,2,3-triazol-1-yl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide
142		2-(2,6-dichlorophenyl)-5-((5-(1-ethyl-1H-1,2,4-triazol-5-yl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide
143		2-(2,6-dichlorophenyl)-5-((5-morpholinopyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide
144		2-(2,6-dichlorophenyl)-5-((5-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide

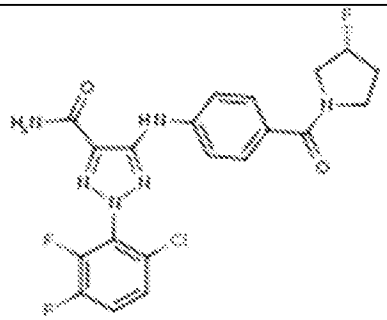
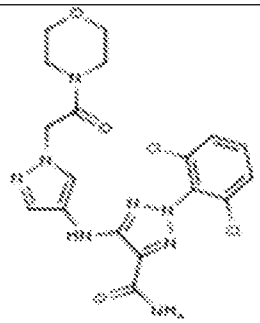
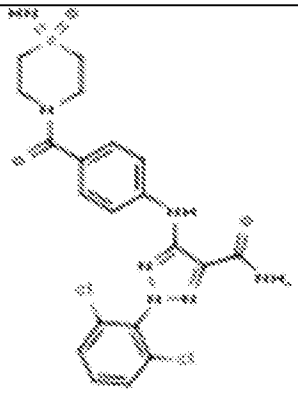
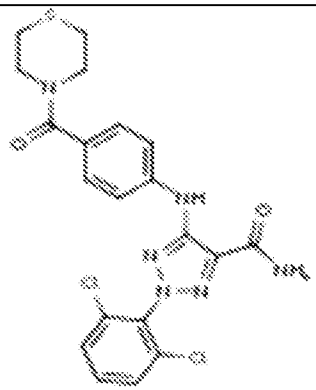
Compound No.	Structure	IUPAC-Name
145		(R)-2-(2,6-dichloro-3-fluorophenyl)-5-((4-(3-fluoropyrrolidine-1-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide
146		(R)-2-(2,6-dichloro-4-fluorophenyl)-5-((4-(3-fluoropyrrolidine-1-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide
147		(R)-2-(2-chloro-3,6-difluorophenyl)-5-((4-(3-fluoropyrrolidine-1-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide
148		(R)-2-(2,6-dichloro-4-cyanophenyl)-5-((4-(3-fluoropyrrolidine-1-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide

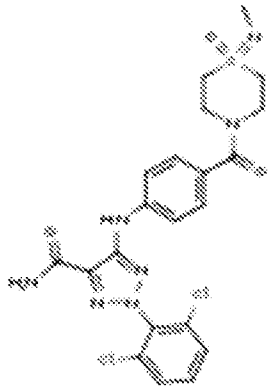
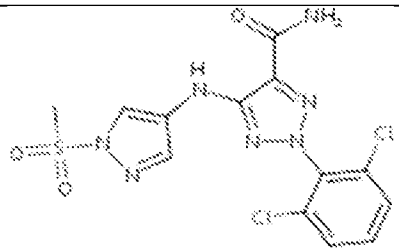
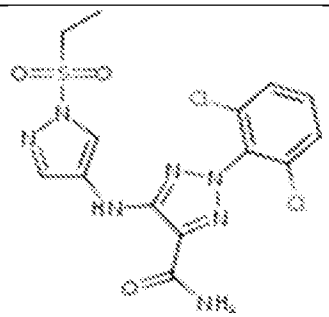
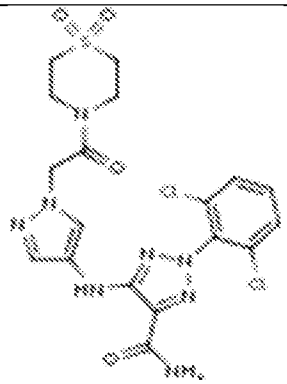
Compound No.	Structure	IUPAC-Name
149		2-(2,6-dichlorophenyl)-5-((5-(4-(dimethylamino)piperidine-1-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide
150		2-(2,6-dichlorophenyl)-5-((5-(4-methyl-1,4-diazepane-1-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide
151		2-(2,6-dichlorophenyl)-5-((6-(2-morpholino-2-oxoethyl)pyridin-3-yl)amino)-2H-1,2,3-triazole-4-carboxamide
152		2-(2,6-dichlorophenyl)-5-((6-(2-(3-fluoroazetidin-1-yl)-2-oxoethyl)pyridin-3-yl)amino)-2H-1,2,3-triazole-4-carboxamide

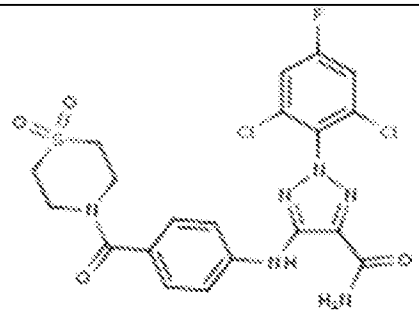
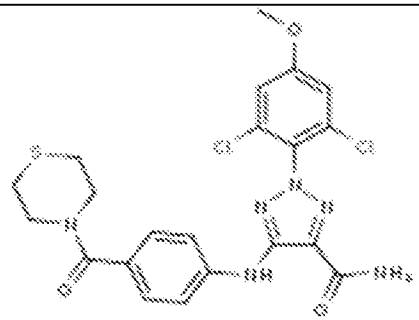
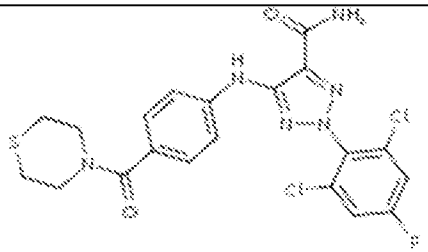
Compound No.	Structure	IUPAC-Name
153		5-((5-(3-cyanoazetidine-1-carbonyl)pyridin-2-yl)amino)-2-(2,6-dichlorophenyl)-2H-1,2,3-triazole-4-carboxamide
154		2-(2,6-dichlorophenyl)-5-((5-(3-hydroxyazetidine-1-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide
155		2-(2,6-dichlorophenyl)-5-((4-(5-(trifluoromethyl)-1H-1,2,3-triazol-1-yl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide
156		2-(2,6-dichlorophenyl)-5-((5-(5-methyl-1H-1,2,4-triazol-1-yl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide
157		2-(2,6-dichlorophenyl)-5-((5-(5-(trifluoromethyl)-1H-1,2,3-triazol-1-yl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide

Compound No.	Structure	IUPAC-Name
158		2-(2,6-dichlorophenyl)-5-((5-(1-methyl-1H-tetrazol-5-yl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide
159		2-(2,6-dichlorophenyl)-5-((6-(5-(trifluoromethyl)-1H-1,2,3-triazol-1-yl)pyridin-3-yl)amino)-2H-1,2,3-triazole-4-carboxamide
160		2-(2,6-dichlorophenyl)-5-((5-(1,1-dioxidothiomorpholine-4-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide
161		2-(2,6-dichlorophenyl)-5-((6-(5-methyl-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)pyridin-3-yl)amino)-2H-1,2,3-triazole-4-carboxamide
162		(R)-2-(2-chloro-6-cyanophenyl)-5-((4-(3-fluoropyrrolidine-1-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide

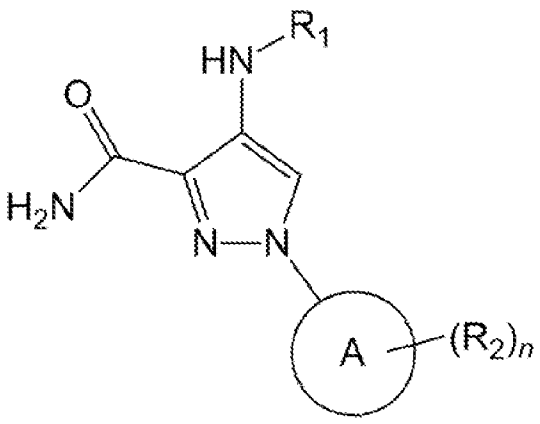
Compound No.	Structure	IUPAC-Name
163		2-(2,6-dichlorophenyl)-5-((4-(1,1-dioxidothiomorpholine-4-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide
164		(R)-2-(2-cyano-6-fluorophenyl)-5-((4-(3-fluoropyrrolidine-1-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide
165		2-(2,6-dichlorophenyl)-5-((5-(3,3-dimethylazetidine-1-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide
166		2-(2,6-dichlorophenyl)-5-((4-(3,3-dimethylazetidine-1-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide

Compound No.	Structure	IUPAC-Name
167		(R)-2-(6-chloro-2,3-difluorophenyl)-5-((4-(3-fluoropyrrolidine-1-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide
168		2-(2,6-dichlorophenyl)-5-((1-(2-morpholino-2-oxoethyl)-1H-pyrazol-4-yl)amino)-2H-1,2,3-triazole-4-carboxamide
169		2-(2,6-dichlorophenyl)-5-((4-(1-imino-1-oxidothiomorpholine-4-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide
170		2-(2,6-dichlorophenyl)-5-((4-(thiomorpholine-4-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide

Compound No.	Structure	IUPAC-Name
171		2-(2,6-dichlorophenyl)-5-((4-(1-(methylimino)-1-oxidothiomorpholine-4-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide
172		2-(2,6-dichlorophenyl)-5-((1-(methylsulfonyl)-1H-pyrazol-4-yl)amino)-2H-1,2,3-triazole-4-carboxamide
173		2-(2,6-dichlorophenyl)-5-((1-(ethylsulfonyl)-1H-pyrazol-4-yl)amino)-2H-1,2,3-triazole-4-carboxamide
174		2-(2,6-dichlorophenyl)-5-((1-(2-(1,1-dioxidothiomorpholino)-2-oxoethyl)-1H-pyrazol-4-yl)amino)-2H-1,2,3-triazole-4-carboxamide

Compound No.	Structure	IUPAC-Name
175		2-(2,6-dichloro-4-fluorophenyl)-5-((4-(1,1-dioxidothiomorpholine-4-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide
176		2-(2,6-dichloro-4-methoxyphenyl)-5-((4-(thiomorpholine-4-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide
177		2-(2,6-dichloro-4-fluorophenyl)-5-((4-(thiomorpholine-4-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide

In an aspect, the invention provides compounds of Formula (I):



(I),

wherein:

R_1 is $C(O)CH_2R_3$, optionally substituted cycloalkyl, optionally substituted cycloheteroalkyl, optionally substituted cycloalkenyl, optionally substituted cycloheteroalkenyl, optionally substituted aryl, or optionally substituted heteroaryl;

each instance of R_2 is independently halo, haloalkyl, cyano, optionally substituted alkoxyl, optionally substituted alkyl, optionally substituted heteroalkyl, optionally substituted alkenyl, optionally substituted heteroalkenyl;

R_3 is optionally substituted cycloalkyl, optionally substituted cycloheteroalkyl, optionally substituted cycloalkenyl, optionally substituted cycloheteroalkenyl, optionally substituted aryl, or optionally substituted heteroaryl;

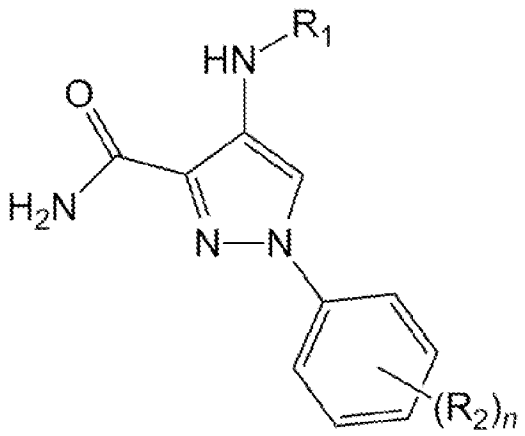
A is cycloalkyl, cycloheteroalkyl, cycloalkenyl, cycloheteroalkenyl, aryl, or heteroaryl; and

n is 0-5.

The optionally substituted aryl in R_1 may be other than a phenyl.

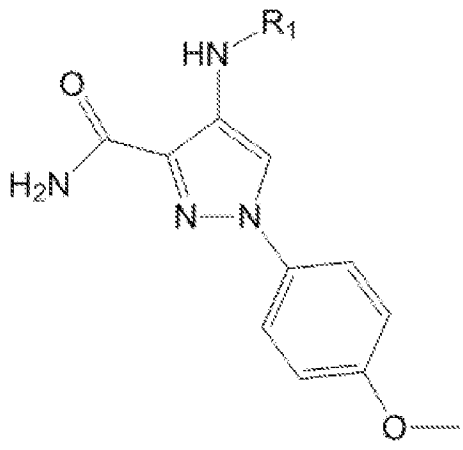
A may be an aryl substituted with 2 or 3 instances of R_2. A may be a phenyl substituted with 2 or 3 instances of R_2. A may be a heteroaryl substituted with 2 or 3 instances of R_2. A may be a six-membered heteroaryl substituted with 2 or 3 instances of R_2.

The compound of Formula (I) may be represented by Formula (Ia):

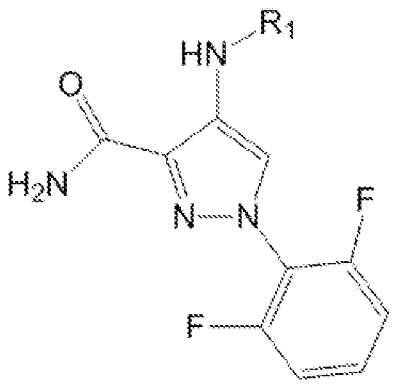


(Ia).

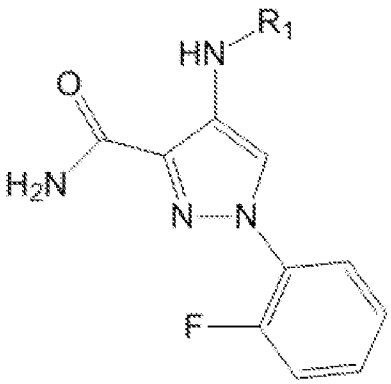
The compound of Formula (Ia) may be represented by one of Formulas (Ia-1), (Ia-2), (Ia-3), (Ia-4), (Ia-5), (Ia-6), and (Ia-7):



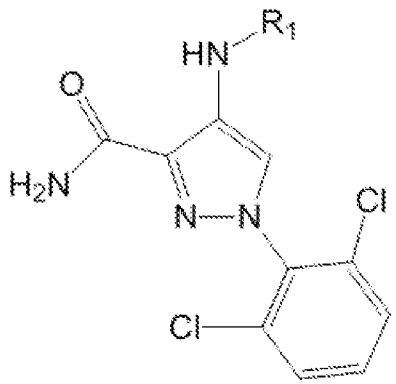
(Ia-1),



(Ia-2),

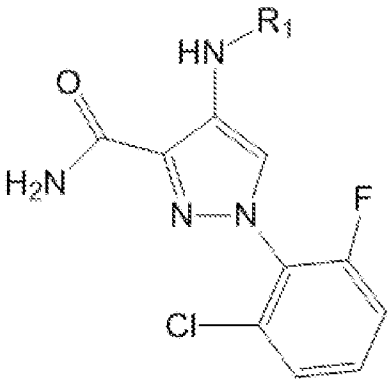


(Ia-3),

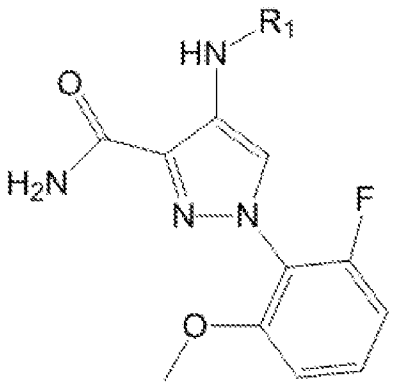


(Ia-4),

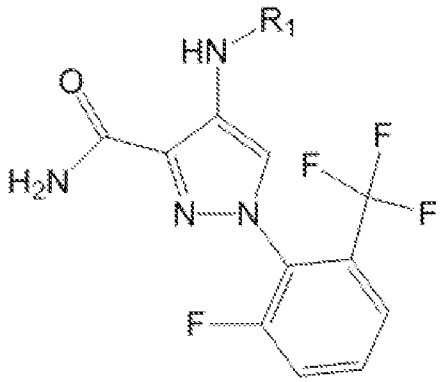
5



(Ia-5),

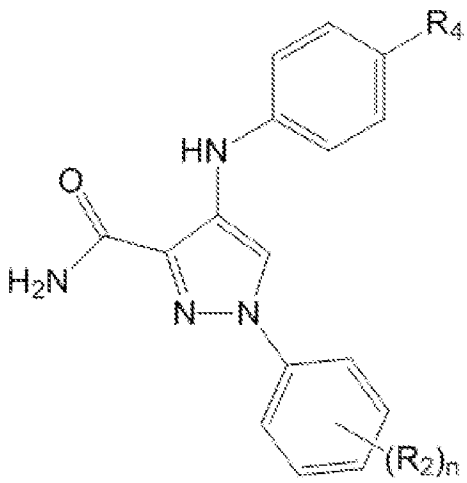


(Ia-6), and



(Ia-7).

The compound of Formula (I) may be represented by Formula (Ib):



(Ib),

wherein:

R_4 is H, $C(O)NR_5R_6$, $C(O)R_5$, $S(O)_2R_5$, $S(O)_2NR_5R_6$, $P(O)R_7R_8$, OR_5, optionally substituted cycloalkyl, optionally substituted cycloheteroalkyl, optionally substituted cycloalkenyl, optionally substituted cycloheteroalkenyl, optionally substituted aryl, or optionally substituted heteroaryl;

either:

R_5 is H, optionally substituted alkyl, optionally substituted heteroalkyl, optionally substituted cycloalkyl, optionally substituted cycloheteroalkyl, optionally substituted cycloalkenyl, optionally substituted cycloheteroalkenyl, optionally substituted aryl, or optionally

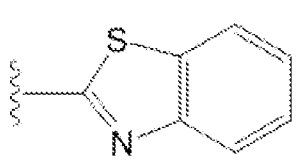
substituted heteroaryl, and R_6, if present, is H, optionally substituted alkyl, or optionally substituted heteroalkyl; or

R_5 and R_6 together form an optionally substituted cycloalkyl or optionally substituted cycloheteroalkyl;

R_7 is optionally substituted alkyl or optionally substituted heteroalkyl; and

R_8 is optionally substituted alkyl or optionally substituted heteroalkyl.

R_1 may be a heteroaryl having one of the following structures: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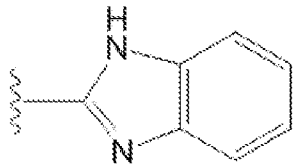
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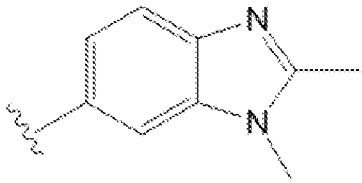
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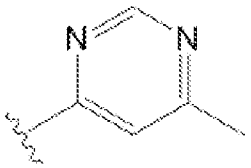
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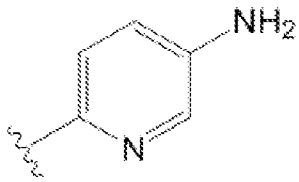
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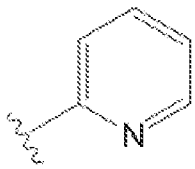
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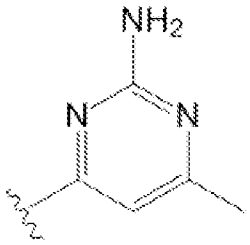
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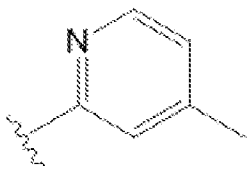
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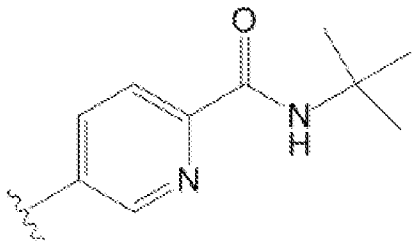
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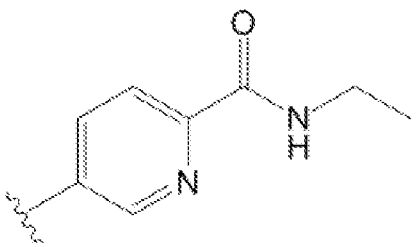
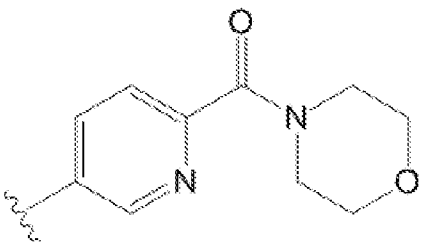
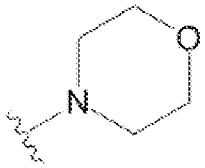
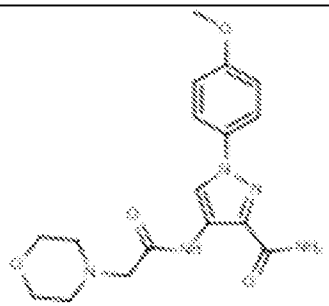
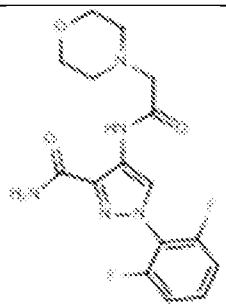
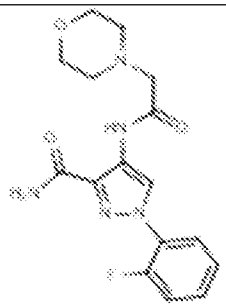

, and

.

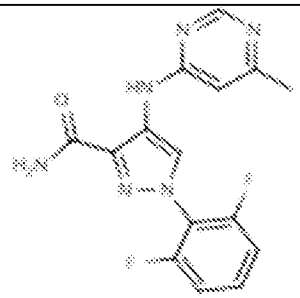
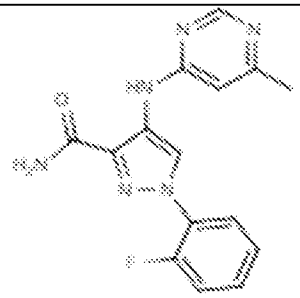
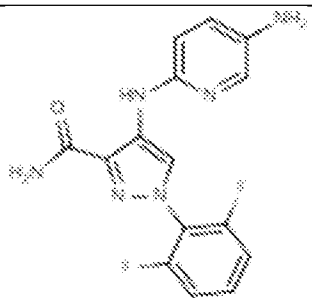
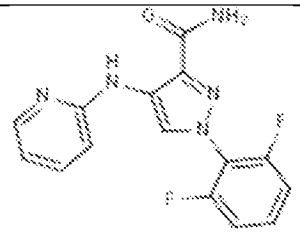
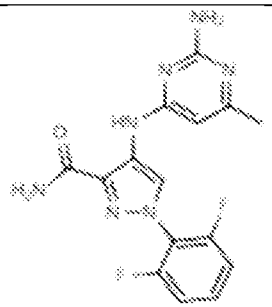
R_3 may have the following structure:

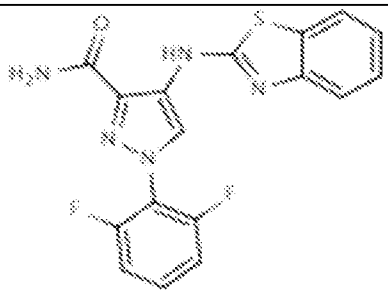
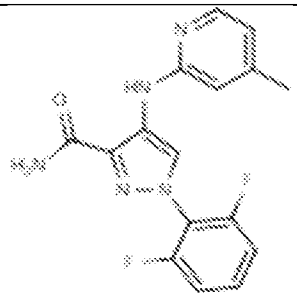
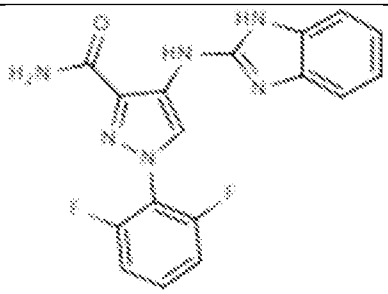
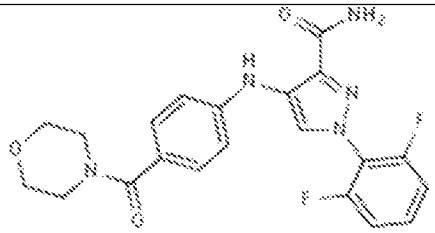
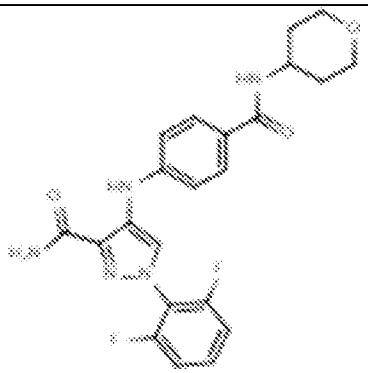


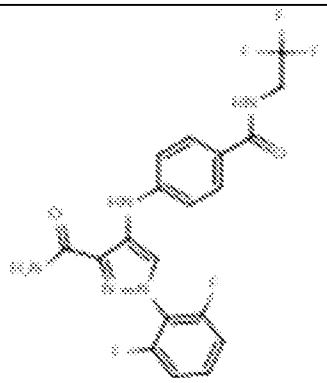
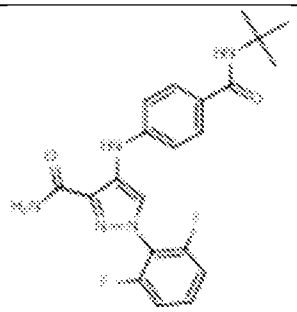
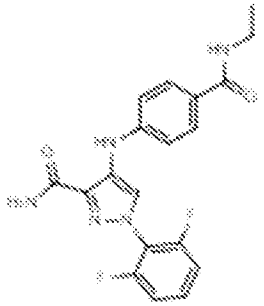
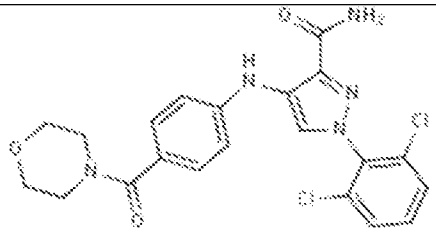
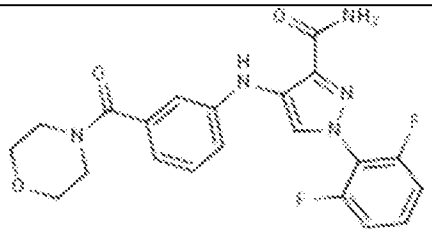
The compound of Formula (I) may have one of the structures shown in Table 1.

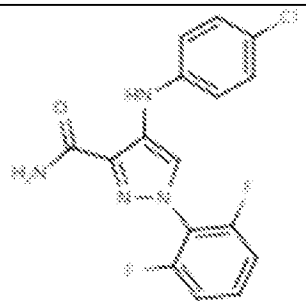
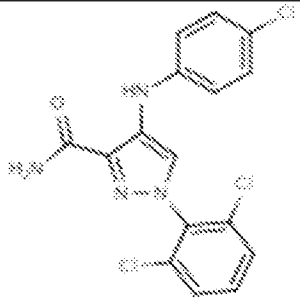
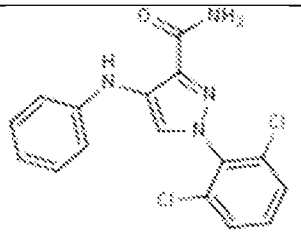
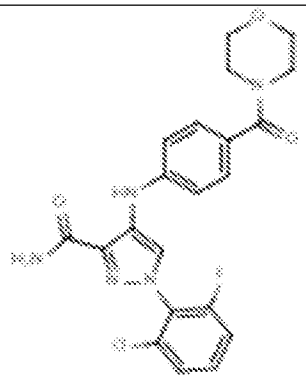
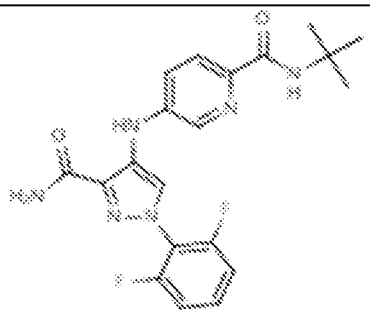
Table 1.

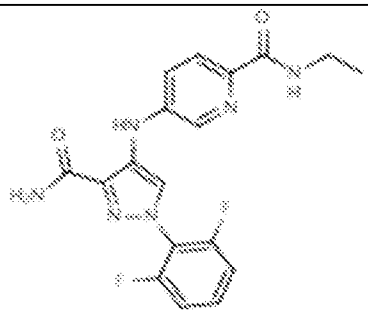
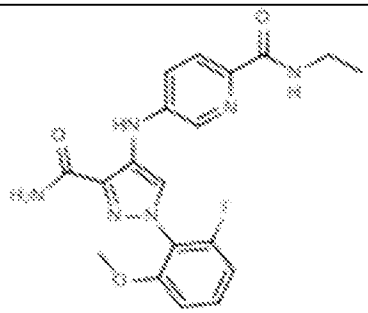
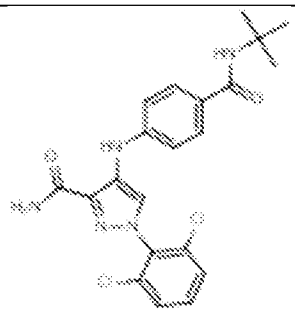
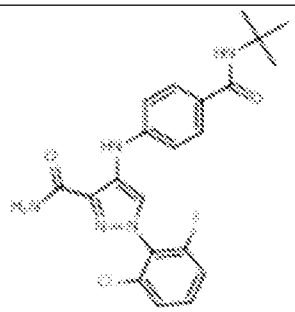
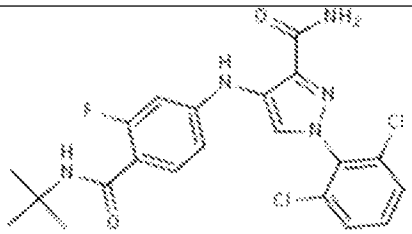
Compound No.	Structure	IUPAC-Name
1		1-(4-methoxyphenyl)-4-(2-morpholinoacetamido)-1H-pyrazole-3-carboxamide
2		1-(2,6-difluorophenyl)-4-(2-morpholinoacetamido)-1H-pyrazole-3-carboxamide
3		1-(2-fluorophenyl)-4-(2-morpholinoacetamido)-1H-pyrazole-3-carboxamide

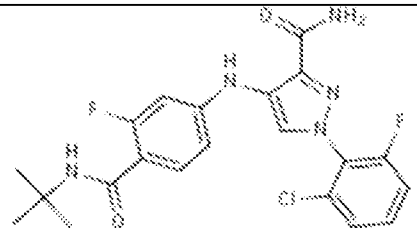
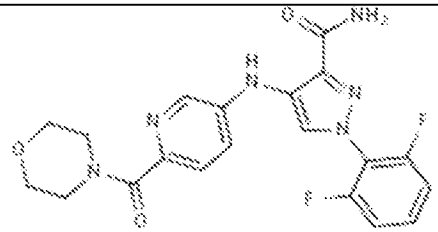
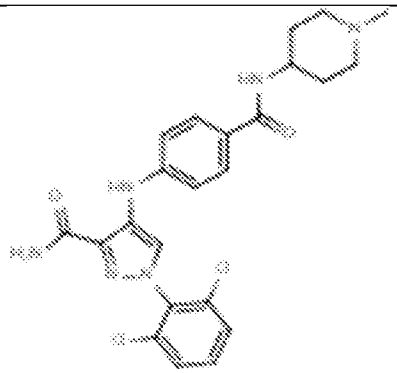
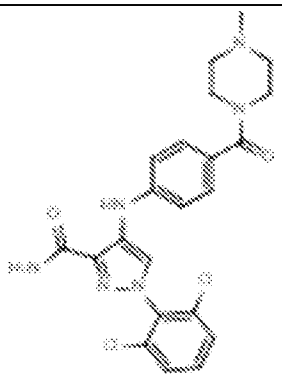
Compound No.	Structure	IUPAC-Name
4		1-(2,6-difluorophenyl)-4-((6-methylpyrimidin-4-yl)amino)-1H-pyrazole-3-carboxamide
5		1-(2-fluorophenyl)-4-((6-methylpyrimidin-4-yl)amino)-1H-pyrazole-3-carboxamide
6		4-((5-aminopyridin-2-yl)amino)-1-(2,6-difluorophenyl)-1H-pyrazole-3-carboxamide
7		1-(2,6-difluorophenyl)-4-(pyridin-2-ylamino)-1H-pyrazole-3-carboxamide
8		4-((2-amino-6-methylpyrimidin-4-yl)amino)-1-(2,6-difluorophenyl)-1H-pyrazole-3-carboxamide

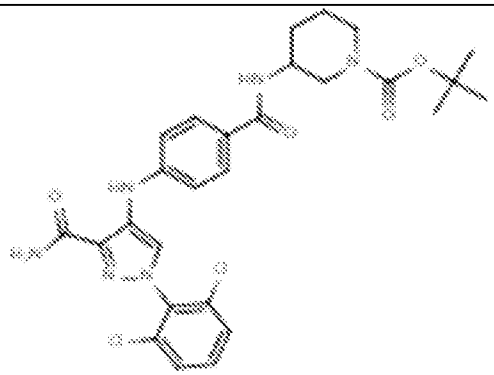
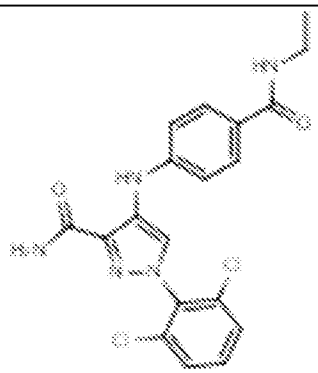
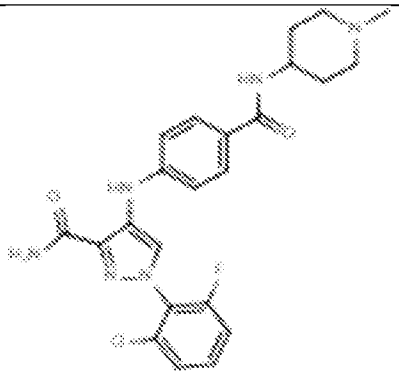
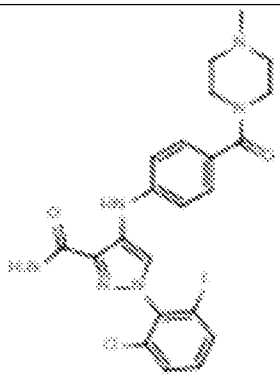
Compound No.	Structure	IUPAC-Name
9		4-(benzo[d]thiazol-2-ylamino)-1-(2,6-difluorophenyl)-1H-pyrazole-3-carboxamide
10		1-(2,6-difluorophenyl)-4-((4-methylpyridin-2-yl)amino)-1H-pyrazole-3-carboxamide
11		4-((1H-benzo[d]imidazol-2-yl)amino)-1-(2,6-difluorophenyl)-1H-pyrazole-3-carboxamide
12		1-(2,6-difluorophenyl)-4-((4-(morpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide
13		1-(2,6-difluorophenyl)-4-((4-((tetrahydro-2H-pyran-4-yl)carbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide

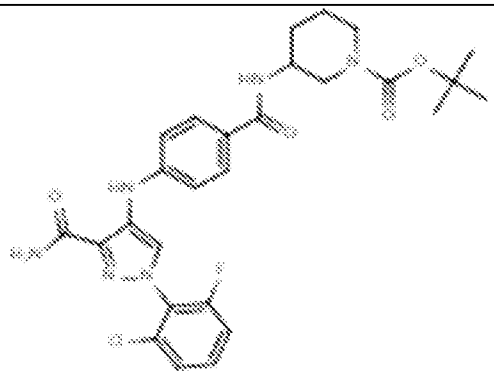
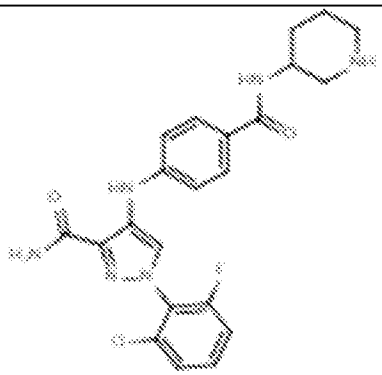
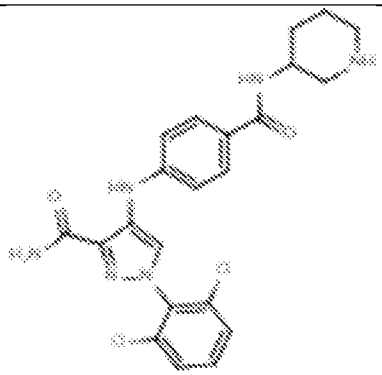
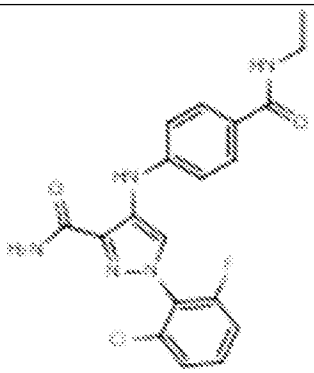
Compound No.	Structure	IUPAC-Name
14		1-(2,6-difluorophenyl)-4-((4-((2,2,2-trifluoroethyl)carbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide
15		4-((4-(tert-butylcarbamoyl)phenyl)amino)-1-(2,6-difluorophenyl)-1H-pyrazole-3-carboxamide
16		1-(2,6-difluorophenyl)-4-((4-(ethylcarbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide
17		1-(2,6-dichlorophenyl)-4-((4-(morpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide
18		1-(2,6-difluorophenyl)-4-((3-(morpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide

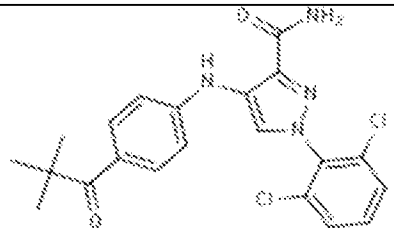
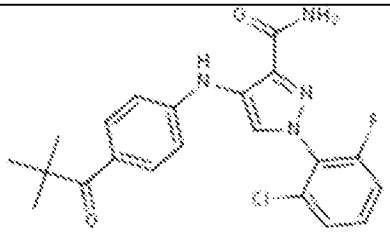
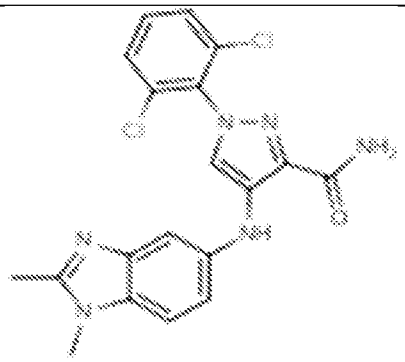
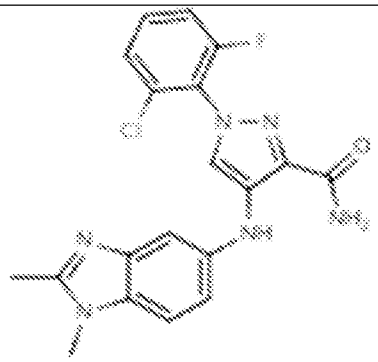
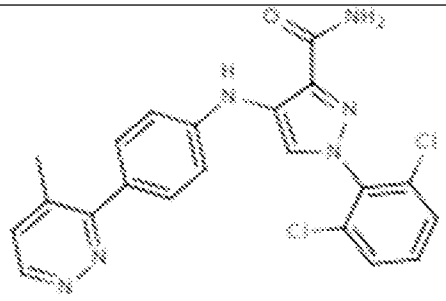
Compound No.	Structure	IUPAC-Name
19		4-((4-chlorophenyl)amino)-1-(2,6-difluorophenyl)-1H-pyrazole-3-carboxamide
20		4-((4-chlorophenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide
21		1-(2,6-dichlorophenyl)-4-(phenylamino)-1H-pyrazole-3-carboxamide
22		1-(2-chloro-6-fluorophenyl)-4-((4-(morpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide
23		N-(tert-butyl)-5-((3-carbamoyl-1-(2,6-difluorophenyl)-1H-pyrazol-4-yl)amino)picolinamide

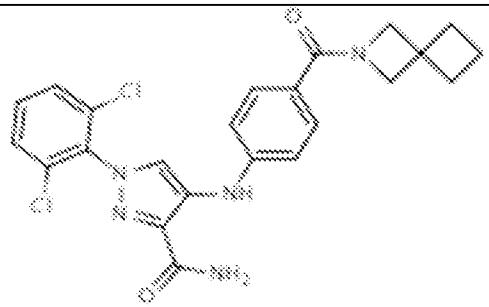
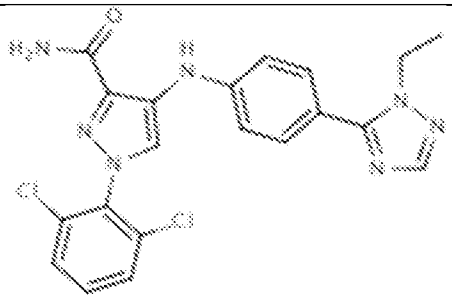
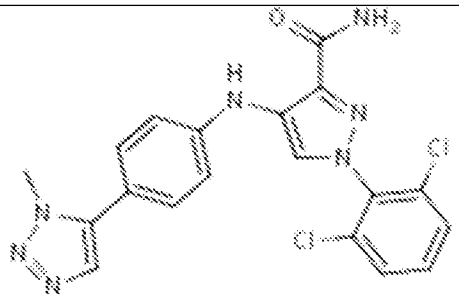
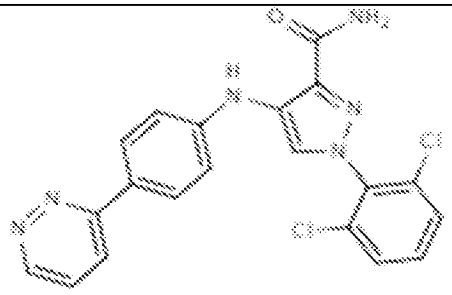
Compound No.	Structure	IUPAC-Name
24		5-((3-carbamoyl-1-(2,6-difluorophenyl)-1H-pyrazol-4-yl)amino)-N-ethylpicolinamide
25		5-((3-carbamoyl-1-(2-fluoro-6-methoxyphenyl)-1H-pyrazol-4-yl)amino)-N-ethylpicolinamide
26		4-((4-(tert-butylcarbamoyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide
27		4-((4-(tert-butylcarbamoyl)phenyl)amino)-1-(2-chloro-6-fluorophenyl)-1H-pyrazole-3-carboxamide
28		4-((4-(tert-butylcarbamoyl)-3-fluorophenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide

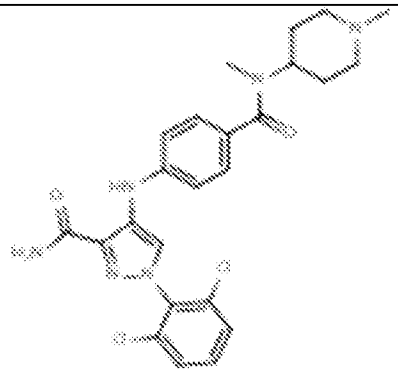
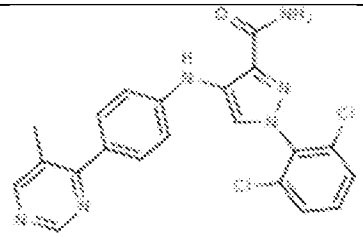
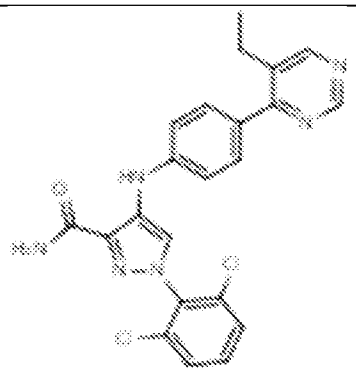
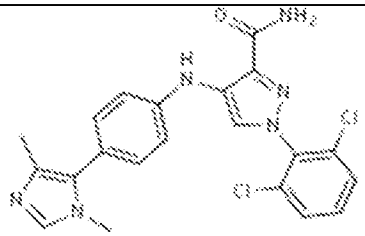
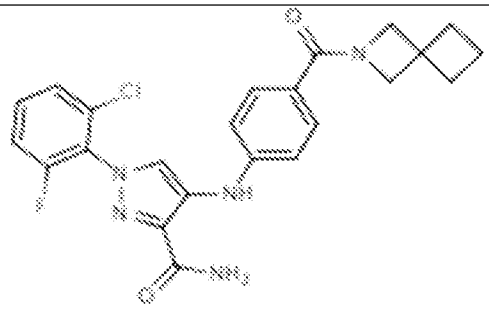
Compound No.	Structure	IUPAC-Name
29		4-((4-(tert-butylcarbamoyl)-3-fluorophenyl)amino)-1-(2-chloro-6-fluorophenyl)-1H-pyrazole-3-carboxamide
30		1-(2,6-difluorophenyl)-4-((6-(morpholine-4-carbonyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide
31		1-(2,6-dichlorophenyl)-4-((4-((1-methylpiperidin-4-yl)carbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide
32		1-(2,6-dichlorophenyl)-4-((4-(4-methylpiperazine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide

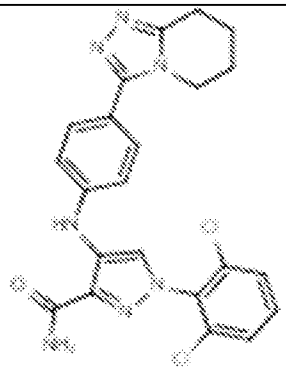
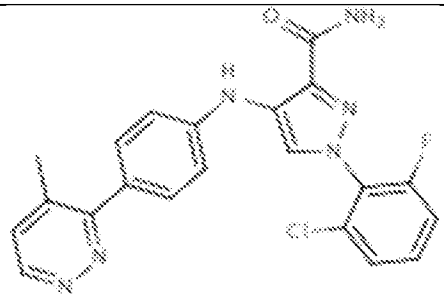
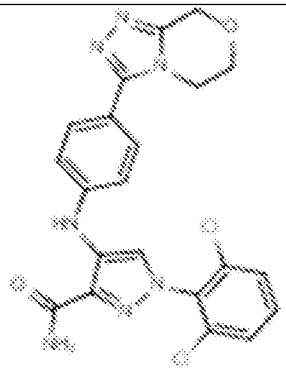
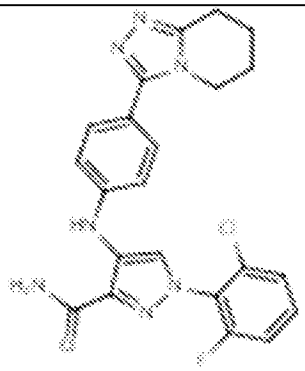
Compound No.	Structure	IUPAC-Name
33		tert-butyl_3-(4-((3-carbamoyl-1-(2,6-dichlorophenyl)-1H-pyrazol-4-yl)amino)benzamido)piperidine-1-carboxylate
34		1-(2,6-dichlorophenyl)-4-((4-(ethylcarbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide
35		1-(2-chloro-6-fluorophenyl)-4-((4-((1-methylpiperidin-4-yl)carbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide
36		1-(2-chloro-6-fluorophenyl)-4-((4-(4-methylpiperazine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide

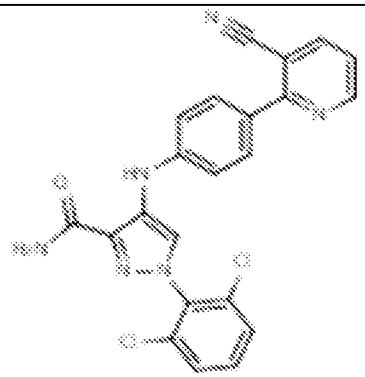
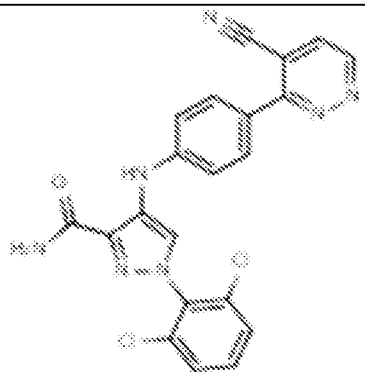
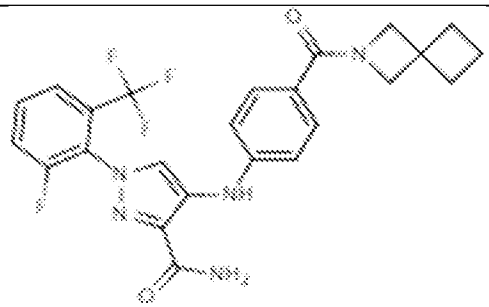
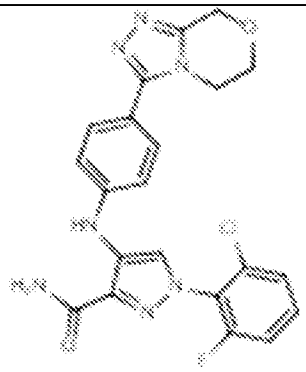
Compound No.	Structure	IUPAC-Name
37		tert-butyl_3-(4-((3-carbamoyl-1-(2-chloro-6-fluorophenyl)-1H-pyrazol-4-yl)amino)benzamido)piperidine-1-carboxylate
38		1-(2-chloro-6-fluorophenyl)-4-((4-(piperidin-3-ylcarbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide
39		1-(2,6-dichlorophenyl)-4-((4-(piperidin-3-ylcarbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide
40		1-(2-chloro-6-fluorophenyl)-4-((4-(ethylcarbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide

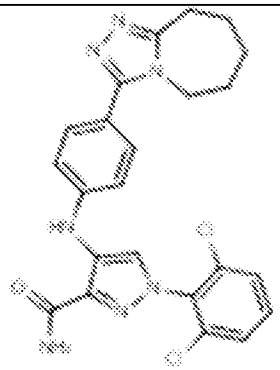
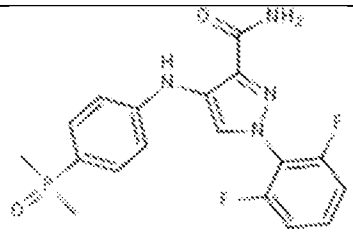
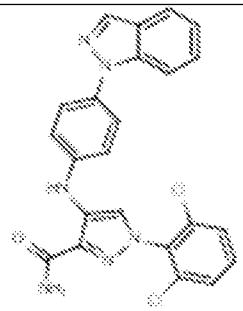
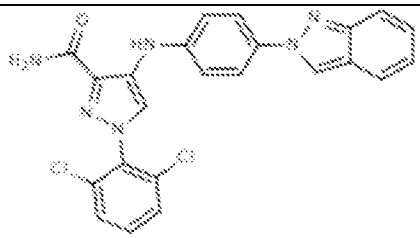
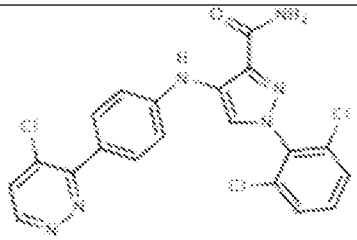
Compound No.	Structure	IUPAC-Name
41		1-(2,6-dichlorophenyl)-4-((4-pivaloylphenyl)amino)-1H-pyrazole-3-carboxamide
42		1-(2-chloro-6-fluorophenyl)-4-((4-pivaloylphenyl)amino)-1H-pyrazole-3-carboxamide
43		1-(2,6-dichlorophenyl)-4-((1,2-dimethyl-1H-benzo[d]imidazol-5-yl)amino)-1H-pyrazole-3-carboxamide
44		1-(2-chloro-6-fluorophenyl)-4-((1,2-dimethyl-1H-benzo[d]imidazol-5-yl)amino)-1H-pyrazole-3-carboxamide
45		1-(2,6-dichlorophenyl)-4-((4-(4-methylpyridazin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide

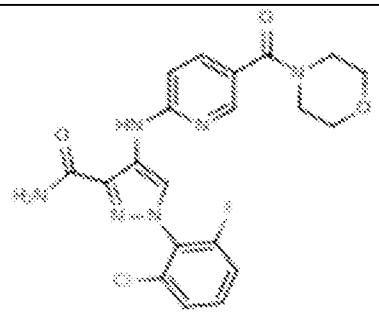
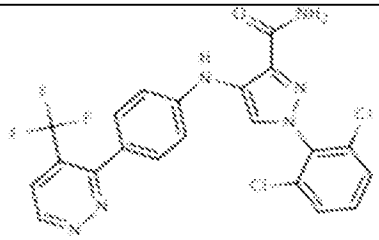
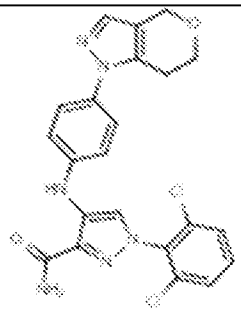
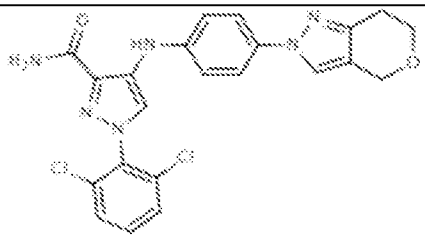
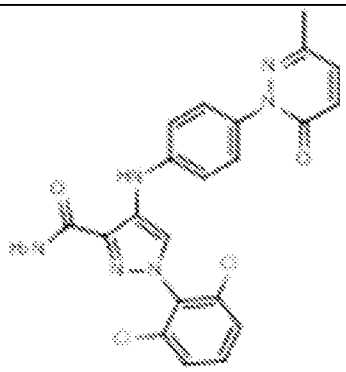
Compound No.	Structure	IUPAC-Name
46		4-((4-(2-azaspiro[3.3]heptane-2-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide
47		1-(2,6-dichlorophenyl)-4-((4-(1-ethyl-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
48		1-(2,6-dichlorophenyl)-4-((4-(1-methyl-1H-1,2,3-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
49		1-(2,6-dichlorophenyl)-4-((4-(pyridazin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide

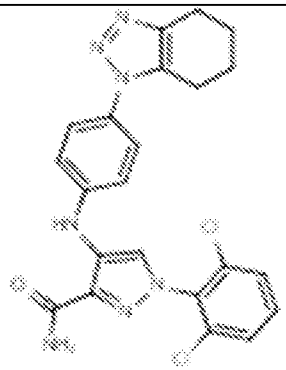
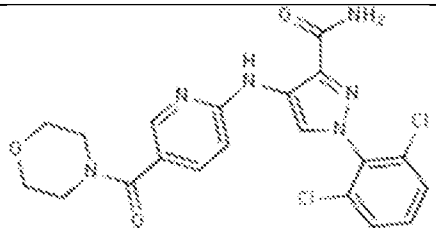
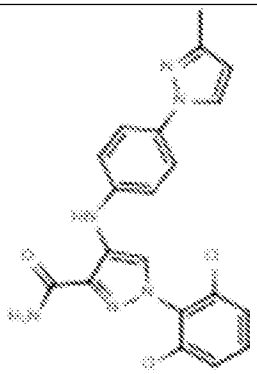
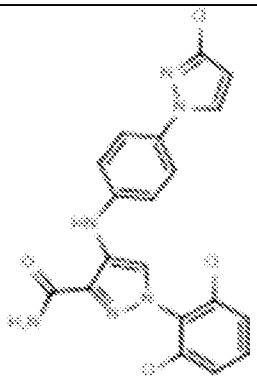
Compound No.	Structure	IUPAC-Name
50		1-(2,6-dichlorophenyl)-4-((4-(methyl(1-methylpiperidin-4-yl)carbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide
51		1-(2,6-dichlorophenyl)-4-((4-(5-methylpyrimidin-4-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
52		1-(2,6-dichlorophenyl)-4-((4-(5-ethylpyrimidin-4-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
53		1-(2,6-dichlorophenyl)-4-((4-(1,4-dimethyl-1H-imidazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
54		4-((4-(2-azaspiro[3.3]heptane-2-carbonyl)phenyl)amino)-1-(2-chloro-6-fluorophenyl)-1H-pyrazole-3-carboxamide

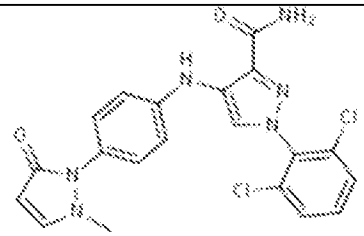
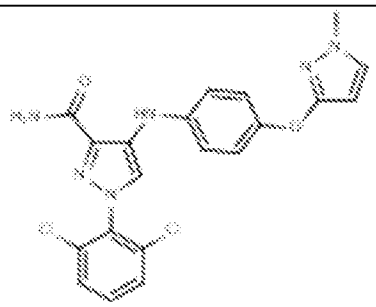
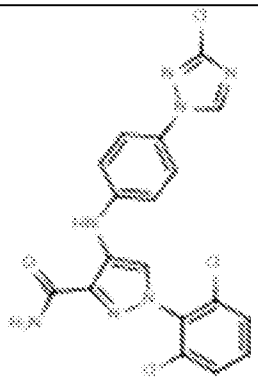
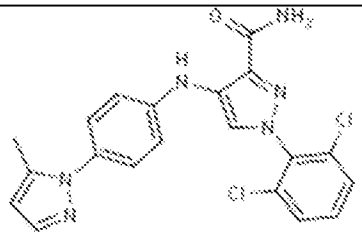
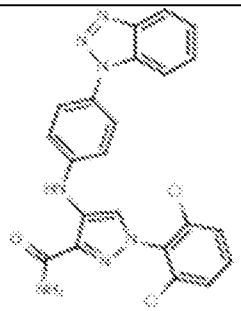
Compound No.	Structure	IUPAC-Name
55		1-(2,6-dichlorophenyl)-4-((4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
56		1-(2-chloro-6-fluorophenyl)-4-((4-(4-methylpyridazin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
57		1-(2,6-dichlorophenyl)-4-((4-(6,8-dihydro-5H-[1,2,4]triazolo[3,4-c][1,4]oxazin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
58		1-(2-chloro-6-fluorophenyl)-4-((4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide

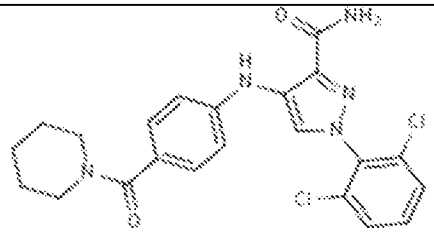
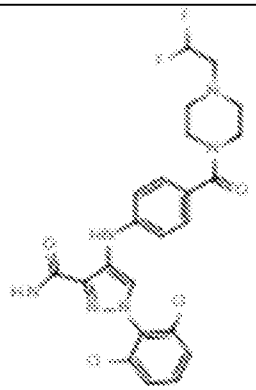
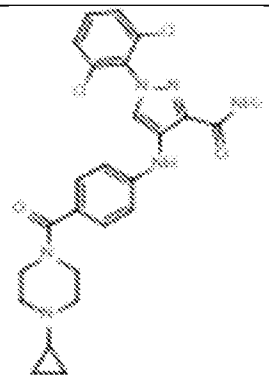
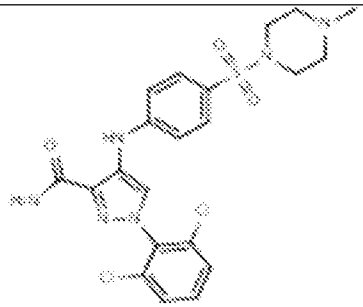
Compound No.	Structure	IUPAC-Name
59		4-((4-(3-cyanopyridin-2-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide
60		4-((4-(4-cyanopyridazin-3-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide
61		4-((4-(2-azaspiro[3.3]heptane-2-carbonyl)phenyl)amino)-1-(2-fluoro-6-(trifluoromethyl)phenyl)-1H-pyrazole-3-carboxamide
62		1-(2-chloro-6-fluorophenyl)-4-((4-(6,8-dihydro-5H-[1,2,4]triazolo[3,4-c][1,4]oxazin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide

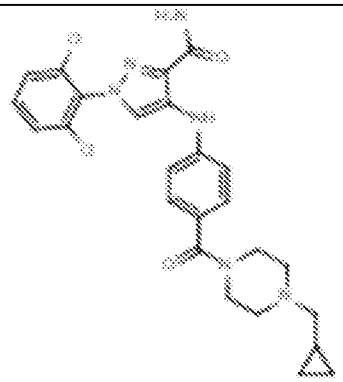
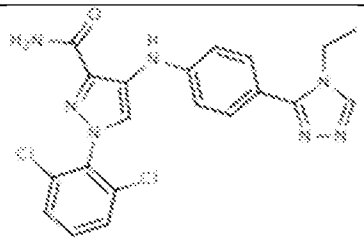
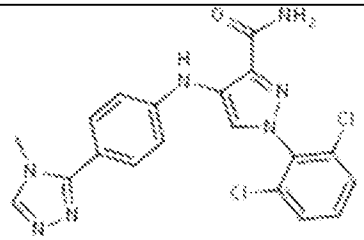
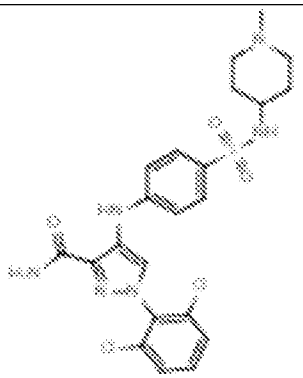
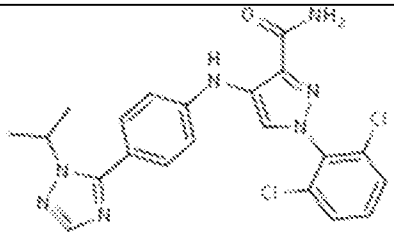
Compound No.	Structure	IUPAC-Name
63		1-(2,6-dichlorophenyl)-4-((4-(6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[4,3-a]azepin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
64		1-(2,6-difluorophenyl)-4-((4-(dimethylphosphoryl)phenyl)amino)-1H-pyrazole-3-carboxamide
65		4-((4-(1H-indazol-1-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide
66		4-((4-(2H-indazol-2-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide
67		4-((4-(4-chloropyridazin-3-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide

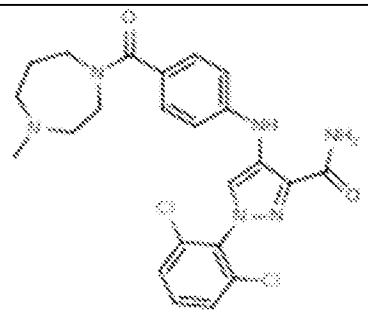
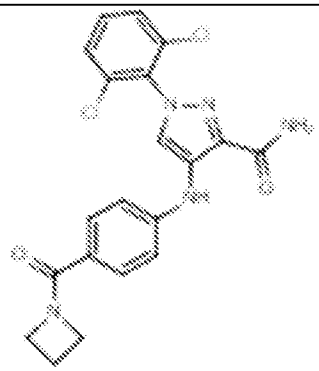
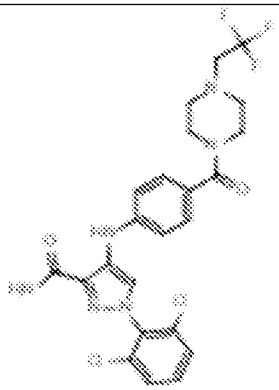
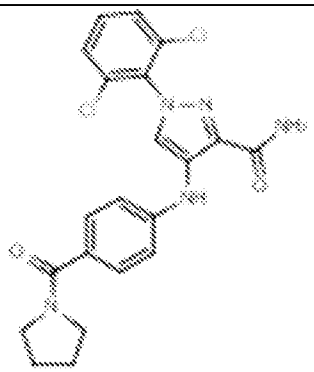
Compound No.	Structure	IUPAC-Name
68		1-(2-chloro-6-fluorophenyl)-4-((5-(morpholine-4-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide
69		1-(2,6-dichlorophenyl)-4-((4-(4-(trifluoromethyl)pyridazin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
70		1-(2,6-dichlorophenyl)-4-((4-(6,7-dihydropyrano[4,3-c]pyrazol-1(4H)-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
71		1-(2,6-dichlorophenyl)-4-((4-(6,7-dihydropyrano[4,3-c]pyrazol-2(4H)-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
72		1-(2,6-dichlorophenyl)-4-((4-(3-methyl-6-oxopyridazin-1(6H)-yl)phenyl)amino)-1H-pyrazole-3-carboxamide

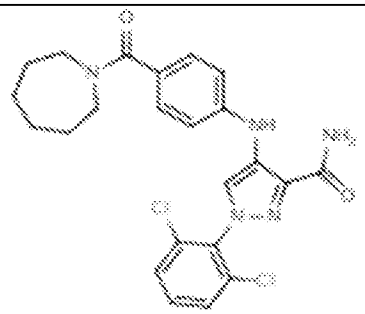
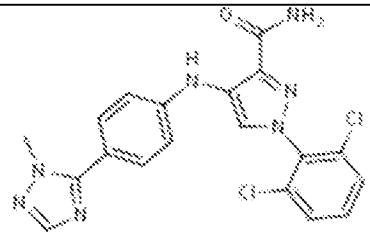
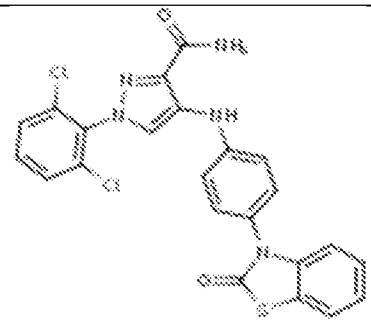
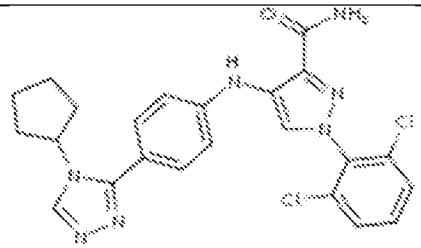
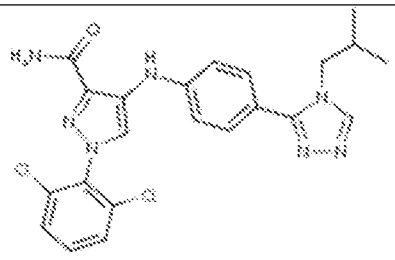
Compound No.	Structure	IUPAC-Name
73		1-(2,6-dichlorophenyl)-4-((4-(4,5,6,7-tetrahydro-1H-benzo[d][1,2,3]triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
74		1-(2,6-dichlorophenyl)-4-((5-(morpholine-4-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide
75		1-(2,6-dichlorophenyl)-4-((4-(3-methyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
76		4-((4-(3-chloro-1H-pyrazol-1-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide

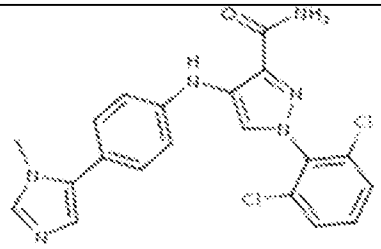
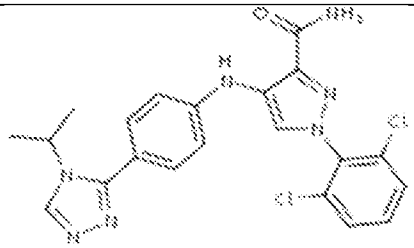
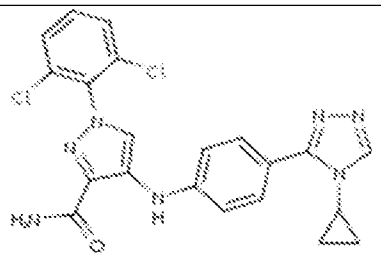
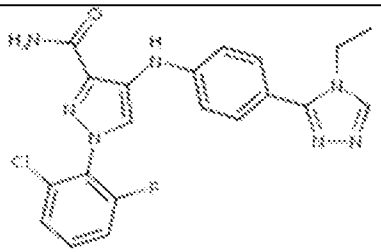
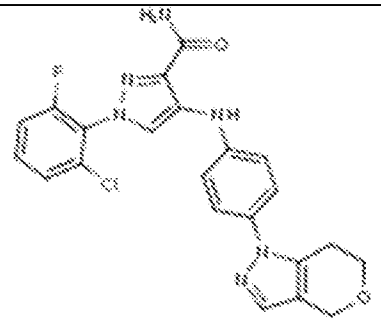
Compound No.	Structure	IUPAC-Name
77		1-(2,6-dichlorophenyl)-4-((4-(2-methyl-5-oxo-2,5-dihydro-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
78		1-(2,6-dichlorophenyl)-4-((4-((1-methyl-1H-pyrazol-3-yl)oxy)phenyl)amino)-1H-pyrazole-3-carboxamide
79		4-((4-(3-chloro-1H-1,2,4-triazol-1-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide
80		1-(2,6-dichlorophenyl)-4-((4-(5-methyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
81		4-((4-(1H-benzo[d][1,2,3]triazol-1-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide

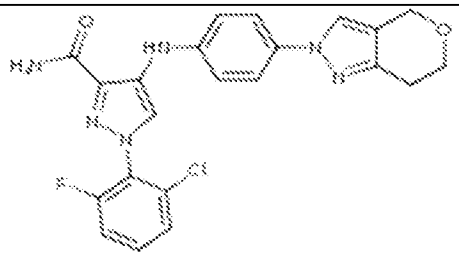
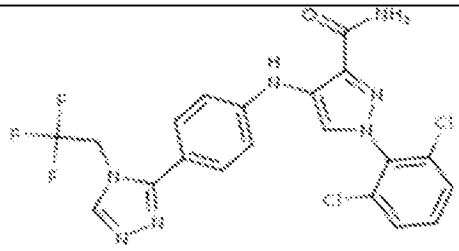
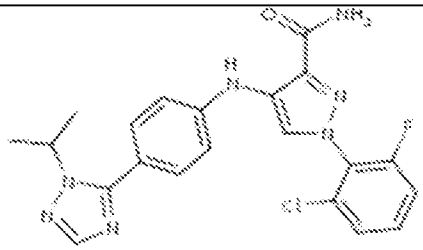
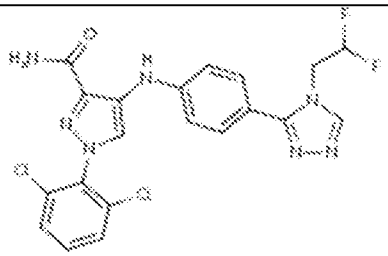
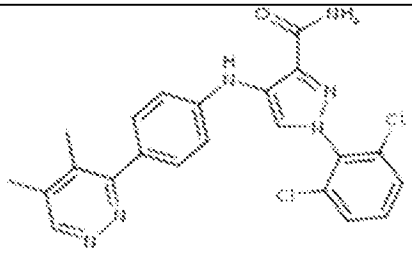
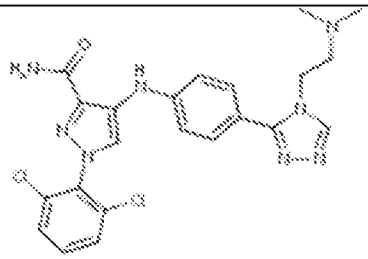
Compound No.	Structure	IUPAC-Name
82		1-(2,6-dichlorophenyl)-4-((4-(piperidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide
83		1-(2,6-dichlorophenyl)-4-((4-(4-(2,2-difluoroethyl)piperazine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide
84		4-((4-(4-cyclopropylpiperazine-1-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide
85		1-(2,6-dichlorophenyl)-4-((4-((4-methylpiperazin-1-yl)sulfonyl)phenyl)amino)-1H-pyrazole-3-carboxamide

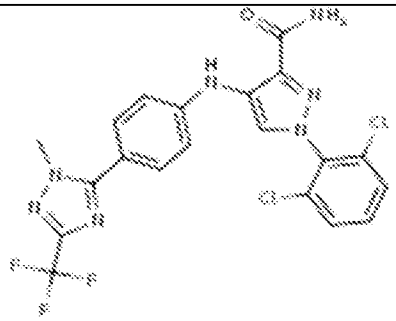
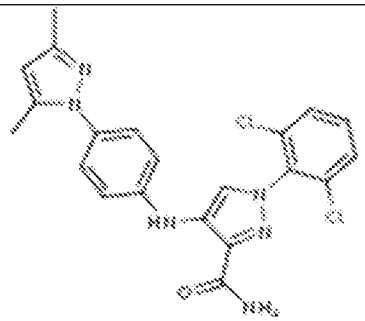
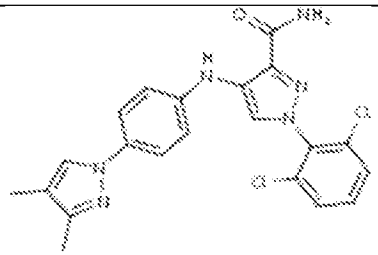
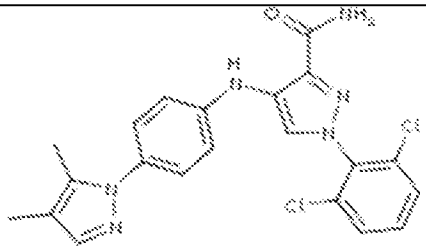
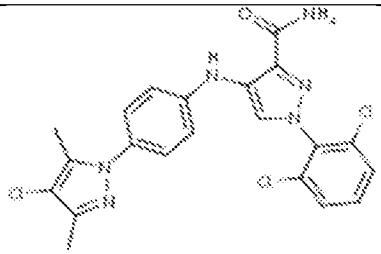
Compound No.	Structure	IUPAC-Name
86		4-((4-(4-(cyclopropylmethyl)piperazine-1-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide
87		1-(2,6-dichlorophenyl)-4-((4-(4-ethyl-4H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
88		1-(2,6-dichlorophenyl)-4-((4-(4-methyl-4H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
89		1-(2,6-dichlorophenyl)-4-((4-(N-(1-methylpiperidin-4-yl)sulfamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide
90		1-(2,6-dichlorophenyl)-4-((4-(1-isopropyl-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide

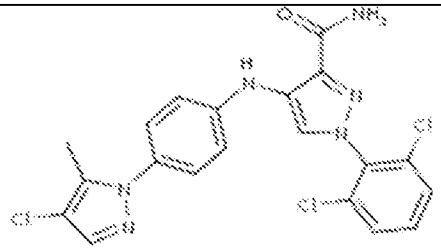
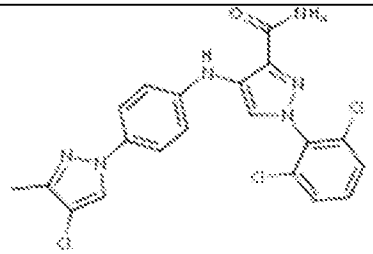
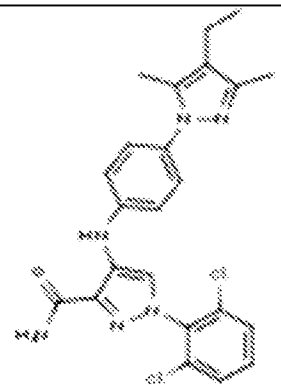
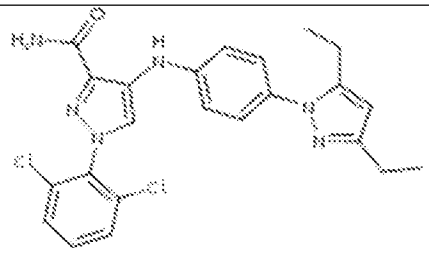
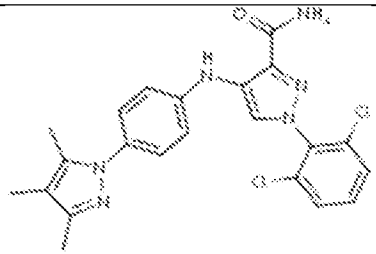
Compound No.	Structure	IUPAC-Name
91		1-(2,6-dichlorophenyl)-4-((4-(4-methyl-1,4-diazepane-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide
92		4-((4-(azetidine-1-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide
93		1-(2,6-dichlorophenyl)-4-((4-(4-(2,2,2-trifluoroethyl)piperazine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide
94		1-(2,6-dichlorophenyl)-4-((4-(pyrrolidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide

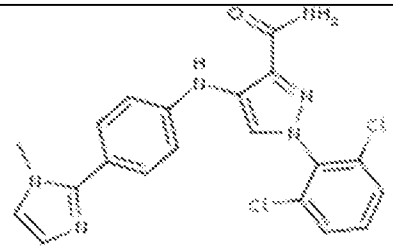
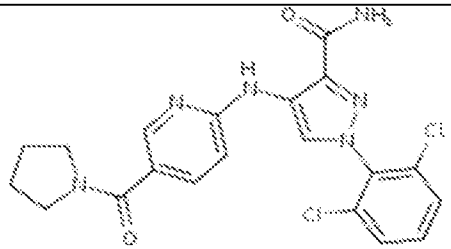
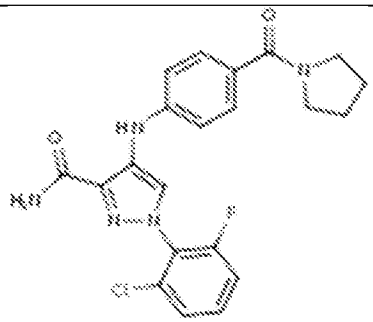
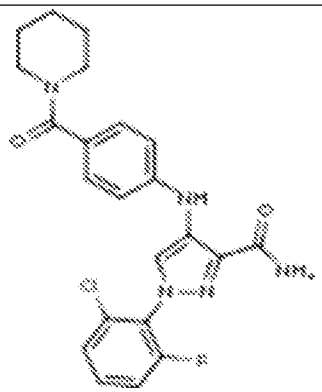
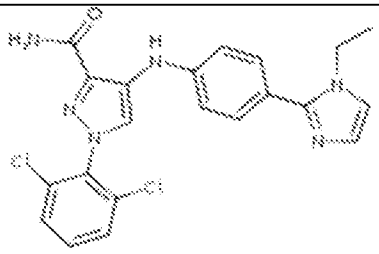
Compound No.	Structure	IUPAC-Name
95		4-((4-(azepane-1-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide
96		1-(2,6-dichlorophenyl)-4-((4-(1-methyl-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
201		1-(2,6-dichlorophenyl)-4-((4-(2-oxobenzo[d]thiazol-3(2H)-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
202		4-((4-(4-cyclopentyl-4H-1,2,4-triazol-3-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide
203		1-(2,6-dichlorophenyl)-4-((4-(4-isobutyl-4H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide

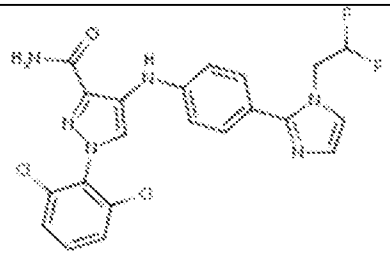
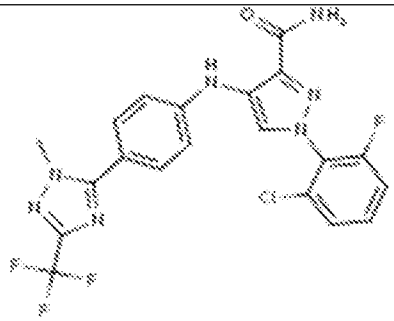
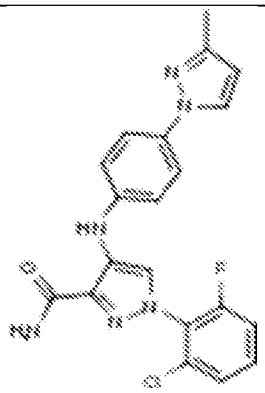
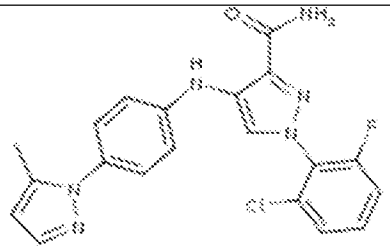
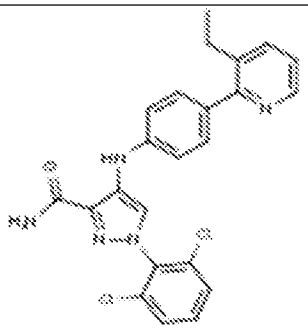
Compound No.	Structure	IUPAC-Name
204		1-(2,6-dichlorophenyl)-4-((4-(1-methyl-1H-imidazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
205		1-(2,6-dichlorophenyl)-4-((4-(4-isopropyl-4H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
206		4-((4-(4-cyclopropyl-4H-1,2,4-triazol-3-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide
207		1-(2-chloro-6-fluorophenyl)-4-((4-(4-ethyl-4H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
208		1-(2-chloro-6-fluorophenyl)-4-((4-(6,7-dihydropyrano[4,3-c]pyrazol-1(4H)-yl)phenyl)amino)-1H-pyrazole-3-carboxamide

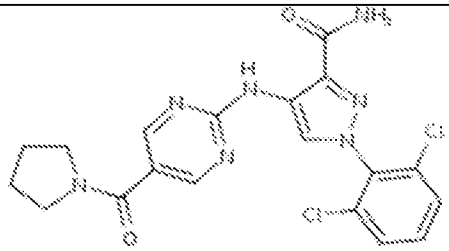
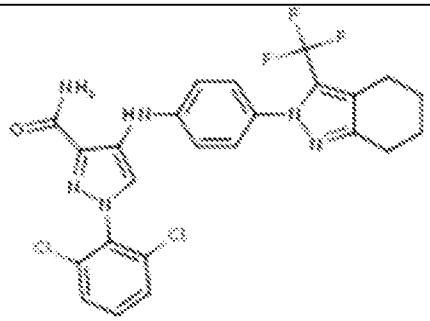
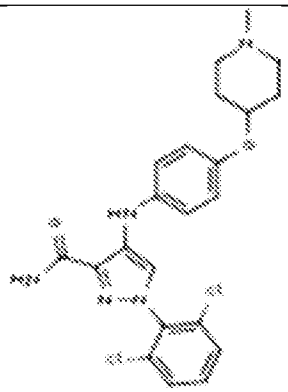
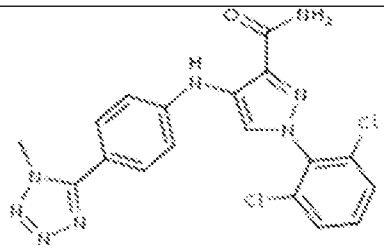
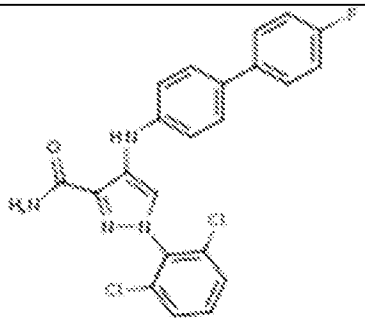
Compound No.	Structure	IUPAC-Name
209		1-(2-chloro-6-fluorophenyl)-4-((4-(6,7-dihydropyrano[4,3-c]pyrazol-2(4H)-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
210		1-(2,6-dichlorophenyl)-4-((4-(4-(2,2,2-trifluoroethyl)-4H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
211		1-(2-chloro-6-fluorophenyl)-4-((4-(1-isopropyl-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
212		1-(2,6-dichlorophenyl)-4-((4-(4-(2,2-difluoroethyl)-4H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
213		1-(2,6-dichlorophenyl)-4-((4-(4,5-dimethylpyridazin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
214		1-(2,6-dichlorophenyl)-4-((4-(4-(2-(dimethylamino)ethyl)-4H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide

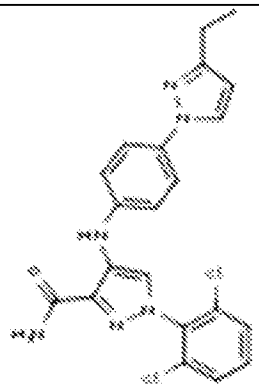
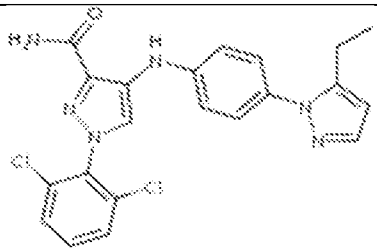
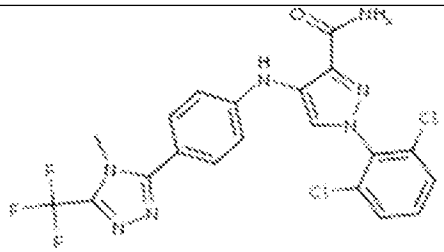
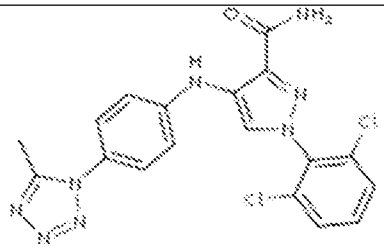
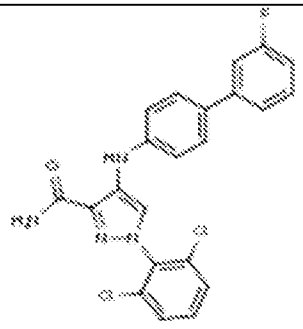
Compound No.	Structure	IUPAC-Name
215		1-(2,6-dichlorophenyl)-4-((4-(1-methyl-3-(trifluoromethyl)-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
216		1-(2,6-dichlorophenyl)-4-((4-(3,5-dimethyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
217		1-(2,6-dichlorophenyl)-4-((4-(3,4-dimethyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
218		1-(2,6-dichlorophenyl)-4-((4-(4,5-dimethyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
219		4-((4-(4-chloro-3,5-dimethyl-1H-pyrazol-1-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide

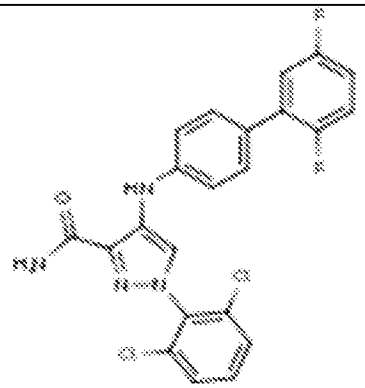
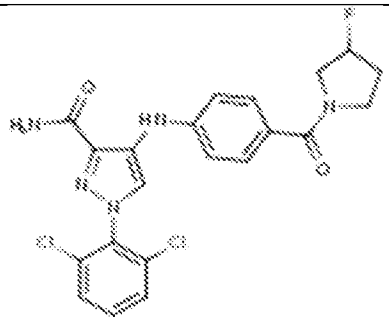
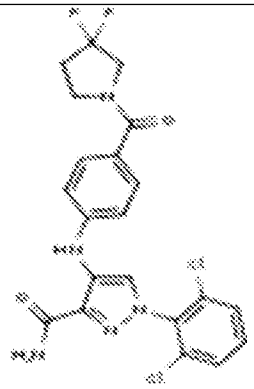
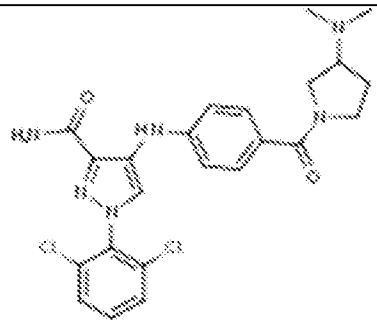
Compound No.	Structure	IUPAC-Name
220		4-((4-(4-chloro-5-methyl-1H-pyrazol-1-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide
221		4-((4-(4-chloro-3-methyl-1H-pyrazol-1-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide
222		1-(2,6-dichlorophenyl)-4-((4-(4-ethyl-3,5-dimethyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
223		1-(2,6-dichlorophenyl)-4-((4-(3,5-diethyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
224		1-(2,6-dichlorophenyl)-4-((4-(3,4,5-trimethyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide

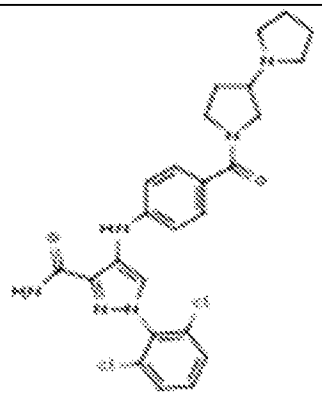
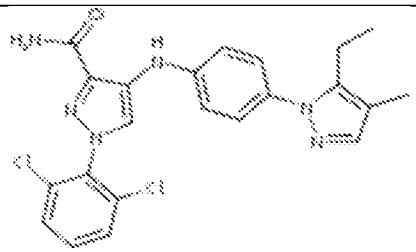
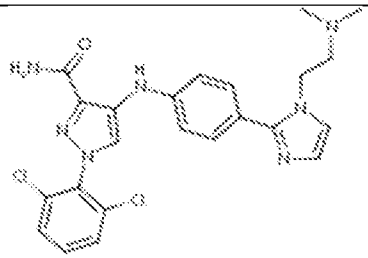
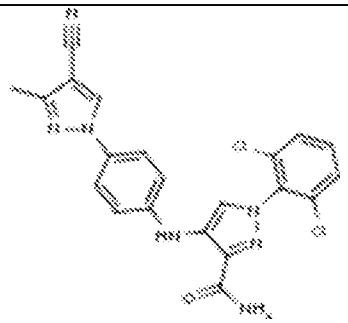
Compound No.	Structure	IUPAC-Name
225		1-(2,6-dichlorophenyl)-4-((4-(1-methyl-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
226		1-(2,6-dichlorophenyl)-4-((5-(pyrrolidine-1-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide
227		1-(2-chloro-6-fluorophenyl)-4-((4-(pyrrolidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide
228		1-(2-chloro-6-fluorophenyl)-4-((4-(piperidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide
229		1-(2,6-dichlorophenyl)-4-((4-(1-ethyl-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide

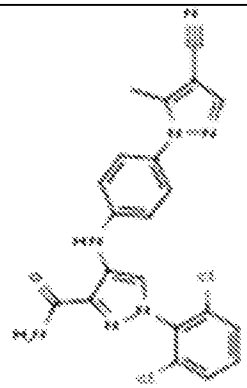
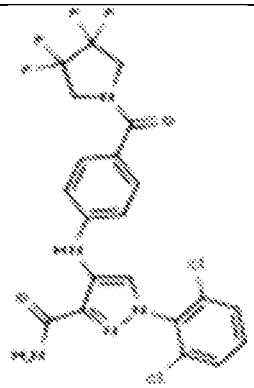
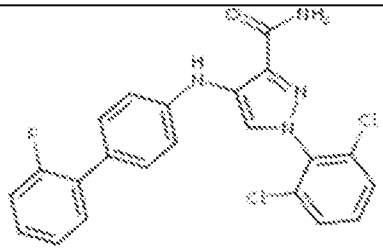
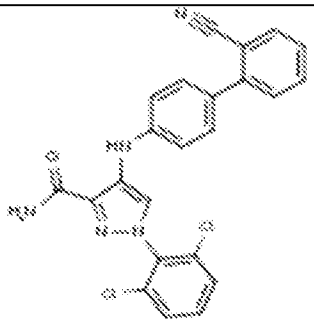
Compound No.	Structure	IUPAC-Name
230		1-(2,6-dichlorophenyl)-4-((4-(1-(2,2-difluoroethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
231		1-(2-chloro-6-fluorophenyl)-4-((4-(1-methyl-3-(trifluoromethyl)-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
232		1-(2-chloro-6-fluorophenyl)-4-((4-(3-methyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
233		1-(2-chloro-6-fluorophenyl)-4-((4-(5-methyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
234		1-(2,6-dichlorophenyl)-4-((4-(3-ethylpyridin-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide

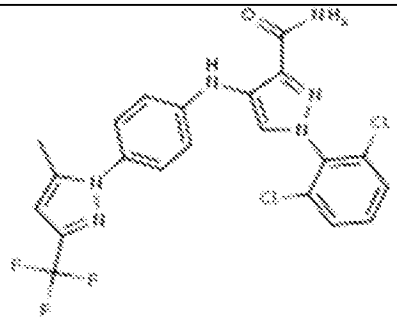
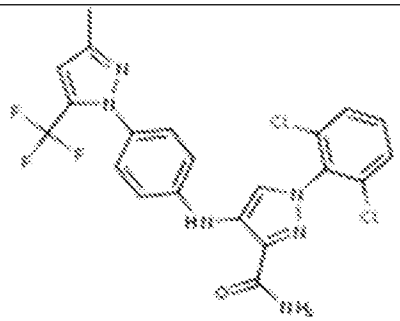
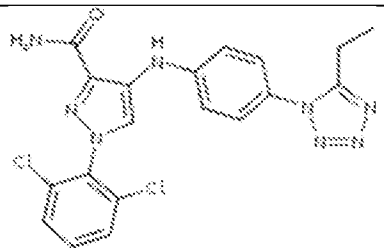
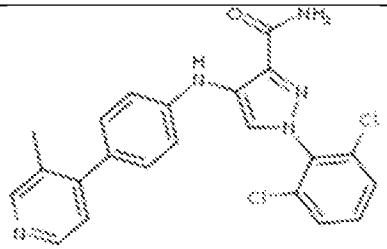
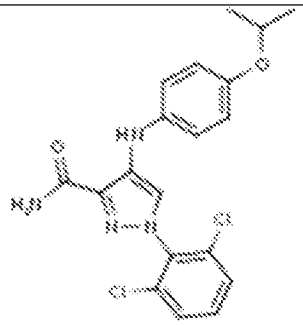
Compound No.	Structure	IUPAC-Name
235		1-(2,6-dichlorophenyl)-4-((5-(pyrrolidine-1-carbonyl)pyrimidin-2-yl)amino)-1H-pyrazole-3-carboxamide
236		1-(2,6-dichlorophenyl)-4-((4-(3-(trifluoromethyl)-4,5,6,7-tetrahydro-2H-indazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
237		1-(2,6-dichlorophenyl)-4-((4-((1-methylpiperidin-4-yl)oxy)phenyl)amino)-1H-pyrazole-3-carboxamide
238		1-(2,6-dichlorophenyl)-4-((4-(1-methyl-1H-tetrazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
239		1-(2,6-dichlorophenyl)-4-((4'-fluoro-[1,1'-biphenyl]-4-yl)amino)-1H-pyrazole-3-carboxamide

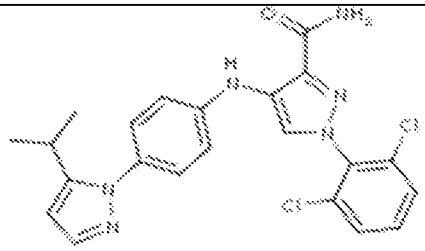
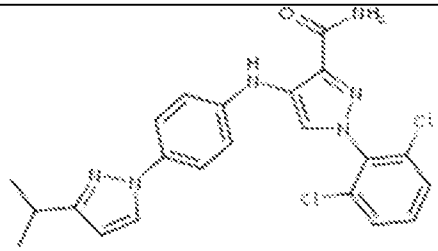
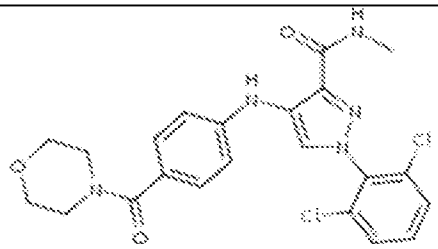
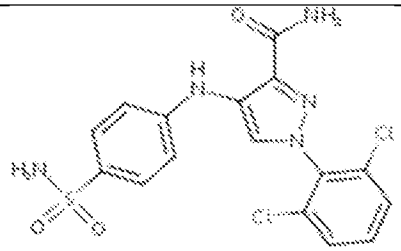
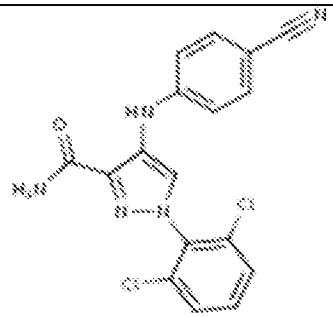
Compound No.	Structure	IUPAC-Name
240		1-(2,6-dichlorophenyl)-4-((4-(3-ethyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
241		1-(2,6-dichlorophenyl)-4-((4-(5-ethyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
242		1-(2,6-dichlorophenyl)-4-((4-(4-methyl-5-(trifluoromethyl)-4H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
243		1-(2,6-dichlorophenyl)-4-((4-(5-methyl-1H-tetrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
244		1-(2,6-dichlorophenyl)-4-((3'-fluoro-[1,1'-biphenyl]-4-yl)amino)-1H-pyrazole-3-carboxamide

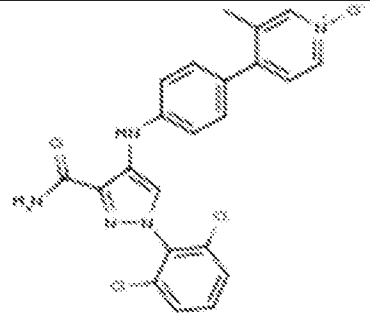
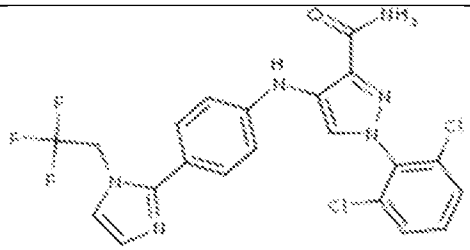
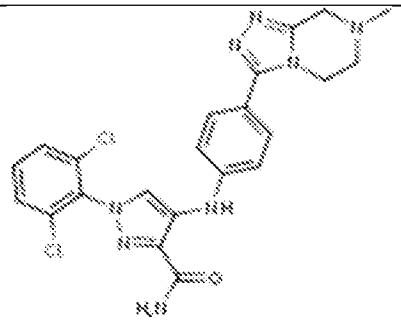
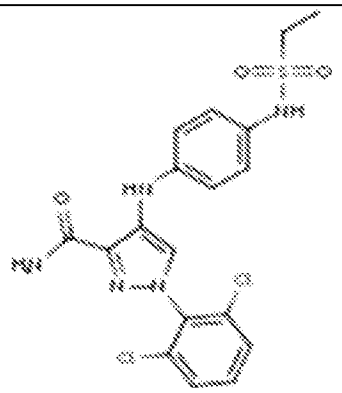
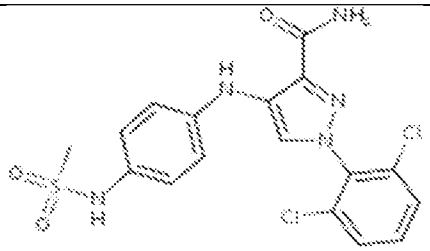
Compound No.	Structure	IUPAC-Name
245		1-(2,6-dichlorophenyl)-4-((2',5'-difluoro-[1,1'-biphenyl]-4-yl)amino)-1H-pyrazole-3-carboxamide
246		1-(2,6-dichlorophenyl)-4-((4-(3-fluoropyrrolidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide
247		1-(2,6-dichlorophenyl)-4-((4-(3,3-difluoropyrrolidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide
248		1-(2,6-dichlorophenyl)-4-((4-(3-(dimethylamino)pyrrolidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide

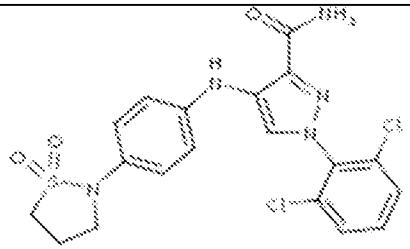
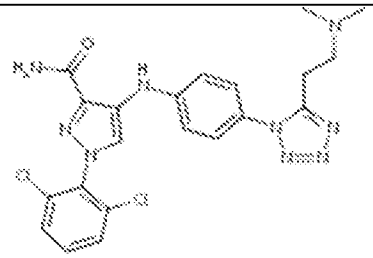
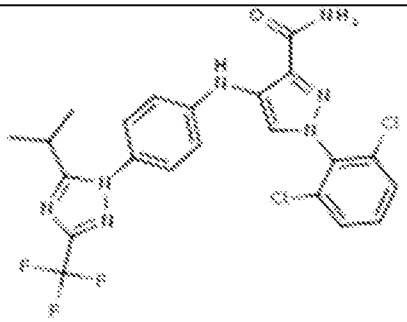
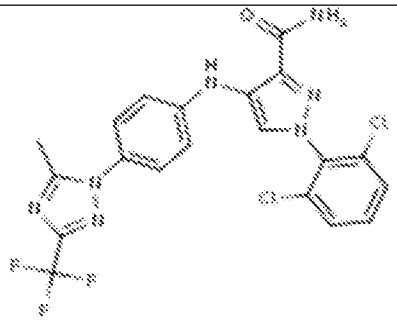
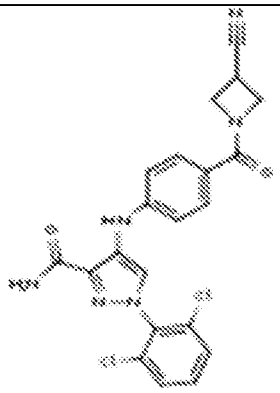
Compound No.	Structure	IUPAC-Name
249		4-((4-([1,3'-bipyrrolidine]-1'-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide
250		1-(2,6-dichlorophenyl)-4-((4-(5-ethyl-4-methyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
251		1-(2,6-dichlorophenyl)-4-((4-(1-(2-(dimethylamino)ethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
252		4-((4-(4-cyano-3-methyl-1H-pyrazol-1-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide

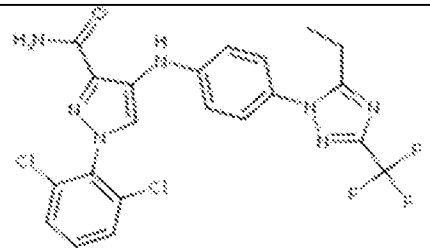
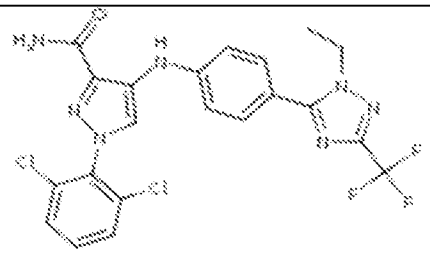
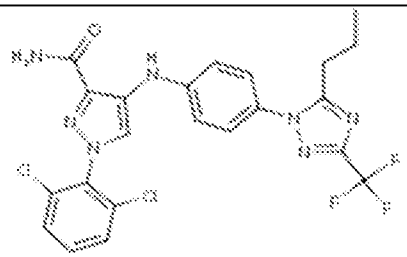
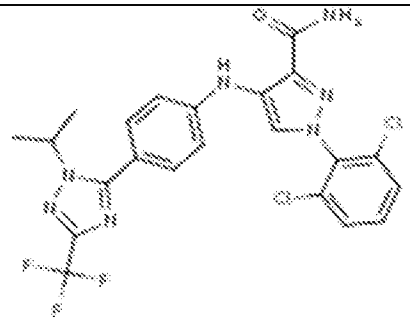
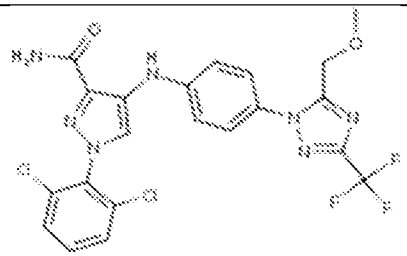
Compound No.	Structure	IUPAC-Name
253		4-((4-(4-cyano-5-methyl-1H-pyrazol-1-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide
254		1-(2,6-dichlorophenyl)-4-((4-(3,3,4,4-tetrafluoropyrrolidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide
255		1-(2,6-dichlorophenyl)-4-((2'-fluoro-[1,1'-biphenyl]-4-yl)amino)-1H-pyrazole-3-carboxamide
256		4-((2'-cyano-[1,1'-biphenyl]-4-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide

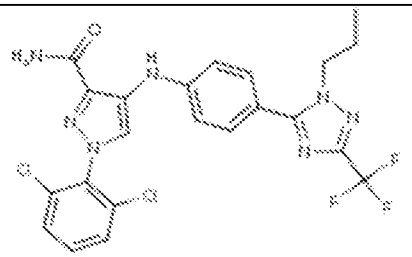
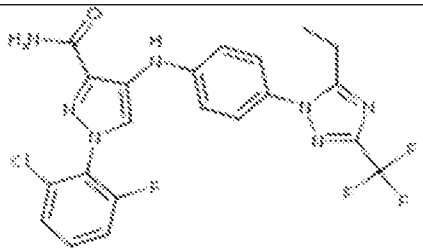
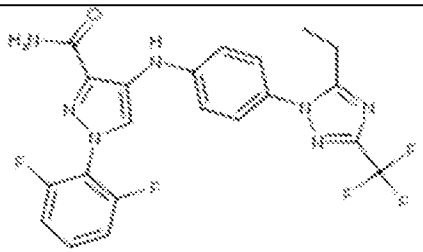
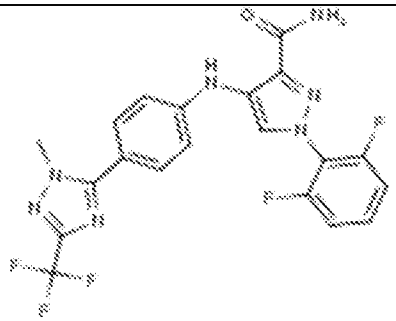
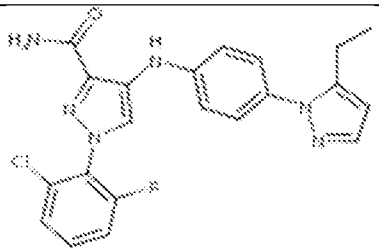
Compound No.	Structure	IUPAC-Name
257		1-(2,6-dichlorophenyl)-4-((4-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
258		1-(2,6-dichlorophenyl)-4-((4-(3-methyl-5-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
259		1-(2,6-dichlorophenyl)-4-((4-(5-ethyl-1H-tetrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
260		1-(2,6-dichlorophenyl)-4-((4-(3-methylpyridin-4-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
261		1-(2,6-dichlorophenyl)-4-((4-isopropoxyphenyl)amino)-1H-pyrazole-3-carboxamide

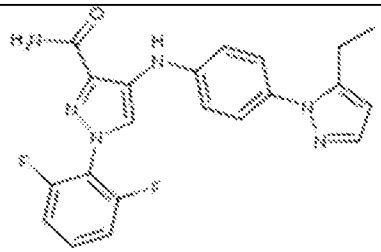
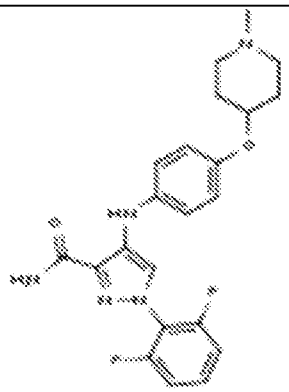
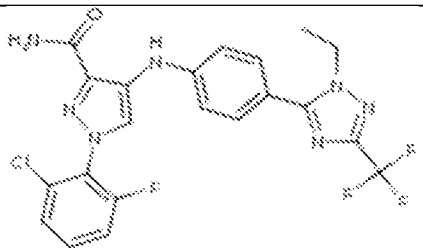
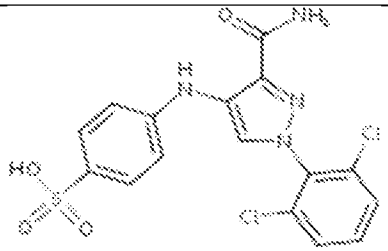
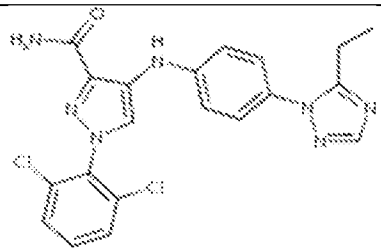
Compound No.	Structure	IUPAC-Name
262		1-(2,6-dichlorophenyl)-4-((4-(5-isopropyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
263		1-(2,6-dichlorophenyl)-4-((4-(3-isopropyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
264		1-(2,6-dichlorophenyl)-N-methyl-4-((4-(morpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide
265		1-(2,6-dichlorophenyl)-4-((4-sulfamoylphenyl)amino)-1H-pyrazole-3-carboxamide
266		4-((4-cyanophenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide

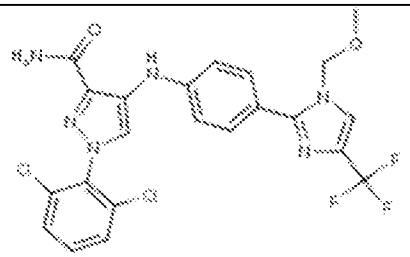
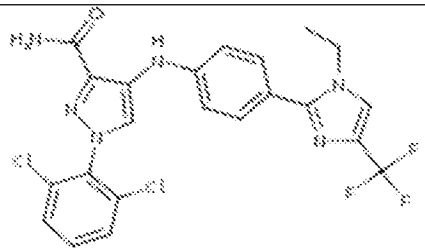
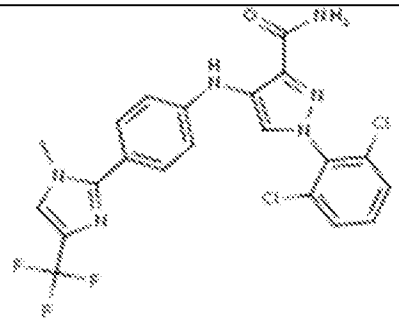
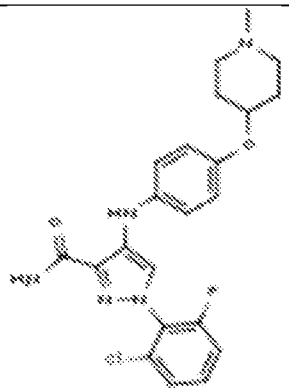
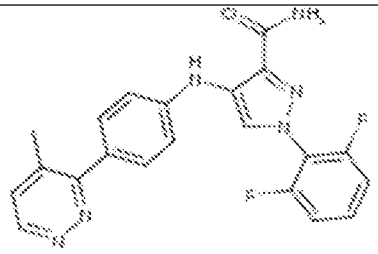
Compound No.	Structure	IUPAC-Name
267		4-(4-((3-carbamoyl-1-(2,6-dichlorophenyl)-1H-pyrazol-4-yl)amino)phenyl)-3-methylpyridine_1-oxide
268		1-(2,6-dichlorophenyl)-4-((4-(1-(2,2,2-trifluoroethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
269		1-(2,6-dichlorophenyl)-4-((4-(7-methyl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
270		1-(2,6-dichlorophenyl)-4-((4-(ethylsulfonamido)phenyl)amino)-1H-pyrazole-3-carboxamide
271		1-(2,6-dichlorophenyl)-4-((4-(methylsulfonamido)phenyl)amino)-1H-pyrazole-3-carboxamide

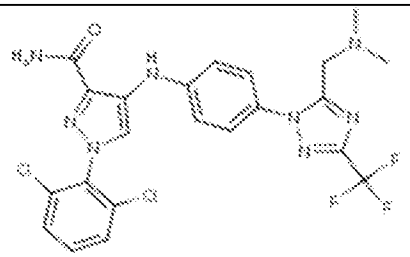
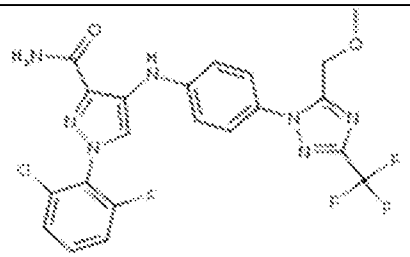
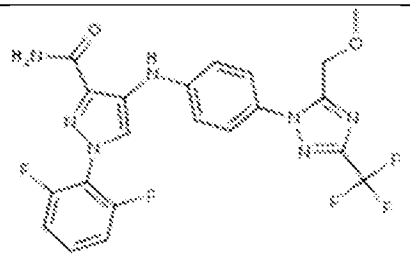
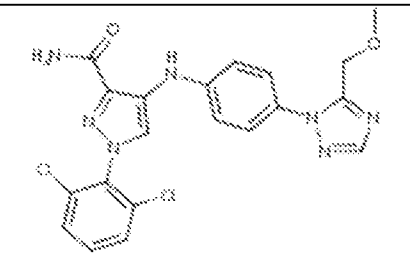
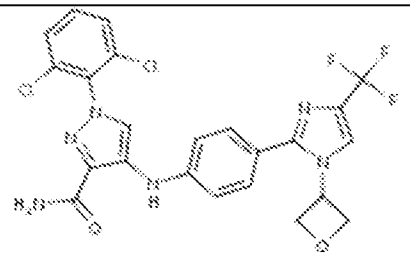
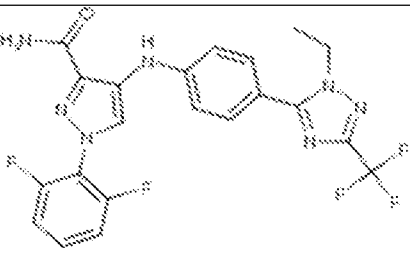
Compound No.	Structure	IUPAC-Name
272		1-(2,6-dichlorophenyl)-4-((4-(1,1-dioxidoisothiazolidin-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
273		1-(2,6-dichlorophenyl)-4-((4-(5-(2-(dimethylamino)ethyl)-1H-tetrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
274		1-(2,6-dichlorophenyl)-4-((4-(5-isopropyl-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
275		1-(2,6-dichlorophenyl)-4-((4-(5-methyl-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
276		4-((4-(3-cyanoazetidine-1-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide

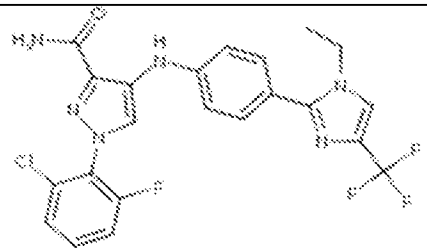
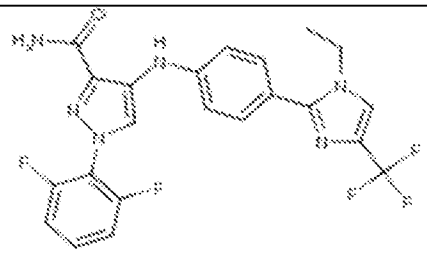
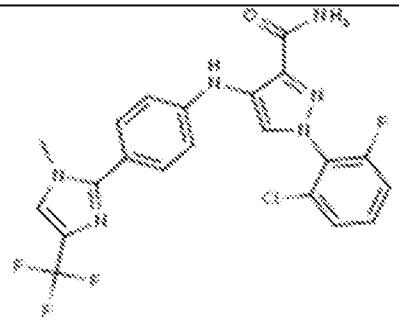
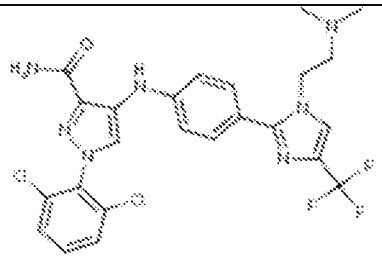
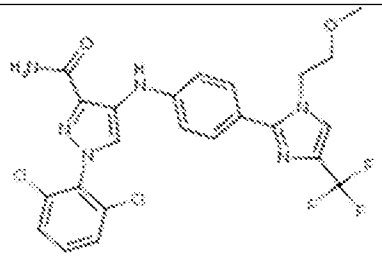
Compound No.	Structure	IUPAC-Name
277		1-(2,6-dichlorophenyl)-4-((4-(5-ethyl-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
278		1-(2,6-dichlorophenyl)-4-((4-(1-ethyl-3-(trifluoromethyl)-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
279		1-(2,6-dichlorophenyl)-4-((4-(5-propyl-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
280		1-(2,6-dichlorophenyl)-4-((4-(1-isopropyl-3-(trifluoromethyl)-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
281		1-(2,6-dichlorophenyl)-4-((4-(5-(methoxymethyl)-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide

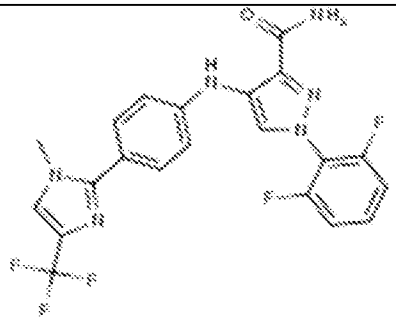
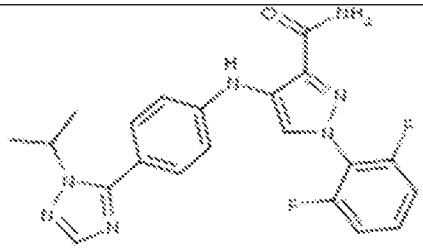
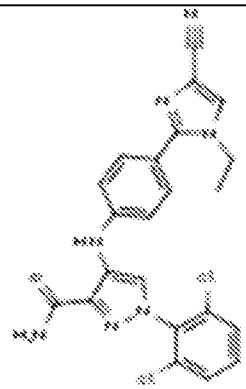
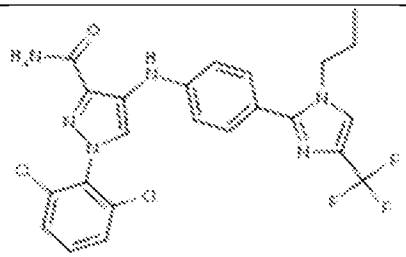
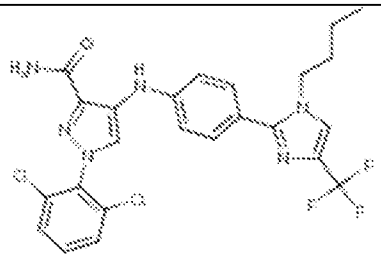
Compound No.	Structure	IUPAC-Name
282		1-(2,6-dichlorophenyl)-4-((4-(1-propyl-3-(trifluoromethyl)-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
283		1-(2-chloro-6-fluorophenyl)-4-((4-(5-ethyl-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
284		1-(2,6-difluorophenyl)-4-((4-(5-ethyl-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
285		1-(2,6-difluorophenyl)-4-((4-(1-methyl-3-(trifluoromethyl)-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
286		1-(2-chloro-6-fluorophenyl)-4-((4-(5-ethyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide

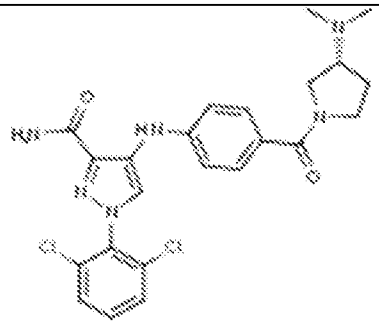
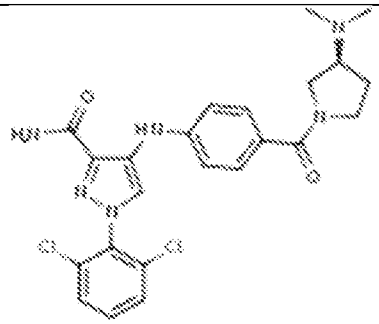
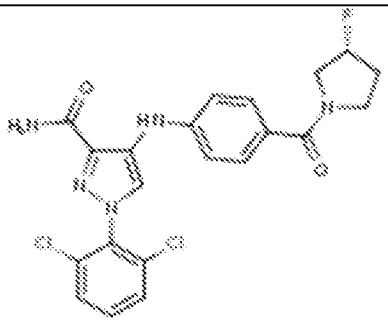
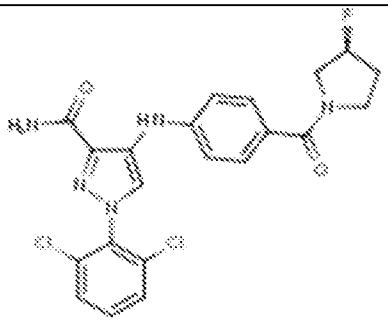
Compound No.	Structure	IUPAC-Name
287		1-(2,6-difluorophenyl)-4-((4-(5-ethyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
288		1-(2,6-difluorophenyl)-4-((4-((1-methylpiperidin-4-yl)oxy)phenyl)amino)-1H-pyrazole-3-carboxamide
289		1-(2-chloro-6-fluorophenyl)-4-((4-(1-ethyl-3-(trifluoromethyl)-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
290		4-((3-carbamoyl-1-(2,6-dichlorophenyl)-1H-pyrazol-4-yl)amino)benzenesulfonic_acid
291		1-(2,6-dichlorophenyl)-4-((4-(5-ethyl-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide

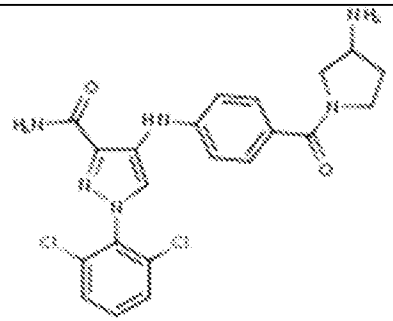
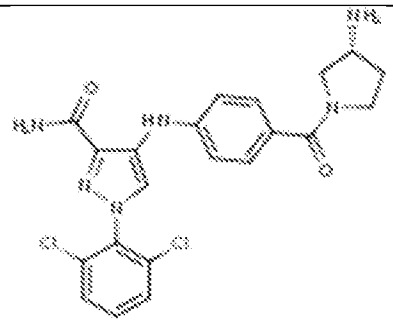
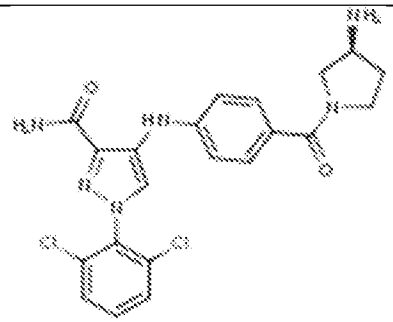
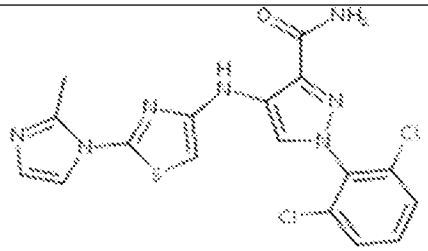
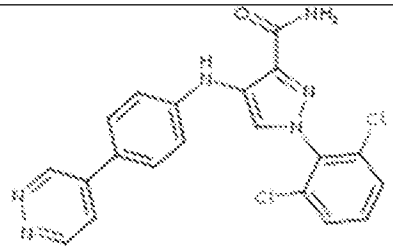
Compound No.	Structure	IUPAC-Name
292		1-(2,6-dichlorophenyl)-4-((4-(1-(methoxymethyl)-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
293		1-(2,6-dichlorophenyl)-4-((4-(1-ethyl-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
294		1-(2,6-dichlorophenyl)-4-((4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
295		1-(2-chloro-6-fluorophenyl)-4-((4-((1-methylpiperidin-4-yl)oxy)phenyl)amino)-1H-pyrazole-3-carboxamide
296		1-(2,6-difluorophenyl)-4-((4-(4-methylpyridazin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide

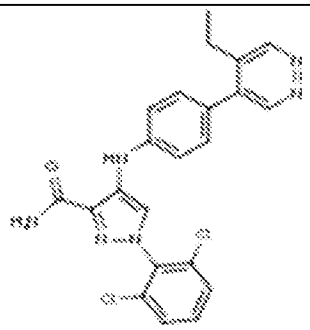
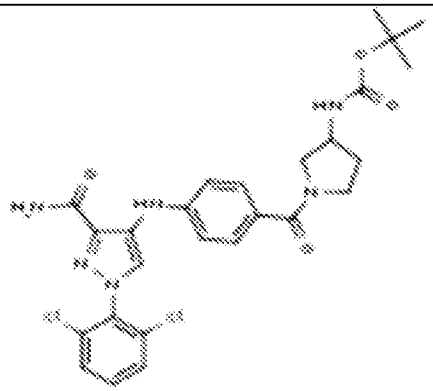
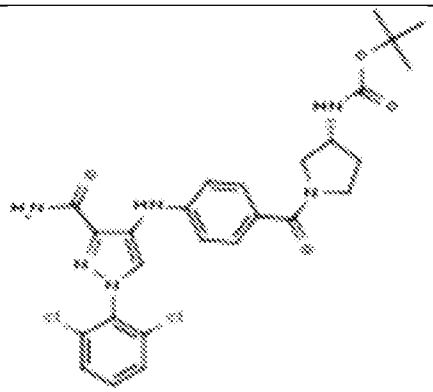
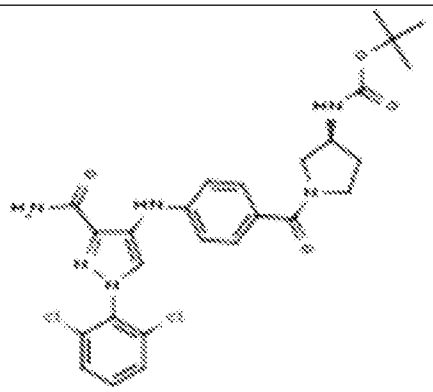
Compound No.	Structure	IUPAC-Name
297		1-(2,6-dichlorophenyl)-4-((4-(5-((dimethylamino)methyl)-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
298		1-(2-chloro-6-fluorophenyl)-4-((4-(5-(methoxymethyl)-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
299		1-(2,6-difluorophenyl)-4-((4-(5-(methoxymethyl)-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
300		1-(2,6-dichlorophenyl)-4-((4-(5-(methoxymethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
301		1-(2,6-dichlorophenyl)-4-((4-(1-(oxetan-3-yl)-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
302		1-(2,6-difluorophenyl)-4-((4-(1-ethyl-3-(trifluoromethyl)-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide

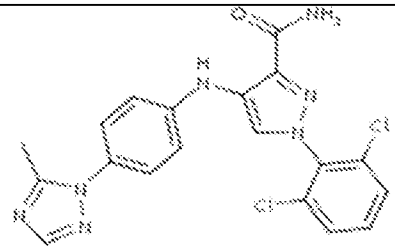
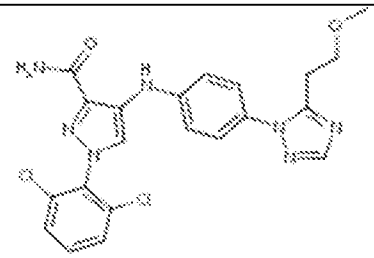
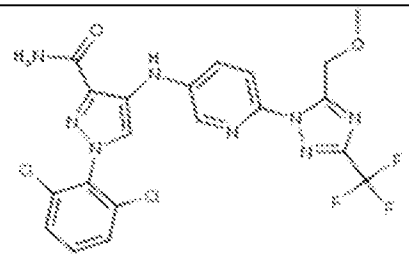
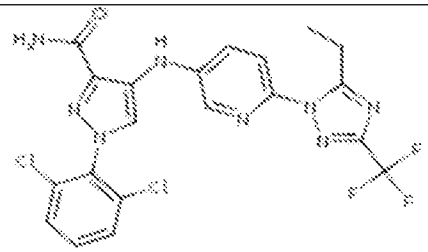
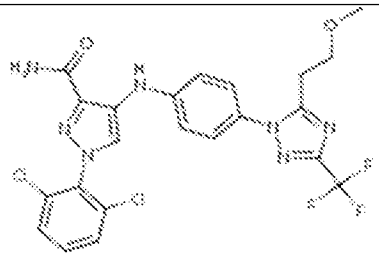
Compound No.	Structure	IUPAC-Name
303		1-(2-chloro-6-fluorophenyl)-4-((4-(1-ethyl-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
304		1-(2,6-difluorophenyl)-4-((4-(1-ethyl-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
305		1-(2-chloro-6-fluorophenyl)-4-((4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
306		1-(2,6-dichlorophenyl)-4-((4-(1-(2-(dimethylamino)ethyl)-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
307		1-(2,6-dichlorophenyl)-4-((4-(1-(2-methoxyethyl)-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide

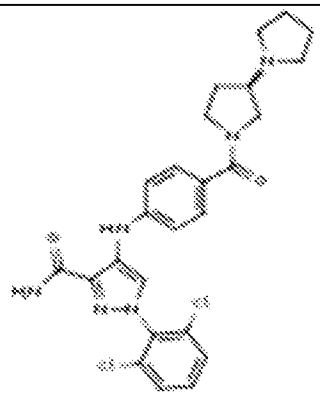
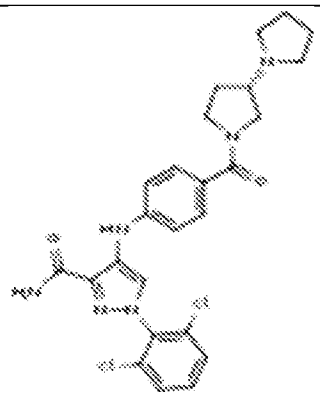
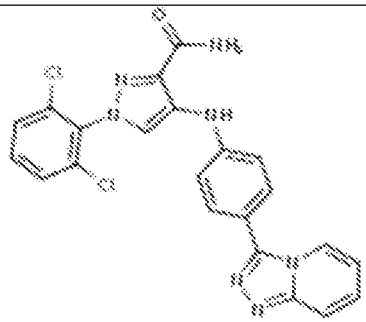
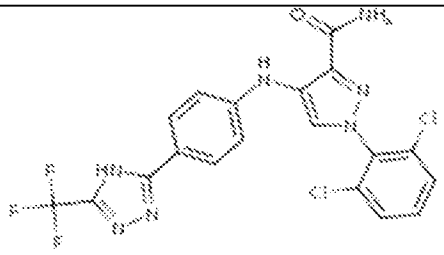
Compound No.	Structure	IUPAC-Name
308		1-(2,6-difluorophenyl)-4-((4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
309		1-(2,6-difluorophenyl)-4-((4-(1-isopropyl-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
310		4-((4-(4-cyano-1-ethyl-1H-imidazol-2-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide
311		1-(2,6-dichlorophenyl)-4-((4-(1-propyl-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
312		4-((4-(1-butyl-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide

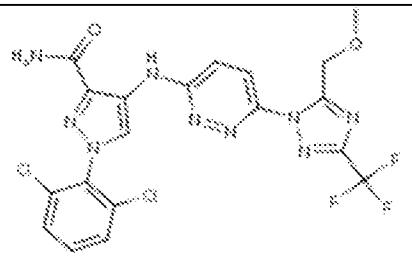
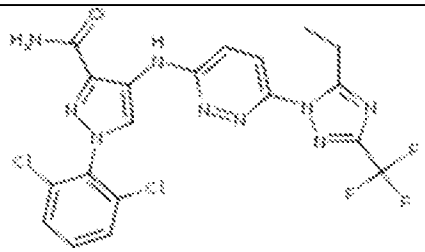
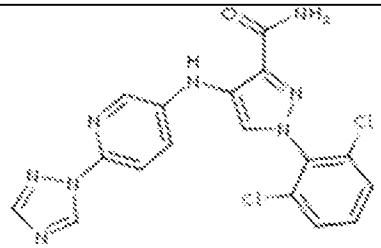
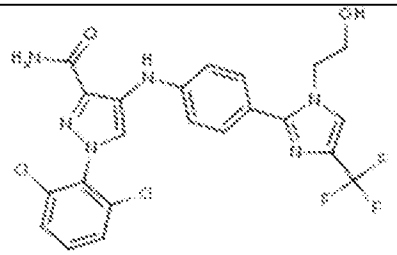
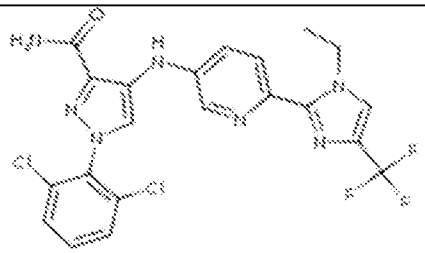
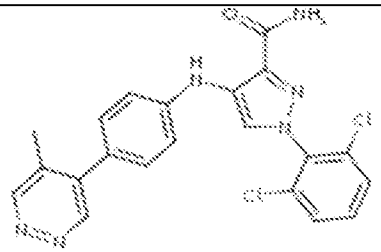
Compound No.	Structure	IUPAC-Name
313		(R)-1-(2,6-dichlorophenyl)-4-((4-(3-(dimethylamino)pyrrolidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide
314		(S)-1-(2,6-dichlorophenyl)-4-((4-(3-(dimethylamino)pyrrolidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide
315		(R)-1-(2,6-dichlorophenyl)-4-((4-(3-fluoropyrrolidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide
316		(S)-1-(2,6-dichlorophenyl)-4-((4-(3-fluoropyrrolidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide

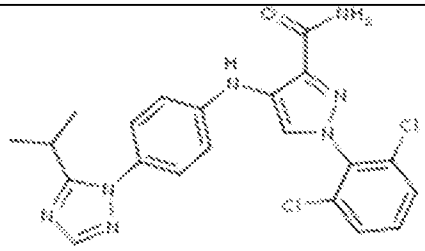
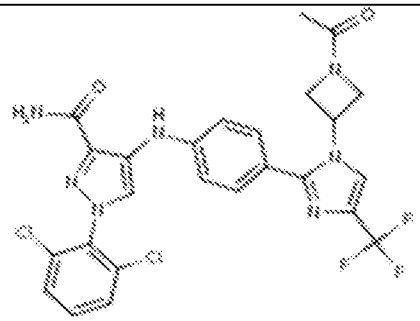
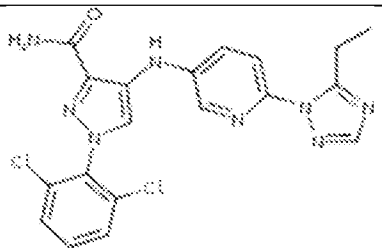
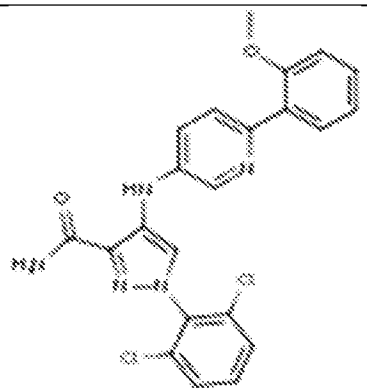
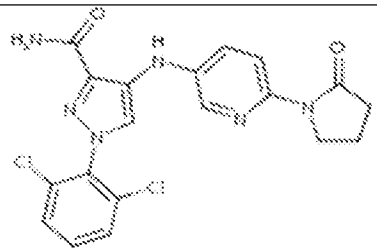
Compound No.	Structure	IUPAC-Name
317		4-((4-(3-aminopyrrolidine-1-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide
318		(R)-4-((4-(3-aminopyrrolidine-1-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide
319		(S)-4-((4-(3-aminopyrrolidine-1-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide
320		1-(2,6-dichlorophenyl)-4-((2-(2-methyl-1H-imidazol-1-yl)thiazol-4-yl)amino)-1H-pyrazole-3-carboxamide
321		1-(2,6-dichlorophenyl)-4-((4-(pyridazin-4-yl)phenyl)amino)-1H-pyrazole-3-carboxamide

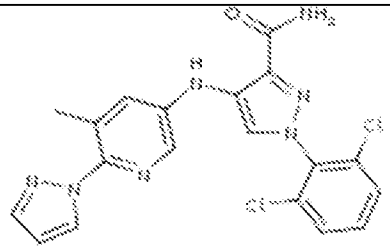
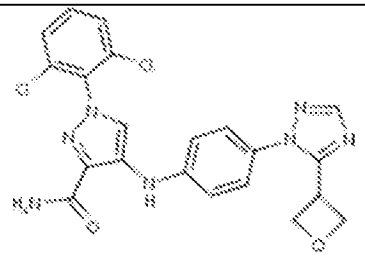
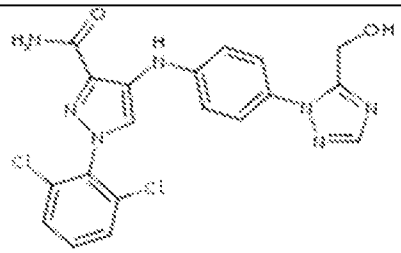
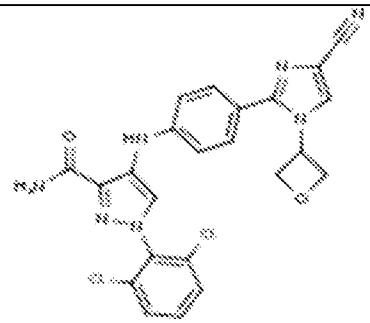
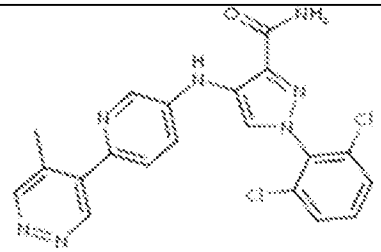
Compound No.	Structure	IUPAC-Name
322		1-(2,6-dichlorophenyl)-4-((4-(5-ethylpyridazin-4-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
323		tert-butyl_(1-(4-((3-carbamoyl-1-(2,6-dichlorophenyl)-1H-pyrazol-4-yl)amino)benzoyl)pyrrolidin-3-yl)carbamate
324		(R)-tert-butyl_(1-(4-((3-carbamoyl-1-(2,6-dichlorophenyl)-1H-pyrazol-4-yl)amino)benzoyl)pyrrolidin-3-yl)carbamate
325		(S)-tert-butyl_(1-(4-((3-carbamoyl-1-(2,6-dichlorophenyl)-1H-pyrazol-4-yl)amino)benzoyl)pyrrolidin-3-yl)carbamate

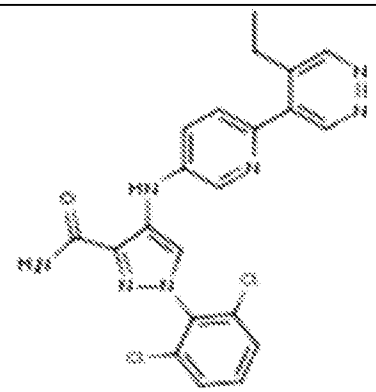
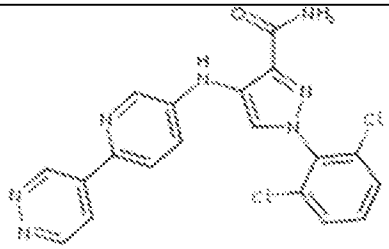
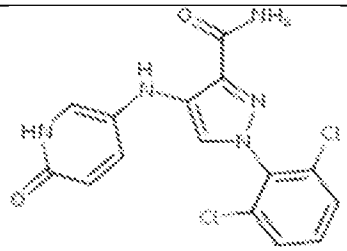
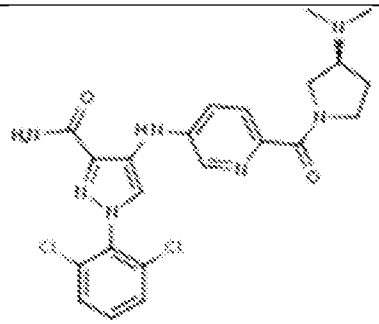
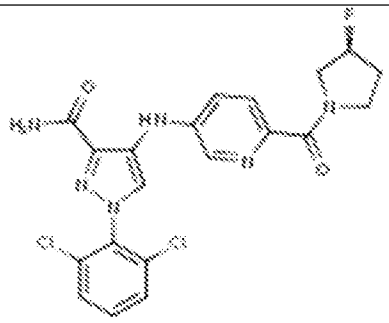
Compound No.	Structure	IUPAC-Name
326		1-(2,6-dichlorophenyl)-4-((4-(5-methyl-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
327		1-(2,6-dichlorophenyl)-4-((4-(5-(2-methoxyethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
328		1-(2,6-dichlorophenyl)-4-((6-(5-(methoxymethyl)-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide
329		1-(2,6-dichlorophenyl)-4-((6-(5-ethyl-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide
330		1-(2,6-dichlorophenyl)-4-((4-(5-(2-methoxyethyl)-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide

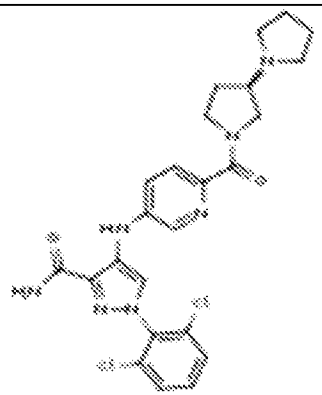
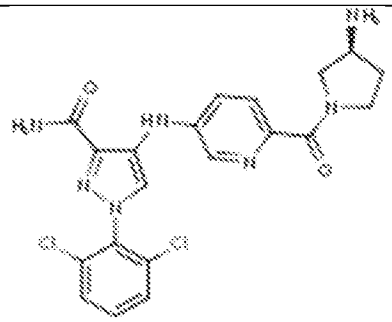
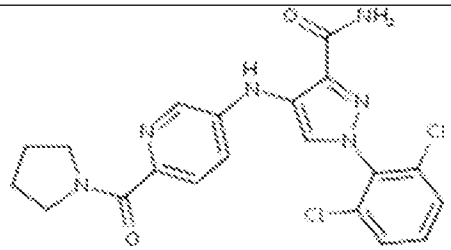
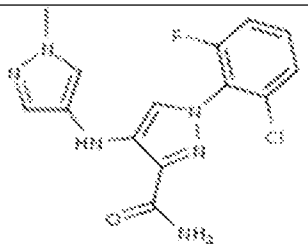
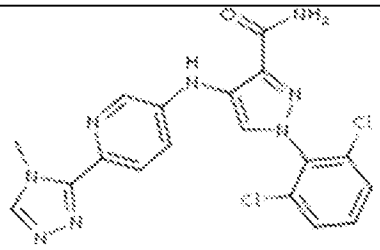
Compound No.	Structure	IUPAC-Name
331		(R)-4-((4-([1,3'-bipyrrolidine]-1'-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide
332		(S)-4-((4-([1,3'-bipyrrolidine]-1'-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide
333		4-((4-([1,2,4]triazolo[4,3-a]pyridin-3-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide
334		1-(2,6-dichlorophenyl)-4-((4-(5-(trifluoromethyl)-1H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide

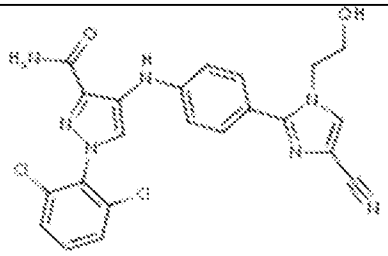
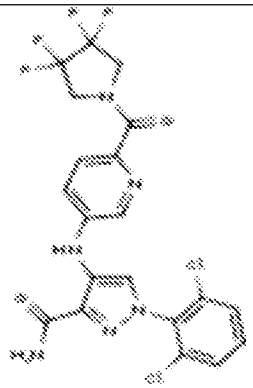
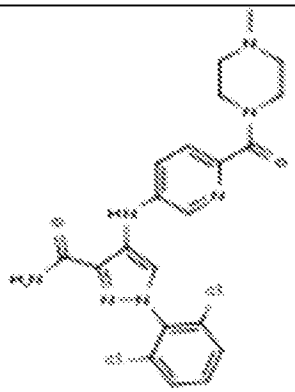
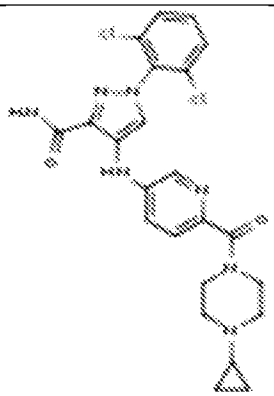
Compound No.	Structure	IUPAC-Name
335		1-(2,6-dichlorophenyl)-4-((6-(5-(methoxymethyl)-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)pyridazin-3-yl)amino)-1H-pyrazole-3-carboxamide
336		1-(2,6-dichlorophenyl)-4-((6-(5-ethyl-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)pyridazin-3-yl)amino)-1H-pyrazole-3-carboxamide
337		4-((6-(1H-1,2,4-triazol-1-yl)pyridin-3-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide
338		1-(2,6-dichlorophenyl)-4-((4-(1-(2-hydroxyethyl)-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
339		1-(2,6-dichlorophenyl)-4-((6-(1-ethyl-4-(trifluoromethyl)-1H-imidazol-2-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide
340		1-(2,6-dichlorophenyl)-4-((4-(5-methylpyridazin-4-yl)phenyl)amino)-1H-pyrazole-3-carboxamide

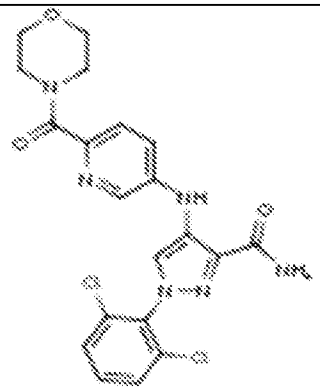
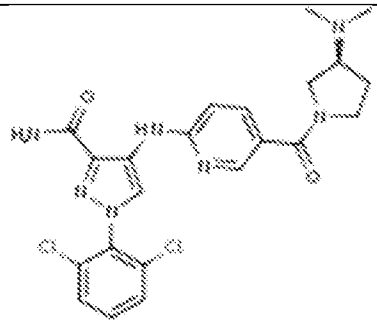
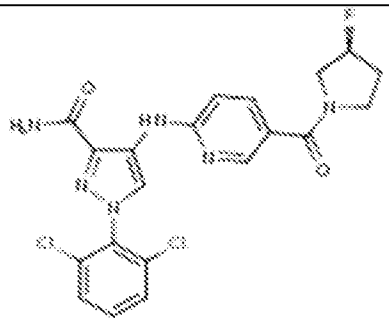
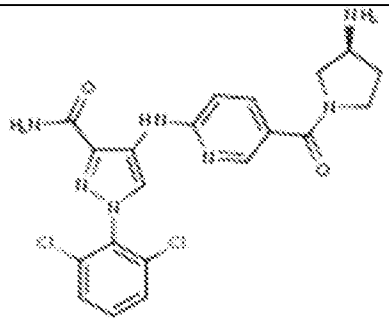
Compound No.	Structure	IUPAC-Name
341		1-(2,6-dichlorophenyl)-4-((4-(5-isopropyl-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
342		4-((4-(1-(1-acetylazetidin-3-yl)-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide
343		1-(2,6-dichlorophenyl)-4-((6-(5-ethyl-1H-1,2,4-triazol-1-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide
344		1-(2,6-dichlorophenyl)-4-((6-(2-methoxyphenyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide
345		1-(2,6-dichlorophenyl)-4-((6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide

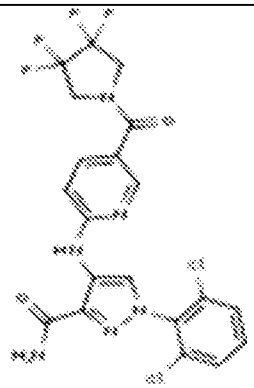
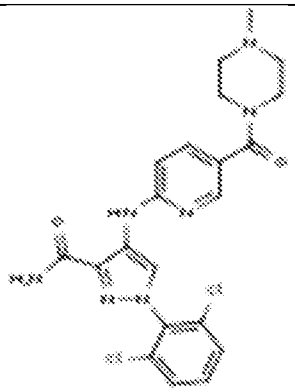
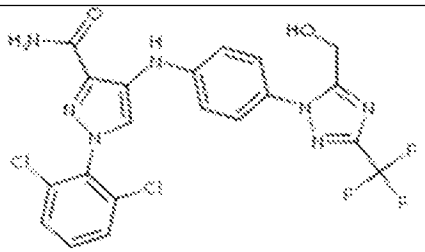
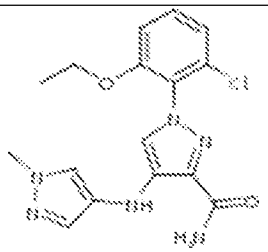
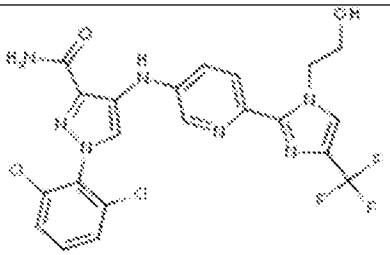
Compound No.	Structure	IUPAC-Name
346		1-(2,6-dichlorophenyl)-4-((5-methyl-6-(1H-pyrazol-1-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide
347		1-(2,6-dichlorophenyl)-4-((4-(5-(oxetan-3-yl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
348		1-(2,6-dichlorophenyl)-4-((4-(5-(hydroxymethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
349		4-((4-(4-cyano-1-(oxetan-3-yl)-1H-imidazol-2-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide
350		1-(2,6-dichlorophenyl)-4-((6-(5-methylpyridazin-4-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide

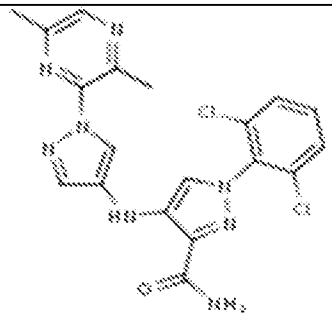
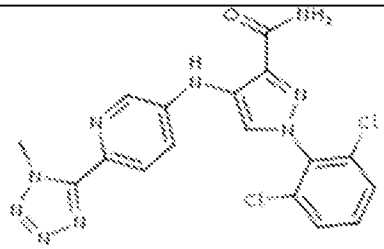
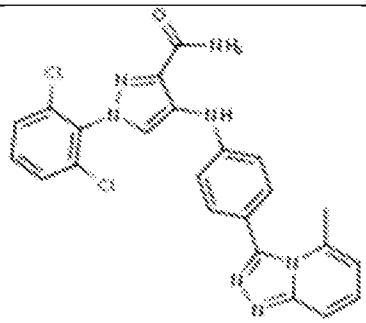
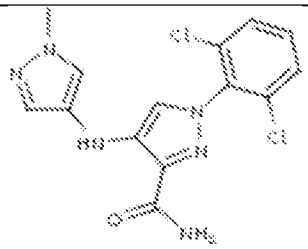
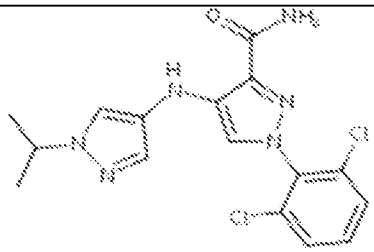
Compound No.	Structure	IUPAC-Name
351		1-(2,6-dichlorophenyl)-4-((6-(5-ethylpyridazin-4-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide
352		1-(2,6-dichlorophenyl)-4-((6-(pyridazin-4-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide
353		1-(2,6-dichlorophenyl)-4-((6-oxo-1,6-dihydropyridin-3-yl)amino)-1H-pyrazole-3-carboxamide
354		(S)-1-(2,6-dichlorophenyl)-4-((6-(3-(dimethylamino)pyrrolidine-1-carbonyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide
355		(S)-1-(2,6-dichlorophenyl)-4-((6-(3-fluoropyrrolidine-1-carbonyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide

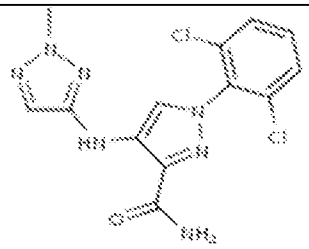
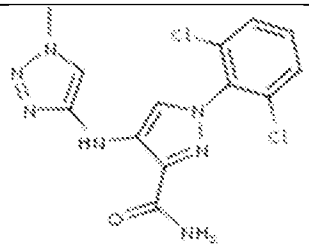
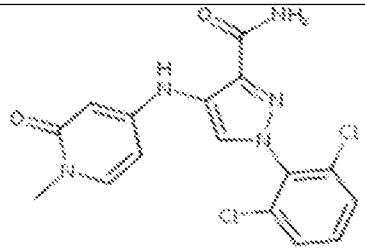
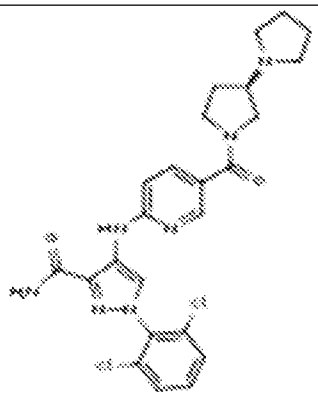
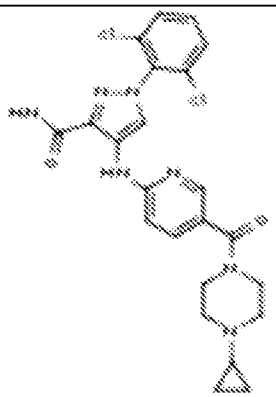
Compound No.	Structure	IUPAC-Name
356		(R)-4-((6-([1,3'-bipyrrolidine]-1'-carbonyl)pyridin-3-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide
357		(S)-4-((6-(3-aminopyrrolidine-1-carbonyl)pyridin-3-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide
358		1-(2,6-dichlorophenyl)-4-((6-(pyrrolidine-1-carbonyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide
359		1-(2-chloro-6-fluorophenyl)-4-((1-methyl-1H-pyrazol-4-yl)amino)-1H-pyrazole-3-carboxamide
360		1-(2,6-dichlorophenyl)-4-((6-(4-methyl-4H-1,2,4-triazol-3-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide

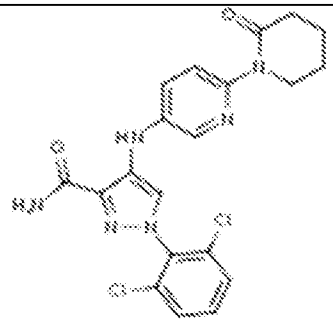
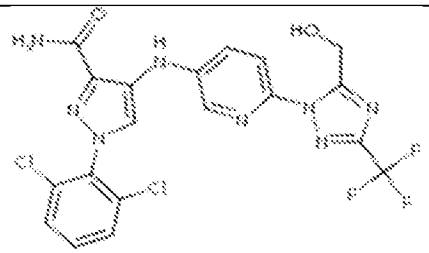
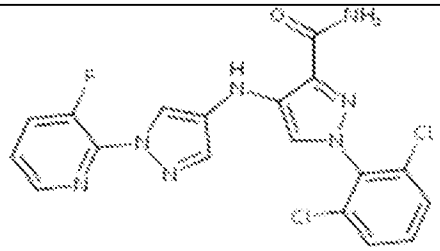
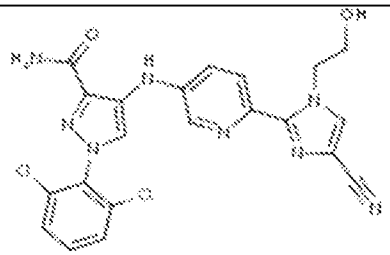
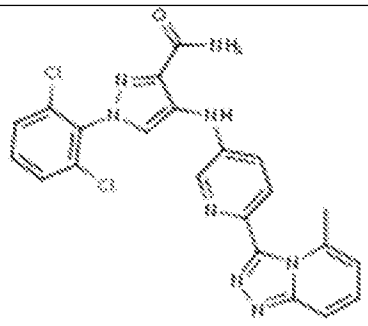
Compound No.	Structure	IUPAC-Name
361		4-((4-(4-cyano-1-(2-hydroxyethyl)-1H-imidazol-2-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide
362		1-(2,6-dichlorophenyl)-4-((6-(3,3,4,4-tetrafluoropyrrolidine-1-carbonyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide
363		1-(2,6-dichlorophenyl)-4-((6-(4-methylpiperazine-1-carbonyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide
364		4-((6-(4-cyclopropylpiperazine-1-carbonyl)pyridin-3-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide

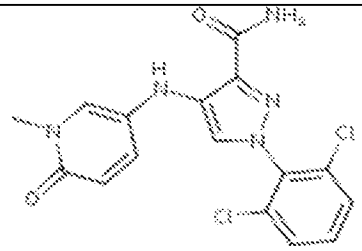
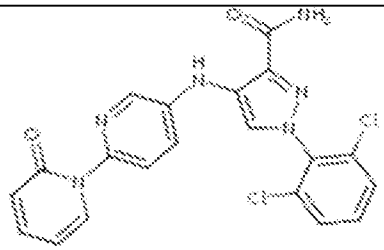
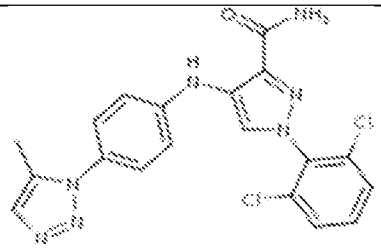
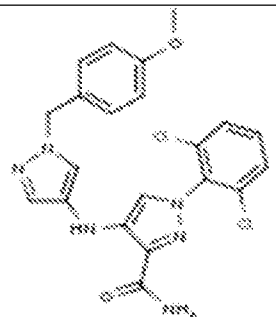
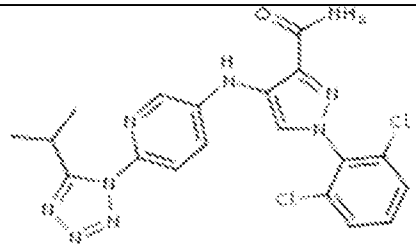
Compound No.	Structure	IUPAC-Name
365		1-(2,6-dichlorophenyl)-4-((6-(morpholine-4-carbonyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide
366		(S)-1-(2,6-dichlorophenyl)-4-((5-(3-(dimethylamino)pyrrolidine-1-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide
367		(S)-1-(2,6-dichlorophenyl)-4-((5-(3-fluoropyrrolidine-1-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide
368		(S)-4-((5-(3-aminopyrrolidine-1-carbonyl)pyridin-2-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide

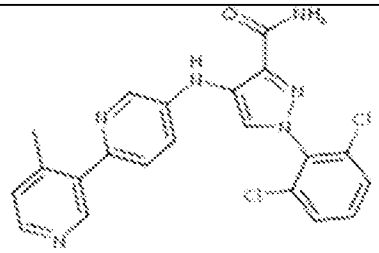
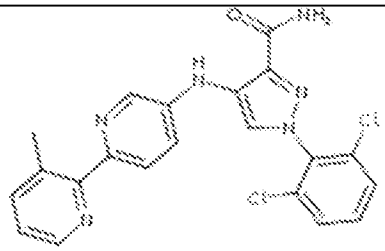
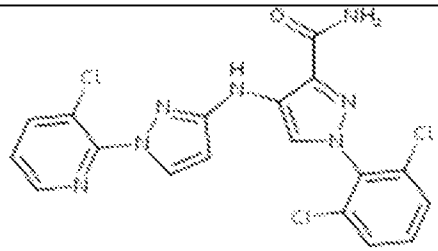
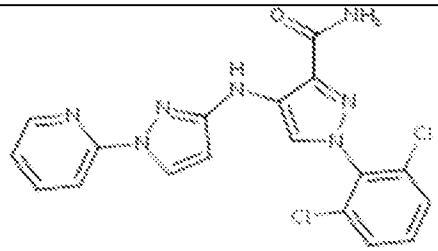
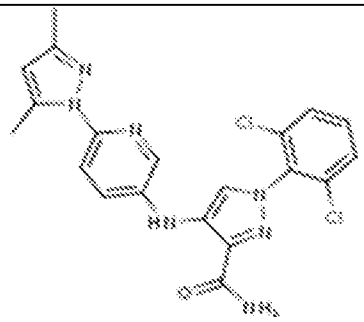
Compound No.	Structure	IUPAC-Name
369		1-(2,6-dichlorophenyl)-4-((5-(3,3,4,4-tetrafluoropyrrolidine-1-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide
370		1-(2,6-dichlorophenyl)-4-((5-(4-methylpiperazine-1-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide
371		1-(2,6-dichlorophenyl)-4-((4-(5-(hydroxymethyl)-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
372		1-(2-chloro-6-ethoxyphenyl)-4-((1-methyl-1H-pyrazol-4-yl)amino)-1H-pyrazole-3-carboxamide
373		1-(2,6-dichlorophenyl)-4-((6-(1-(2-hydroxyethyl)-4-(trifluoromethyl)-1H-imidazol-2-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide

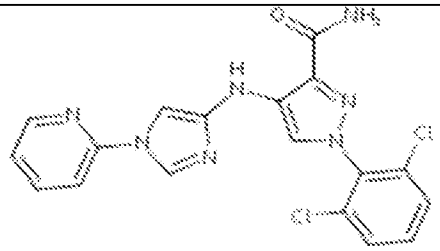
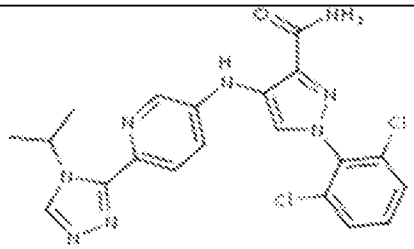
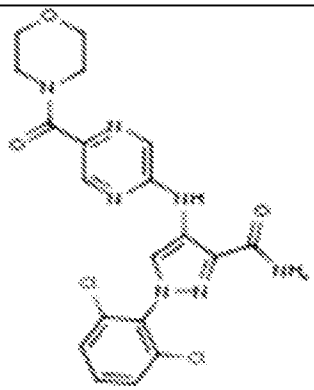
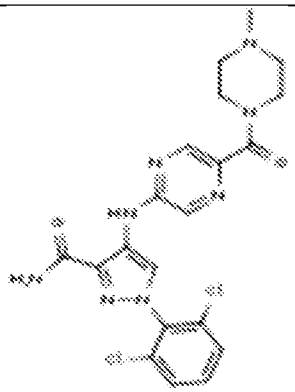
Compound No.	Structure	IUPAC-Name
374		1-(2,6-dichlorophenyl)-4-((1-(3,6-dimethylpyrazin-2-yl)-1H-pyrazol-4-yl)amino)-1H-pyrazole-3-carboxamide
375		1-(2,6-dichlorophenyl)-4-((6-(1-methyl-1H-tetrazol-5-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide
376		1-(2,6-dichlorophenyl)-4-((4-(5-methyl-[1,2,4]triazolo[4,3-a]pyridin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
377		1-(2,6-dichlorophenyl)-4-((1-methyl-1H-pyrazol-4-yl)amino)-1H-pyrazole-3-carboxamide
378		1-(2,6-dichlorophenyl)-4-((1-isopropyl-1H-pyrazol-4-yl)amino)-1H-pyrazole-3-carboxamide

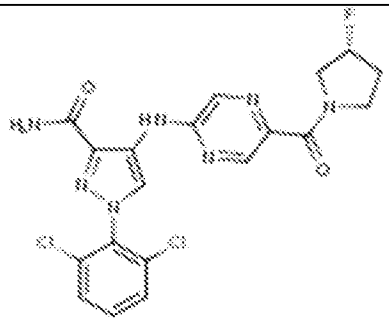
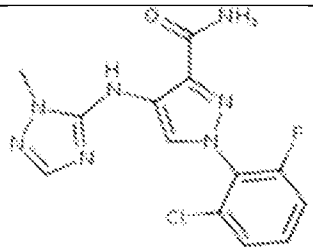
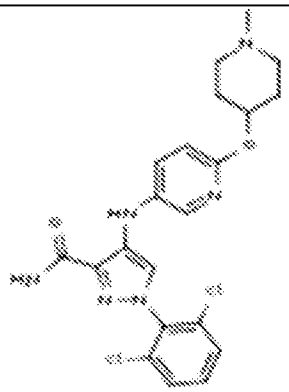
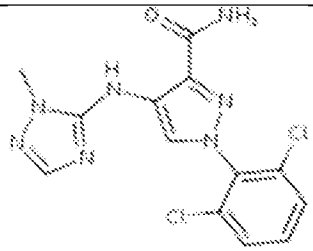
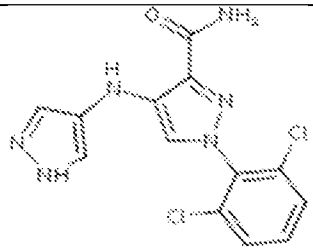
Compound No.	Structure	IUPAC-Name
379		1-(2,6-dichlorophenyl)-4-((2-methyl-2H-1,2,3-triazol-4-yl)amino)-1H-pyrazole-3-carboxamide
380		1-(2,6-dichlorophenyl)-4-((1-methyl-1H-1,2,3-triazol-4-yl)amino)-1H-pyrazole-3-carboxamide
381		1-(2,6-dichlorophenyl)-4-((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)amino)-1H-pyrazole-3-carboxamide
382		(R)-4-((5-([1,3'-bipyrrolidine]-1'-carbonyl)pyridin-2-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide
383		4-((5-(4-cyclopropylpiperazine-1-carbonyl)pyridin-2-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide

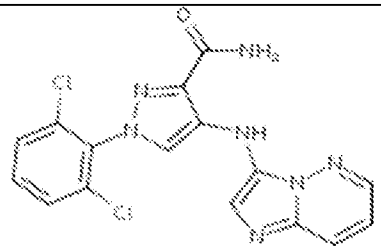
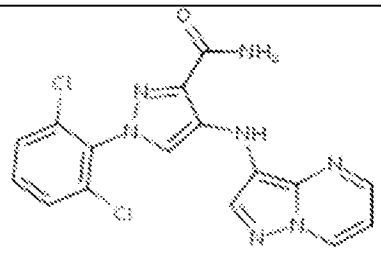
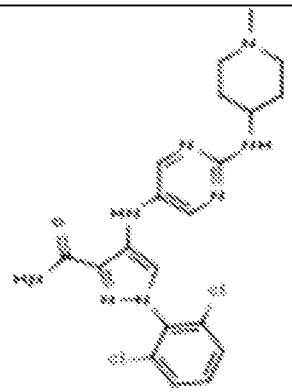
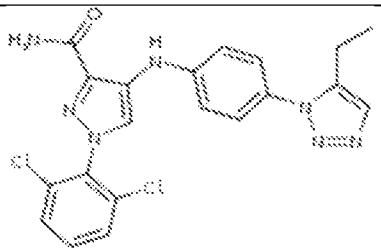
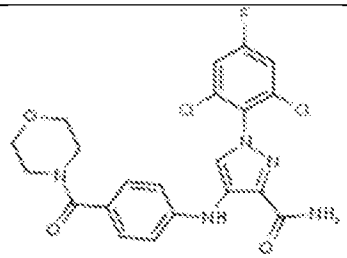
Compound No.	Structure	IUPAC-Name
384		1-(2,6-dichlorophenyl)-4-((6-(2-oxopiperidin-1-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide
385		1-(2,6-dichlorophenyl)-4-((6-(5-(hydroxymethyl)-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide
386		1-(2,6-dichlorophenyl)-4-((1-(3-fluoropyridin-2-yl)-1H-pyrazol-4-yl)amino)-1H-pyrazole-3-carboxamide
387		4-((6-(4-cyano-1-(2-hydroxyethyl)-1H-imidazol-2-yl)pyridin-3-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide
388		1-(2,6-dichlorophenyl)-4-((6-(5-methyl-[1,2,4]triazolo[4,3-a]pyridin-3-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide

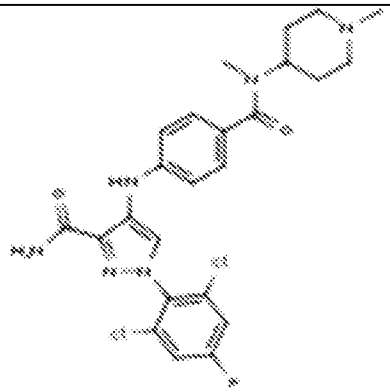
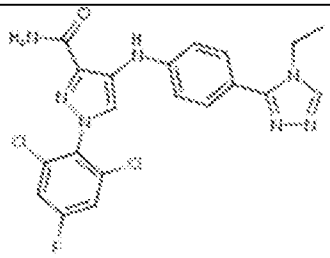
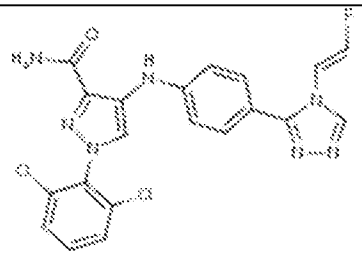
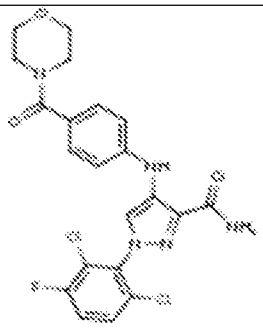
Compound No.	Structure	IUPAC-Name
389		1-(2,6-dichlorophenyl)-4-((1-methyl-6-oxo-1,6-dihydropyridin-3-yl)amino)-1H-pyrazole-3-carboxamide
390		1-(2,6-dichlorophenyl)-4-((2-oxo-2H-[1,2'-bipyridin]-5'-yl)amino)-1H-pyrazole-3-carboxamide
391		1-(2,6-dichlorophenyl)-4-((4-(5-methyl-1H-1,2,3-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
392		1-(2,6-dichlorophenyl)-4-((1-(4-methoxybenzyl)-1H-pyrazol-4-yl)amino)-1H-pyrazole-3-carboxamide
393		1-(2,6-dichlorophenyl)-4-((6-(5-isopropyl-1H-tetrazol-1-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide

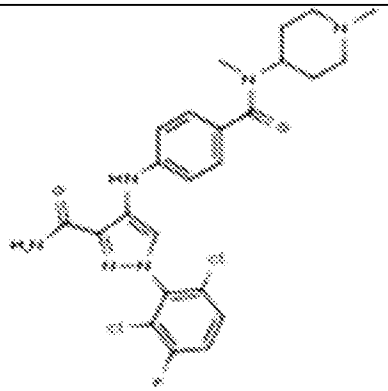
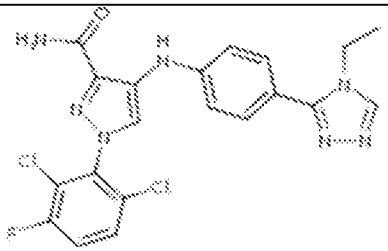
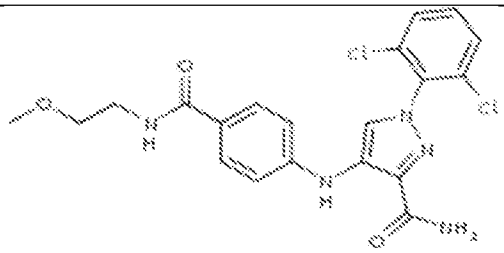
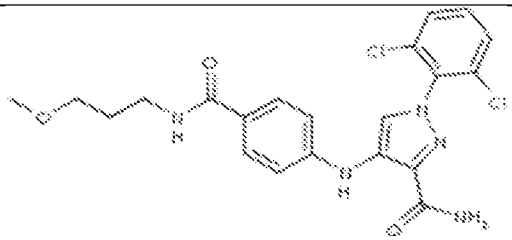
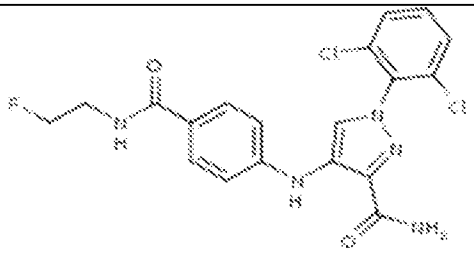
Compound No.	Structure	IUPAC-Name
394		1-(2,6-dichlorophenyl)-4-((4'-methyl-[2,3'-bipyridin]-5-yl)amino)-1H-pyrazole-3-carboxamide
395		1-(2,6-dichlorophenyl)-4-((3'-methyl-[2,2'-bipyridin]-5-yl)amino)-1H-pyrazole-3-carboxamide
396		4-((1-(3-chloropyridin-2-yl)-1H-pyrazol-3-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide
397		1-(2,6-dichlorophenyl)-4-((1-(pyridin-2-yl)-1H-pyrazol-3-yl)amino)-1H-pyrazole-3-carboxamide
398		1-(2,6-dichlorophenyl)-4-((6-(3,5-dimethyl-1H-pyrazol-1-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide

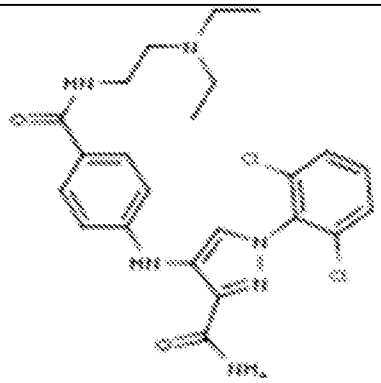
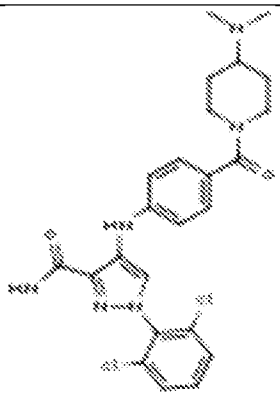
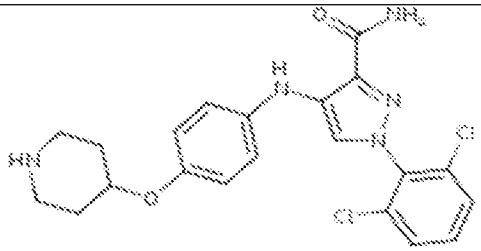
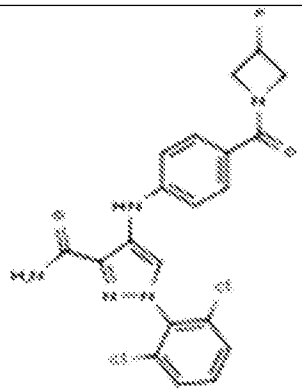
Compound No.	Structure	IUPAC-Name
399		1-(2,6-dichlorophenyl)-4-((1-(pyridin-2-yl)-1H-imidazol-4-yl)amino)-1H-pyrazole-3-carboxamide
400		1-(2,6-dichlorophenyl)-4-((6-(4-isopropyl-4H-1,2,4-triazol-3-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide
401		1-(2,6-dichlorophenyl)-4-((5-(morpholine-4-carbonyl)pyrazin-2-yl)amino)-1H-pyrazole-3-carboxamide
402		1-(2,6-dichlorophenyl)-4-((5-(4-methylpiperazine-1-carbonyl)pyrazin-2-yl)amino)-1H-pyrazole-3-carboxamide

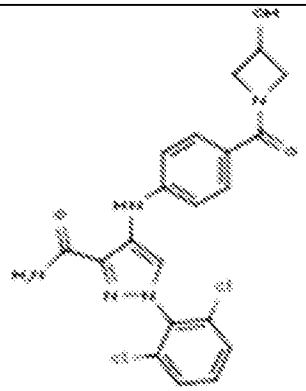
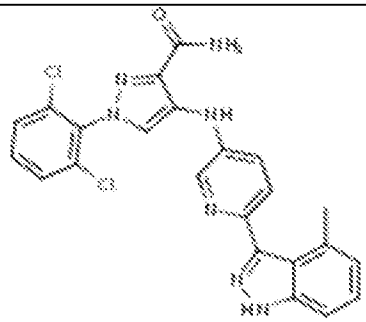
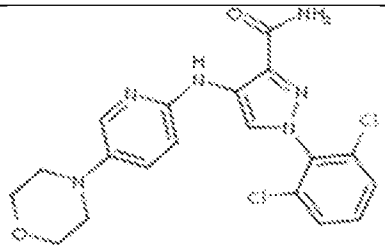
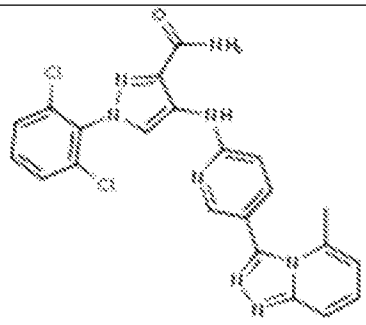
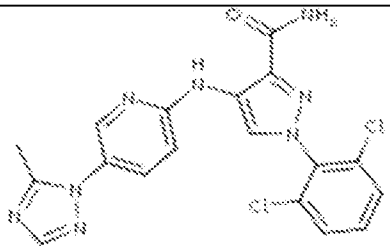
Compound No.	Structure	IUPAC-Name
403		(R)-1-(2,6-dichlorophenyl)-4-((5-(3-fluoropyrrolidine-1-carbonyl)pyrazin-2-yl)amino)-1H-pyrazole-3-carboxamide
404		1-(2-chloro-6-fluorophenyl)-4-((1-methyl-1H-1,2,4-triazol-5-yl)amino)-1H-pyrazole-3-carboxamide
405		1-(2,6-dichlorophenyl)-4-((6-((1-methylpiperidin-4-yl)oxy)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide
406		1-(2,6-dichlorophenyl)-4-((1-methyl-1H-1,2,4-triazol-5-yl)amino)-1H-pyrazole-3-carboxamide
407		4-((1H-pyrazol-4-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide

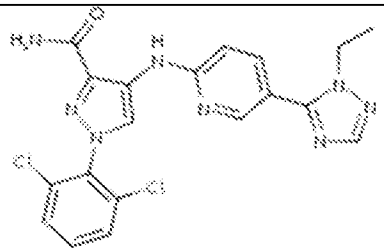
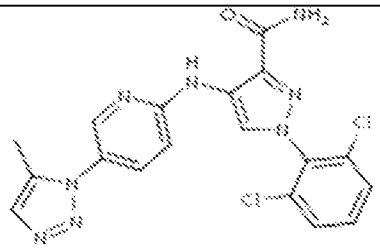
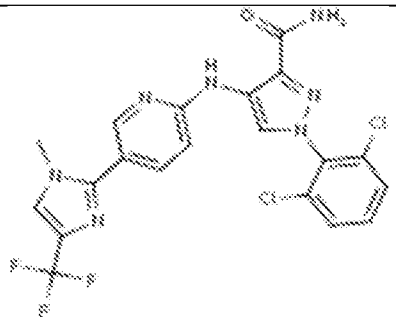
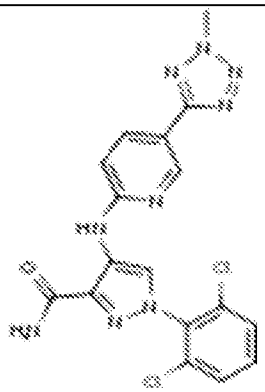
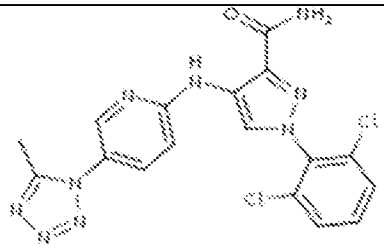
Compound No.	Structure	IUPAC-Name
408		1-(2,6-dichlorophenyl)-4-(imidazo[1,2-b]pyridazin-3-ylamino)-1H-pyrazole-3-carboxamide
409		1-(2,6-dichlorophenyl)-4-(pyrazolo[1,5-a]pyrimidin-3-ylamino)-1H-pyrazole-3-carboxamide
410		1-(2,6-dichlorophenyl)-4-((2-((1-methylpiperidin-4-yl)amino)pyrimidin-5-yl)amino)-1H-pyrazole-3-carboxamide
411		1-(2,6-dichlorophenyl)-4-((4-(5-ethyl-1H-1,2,3-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
412		1-(2,6-dichloro-4-fluorophenyl)-4-((4-(morpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide

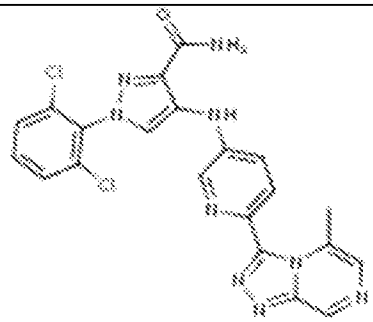
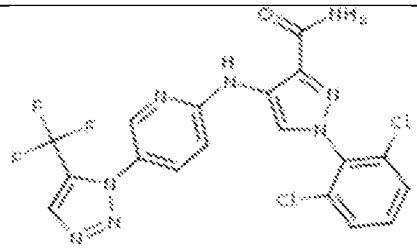
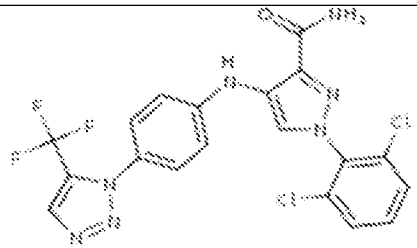
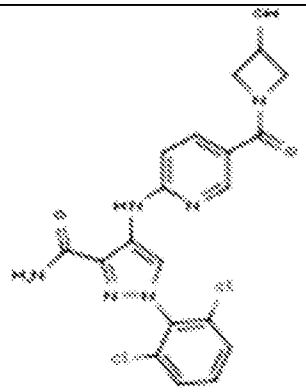
Compound No.	Structure	IUPAC-Name
413		1-(2,6-dichloro-4-fluorophenyl)-4-((4-(methyl(1-methylpiperidin-4-yl)carbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide
414		1-(2,6-dichloro-4-fluorophenyl)-4-((4-(4-ethyl-4H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
415		(E)-1-(2,6-dichlorophenyl)-4-((4-(4-(2-fluorovinyl)-4H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
416		1-(2,6-dichloro-3-fluorophenyl)-4-((4-(morpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide

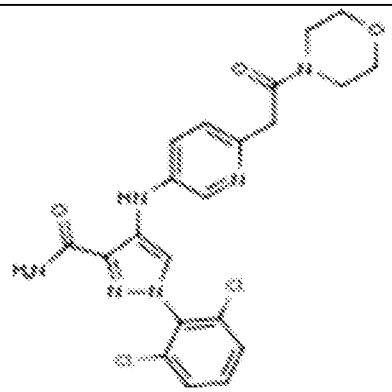
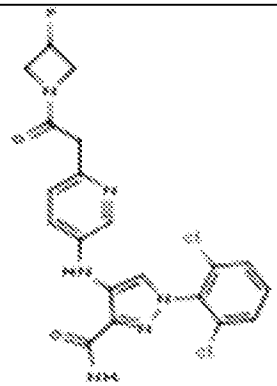
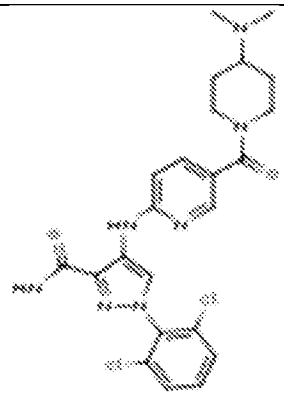
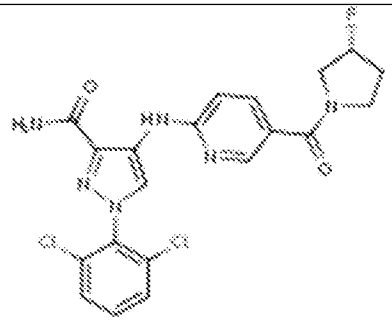
Compound No.	Structure	IUPAC-Name
417		1-(2,6-dichloro-3-fluorophenyl)-4-((4-(methyl(1-methylpiperidin-4-yl)carbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide
418		1-(2,6-dichloro-3-fluorophenyl)-4-((4-(4-ethyl-4H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
419		1-(2,6-dichlorophenyl)-4-((4-((2-methoxyethyl)carbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide
420		1-(2,6-dichlorophenyl)-4-((4-((3-methoxypropyl)carbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide
421		1-(2,6-dichlorophenyl)-4-((4-((2-fluoroethyl)carbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide

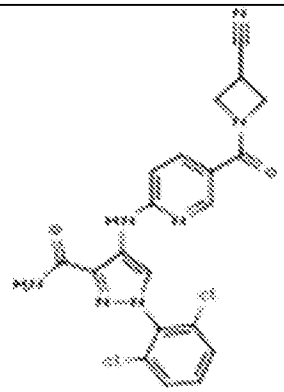
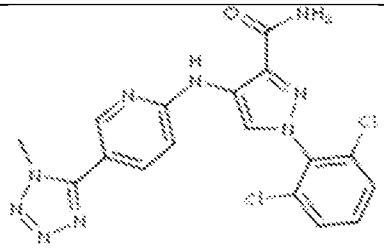
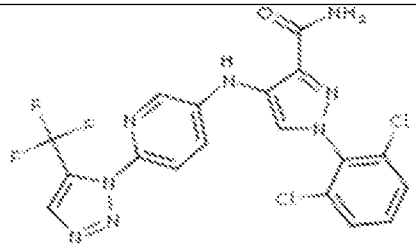
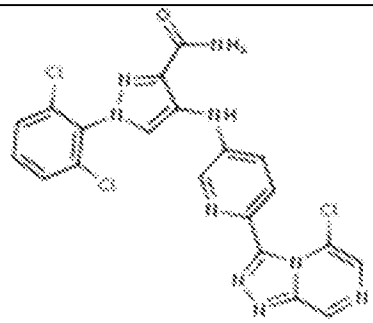
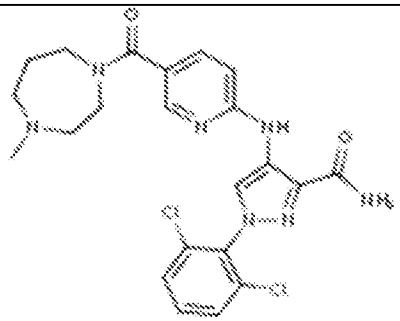
Compound No.	Structure	IUPAC-Name
422		1-(2,6-dichlorophenyl)-4-((4-((2-(diethylamino)ethyl)carbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide
423		1-(2,6-dichlorophenyl)-4-((4-(4-(dimethylamino)piperidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide
424		1-(2,6-dichlorophenyl)-4-((4-(piperidin-4-yloxy)phenyl)amino)-1H-pyrazole-3-carboxamide
425		1-(2,6-dichlorophenyl)-4-((4-(3-fluoroazetidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide

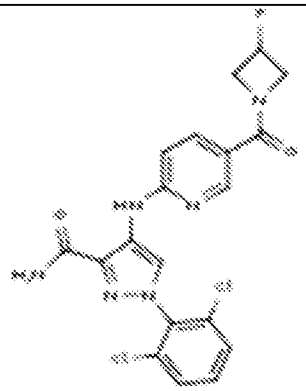
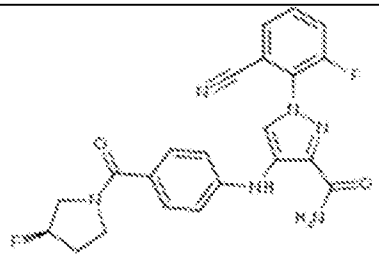
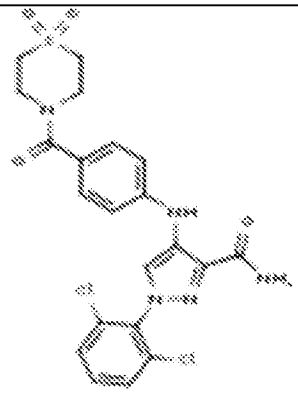
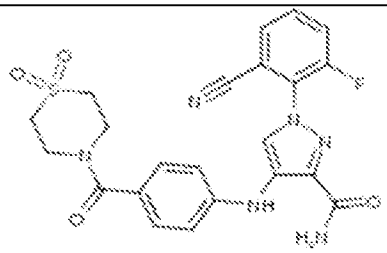
Compound No.	Structure	IUPAC-Name
426		1-(2,6-dichlorophenyl)-4-((4-(3-hydroxyazetidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide
427		1-(2,6-dichlorophenyl)-4-((6-(4-methyl-3H-indazol-3-ylidene)-1,6-dihydropyridin-3-yl)amino)-1H-pyrazole-3-carboxamide
428		1-(2,6-dichlorophenyl)-4-((5-morpholinopyridin-2-yl)amino)-1H-pyrazole-3-carboxamide
429		1-(2,6-dichlorophenyl)-4-((5-(5-methyl-[1,2,4]triazolo[4,3-a]pyridin-3-yl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide
430		1-(2,6-dichlorophenyl)-4-((5-(5-methyl-1H-1,2,4-triazol-1-yl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide

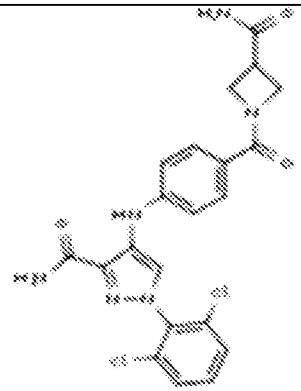
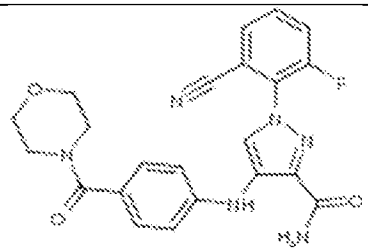
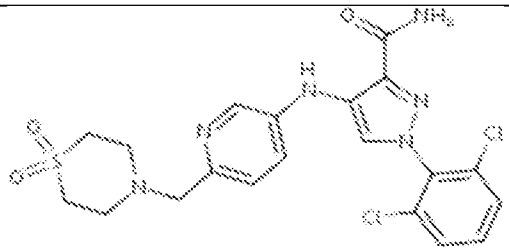
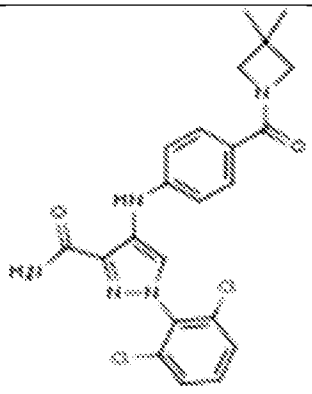
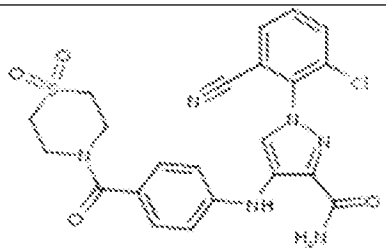
Compound No.	Structure	IUPAC-Name
431		1-(2,6-dichlorophenyl)-4-((5-(1-ethyl-1H-1,2,4-triazol-5-yl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide
432		1-(2,6-dichlorophenyl)-4-((5-(5-methyl-1H-1,2,3-triazol-1-yl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide
433		1-(2,6-dichlorophenyl)-4-((5-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide
434		1-(2,6-dichlorophenyl)-4-((5-(2-methyl-2H-tetrazol-5-yl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide
435		1-(2,6-dichlorophenyl)-4-((5-(5-methyl-1H-tetrazol-1-yl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide

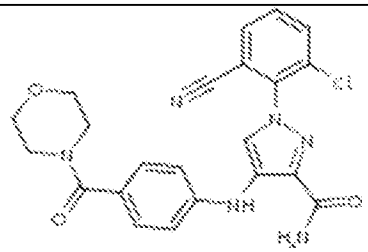
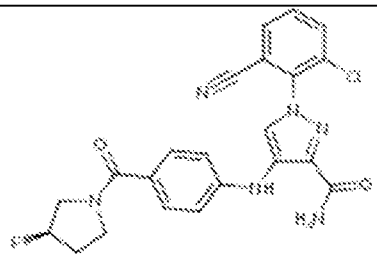
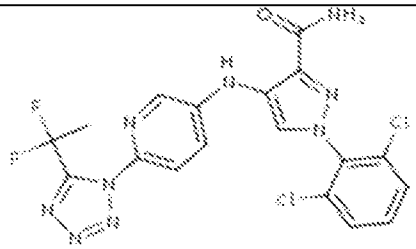
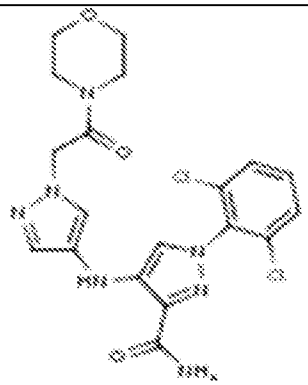
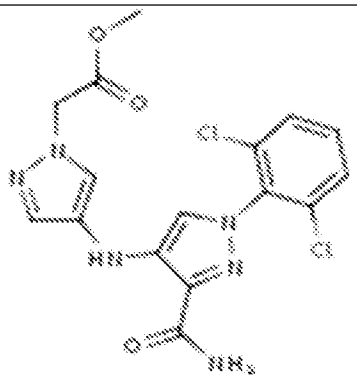
Compound No.	Structure	IUPAC-Name
436		1-(2,6-dichlorophenyl)-4-((6-(5-methyl-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide
437		1-(2,6-dichlorophenyl)-4-((5-(5-(trifluoromethyl)-1H-1,2,3-triazol-1-yl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide
438		1-(2,6-dichlorophenyl)-4-((4-(5-(trifluoromethyl)-1H-1,2,3-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide
439		1-(2,6-dichlorophenyl)-4-((5-(3-hydroxyazetidine-1-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide

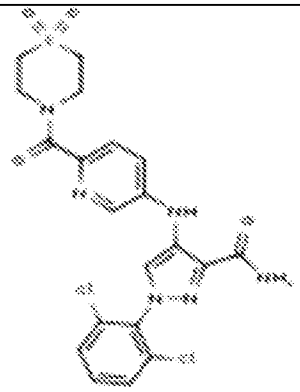
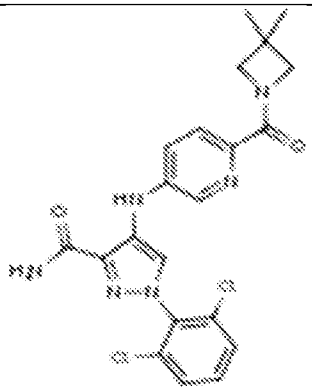
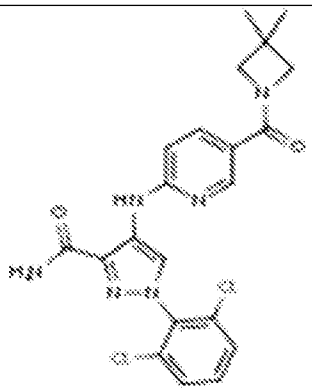
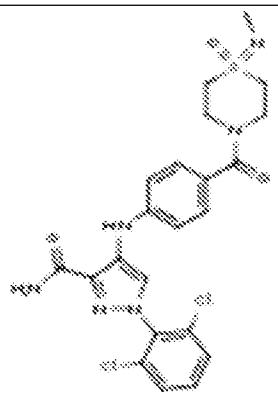
Compound No.	Structure	IUPAC-Name
440		1-(2,6-dichlorophenyl)-4-((6-(2-morpholino-2-oxoethyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide
441		1-(2,6-dichlorophenyl)-4-((6-(2-(3-fluoroazetidin-1-yl)-2-oxoethyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide
442		1-(2,6-dichlorophenyl)-4-((5-(4-(dimethylamino)piperidine-1-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide
443		(R)-1-(2,6-dichlorophenyl)-4-((5-(3-fluoropyrrolidine-1-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide

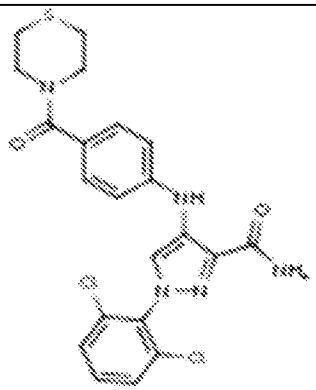
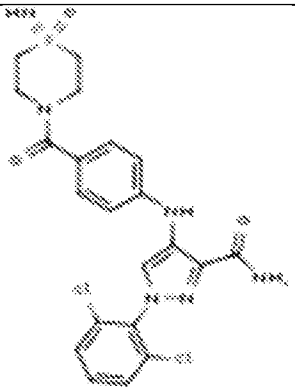
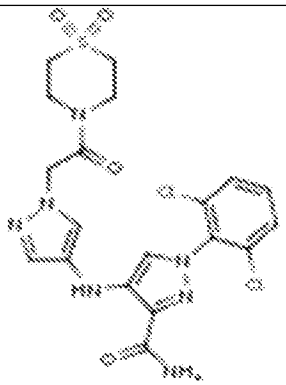
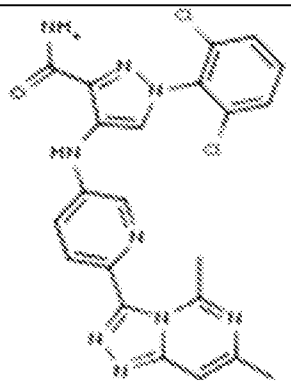
Compound No.	Structure	IUPAC-Name
444		4-((5-(3-cyanoazetidine-1-carbonyl)pyridin-2-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide
445		1-(2,6-dichlorophenyl)-4-((5-(1-methyl-1H-tetrazol-5-yl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide
446		1-(2,6-dichlorophenyl)-4-((6-(5-(trifluoromethyl)-1H-1,2,3-triazol-1-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide
447		4-((6-(5-chloro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)pyridin-3-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide
448		1-(2,6-dichlorophenyl)-4-((5-(4-methyl-1,4-diazepane-1-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide

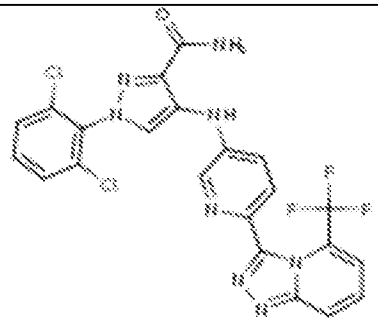
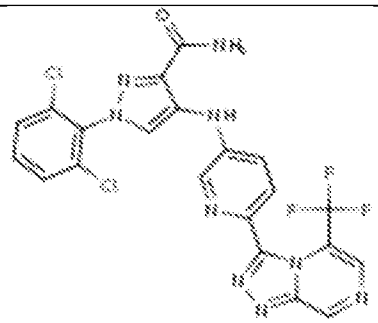
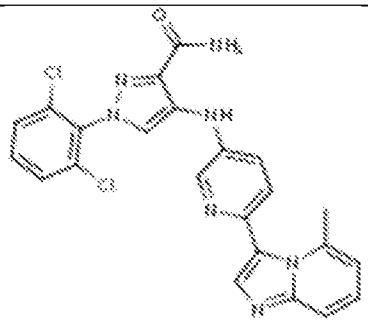
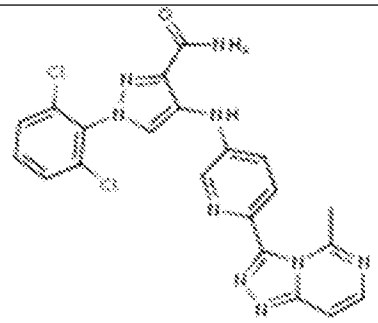
Compound No.	Structure	IUPAC-Name
449		1-(2,6-dichlorophenyl)-4-((5-(3-fluoroazetidine-1-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide
450		(R)-1-(2-cyano-6-fluorophenyl)-4-((4-(3-fluoropyrrolidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide
451		1-(2,6-dichlorophenyl)-4-((4-(1,1-dioxidothiomorpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide
452		1-(2-cyano-6-fluorophenyl)-4-((4-(1,1-dioxidothiomorpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide

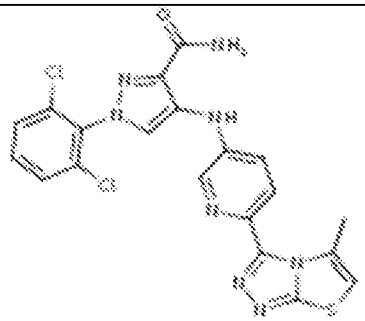
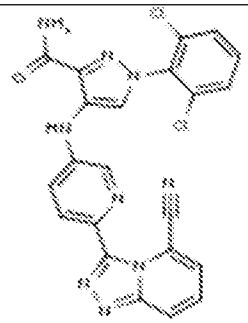
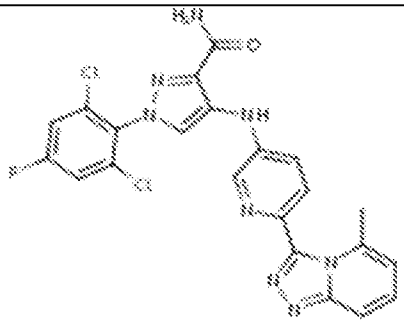
Compound No.	Structure	IUPAC-Name
453		4-[4-(3-Carbamoyl-azetidine-1-carbonyl)-phenylamino]-1-(2,6-dichloro-phenyl)-1H-pyrazole-3-carboxylic acid amide
454		1-(2-cyano-6-fluorophenyl)-4-((4-(morpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide
455		1-(2,6-dichlorophenyl)-4-((6-((1,1-dioxidothiomorpholino)methyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide
456		1-(2,6-dichlorophenyl)-4-((4-(3,3-dimethylazetidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide
457		1-(2-chloro-6-cyanophenyl)-4-((4-(1,1-dioxidothiomorpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide

Compound No.	Structure	IUPAC-Name
458		1-(2-chloro-6-cyanophenyl)-4-((4-(morpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide
459		1-(2-Chloro-6-cyano-phenyl)-4-[4-((R)-3-fluoro-pyrrolidine-1-carbonyl)-phenylamino]-1H-pyrazole-3-carboxylic acid amide
460		1-(2,6-dichlorophenyl)-4-((6-(5-(1,1-difluoroethyl)-1H-tetrazol-1-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide
461		1-(2,6-dichlorophenyl)-4-((1-(2-morpholino-2-oxoethyl)-1H-pyrazol-4-yl)amino)-1H-pyrazole-3-carboxamide
462		methyl_2-(4-((3-carbamoyl-1-(2,6-dichlorophenyl)-1H-pyrazol-4-yl)amino)-1H-pyrazol-1-yl)acetate

Compound No.	Structure	IUPAC-Name
463		1-(2,6-dichlorophenyl)-4-((6-(1,1-dioxidothiomorpholine-4-carbonyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide
464		1-(2,6-dichlorophenyl)-4-((6-(3,3-dimethylazetidine-1-carbonyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide
465		1-(2,6-dichlorophenyl)-4-((5-(3,3-dimethylazetidine-1-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide
466		1-(2,6-dichlorophenyl)-4-((4-(1-(methylimino)-1-oxidothiomorpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide

Compound No.	Structure	IUPAC-Name
467		1-(2,6-dichlorophenyl)-4-((4-(thiomorpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide
468		1-(2,6-dichlorophenyl)-4-((4-(1-imino-1-oxidothiomorpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide
469		1-(2,6-dichlorophenyl)-4-((1-(2-(1,1-dioxidothiomorpholino)-2-oxoethyl)-1H-pyrazol-4-yl)amino)-1H-pyrazole-3-carboxamide
470		1-(2,6-dichlorophenyl)-4-((6-(5,7-dimethyl-[1,2,4]triazolo[4,3-c]pyrimidin-3-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide

Compound No.	Structure	IUPAC-Name
471		1-(2,6-dichlorophenyl)-4-((6-(5-(trifluoromethyl)-[1,2,4]triazolo[4,3-a]pyridin-3-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide
472		1-(2,6-dichlorophenyl)-4-((6-(5-(trifluoromethyl)-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide
473		1-(2,6-dichlorophenyl)-4-((6-(5-methylimidazo[1,2-a]pyridin-3-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide
474		1-(2,6-dichlorophenyl)-4-((6-(5-methyl-[1,2,4]triazolo[4,3-c]pyrimidin-3-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide

Compound No.	Structure	IUPAC-Name
475		1-(2,6-dichlorophenyl)-4-((6-(5-methylthiazolo[2,3-c][1,2,4]triazol-3-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide
476		4-((6-(5-cyano-[1,2,4]triazolo[4,3-a]pyridin-3-yl)pyridin-3-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide
477		1-(2,6-dichloro-4-fluorophenyl)-4-((6-(5-methyl-[1,2,4]triazolo[4,3-a]pyridin-3-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide
478		4-((4-(3-carbamoylazetidine-1-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide

Pharmaceutical compositions

The present invention provides pharmaceutical compositions containing one or more compounds described above, or a pharmaceutically acceptable ester, prodrug, hydrate, solvate or salt of such a compound, optionally in combination with a pharmaceutically acceptable carrier. The invention further provides such compounds for the preparation of a medicament for the treatment of one or more diseases mentioned herein.

A pharmaceutical composition may contain one or more compounds of the invention in a therapeutically effective amount. A therapeutically effective amount of a compound in accordance with this invention means an amount of compound that is effective to prevent, alleviate or ameliorate symptoms of disease or prolong the survival of the subject being treated. Determination of a therapeutically effective amount is within the skill in the art.

The therapeutically effective amount or dosage of a compound according to this invention can vary within wide limits and may be determined in a manner known in the art. Such dosage may be adjusted to the individual requirements in each particular case including the specific compound being administered, the route of administration, the condition being treated, as well as the patient being treated.

Compositions of the invention may include a vehicle for delivery of one or more compounds of the invention. For example, the composition may contain particles, such as nanoparticles, microparticles, liposomes, micelles, and virus particles.

Examples of pharmacologically acceptable salts of sufficiently basic compounds of the invention are salts of physiologically acceptable mineral acids like hydrochloric, hydrobromic, sulfuric and phosphoric acid; or salts of organic acids like methanesulfonic, p-toluenesulfonic, lactic, acetic, trifluoroacetic, citric, succinic, fumaric, maleic and salicylic acid. Further, a sufficiently acidic compound of the invention may form alkali or alkaline earth metal salts, for example sodium, potassium, lithium, calcium or magnesium salts; ammonium salts; or organic base salts, for example methylamine, dimethylamine, trimethylamine, triethylamine, ethylenediamine, ethanolamine, choline hydroxide, meglumin, piperidine, morpholine, tris-(2-hydroxyethyl)amine, lysine or arginine salts; all of which are also further examples of salts of the invention. Compounds of the invention may be solvated, especially hydrated. The solvation may occur during the process of production or as a consequence of the hygroscopic nature of the

initially water free compounds of the invention. The solvates and/or hydrates may e.g. be present in solid or liquid form.

It should be appreciated that certain compounds of the invention may have tautomeric forms from which only one might be specifically mentioned or depicted in the following description, different geometrical isomers (which are usually denoted as cis/trans isomers or more generally as (E) and (Z) isomers) or different optical isomers as a result of one or more chiral carbon atoms (which are usually nomenclatured under the Cahn-Ingold-Prelog or R/S system). All these tautomeric forms, geometrical or optical isomers (as well as racemates and diastereomers) and polymorphous forms are included in the invention. Since the compounds of the invention may contain asymmetric C-atoms, they may be present either as achiral compounds, mixtures of diastereomers, mixtures of enantiomers or as optically pure compounds. The present invention comprises both all pure enantiomers and all pure diastereomers, and also the mixtures thereof in any mixing ratio.

According to a further embodiment of the present invention, one or more hydrogen atoms of the compounds of the present invention may be replaced by deuterium. Deuterium modification improves the metabolic properties of a drug with little or no change in its intrinsic pharmacology. Deuterium substitution at specific molecular positions improves metabolic stability, reduces formation of toxic metabolites and/or increases the formation of desired active metabolites. Accordingly, the present invention also encompasses the partially and fully deuterated compounds of the invention. The term hydrogen also encompasses deuterium.

The therapeutic use of compounds according to the invention, their pharmacologically acceptable salts, solvates and hydrates, respectively, as well as formulations and pharmaceutical compositions also lie within the scope of the present invention. The pharmaceutical compositions according to the present invention may comprise at least one compound of the invention as an active ingredient and, optionally, carrier substances and/or adjuvants.

The present invention also relates to prodrugs which are composed of a compound of the invention and at least one pharmacologically acceptable protective group which will be cleaved under physiological conditions, such as an alkoxy-, arylalkyloxy-, acyl-, acyloxymethyl group (e.g. pivaloyloxymethyl), an 2-alkyl-, 2-aryl- or 2-arylalkyl oxycarbonyl-2-alkylidene ethyl group or an acyloxy group as defined herein, e.g. ethoxy, benzyloxy, acetyl or acetyloxy or,

especially for a compound of the invention, carrying a hydroxy group (-OH): a sulfate, a phosphate (-OPO_3 or -OCH_2OPO_3) or an ester of an amino acid. For example, compositions may contain pro-drugs of the hydroxy group of a compound of the invention.

As used herein, the term pharmaceutically acceptable ester especially refers to esters which hydrolyze in vivo and include those that break down readily in the human body to leave the parent compound or a salt thereof. Suitable ester groups include, for example, those derived from pharmaceutically acceptable aliphatic carboxylic acids, particularly alkanoic, alkenoic, cycloalkanoic and alkanedioic acids, in which each alkyl or alkenyl moiety advantageously has not more than 6 carbon atoms. Examples of particular esters include, but are not limited to, formates, acetates, propionates, butyrates, acrylates and ethylsuccinates.

The present invention also relates to a prodrug, a biohydrolyzable ester, a biohydrolyzable amide, a polymorph, tautomer, stereoisomer, metabolite, N-oxide, biohydrolyzable carbamate, biohydrolyzable ether, physiologically functional derivative, atropisomer, or in vivo-hydrolysable precursor, diastereomer or mixture of diastereomers, chemically protected form, affinity reagent, complex, chelate and a stereoisomer of the compounds of the invention.

As mentioned above, therapeutically useful agents that contain compounds of the invention, their solvates, salts or formulations are also comprised in the scope of the present invention. In general, compounds of the invention will be administered by using the known and acceptable modes known in the art, either alone or in combination with any other therapeutic agent.

For oral administration such therapeutically useful agents can be administered by one of the following routes: oral, e.g. as tablets, dragees, coated tablets, pills, semisolids, soft or hard capsules, for example soft and hard gelatin capsules, aqueous or oily solutions, emulsions, suspensions or syrups, parenteral including intravenous, intramuscular and subcutaneous injection, e.g. as an injectable solution or suspension, rectal as suppositories, by inhalation or insufflation, e.g. as a powder formulation, as microcrystals or as a spray (e.g. liquid aerosol), transdermal, for example via an transdermal delivery system (TDS) such as a plaster containing the active ingredient or intranasal. For the production of such tablets, pills, semisolids, coated tablets, dragees and hard, e.g. gelatin, capsules, the therapeutically useful product may be mixed with pharmaceutically inert, inorganic or organic excipients as are e.g. lactose, sucrose, glucose,

gelatin, malt, silica gel, starch or derivatives thereof, talc, stearinic acid or their salts, dried skim milk, and the like. For the production of soft capsules, one may use excipients as are e.g. vegetable, petroleum, animal or synthetic oils, wax, fat, polyols. For the production of liquid solutions, emulsions or suspensions or syrups one may use as excipients e.g. water, alcohols, aqueous saline, aqueous dextrose, polyols, glycerin, lipids, phospholipids, cyclodextrins, vegetable, petroleum, animal or synthetic oils. Particularly useful are lipids, such as phospholipids (e.g., natural origin and/or with a particle size between 300 to 350 nm) in phosphate buffered saline (pH = 7 to 8, e.g., 7.4). For suppositories one may use excipients as are e.g. vegetable, petroleum, animal or synthetic oils, wax, fat and polyols. For aerosol formulations one may use compressed gases suitable for this purpose, as are e.g. oxygen, nitrogen and carbon dioxide. The pharmaceutically useful agents may also contain additives for conservation, stabilization, e.g. UV stabilizers, emulsifiers, sweetener, aromatizers, salts to change the osmotic pressure, buffers, coating additives and antioxidants.

In general, in the case of oral or parenteral administration to adult humans weighing approximately 80 kg, a daily dosage of about 10 mg to about 10,000 mg, or from about 20 mg to about 1,000 mg, should be appropriate, although the upper limit may be exceeded when indicated. The daily dosage can be administered as a single dose or in divided doses, or for parenteral administration, it may be given as continuous infusion or subcutaneous injection.

Methods of making compounds

The invention also provides methods of making compounds of the invention, such as those described above. Synthesis schemes for making specific compounds of Formula (I) are provided in the Examples below.

Methods of treating conditions

The compounds and compositions of the invention modulate activity of one or more protein kinases. The compounds and compositions may inhibit, activate, or otherwise alter kinase activity. Consequently, the compounds and compositions may be used to diagnose, treat, or prevent a condition, such as a disease, disorder, or other condition for which modulation of kinase activity provides therapeutic benefit.

Diseases, disorders, and conditions that can be diagnosed and/or treated using compositions and methods of the invention include (but are not restricted to) those associated with aberrant activity, e.g., increased activity or decreased activity, of one or more kinases. The kinase may be a serine-threonine kinase or a tyrosine kinase, e.g., a receptor tyrosine kinase or non-receptor tyrosine kinase. The kinase may be a member of the JAK family. For example and without limitation, the kinase may be leucine-rich repeat kinase 2 (LRRK2), NUAK family SNF1-like kinase 1 (NUAK1, also known as AMPK-related protein kinase 5 or ARK5), JAK1, JAK2, or non-receptor tyrosine-protein kinase TYK2 (TYK2), including mutants of any of the aforementioned kinases.

The disease, disorder, or condition may be associated with aberrant LRRK2 activity, such as Alzheimer's disease, Crohn's disease, inflammatory bowel disease, an inflammatory disease, leprosy, neurodegenerative diseases, a non-skin cancer, or Parkinson's disease, including familial Parkinson's disease, sporadic Parkinson's disease, late-onset Parkinson's disease (PD), and type 8 Parkinson's disease.

The disease, disorder, or condition may be associated with aberrant NUAK1 activity, such as cancer, e.g., colorectal cancer, stomach cancer, endometrial cancer, or multiple myeloma, diabetes, fibrosis, a neurodegenerative disease, or omphalocele.

The disease, disorder, or condition may be associated with aberrant TYK2 activity, such as autoimmune disorders, Crohn's disease, hyperimmunoglobulin E syndrome, inflammatory bowel disease, multiple sclerosis (MS), psoriasis, rheumatoid arthritis, systemic lupus erythematosus (SLE), type 1 diabetes (T1D), or ulcerative colitis.

The disease, disorder, or condition may be or include a respiratory tract/obstructive airways disease or disorder, such as rhinorrhea, tracheal constriction, airway contraction, acute-, allergic, atrophic rhinitis or chronic rhinitis (such as rhinitis caseosa, hypertrophic rhinitis, rhinitis purulenta, rhinitis sicca), rhinitis medicamentosa, membranous rhinitis (including croupous, fibrinous and pseudomembranous rhinitis), scrofulous rhinitis, perennial allergic rhinitis, seasonal rhinitis (including rhinitis nervosa (hay fever) and vasomotor rhinitis), pollinosis, asthma (such as bronchial, atopic, allergic, intrinsic, extrinsic, exercise-induced, cold air-induced, occupational, bacterial infection-induced, and dust asthma particularly chronic or inveterate asthma (e.g. late asthma and airways hyper-responsiveness)), bronchitis (including chronic, acute, arachidic, catarrhal, croupus, phthinoid and eosinophilic bronchitis),

cardiobronchitis, pneumoconiosis, chronic inflammatory disease of the lung which result in interstitial fibrosis, such as interstitial lung disease (ILD) (e.g., idiopathic pulmonary fibrosis, or ILD associated with rheumatoid arthritis, or other autoimmune conditions), acute lung injury (ALI), adult respiratory distress syndrome (ARDS), chronic obstructive pulmonary, airways or lung disease (CORD, COAD, COLD or COPD, such as irreversible COPD), chronic sinusitis, conjunctivitis (e.g. allergic conjunctivitis), cystic fibrosis, extrinsic allergic alveolitis (like farmer's lung and related diseases), fibroid lung, hypersensitivity lung diseases, hypersensitivity pneumonitis, idiopathic interstitial pneumonia, nasal congestion, nasal polyposis, otitis media, and cough (chronic cough associated with inflammation or iatrogenic induced), pleurisy, pulmonary congestion, emphysema, bronchiectasis, sarcoidosis, lung fibrosis, including cryptogenic fibrosing alveolitis, fibrosis complicating anti-neoplastic therapy and chronic infection, including tuberculosis and aspergillosis and other fungal infections, vasculitic and thrombotic disorders of the lung vasculature, and pulmonary hypertension, acute viral infection including the common cold, and infection due to respiratory syncytial virus, influenza, coronavirus (including SARS) and adenovirus, allergic bronchopulmonary mycosis, emphysema, diffuse panbronchiolitis, systemic anaphylaxis or hypersensitivity responses, drug allergies (e.g., to penicillin, cephalosporins), insect sting allergies, and food related allergies which may have effects remote from the gut (such as migraine, rhinitis and eczema), anaphylactic shock, or vascular spasms.

The disease, disorder, or condition may be or include a bone and joint related disease or disorder, such as osteoporosis, arthritis (including rheumatic, infectious, autoimmune, chronic, malignant), seronegative spondyloarthropathies (such as ankylosing spondylitis, rheumatoid spondylitis, psoriatic arthritis, enthesopathy, Bechet's disease, Marie-Strumpell arthritis, arthritis of inflammatory bowel disease, and Reiter's disease), systemic sclerosis, osteoarthritis, osteoarthrosis, both primary and secondary to e.g. congenital hip dysplasia, cervical and lumbar spondylitis, and low back and neck pain, Still's disease, reactive arthritis and undifferentiated spondarthropathy, septic arthritis and other infection-related arthropathies and bone disorders such as tuberculosis, including Pott's disease and Poncet's syndrome, acute and chronic crystal-induced synovitis including urate gout, calcium pyrophosphate deposition disease, and calcium apatite related tendon, bursar and synovial inflammation, primary and secondary Sjogren's syndrome, systemic sclerosis and limited scleroderma, mixed connective tissue disease, and

undifferentiated connective tissue disease, inflammatory myopathies including, polymyalgia rheumatica, juvenile arthritis including idiopathic inflammatory arthritides of whatever joint distribution and associated syndromes, other joint disease (such as intervertebral disc degeneration or temporomandibular joint degeneration), rheumatic fever and its systemic complications, vasculitides including giant cell arteritis, Takayasu's arteritis, polyarteritis nodosa, microscopic polyarteritis, and vasculitides to associated with viral infection, hypersensitivity reactions, cryoglobulins, paraproteins, low back pain, Familial Mediterranean fever, Muckle-Wells syndrome, and Familial Hibenian Fever, Kikuchi disease, drug-induced arthralgias, tendonititides, polychondritis, and myopathies, osteoporosis, osteomalacia like osteoporosis, osteopenia, osteogenesis imperfects, osteopetrosis, osteofibrosis, osteonecrosis, Paget's disease of bone, hypophosphatemia, Felty's syndrome, Still's disease, slack of artificial joint implant, sprain or strain of muscle or joint, tendinitis, fasciitis, periarthritis humeroscapularis, cervico-omo-brachial syndrome, or tenosynovitis.

The disease, disorder, or condition may be or include a skin or eye related disease or disorder, such as glaucoma, ocular hypertension, cataract, retinal detachment, psoriasis (including psoriasis vulgaris, pustular psoriasis, arthritic psoriasis, erythroderma psoriaticum), palmoplantar pustulosis, xerodoma, eczematous diseases (like atopic dermatitis, ultraviolet radiation dermatitis, contact dermatitis, and seborrheic dermatitis), phytodermatitis, photodermatitis, cutaneous eosinophilias, chronic skin ulcers, cutaneous lupus erythematosus, contact hypersensitivity/allergic contact dermatitis (including sensitivity to poison ivy, sumac, or oak), and eosinophilic folliculitis (Ofuji's disease), pruritus, drug eruptions, urticaria (acute or chronic, allergic or non-allergic), acne, erythema, dermatitis herpetiformis, scleroderma, vitiligo, lichen planus, lichen sclerosus et atrophica, pyodenna gangrenosum, skin sarcoid, pemphigus, ocular pemphigus, pemphigoid, epidermolysis bullosa, angioedema, vasculitides, toxic erythemas, cutaneous eosinophilias, alopecia areata, male-pattern baldness, Sweet's syndrome, Stevens-Johnson syndrome, Weber-Christian syndrome, erythema multiforme, cellulitis, both, infective and non infective, panniculitis, cutaneous Lymphomas, non¬ melanoma skin cancer and other dysplastic lesions, blepharitis, iritis, anterior and posterior uveitis, choroiditis, autoimmune, degenerative or inflammatory disorders affecting the retina, ophthalmitis including sympathetic ophthalmitis, sarcoidosis, xerosis infections including viral, fungal, and bacterial, allergic conjunctivitis, increased fibrosis, keloids, keloplasty, post surgical scars, epidermolysis

bullosa, dry eye, ocular inflammation, allergic conjunctivitis, vernal conjunctivitis, vernal keratoconjunctivitis, and giant papillary conjunctivitis, ocular angiogenesis, cornea damage and scar, all forms of macular degeneration, macular edema, macular dystrophy, abnormal wound healing, scleritis, episcleritis, pachydermia, peripheral ulcerative keratitis, fungal keratitis, herpetic keratitis, invasive aspergillosis; conical cornea, dystorphia epithelialis comeae, or severe intraocular inflammation.

The disease, disorder, or condition may be or include a gastrointestinal tract and abdominal related disease or disorder, such as celiac/coeliac disease (e.g. celiac sprue), cholecystitis, enteritis (including infectious, ischemic, radiation, drug-induced, and eosinophilic gastroenteritis), eosinophilic esophagitis, eosinophilic gastrointestinal inflammation, allergen induced diarrhea, enteropathy associated with seronegative arthropathies, gastritis, autoimmune atrophic gastritis, ischemic bowel disease, inflammatory bowel disease (Crohn's disease and ulcerative colitis), colitis, Mooren's ulcer, irritable bowel syndrome, necrotizing enterocolitis, gut ischemia, glossitis, gingivitis, periodontitis, oesophagitis, including reflex, proctitis, fibrosis and cirrhosis of the liver, pancreatitis, both acute and chronic, pancreatic fibrosis, pancreatic sclerosis, pancreatolithiasis, hepatic cirrhosis, hepatitis (congestive, autoimmune, acute, fulminant, chronic, drug-induced, alcoholic, lupoid, steatohepatitis and chronic viral), fatty liver, primary biliary cirrhosis, hepatic porphyria, and gastrointestinal related allergic disorders, spastic colon, diverticulitis, gastroenteric bleeding, Behcet's disease; partial liver resection, acute liver necrosis (e.g. necrosis caused by toxins, viral hepatitis, shock or anoxia), or hemolytic uremic syndrome.

The disease, disorder, or condition may be or include a hematological disease or disorder, such as anemias, coagulation, myeloproliferative disorders, hemorrhagic disorders, leukopenia, eosinophilic disorders, leukemias (e.g. myelogenous, lymphomas, plasma cell dyscrasias, disorders of the spleen, Band's disease, hemophilia, purpura (including idiopathic thrombocytopenic purpura), or Wiskott-Aldrich syndrome.

The disease, disorder, or condition may be or include a metabolic disease or disorder, such as obesity, amyloidosis, disturbances of the amino and acid metabolism like branched chain disease, hyperaminoacidemia, hyperaminoaciduria, disturbances of the metabolism of urea, hyperammonemia, mucopolysaccharidoses e.g. Maroteaux-Lamy syndrome, storage disease like glycogen storage diseases and lipid storage diseases, glycogenosis I diseases like Cori's disease,

malabsorption diseases like intestinal carbohydrate malabsorption, oligosaccharidase deficiency like maltase-, lactase-, sucrase-insufficiency, disorders of the metabolism of fructose, disorders of the metabolism of galactose, galactosaemia, disturbances of carbohydrate utilization like diabetes, hypoglycemia, disturbances of pyruvate metabolism, hypolipidemia, hypolipoproteinemia, hyperlipidemia, hyperlipoproteinemia, carnitine or carnitine acyltransferase deficiency, disturbances of the porphyrin metabolism, porphyrins, disturbances of the purine metabolism, lysosomal diseases, metabolic diseases of nerves and nervous systems like gangliosidoses, sphingolipidoses, sulfatidoses, leucodystrophies, or Lesch Nyhan syndrome.

The disease, disorder, or condition may be or include a cerebellar dysfunction or disturbance of brain metabolism, such as dementia, Alzheimer's disease, Huntington's chores, Parkinson's disease, Pick's disease, toxic encephalopathy, demyelinating neuropathies like inflammatory neuropathy, Guillain-Barre syndrome; Meniere's disease and radiculopathy, primary and secondary metabolic disorders associated with hormonal defects like any disorder stemming from either an hyperfunction or hypofunction of some hormone- secreting endocrine gland and any combination thereof. Sipple's syndrome, pituitary gland dysfunction and its effects on other endocrine glands, such as the thyroid, adrenals, ovaries, and testes, acromegaly, hyper- and hypothyroidism, euthyroid goiter, euthyroid sick syndrome, thyroiditis, and thyroid cancer, over or underproduction of the adrenal steroid hormones, adrenogenital syndrome, Cushing's syndrome, Addison's disease of the adrenal cortex, Addison's pernicious anemia, primary and secondary aldosteronism, diabetes insipidus, diabetes mellitus, carcinoid syndrome, disturbances caused by the dysfunction of the parathyroid glands, pancreatic islet cell dysfunction, diabetes, disturbances of the endocrine system of the female like estrogen deficiency, resistant ovary syndrome; muscle weakness, myotonia. Duchenne's and other muscular dystrophies, dystrophia myotonica of Steinert, mitochondrial myopathies like disturbances of the catabolic metabolism in the muscle, carbohydrate and lipid storage myopathies, glycogenoses, myoglobinuria, malignant hyperthermia, polymyalgia rheumatics, dermatomyositis, multiple myositis, primary myocardial disease, cardiomyopathy; disorders of the ectoderm, neurofibromatosis, scleroderma and polyar teritis, Louis-Bar syndrome, von Hippel-Lindau disease, Sturge-Weber syndrome, tuberous sclerosis, amyloidosis, porphyria; sexual dysfunction of the male and female; confused states and seizures due to inappropriate secretion of antidiuretic hormone from the pituitary gland, Liddle's syndrome, Bartter's syndrome, Fanconi's I syndrome, or renal electrolyte wasting.

The disease, disorder, or condition may be or include a transplant rejection related condition, such as acute and chronic allograft rejection following solid organ transplant, for example, transplantation of kidney, heart, liver, lung, and cornea, chronic graft versus host disease, skin graft rejection, and bone marrow transplant rejection, or immunosuppression.

The disease, disorder, or condition may be or include a genitourinary related condition, such as nephritis (interstitial, acute interstitial (allergic), and glomerulonephritis), nephrotic syndrome, cystitis including acute and chronic (interstitial) cystitis and Hunner's ulcer, acute and chronic urethritis, prostatitis, epididymitis, oophoritis, salpingitis, vulvo vaginitis, vulvovaginal candidiasis, Peyronie's disease, and erectile dysfunction, renal disease, renal fibrosis, nephropyelitis, secondary contracted kidney, steroid dependent and steroid-resistant nephrosis, or Goodpasture's syndrome.

The disease, disorder, or condition may be or include a CNS related disease or disorder, such as neurodegenerative diseases, Alzheimer's disease and other cementing disorders including CJD and nvCJD, amyloidosis, and other demyelinating syndromes, cerebral atherosclerosis and vasculitis, temporal arteritis, myasthenia gravis, acute and chronic so pain (acute, intermittent or persistent, whether of central or peripheral origin) including post-operative, visceral pain, headache, migraine, neuralgia (including trigeminal), atypical facial pain, joint and bone pain, pain arising from cancer and tumor invasion, neuropathic pain syndromes including diabetic, post-herpetic, and HIV-associated neuropathies, neurosarcoidosis, to brain injuries, cerebrovascular diseases and their consequences, Parkinson's disease, corticobasal degeneration, motor neuron disease, dementia, including ALS (Amyotrophic-lateral sclerosis), multiple sclerosis, traumatic brain injury, stroke, post-stroke, post- traumatic brain injury, and small-vessel cerebrovascular disease, dementias, vascular dementia, dementia with Lewy bodies, frontotemporal dementia and Parkinsonism linked 1 to chromosome 17, frontotemporal dementias, including Pick's disease, progressive supranuclear palsy, corticobasal degeneration, Huntington's disease, thalamic degeneration, HIV dementia, schizophrenia with dementia, and Korsakoffs psychosis, within the meaning of the definition are also considered to be CNS disorders central and peripheral nervous system complications of malignant, infectious or autoimmune processes, algesia, cerebral infarction, attack, cerebral ischemia, head injury, spinal cord injury, myelopathic muscular atrophy, Shy-Drager syndrome, Reye's syndrome, progressive multifocal leukoencephalopathy, normal pressure hydrocephalus, sclerosing panencephalitis,

frontal lobe type dementia, acute anterior poliomyelitis (poliomyelitis), poliomyelitis neurosis, viral encephalitis, allergic encephalomyelitis, epileptic encephalopathies, Creutzfeldt-Jakob disease, Kuru disease, bovine spongiform encephalopathy (mad cow disease), scrapie, epilepsy, cerebral amyloid angiopathy, depression, mania, manic-depressive psychosis, hereditary cerebellar ataxia, peripheral neuropathy, Nasu-Hakola syndrome, or Machado-Joseph disease.

The disease, disorder, or condition may be or include an inflammatory or immunological disease or disorder, such as general inflammation (of the ocular, nasal, pulmonary, and gastrointestinal passages), mastocytosis/mast cell disorders (cutaneous, systemic, mast cell activation syndrome, and pediatric mast cell diseases), mastitis (mammary gland), vaginitis, vasculitis (e.g., necrotizing, cutaneous, and hypersensitivity vasculitis), Wegener granulamatosis, myyositis (including polymyositis, dermatomyositis), basophil related diseases including basophilic leukemia and basophilic leukocytosis, and eosinophil related diseases such as Churg-Strauss syndrome, eosinophilic granuloma, lupus erythematosus (such as, systemic lupus erythematosus, subacute cutaneous lupus erythematosus, and discoid lupus erythematosus), chronic thyroiditis, Hashimoto's thyroiditis, Grave's disease, type I diabetes, complications arising from diabetes mellitus, other immune disorders, eosinophilia fasciitis, hyper IgE syndrome, Addison's disease, antiphospholipid syndrome, immunodeficiency disease, acquired immune deficiency syndrome (AIDS), leprosy, Sezary syndrome, paraneoplastic syndromes, and other autoimmune disorders, fervescence, myositis, nervous diseases selected from multiple myositis, bursitis, Evans syndrome, leukotriene B4-mediated diseases, idiopathic hypoparathyroidism, nephrotic syndrome lupus, or immunosuppression.

The disease, disorder, or condition may be or include a cardiovascular disease or disorder, such as congestive heart failure, myocardial infarction, ischemic diseases of the heart, all kinds of atrial and ventricular arrhythmias, hypertension, cerebral trauma, occlusive vascular disease, stroke, cerebrovascular disorder, atherosclerosis, restenosis, affecting the coronary and peripheral is circulation, pericarditis, myocarditis, inflammatory and auto-immune cardiomyopathies including myocardial sarcoid, endocarditis, valvulitis, and aortitis including infective (e.g. syphilitic), hypertensive vascular diseases, peripheral vascular diseases, and atherosclerosis, vasculitides, disorders of the proximal and peripheral veins including phlebitis and thrombosis, including deep vein thrombosis and complications of varicose veins, aortic

aneurism, periarteritis nodosa, cardiac fibrosis, post-myocardial infarction, idiopathic cardiomyopathy, or angioplasty.

The disease, disorder, or condition may be or include an oncological disease or disorder, such as common cancers (prostate, breast, lung, ovarian, pancreatic, bowel and colon, abdomen, stomach (and any other digestive system cancers), liver, pancreas, peritoneum, endocrine glands (adrenal, parathyroid, pituitary, testicles, ovary, thymus, thyroid), eye, head, neck, nervous system (central and peripheral), lymphatic system, blood, pelvic, skin, bone, soft tissue, spleen, thoracic, urogenital, and brain tumors), breast cancer, genitourinary cancer, lung cancer, gastrointestinal cancer, epidermoid cancer, melanoma, ovarian cancer, pancreas cancer, neuroblastoma, malignancies affecting the bone marrow (including the leukemias) and lymphoproliferative systems, such as Hodgkin's and non-Hodgkin's lymphoma, B-cell lymphoma, follicular lymphoma, metastatic disease and tumor recurrences, and paraneoplastic syndromes, as well as hypergammaglobulinemia, lymphoproliferative diseases, disorders, and/or conditions, paraproteinemias, purpura (including idiopathic thrombocytopenic purpura), Waldenstron's Macroglobulinemia, Gaucher's Disease, histiocytosis, retinoblastoma and any other hyperproliferative disease, sarcomata, cachexia, tumor growth, tumor invasion, metastasis, AIDS-related lymphomas, malignant immunoproliferative diseases, multiple myeloma and malignant plasma cell neoplasms, lymphoid leukemia, acute or chronic myeloid leukemia, acute or chronic lymphocytic leukemia, monocytic leukemia, other leukemias of specified cell type, leukemia of unspecified cell type, other and unspecified malignant neoplasms of lymphoid, hematopoietic and related tissues, for example diffuse large cell lymphoma, T-cell lymphoma or cutaneous T-cell lymphoma). Myeloid cancer includes e.g. acute or chronic myeloid leukemia, or keratoleukoma.

The disease, disorder, or condition may be or include another disease or disorder, such as pain, migraine, sleep disorders, fever, sepsis, idiopathic thrombocytopenia purpura, post-operative adhesions, flushing, ischemic/reperfusion injury in the heart, brain, peripheral limbs, bacterial infection, viral infection, fungal infection, thrombosis, endotoxin shock, septic shock, thermal regulation including fever, Raynaud's disease, gangrene, diseases requiring anti-coagulation therapy, congestive heart failure, mucus secretion disorders, pulmonary hypotension, prostanoid- induced smooth muscle contract associated with dysmenorrhea and premature labor, premature delivery, reperfusion injury, bum, thermal injury, hemorrhage or traumatic shock,

menstrual pain, menstrual cramp, dysmenorrhea, periodontosis, rickettsial infectious disease, protozoal disease, reproduction disease, toothache, pain after tooth extraction, Herpes zoster, Herpes simplex, retroperitoneal fibrosis, or various radiation injuries.

In certain embodiments, the disease is selected from the group consisting of an inflammatory disease, an autoimmune disease, an allergic disorder, and an ocular disorder. In certain embodiments, the disease is selected from the group consisting of pruritus, eczema, asthma, rhinitis, dry eye, ocular inflammation, allergic conjunctivitis, vernal conjunctivitis, vernal keratoconjunctivitis, giant papillary conjunctivitis, fungal keratitis and uveitis.

The method may include modulating the activity of one or more kinases in a subject, such as any of the kinase described above. The method may include inhibiting a kinase. The method may include activating, e.g., stimulating or enhancing the activity of, a kinase. The method may include modulating activity of a single kinase or preferentially modulating activity of a specific kinase over others. The method may include modulating activity of multiple kinases or preferentially modulating activity of two more specific kinases over others.

The method may include providing a compound of the invention. The method may include providing multiple compounds of the invention.

The method may include contacting cells containing a kinase with one or more compounds of the invention. For example and without limitation, contacting a cell with a compound may include exposing a cell to a compound, e.g., in a formulation, such as any of those described above; delivering a compound inside a cell; providing a compound to a subject and allowing a cell in the subject to become exposed to the compound. Contacting may be performed in vivo or in vitro. In vitro contact may include exposure of cells or tissue isolated from a subject. The method may include contacting cells with a single compound of the invention. The method may include contact cells with multiple compounds of the invention.

The method may include administration of a composition to a subject. The compositions may be provided by any suitable route of administration. For example and without limitation, the compositions may be administered buccally, by injection, dermally, enterally, intraarterially, intravenously, intranasally, e.g., by inhalation, intraocularly, orally, parenterally, pulmonarily, rectally, subcutaneously, systemically, topically, e.g., to the skin or eye, transdermally, or with or on an implantable medical device (e.g., stent or drug-eluting stent or balloon equivalents).

The method may include using a composition of the invention to diagnose a disease,

disorder, or condition in a subject. For example, a radiolabeled form of a compound may be used a tracer in positron emission tomography (PET) to identify anatomical locations of aberrant kinase activity. PET is known in the art and described in, for example, Wadsak Wolfgang, Mitterhauser Markus (2010), "Basics and principles of radiopharmaceuticals for PET/CT", European Journal of Radiology, 73 (3): 461–469. doi:10.1016/j.ejrad.2009.12.022; Bailey, D.L; D.W. Townsend; P.E. Valk; M.N. Maisey (2005), Positron Emission Tomography: Basic Sciences. Secaucus, NJ: Springer-Verlag, ISBN 1-85233-798-2; and Carlson, Neil (January 22, 2012). Physiology of Behavior. Methods and Strategies of Research, 11th edition, Pearson, p. 151, ISBN 0205239390, the contents of each of which are incorporated herein by reference. The invention may include administering one or more compositions of the invention for both diagnostic and therapeutic purposes.

Examples

Example 1

The following methods were used in synthesis of compounds described herein.

Flash chromatography: Flash chromatography was performed on a Biotage Isolera(R) or Selekt® system using SNAP or SFÄR silica cartridges and ethyl acetate/cyclohexane/methanol or dichloromethane/methanol gradients as eluent.

Microwave conditions: Reactions under microwave conditions are performed in a Biotage initiator(R) microwave system.

SEMIprep reversed phase chromatography: The following instrumentation was used for SEMIprep reversed phase chromatography: 2x Varian PrepStar SD-1, 1x Dionex P580 Pump 1 Channel(MakeUP I), 1x Dionex AXP-MS (MakeUP II), 1x Dionex MSQ, 1x Dionex UVD 340V – Prep Flow Cell, Gilson 215 Liquid Handler, SunFire Prep C18 OBD 5 µm,19x50 mm column, 1x G7159B 1290 Infinity II Preparative Open-Bed Sampler/Collector, 1x G7161B 1290 Infinity II Preparative Binary Pump, 1x G7111B 1260 Infinity II Quaternary Pump (Modifier), 1x G7111B 1260 Infinity II Quaternary Pump (Analyltic / MakeUp), 1x G7165A 1260 Infinity II Multiple Wavelength Detector incl. Flow Cell (Product# G1315-60022, Serial# DE185H6157, Path Length 10.00 mm, Volume 13.00 µl), 1x G7170B 1290 Infinity II MS Flow Modulator, 1x G6125B MSD 6100 Series Single Quadrupole incl. G1948B Electrospray Interface, and 3x G1170A 1290 Infinity Valve Drive (14 Ports, 6 Positions Valve Head for Analytic Column

Selection; 14 Ports, 6 Positions Valve Head for Preparative Column Selection; 14 Ports, 2 Positions Valve Head for Analytic / Preparative Mode Selection).

Preparative columns: Waters SunFire Prep C18 5 μm OBD 30x100 mm, #186002572, Waters Atlantis T3 Prep 5µm OBD 30x100 mm, #186003702, and Waters XSelect CSH Prep C18 5 μm OBD 30x100 mm, #186005425

Analytical columns: Waters SunFire C18 2.5 μm 3.0x75mm, #186005636, Waters Atlantis T3 3µm 3.0 x75 mm, #186005653, and Waters XSelect CSH C18 2.5 μm 3.0 x 75mm, #186006106.

Typical chromatography conditions are as follows:

Column flow was 30 mL/min, Solvent A was methanol containing 0.3% acetic acid, and Solvent B was water containing 0.3% acetic acid. Typical times and relative volumes of Solvent and Solvent B are shown in Table 2.

Table 2.

Time (min)	Solv. A	Solv. B
0.0	30.00	70.00
10.0	100.00	0.00
14.0	100.00	0.00
14.4	30.00	70.00
16.4	30.00	70.00

Typical preparative method: Column flow was 60 mL/min, Solvent A was acetonitrile, and Solvent B was water. Preparation included Modifier Flow: 1.8 mL/min Modifier Flow containing 10% Acetic Acid in Acetonirile/Water 1:1 => resulting 0.3% Acetic Acid in Flow; and 0.5M NH_4Ac/NH_4OH-Buffer (pH 9.2) in Acetonitrile/Water 1:9 => resulting 15 mM Buffer Concentration in Flow

MS MakeUp: 0.9 mL/min 0.05% Acetic Acid in Acetonirile/Water 1:1.

Typical Focused Gradient Timetable for e.g. 59.7% Elution Point is shown in Table 3.

Table 3.

Time (min)	Solv. A	Solv. B
-2.37	18.6	84.4
0.00	18.6	84.4
1.15	18.6	84.4
1.16	43.5	56.5
8.46	63.5	36.5
8.47	100	0
10.77	100	0
10.78	18.6	84.4

Typical Analytical Modifier: Column flow was 1 mL/min, Solvent A was acetonitrile, Solvent B was water, and Solvent C was 5% acetic Acid in acetonitrile/water 1:1. Typical times and relative volumes of Solvent, Solvent B, Solvent C are shown in Table 4.

Table 4.

Time (min)	Solv. A	Solv. B	Solv. C
0	2	96	2
0.5	2	96	2
5.5	96	2	2
5.6	98	0	2
6.9	98	0	2
7.0	2	2	2

A Mass Spectrometer Detector (API-ES, positive) at UV 220 nm, 254 nm, or 310 nm was used for detection.

Example 2

Terms and abbreviations used in the Examples are provided in Table 5.

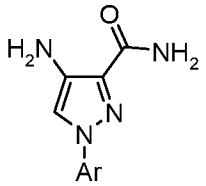
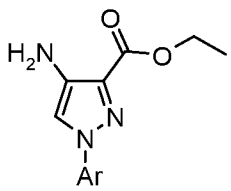
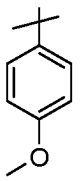
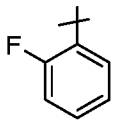
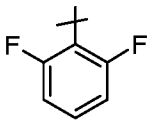
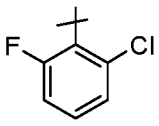
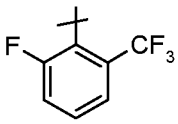
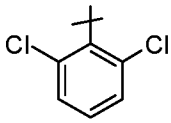
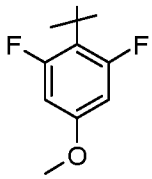
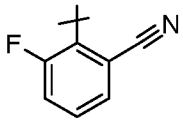
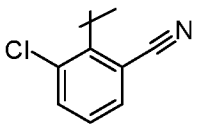
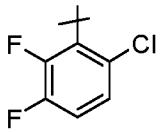
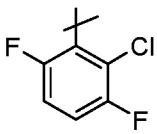
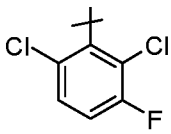
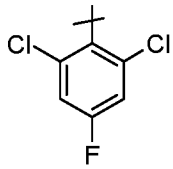
Table 5.

Pd dppf - [1,1′-Bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane CAS 95464-05-4
DCM - dichloromethane
THF- tetrahydofuran
MeOH- methanol
celite - Diatomaceous earth, celite (R) CAS 61790-53-2
diborolane – 4,4,5,5,4',4',5',5'-Octamethyl-[2,2']bi[[1,3,2]dioxaborolanyl] CAS 73183-34-3
pinacolborane – 4,4,5,5-Tetramethyl-[1,3,2]dioxaborolane CAS 25015-63-8
o.n. - over night
r.t. - room temperature
eq. - equivalent
dioxane – 1,4-dioxane
brine – saturated aqueous solution of NaCl
h – hour
TFA – trifluoroacetic acid
Boc - *tert*-Butyloxycarbonyl
catacxium- cataCXium® A, Di(1-adamantyl)-*n*-butylphosphine, CAS 321921-71-5
LiHMDS - Lithium bis(trimethylsilyl)amide CAS 4039-32-1
$Pd(PPh_3)_4$ - Palladium-tetrakis(triphenylphosphine) CAS 14221-01-3
PYBOP - (Benzotriazol-1-yloxy)tripyrrolidinophosphonium hexafluorophosphate CAS 128625-52-5
DIPEA – *N,N*-Diisopropylethylamine CAS 7087-68-5
DMF - *N,N*-Dimethylformamide CAS 68-12-2
DBAD - Di-*tert*-butyl azodicarboxylate CAS 870-50-8
PPh_3 – Triphenylphosphine CAS 603-35-0
HOBT - 1-Hydroxybenzotriazole hydrate CAS 123333-53-9
HATU - 1-[Bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxide hexafluorophosphate CAS 148893-10-1
EDCI - *N*-(3-Dimethylaminopropyl)-N′-ethylcarbodiimide hydrochloride CAS 25952-53-8

T3P - T3P® 2,4,6-Tripropyl-1,3,5,2,4,6-trioxatriphosphorinane-2,4,6-trioxide CAS 68957-94-8
NaO*t*Bu Sodium *tert*-butoxide CAS 865-48-5
X-Phos Pd G2 - CAS 1310584-14-5
XPhos - CAS 564483-18-7
tBuBrettPhos Pd G3 - CAS 1536473-72-9

Example 3

Certain compounds that were used as reagents in synthesis schemes described herein were prepared by the following schemes.

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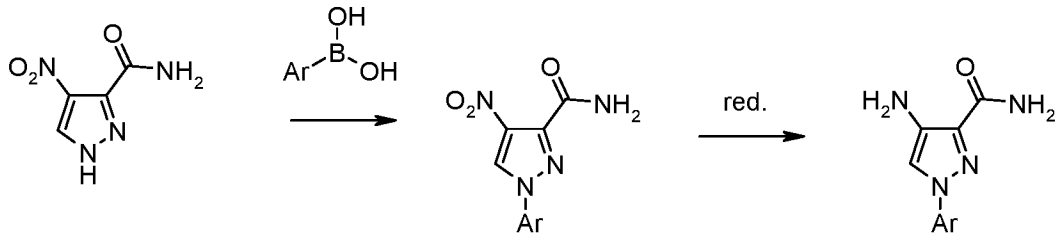
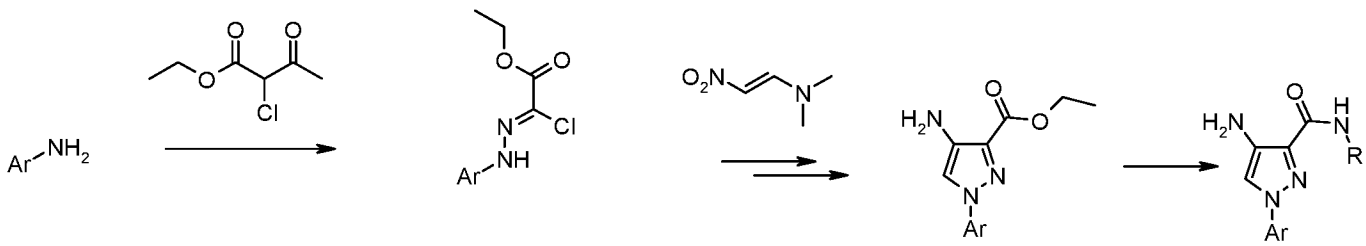


Route 2:



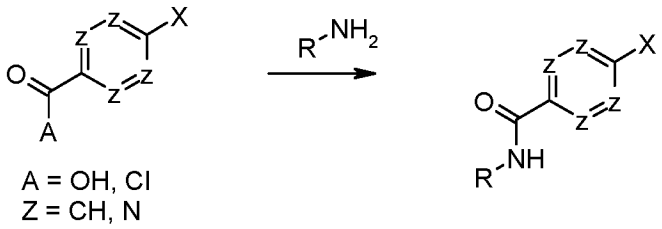
R =H, Me

Routes 1 and 2 are known in the art and described in, for example, International Patent Publication Nos. WO2006/115845, WO2007/2248, WO2007/55941, WO2007/55942, WO2007/87129, WO2011/154327, WO2017/7756, and WO2018/64135; U.S. Patent Publication Nos. US2007/117824, US2011/306589, and US2019/192668; European Patent Publication No. EP1566384; *Bioorganic and Medicinal Chemistry Letters*, vol. 24, 12 (2016), p. 2794–2808; *Med.Chem .Commun.*, vol. 4, nb. 2 (2013), p. 456–462; *Journal of Medicinal Chemistry*, vol. 52, nb. 23 (2009), p. 7640–7652; *Zeitschrift fur Naturforschung, B, Chemical Sciences*, vol. 59, nb. 10 (2004), p. 1132–1136; *Tetrahedron*; vol. 53, nb. 25 (1997), p. 8585–8598; Indian Journal of Chemistry - Section B *Organic and Medicinal Chemistry*, vol. 28, nb. 1 (1989), p. 56–60; and *Gazzetta Chimica Italiana*, vol. 98 (1968), p. 949, the contents of each of which are incorporated herein by reference.

Example 4

Intermediates: Anilines.

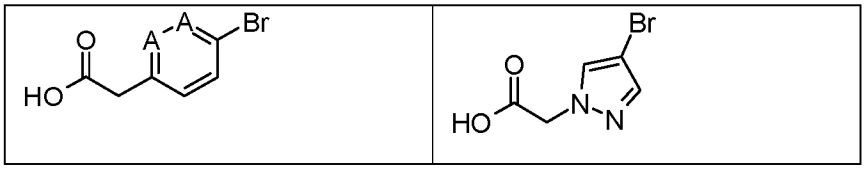
Peptide coupling:



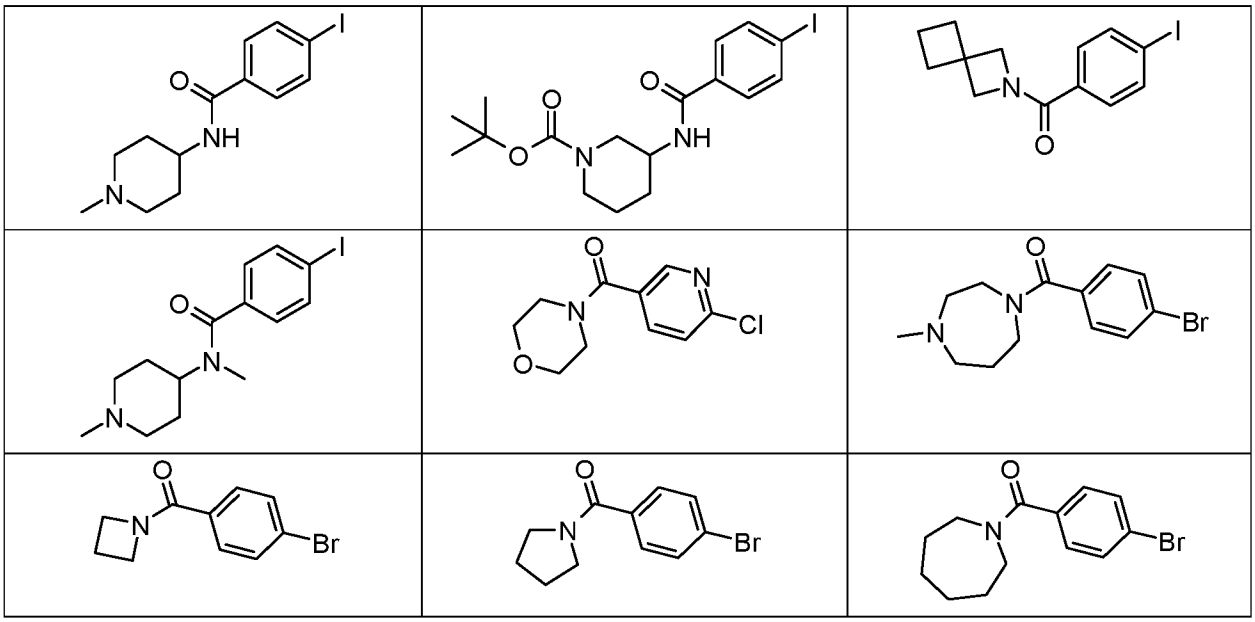
Starting from acid chloride: The amine was dissolved in DCM, cooled to 0°C, triethylamine (2eq). and the corresponding acid chloride were added. The mixture was stirred at r.t. for 2h. The reaction was diluted with $NaHCO_3$ aq., extracted with DCM, dried (Na_2SO_4), filtered and concentrated under reduced pressure.

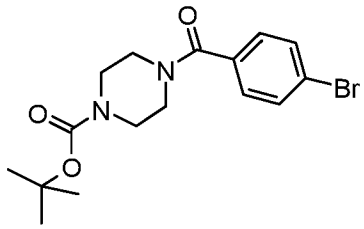
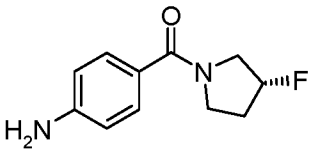
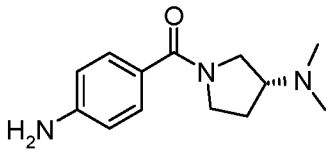
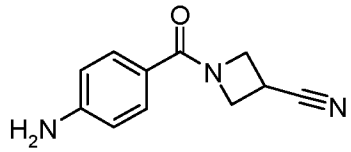
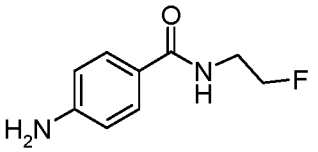
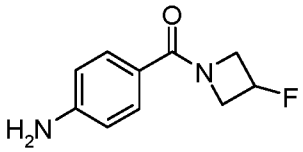
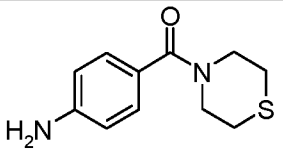
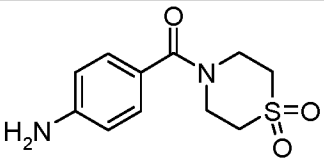
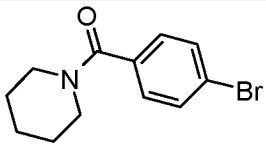
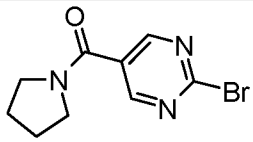
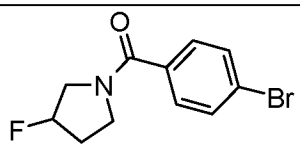
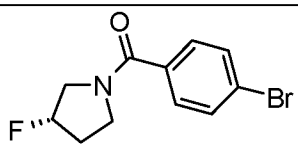
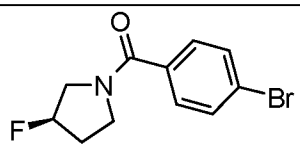
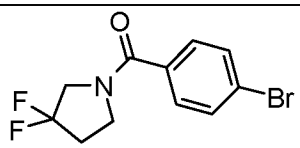
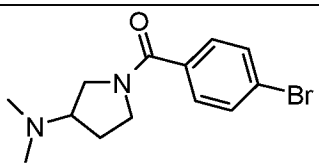
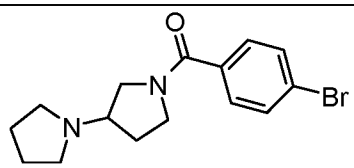
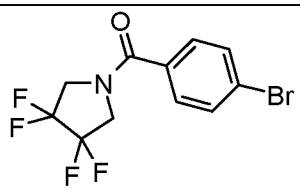
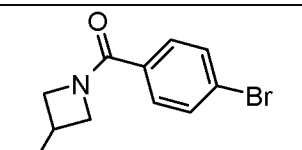
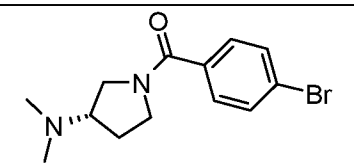
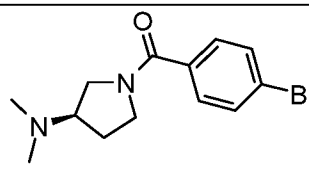
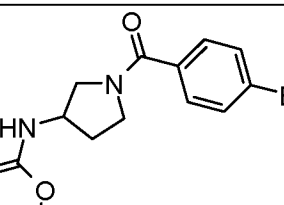
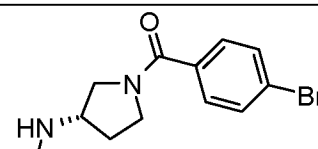
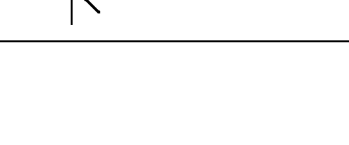
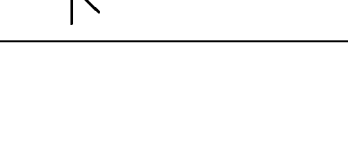
Alternatively, standard peptide coupling protocols, e.g., using HOBT, EDCI, DIPEA or HATU, DIPEA were used.

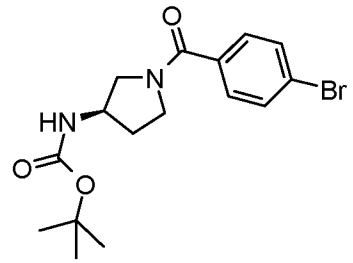
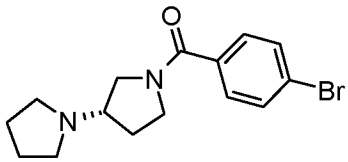
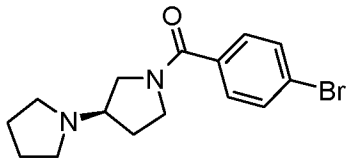
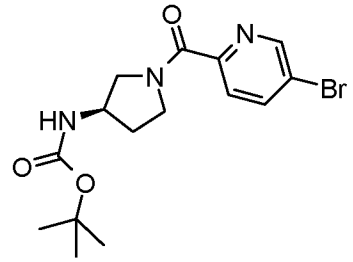
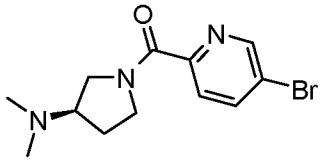
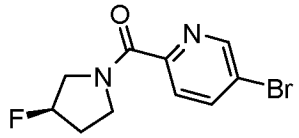
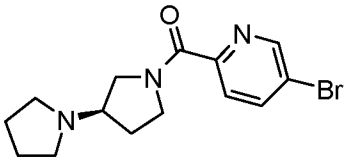
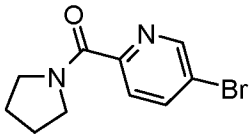
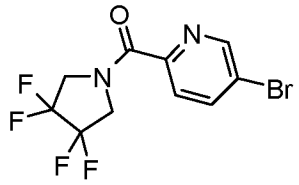
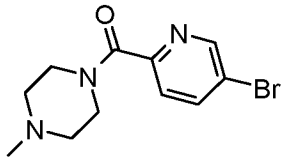
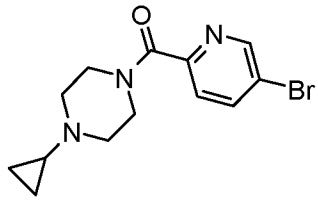
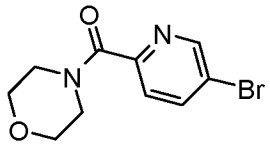
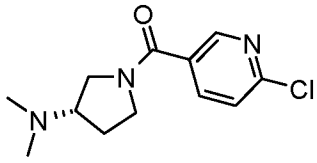
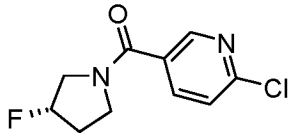
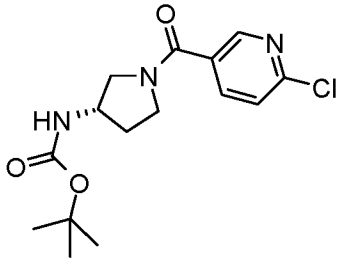
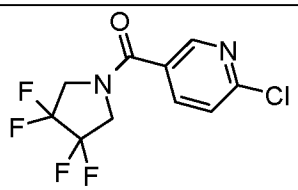
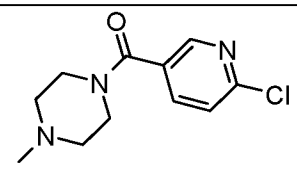
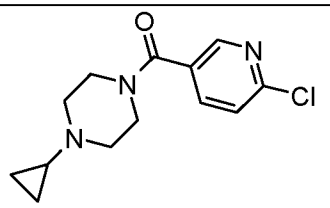
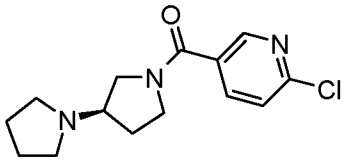
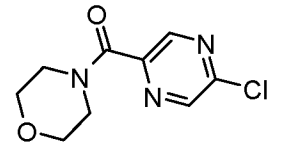
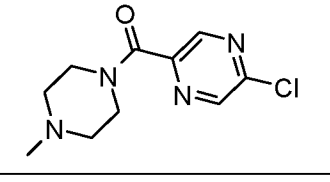
Alternatively the following acids are used for the corresponding intermediates:

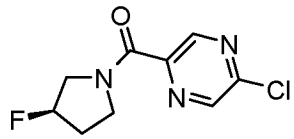
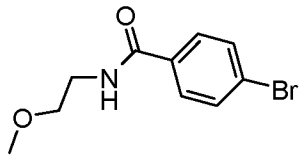
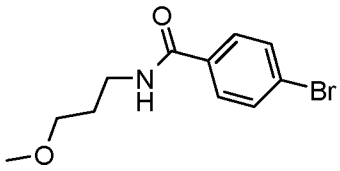
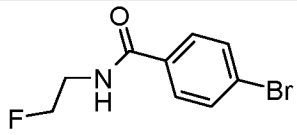
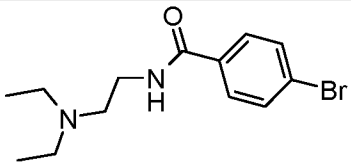
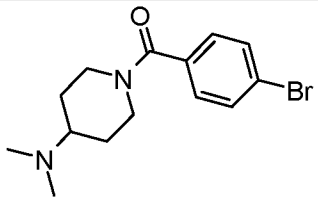
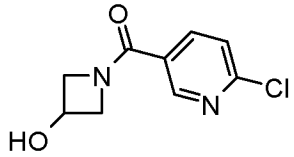
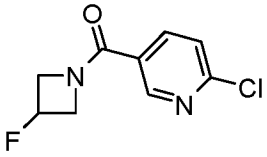
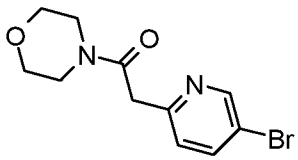
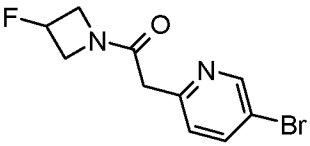
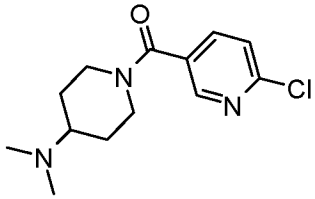
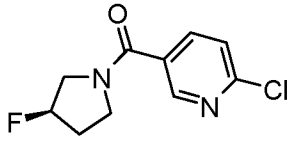
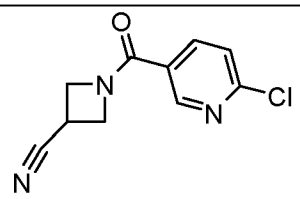
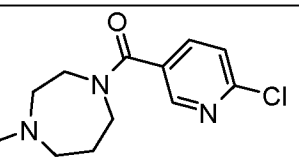
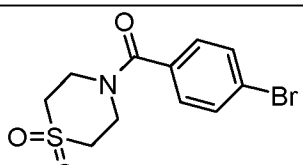
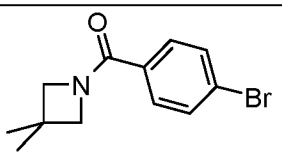
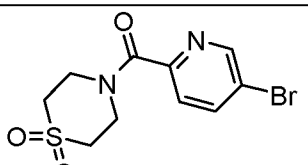
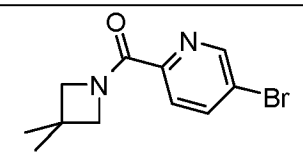
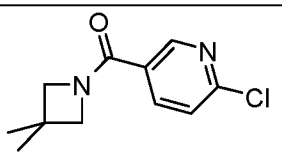


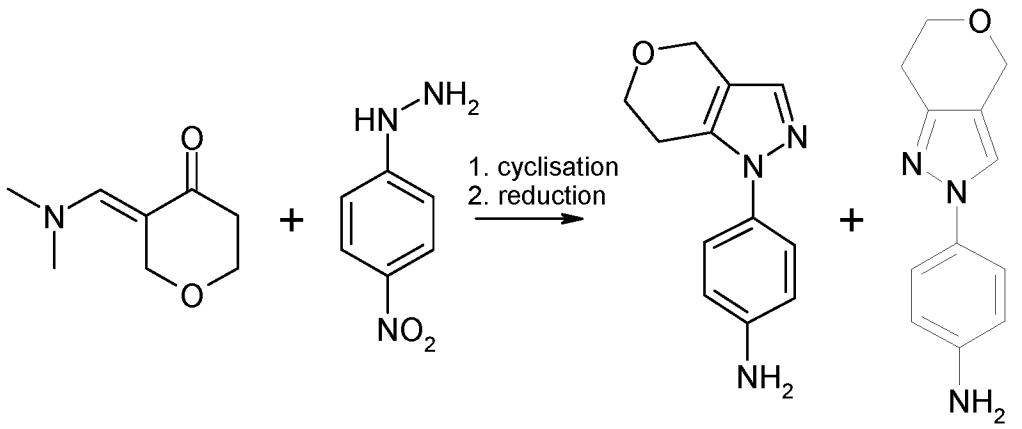
The following intermediates were synthesized using this method:





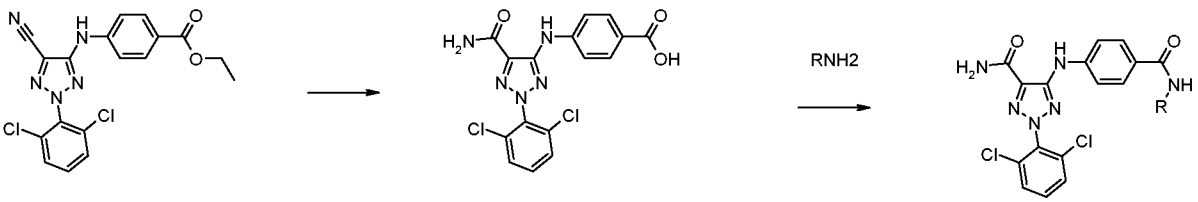
These anilines were synthesized as described in International Patent Pub. No. WO 2017/139778, the contents of which are incorporated herein by reference. The two intermediates were used as mixture and separated at the stage of the examples.

The aniline were obtained commercially or were synthesized as described above.

This method was used to synthesize Compound Nos. 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 119, 123, 124, 128, 129, 145, 146, 147, 148, 162, 164, 167, 175, 176, and 177.

Compound No. 120, 2-(2,6-dichlorophenyl)-5-((4-(piperidin-4-yloxy)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide, was synthesized using method A with the corresponding Boc protected reagent, followed by HCl treatment and reversed phase HPLC purification.

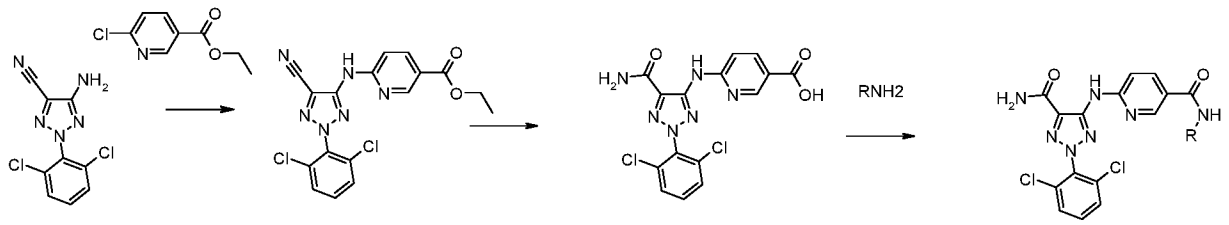
The following intermediate was synthesized using Route A to step 2A.



This intermediate was treated with NaOH 1M in water/THF 1/1 at 35°C over three days. The mixture was concentrated to remove organic solvent, adjusted to pH 3-4 (HCl 1M) and extracted with EtOAc. The organic layer was dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude product was used without further purification.

The amination was performed using the conditions of aniline amide synthesis above.

This method was used to synthesize Compound Nos. 122, 163, and 166.

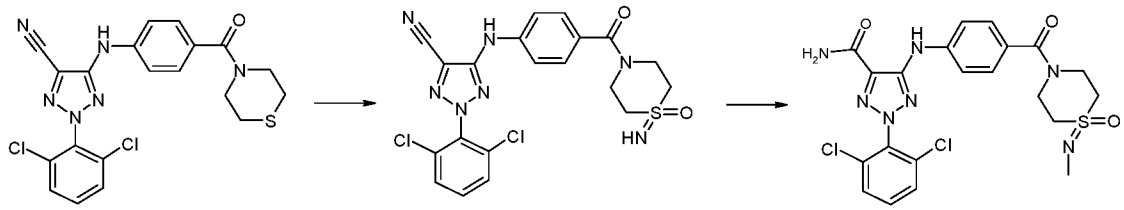


In the scheme shown above, the acid intermediate was synthesized using Route A to step 2A. This was dissolved in DMF, chloronicotinate (1eq.) and $CsCO_3$ (5eq.) was added. The mixture was heated at 60°C o.n. The mixture was diluted with water and extracted with EtOAc. The organic layer was dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude product was purified with gradient flash chromatography.

This intermediate was treated with NaOH 1M in water/THF 1/1 at 35°C o.n. The mixture was concentrated to remove organic solvent, adjusted to pH 3-4 (HCl 1M) and extracted with EtOAc. The organic layer was dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude product was used without further purification.

The amination was performed using the conditions of aniline amide synthesis above.

This method was used to synthesize Compound Nos. 133, 149, 150, 153, 154, and 165.



In the scheme shown above, the thiomorpholine intermediate was synthesized following Route A to step 2A. This intermediate was dissolved in MeOH, ammonium acetate (2 eq.) and iodobenzene diacetate (3eq.) were added. The mixture was stirred for 2.5 h at r.t., then concentrated, diluted with water and extracted with DCM. The organic layer was dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude product was purified by gradient flash chromatography.

The product from the step before was dissolved in MeOH. Formaldehyde (10 eq., 37% in water) was added, the pH was adjusted with NaOH 1M and HOAc against bromocresole green, followed by sodium cyanoborohydride (2.5eq.). The mixture was stirred for 2h, the adjustment and the addition of cyano borohydride was repeated. The mixture was cooled to 0°C, water and $NaHCO_3$ aq. sat was added an the mixture extracted with DCM. The organic layer was dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude product was used without further purification.

The hydrolysis to the amide was following step 3A.

Compound No. 172, 2-(2,6-dichlorophenyl)-5-((1-(methylsulfonyl)-1H-pyrazol-4-yl)amino)-2H-1,2,3-triazole-4-carboxamide, was synthesized using this procedure.

Route B was used to synthesize Compound Nos. 121, 125, 126, 131, and 132.

The halogenids were obtained commercially or synthesized as described above:

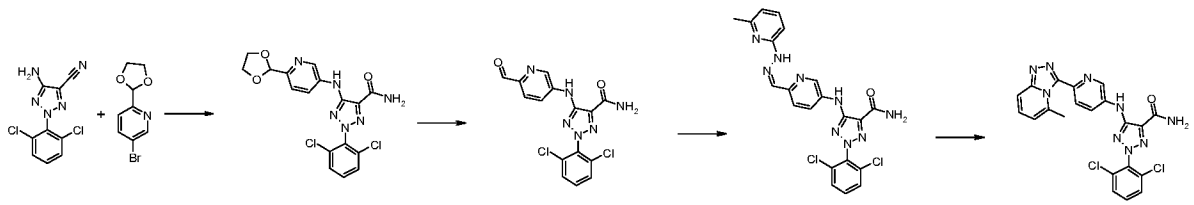
Route C, using the condition A2.2 from pyrazole section, was used to synthesize Compound Nos. 127, 130, 136, 137, and 140.

The halogenids were obtained commercially or synthesized as described above.

Route C, using the condition A2.3 from pyrazole section, was used to synthesize Compound Nos. 112, 113, 114, 115, 141, 142, 143, 144, 152, 155, 156, 157, 158, 159, 160, 168, 172, and 173.

The halogenids were obtained commercially or synthesized as described above.

Route D was used to synthesize Compound Nos. 151, 169, and 170.



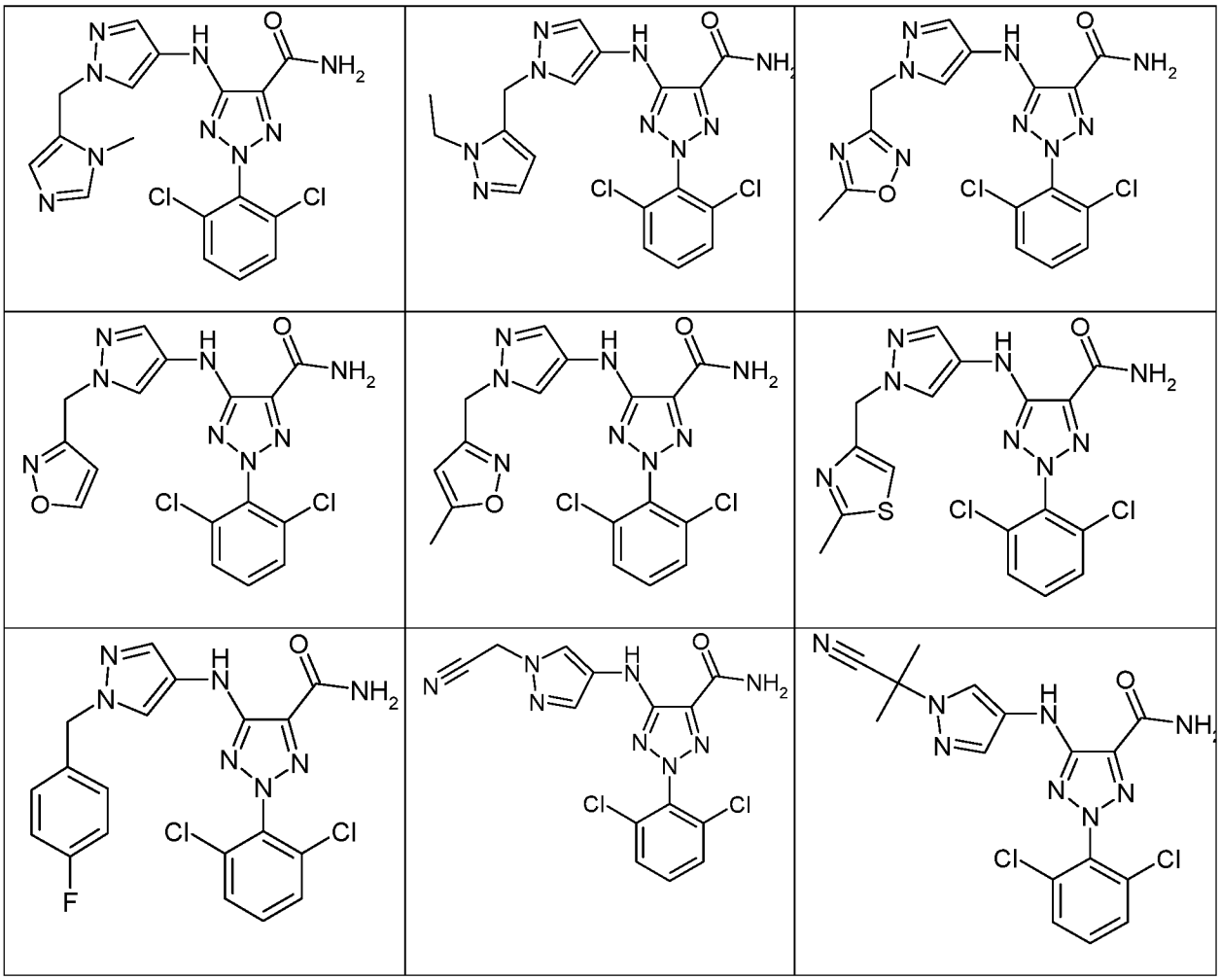
In the scheme shown above, the intermediate form step 2C was reacted under the conditions of A2.3 (pyrazole section), followed by treatment with 2m HCl aq. in THF for 2. The mixture was concentrated, diluted with water and extracted with EtOAc. The organic layer was dried (Na_2SO_4), filtered and concentrated under reduced pressure.

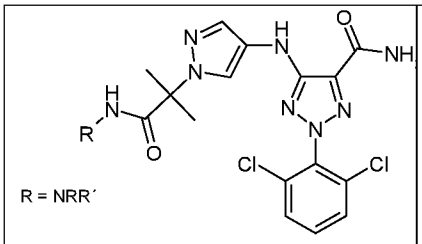
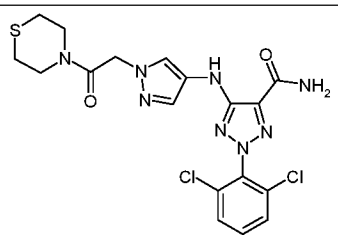
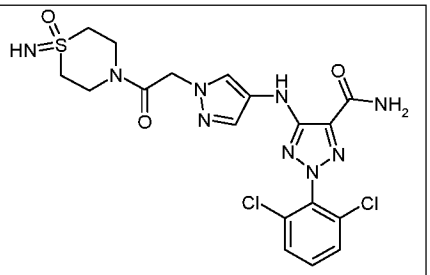
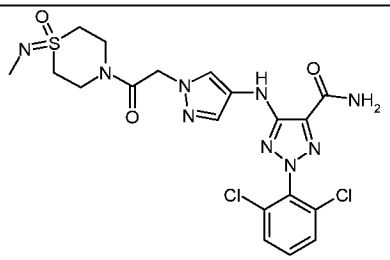
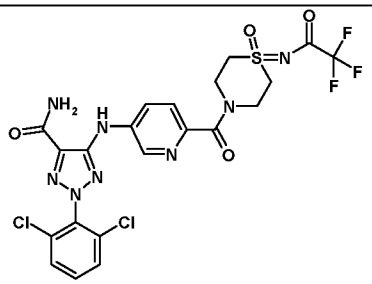
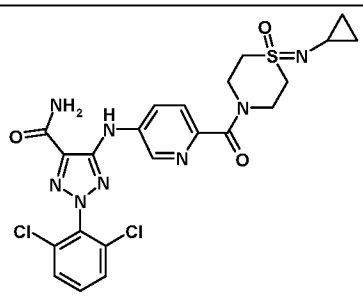
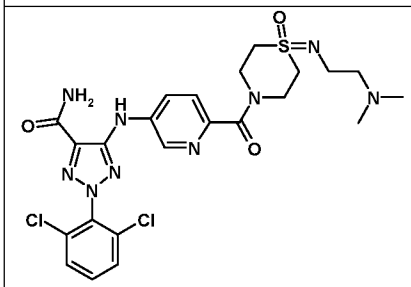
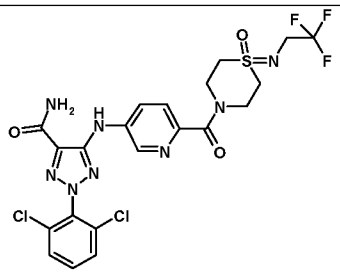
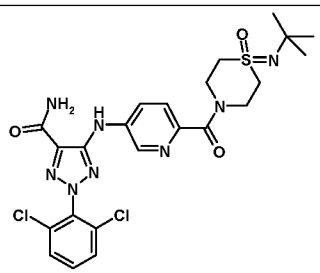
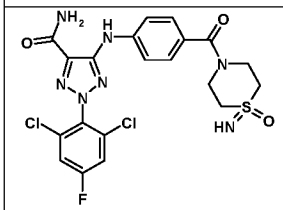
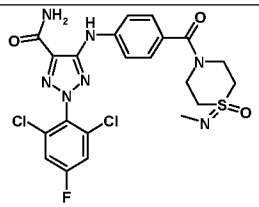
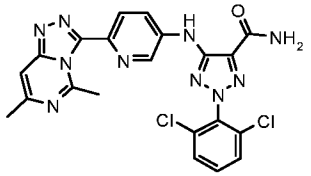
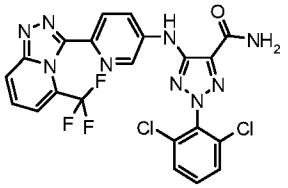
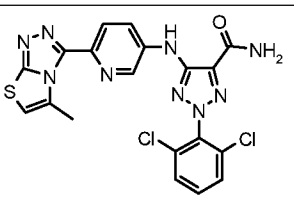
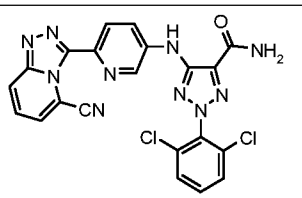
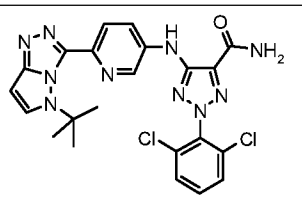
The aldehyde building block was dissolved in EtOH. The hydrazine derivative was added and the mixture refluxed for 1h. The mixture was concentrated under reduced pressure. The crude product was used without further purification.

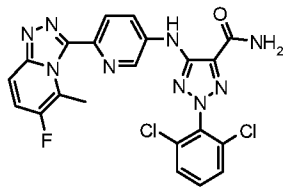
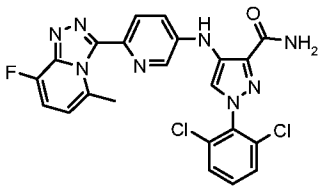
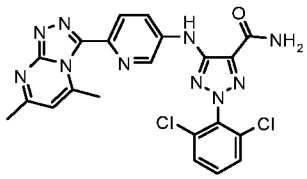
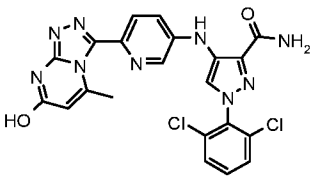
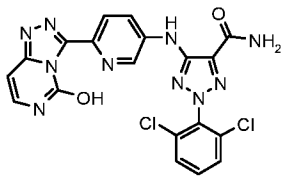
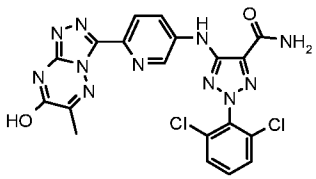
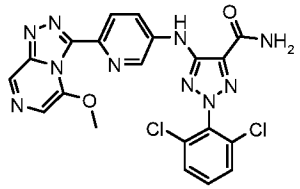
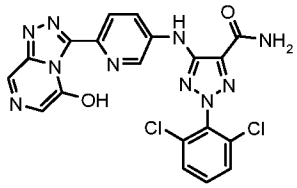
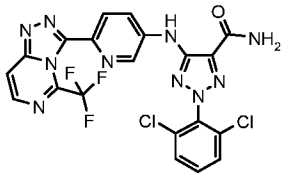
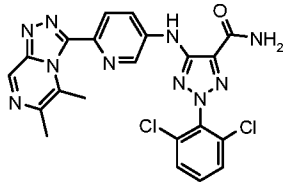
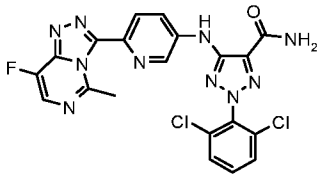
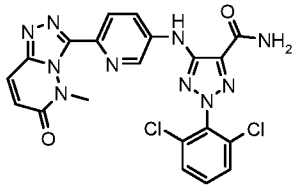
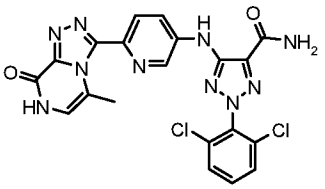
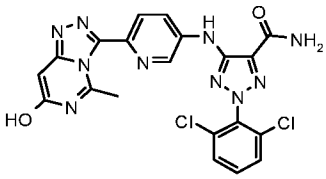
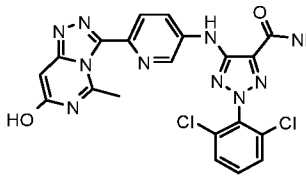
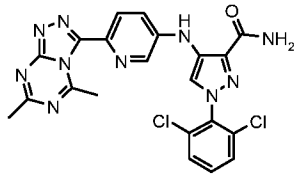
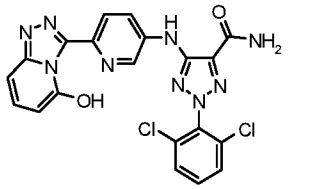
This intermediate was dissolved in DCM. Iodobenzene diacetate (10 eq.) was added and the mixture was stirred for 3h at r.t. The mixture was filtered through celite, concentrated and purified by reversed phase HPLC.

This method, with appropriate hydrazine derivatives, was used to synthesize Compound Nos. 139 and 161.

Other compounds that may be made using the schemes described above are shown below.

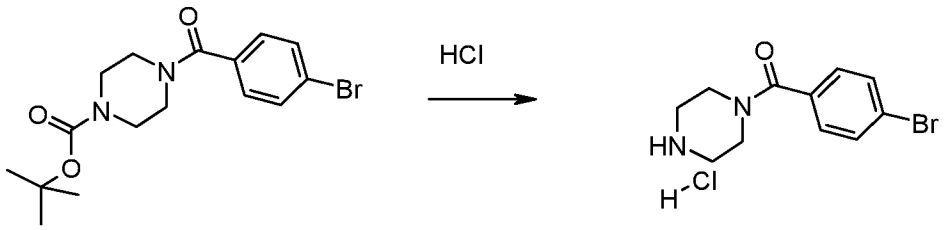


 R = NRR´		
		
		
		
		
		

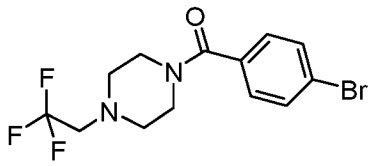
		
		
		
		
		
		

Example 5

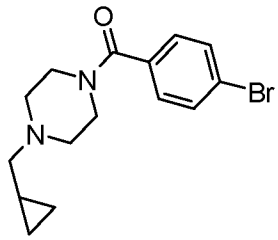
Piperazine modifications:



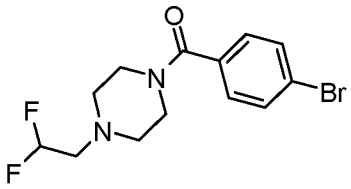
The Boc protected piperazine was dissolved in dry MeOH followed by the addition of 4M HCl in dioxane (40% v/v). The mixture was stirred o.n. The product was collected by filtration and used without further purification.



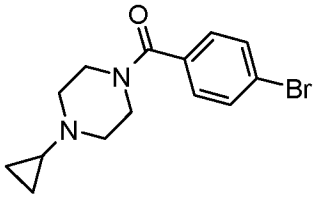
The HCl salt from above was suspended in THF (dry), followed by the addition of 2,2,2-trifluoroethyl trifluoromethanesulfonate (3eq.) and DIPEA (4eq.). The mixture was stirred at 65°C o.n. The mixture was diluted with ethyl acetate and washed with $NaHCO_3$ aq. The organic layer was dried (Na_2SO_4) filtered and concentrated under reduced pressure. The crude product was purified by gradient flash chromatography.



The HCl salt from above and cyclopropyl aldehyde (1.2eq.) were dissolved in DCE DCE or DCM? If DCE need to define in the table of abbreviations *vide supra*. After 10min sodium triacetoxyborohydride (1.5.eq.) was added. The mixture was stirred at r.t. o.n. The mixture was diluted with ethyl acetate and washed with $NaHCO_3$ aq. The organic layer was dried (Na_2SO_4) filtered and concentrated under reduced pressure. The crude product was purified by gradient flash chromatography.

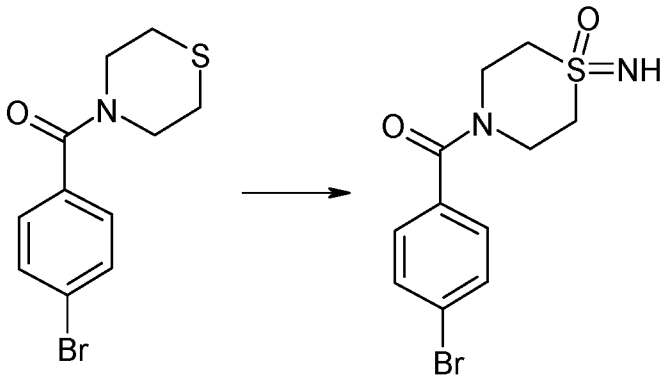


The HCl salt from above was suspended in THF (dry), followed by the addition of 2,2-difluoroethyl trifluoromethanesulfonate (3eq.) and DIPEA (4eq.). The mixture was stirred at 65°C o.n. The mixture was diluted with ethyl acetate and washed with $NaHCO_3$ aq. The organic layer was dried (Na_2SO_4) filtered and concentrated under reduced pressure. The crude product was purified by gradient flash chromatography.

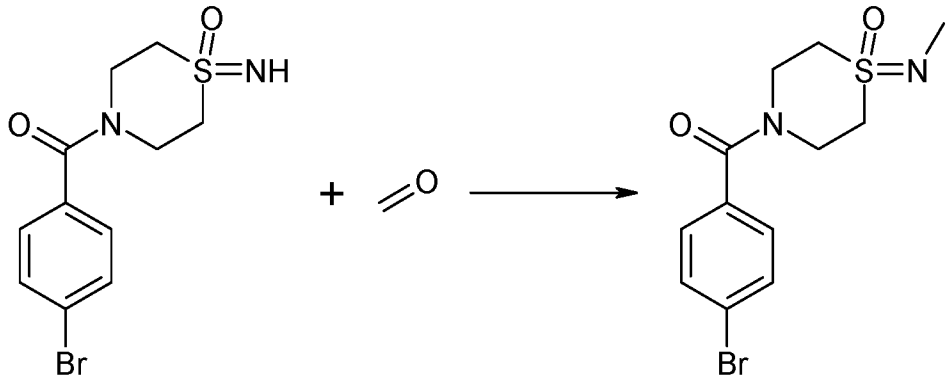


The HCl salt from above and (1-Ethoxycyclopropoxy)trimethylsilane (10eq.) were dissolved in MeOH. Acetic acid (16eq.) was added dropwise, followed by sodium cyanoborohydride (12.eq.).). The mixture was stirred at r.t. o.n. The mixture was diluted with ethyl acetate and washed with $NaHCO_3$ aq. The organic layer was dried (Na_2SO_4) filtered and concentrated under reduced pressure. The crude product was purified by gradient flash chromatography.

Special modifications



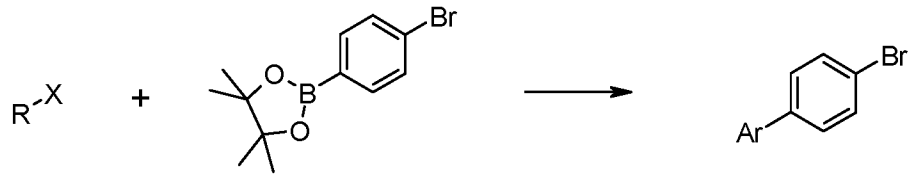
The thiomorpholine amide was dissolved in MeOH, followed by the addition of ammonium acetate (2eq.) and iodobenzene diacetate (2.5 eq.). The mixture was stirred for 30 min at r.t. The mixture was concentrated, diluted with water and extracted with DCM. The organic layer was dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude product was purified by gradient flash chromatography.



The imino-oxidothiomorpholino derivative was dissolved in MeOH, formaldehyde (10 eq., 37% in water) and sodium cyano borohydride (2.5 eq.) was added. The mixture was basified with NaOH 1M until the color change of bromcresol green. After 20 min additional $NaBH_3CN$(2.5 eq.). The pH was adjusted with HOAc. This was repeated three times. The mixture was basified with NaOH 1M and $NaHCO_3$ aq. sat. The mixture was extracted with DCM, the organic layer dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude product was purified by gradient flash chromatography.

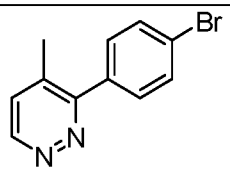
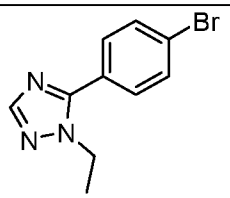
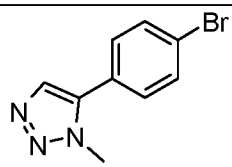
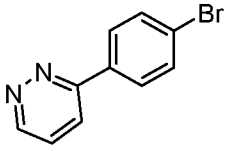
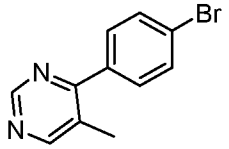
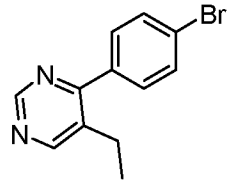
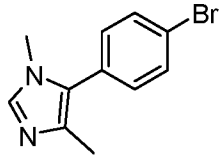
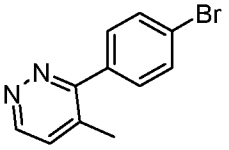
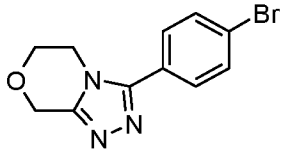
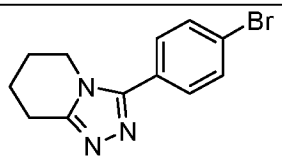
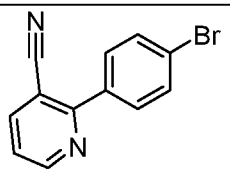
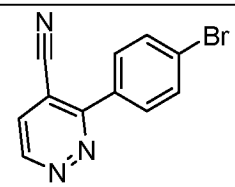
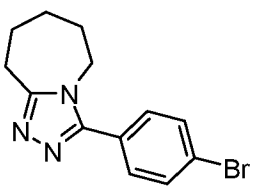
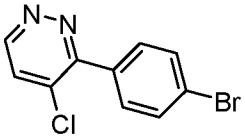
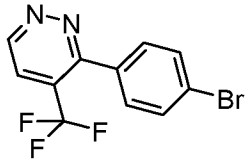
Example 6

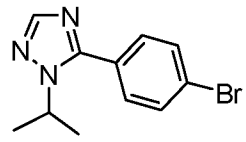
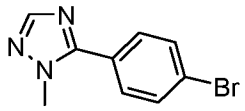
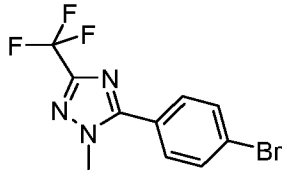
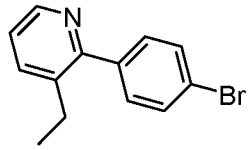
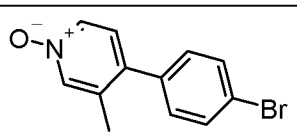
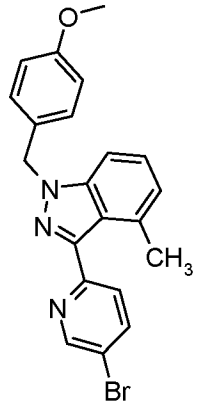
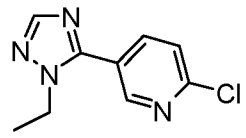
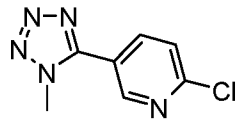
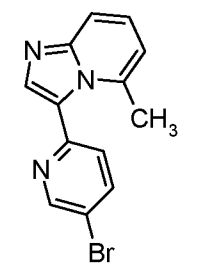
Suzuki type coupling:



General procedure: Bromophenyl boronic ester, haloarene (2eq.), K_2CO_3 (3eq.) were dissolved in dioxane water (5/1). The mixture is degassed with N_2, then $Pd(PPh_3)_4$ (0,1eq.) was added. The mixture was heated at 100°C o.n. The solvent was evaporated under reduced pressure. The crude product was purified by gradient flash chromatography.

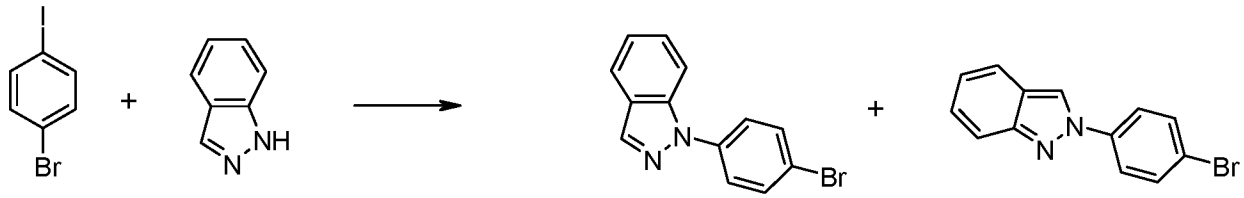
The following intermediates were synthesized using this method:

Example 7

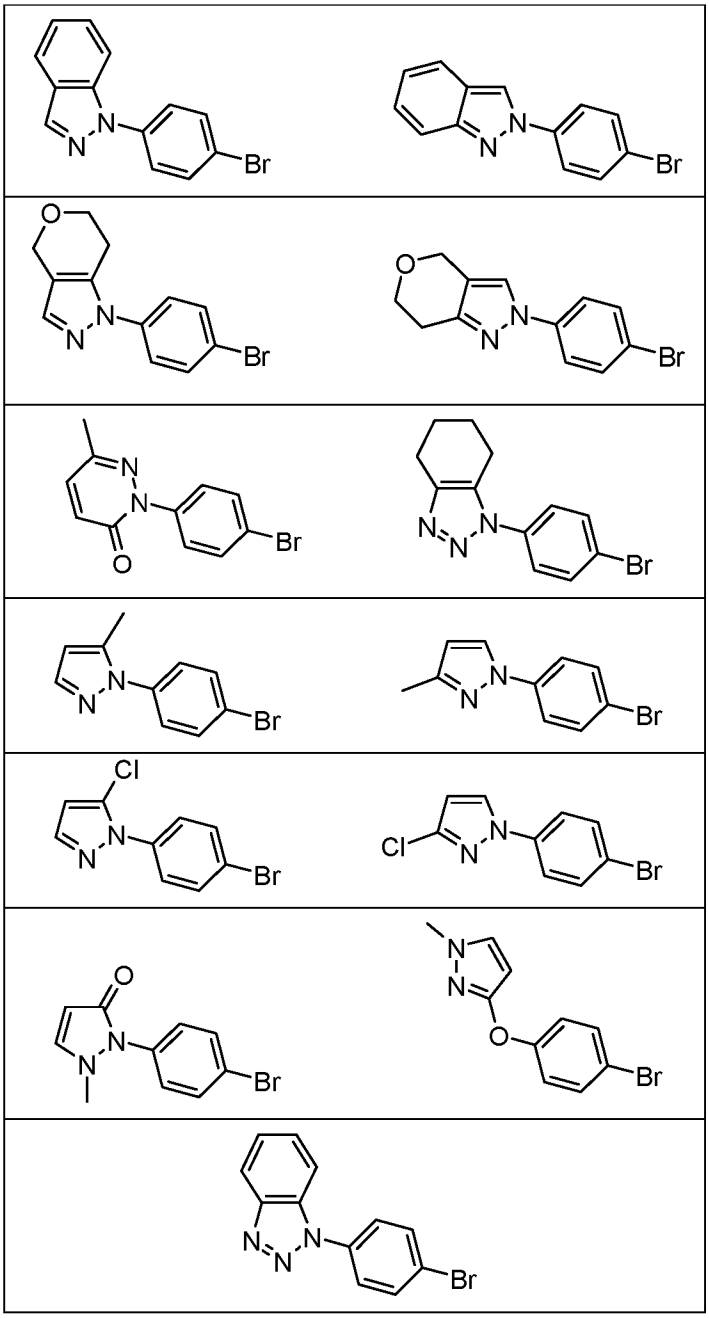
Ullmann type coupling

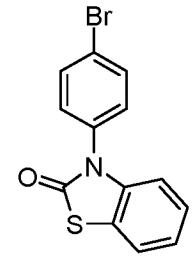
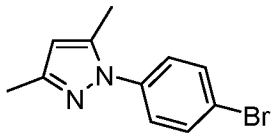
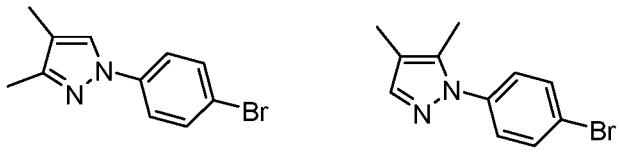
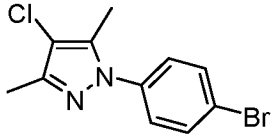
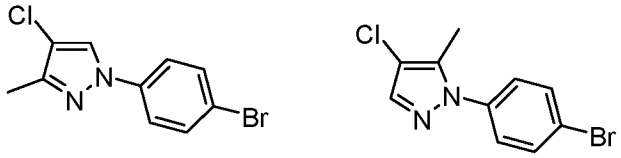
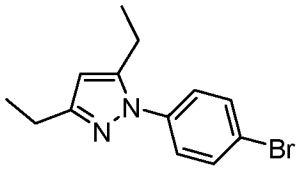
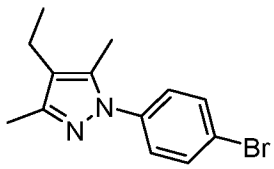
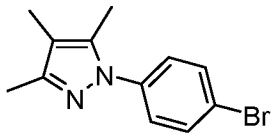
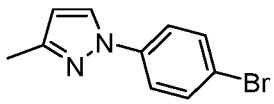


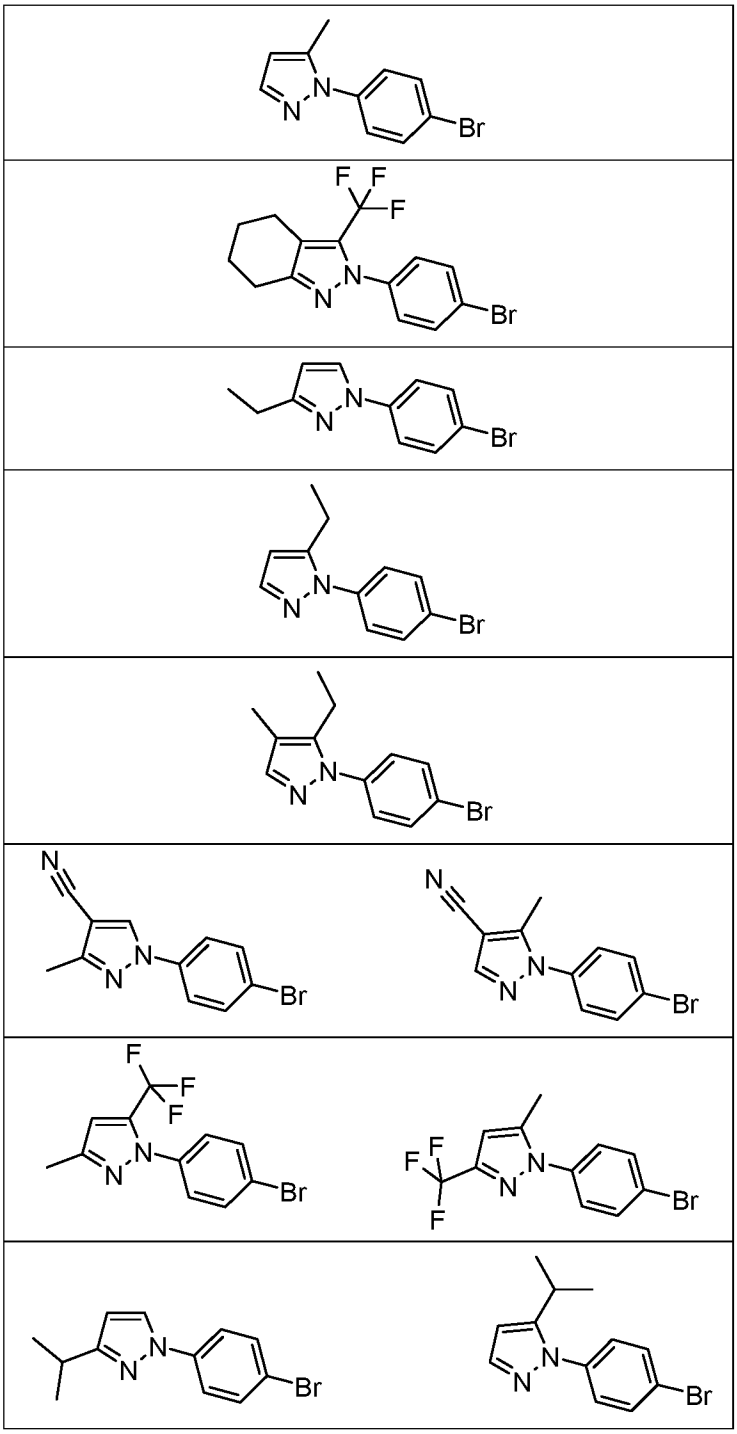
General procedure: Bromoiodobenzene, pyrazolo compound (1eq.); K_2CO_3 (2.1 eq.) dimethyl glycine and CuI were dissolved in DMSO. During the degassing the reaction turned blue. The reaction was stirred at 100°C for 1h. The mixture was diluted with ethyl acetate and water. The aq. layer was extracted with ethyl acetate several times. The combined organic layers were washed with NH_4Cl aq, and brine. The organic layer was dried (Na_2SO_4), filtered and

concentrated under reduced pressure. The resulting product was used without further purification as a mixture of isomers.

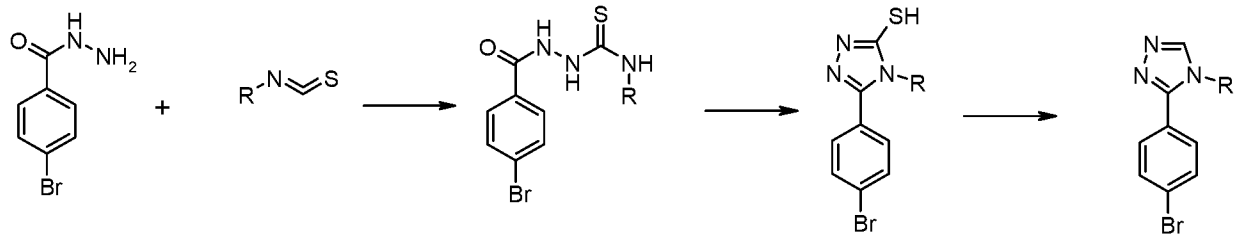
The following intermediates were synthesized using this procedure:



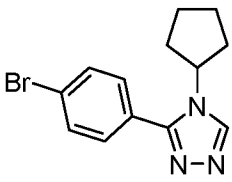
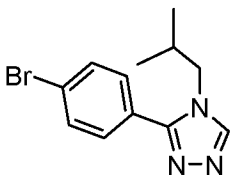
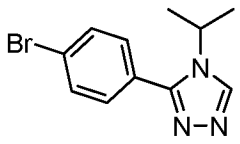
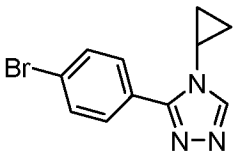
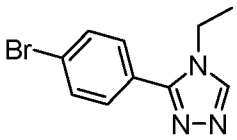
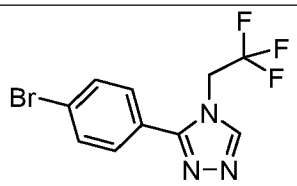
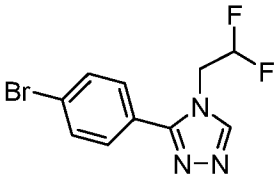
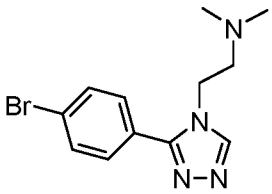












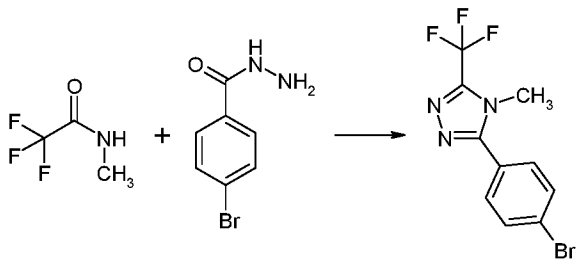
3-Aryl,4-Alky 1,2,4 triazole formation.



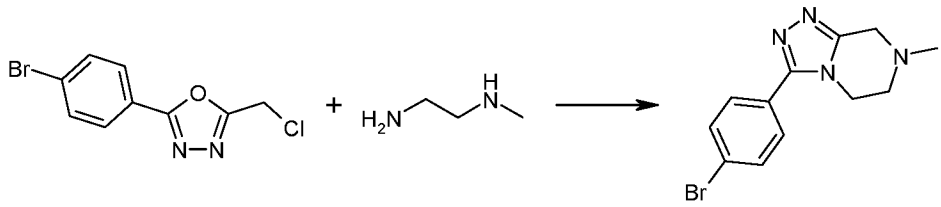
The following intermediates were synthesized in procedures known in the art and described in, for example, Journal of Medicinal Chemistry, 2018, vol. 61, no. 18, p. 8226 – 8240, the contents of which are incorporated herein by reference.

Special examples:

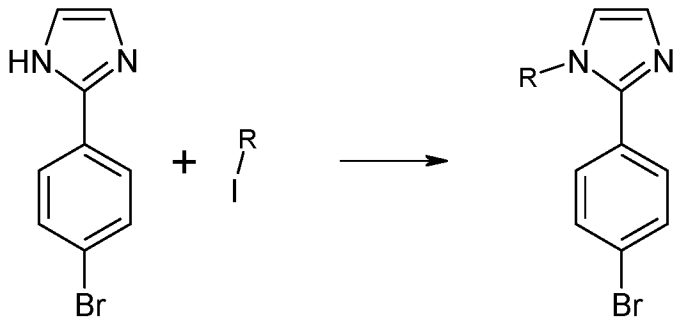


The intermediate shown above was synthesized as described in Org. Lett. 2015, 17, 1184-1187, the contents of which are incorporated herein by reference.

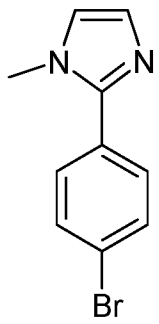
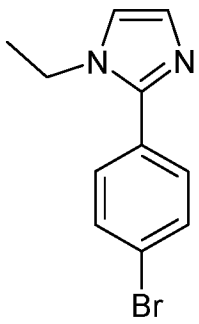
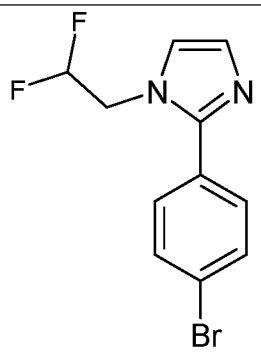


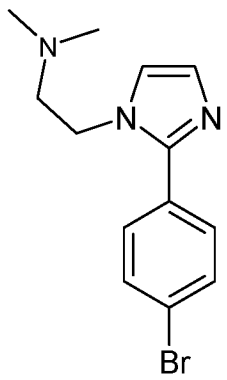
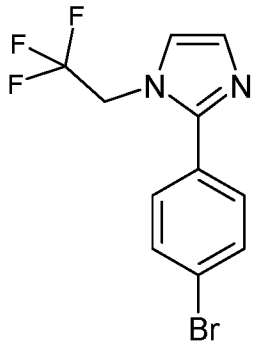
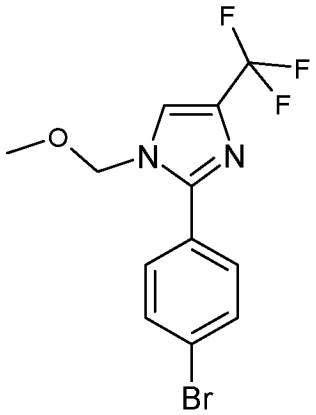
The intermediate shown above was synthesized as described in Org. Lett. 2005, 7, 6, 1039-1042, the contents of which are incorporated herein by reference.

1-Alky-2-arylimidazole

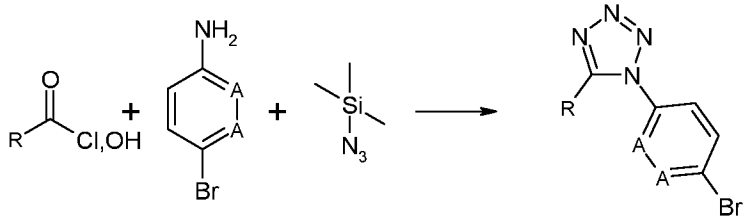


The following compounds were synthesized as described in Org. Lett. 2017, 19, 6, 1450-1453, the contents of which are incorporated herein by reference.

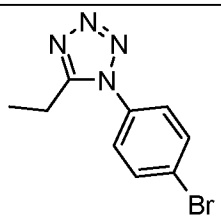
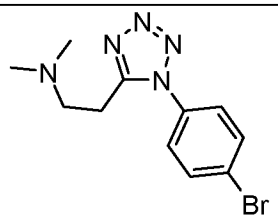
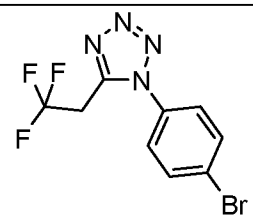
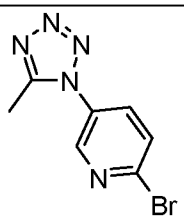
		

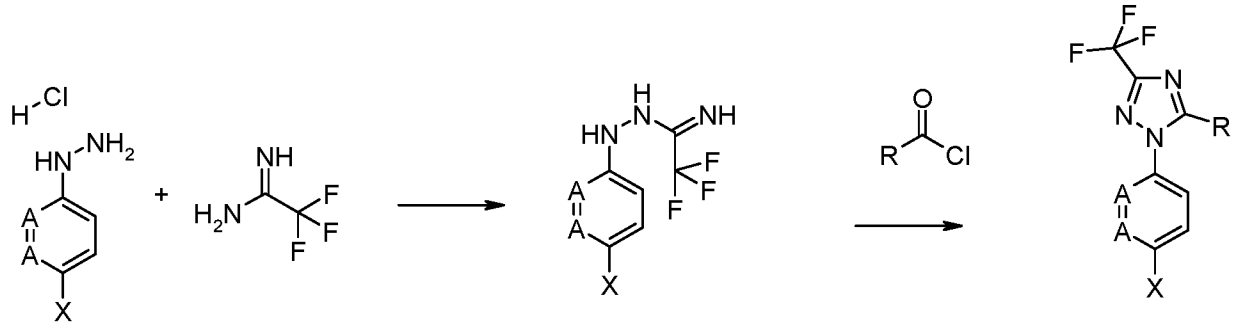
1-Aryl,5-Alkyl tetrazoles



The following compounds were synthesized as described in EUR JOC 2016, 2383-2387, the contents of which are incorporated herein.

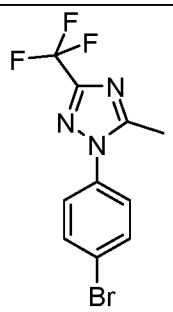
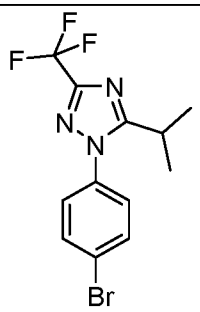
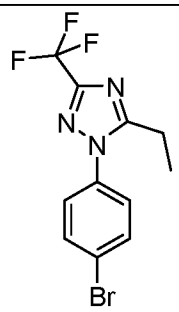
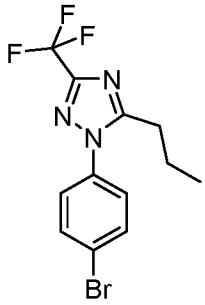
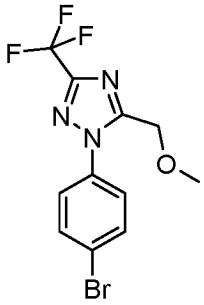
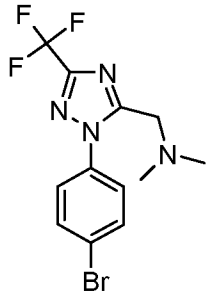
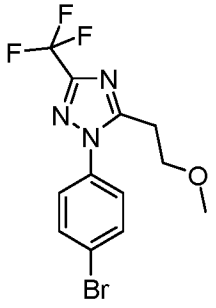
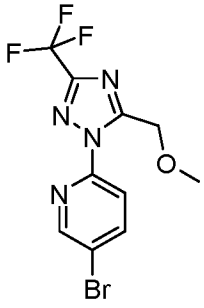
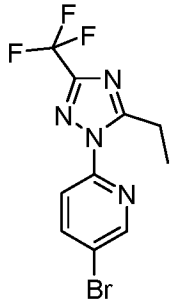
		
		

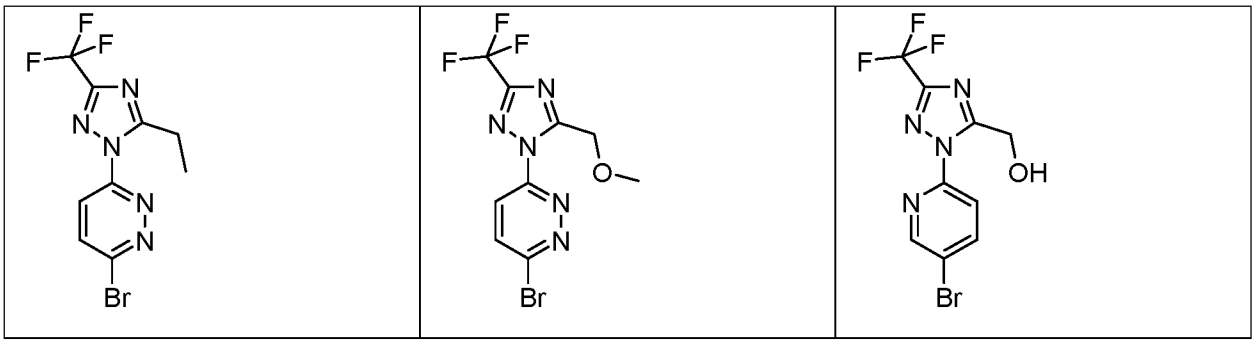
3-Trifluoromethyl, 5-Alkyl, 1H-triazole



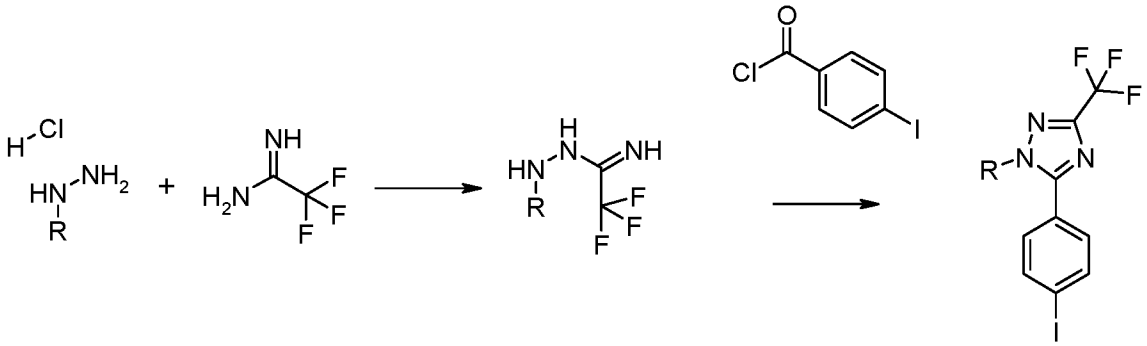
A = N,CH X = Cl, Br, I

The following compounds were synthesized as described in, e.g., US2004/106612 A1, WO2018/48969 A1, US2005/75507 A1, the contents of which are incorporated herein by reference.



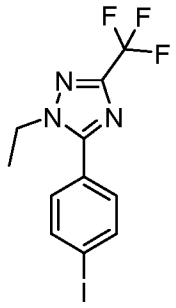
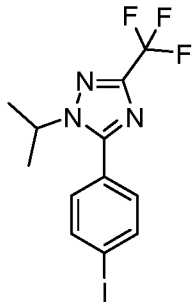
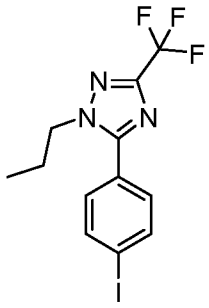
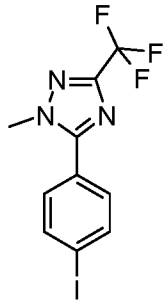
5-Aryl-1-alkyl-3-(trifluoromethyl)-1H-1,2,4-triazoles



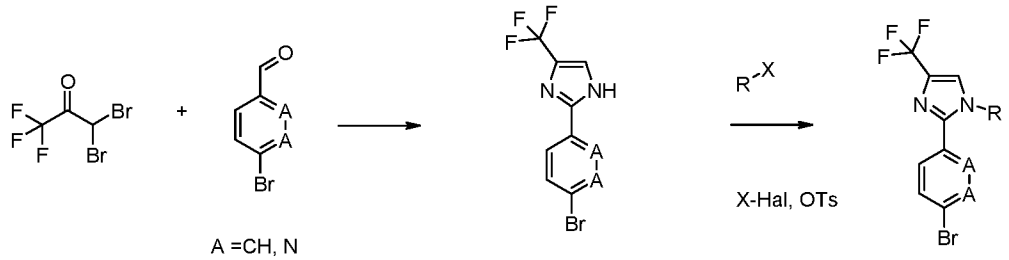
The corresponding hydrazine hydrochloride was dissolved in THF/MeOH, followed by triethylamine (1.1 eq.). After 30min trifluoro amidine (1.1.eq.) The mixture was stirred for 6h, diluted with water and extracted with EtOAc. The organic layer was dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude product was used without further purification.

The product from step1 was dissolved in dioxane, pyridine (1eq.) was added and the was degassed with N2. After 10 min the acid chloride was added. The mixture was stirred at 105°C o.n. The mixture was diluted with water and extracted with EtOAc. The organic layer was dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude product was purified by gradient flash chromatography.

The following intermediates were synthesized according to this procedure:

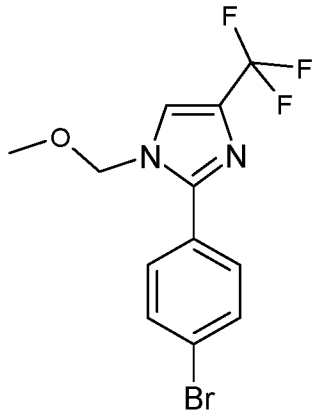
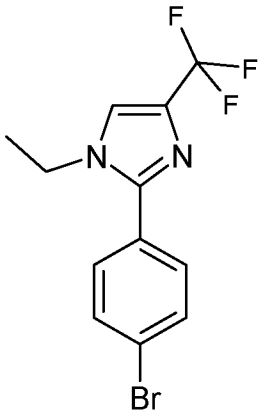
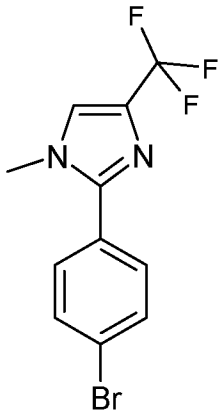
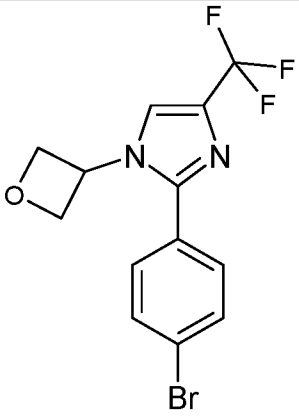
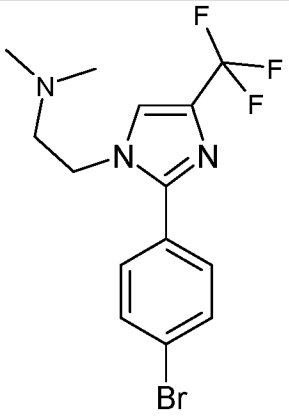
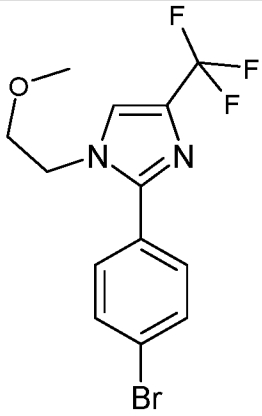
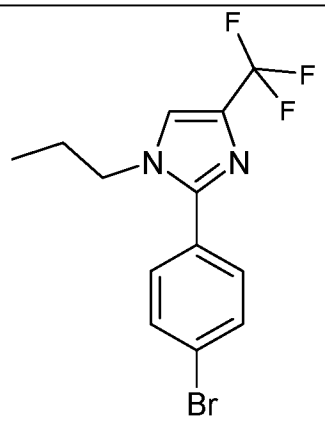
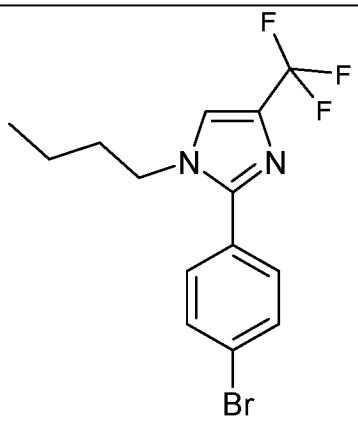
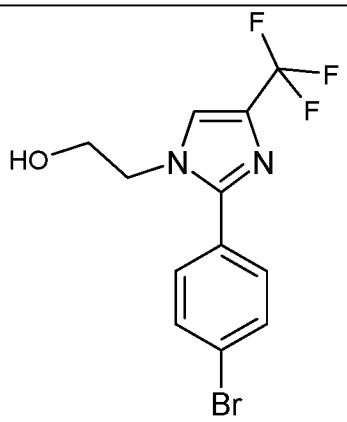
		
		

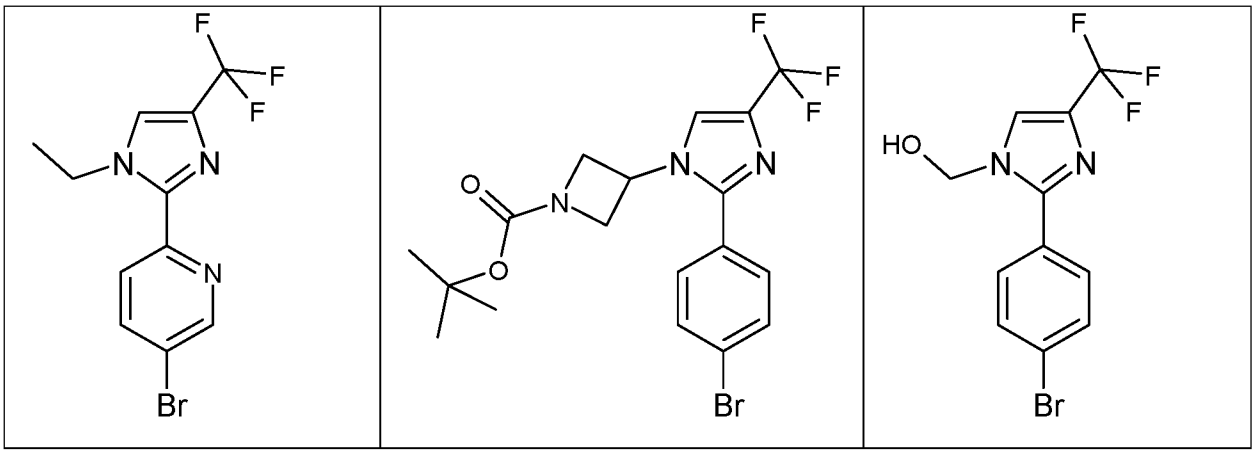
1-Alkyl,2-aryl,4-trifluoromethyl imidazole



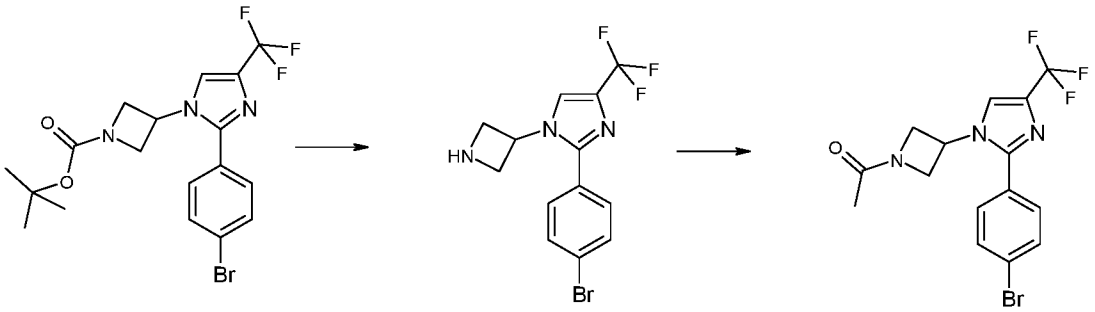
5

The syntheses were performed as described in US20200079776A1, the contents of which are incorporated herein by reference.



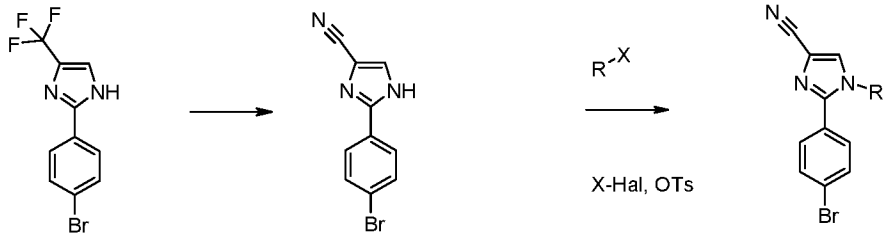
Later modifications:



The protected compound was dissolved in DCM/TFA (2/1) and stirred for 5h. The reaction was quenched by adding $NaHCO_3$ aq. and extracted with DCM/MeOH (9/1). The organic layer was washed with brine, dried, filtered and concentrated under reduced pressure. The product was used without further purification.

The product from the first step was dissolved in THF, AcCl (1,5eq.) and Net3 (3eq.) were added and the mixture stirred for 10 min. The mixture was concentrated, partitioned between water and DCM, the organic layer dried (Na_2SO_4), filtered and concentrated under reduced pressure. The product was used without further purification.

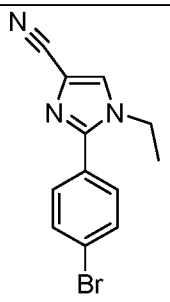
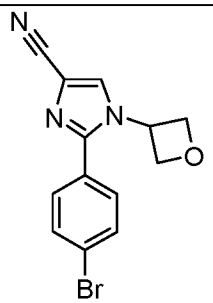
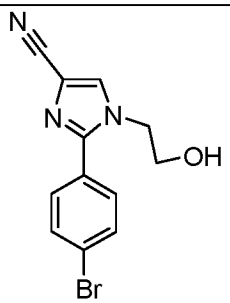
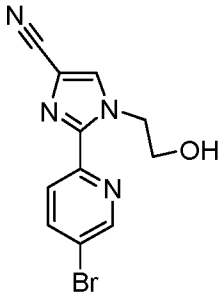
1-Alkyl,2-aryl,4-cyano imidazole



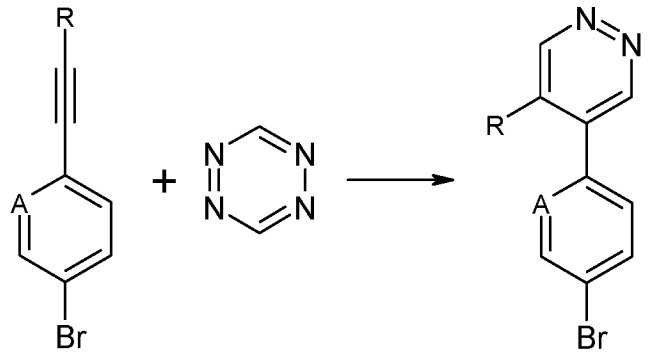
The trifluoro aryl imidazole was dissolved in MeOH, ammonia (20mL/mmol: 25%aq.) was added and the mixture hearted to 60°C for 2h. The mixture was extracted with EtOAc. The organic layer washed with brine, dried (Na_2SO_4), filtered and concentrated und reduced pressure. The product was used without further purification.

The alkylation was performed as described in US20200079776A1, the contents of which are incorporated by reference.

The following intermediates were synthesized using this method

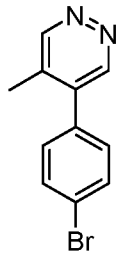
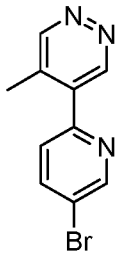
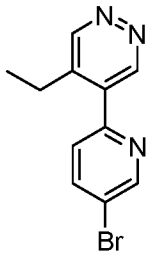
4-(aryl)-5-alky pyridazines



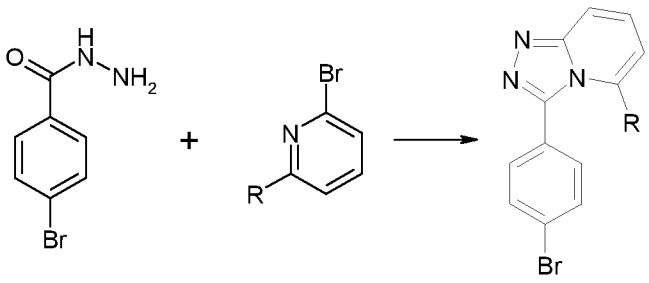
A = CH, N

The acetylene and tetrazine were mixed in o-xylene and heated at 140°C. The desired product was isolated by evaporation and used without purification.

The following intermediates were synthesized using this method.

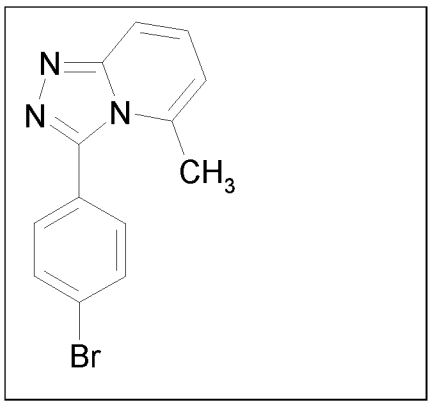
12. 5 substituted 3-(4-aryl)-l-[1,2,4]triazolo[4,3-a]pyridines



The pyridine derivative and hydrazide were dissolved in DCM, cooled to 0°C and Tf2O (1eq) was added slowly. The mixture was stirred for 15 min at 0°C the at r.t. o.n. The reaction was quenched with $NaHCO_3$ aq. sat., extracted with DCM. The organic layer dried (Na_2SO_4),

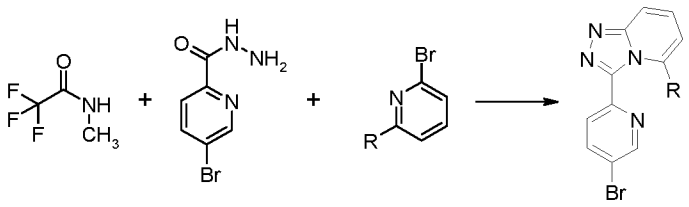
filtered and concentrated under reduced pressure. The crude product was purified by gradient flash chromatography.

The following intermediate was synthesized using this method:



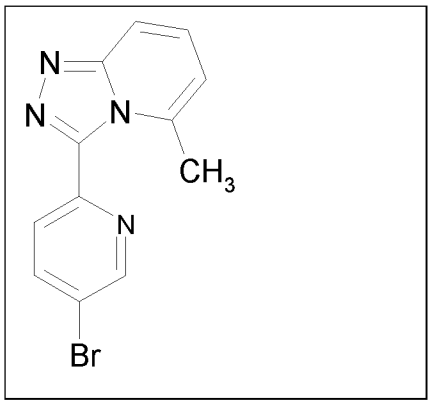
5

5 substituted 3-(4-pyridyl)-l-[1,2,4]triazolo[4,3-a]pyridines

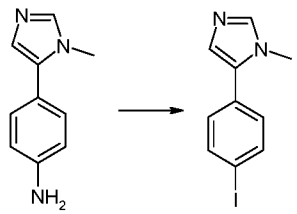


10 The pyridine derivative and, CF_3-aminde were dissolved in DCM, cooled to 0°C and Tf2O (1eq) was added slowly. The mixture was stirred for 15 min at 0°C then hydrazide was added. The mixture was heated at 120°C for 10 min under microwave irradiation. The reaction was quenched with $NaHCO_3$ aq. sat., extracted with DCM. The organic layer dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude product was purified by gradient
15 flash chromatography.

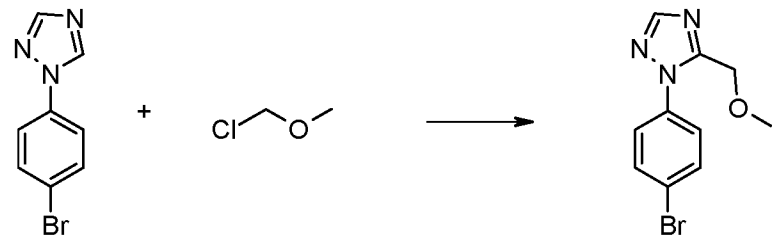
The following intermediate was synthesized using this method:



Special examples:



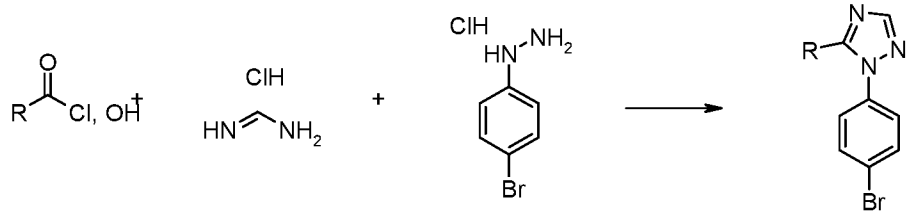
The aniline 1eq. was dissolved in HCl conc. (3mL/mmol) A solution of $NaNO_2$ (1,1eq.)in water was added dropwise at 0°C. The solution was stirred at 0°C for 1h. Acetone (3mL/mL), KI (1.1 eq) and CuI were added, and the mixture stirred at r.t. o.n. The mixture was quench by adding pH 7 buffer, extracted with EtOAc and the organic layer washed with brine, dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude product was purified by gradient flash chromatography.



The triazole was dissolved in dry THF, cooled to -78°C and n-BuLi (1,5 eq, 2,5M in hexanes) was added. After 0,5h MOM-Cl was added. The mixture was allowed to warm to r.t. The reaction mixture was diluted with water and extracted with EtOAc. The organic layer was

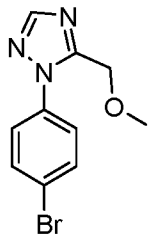
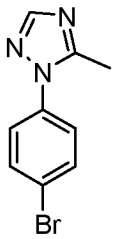
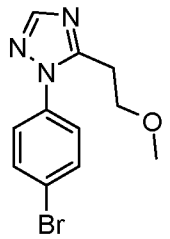
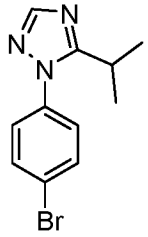
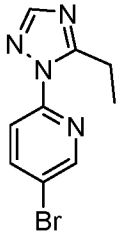
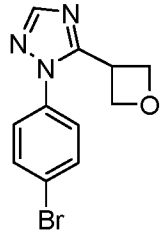
dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude product was purified by gradient flash chromatography.

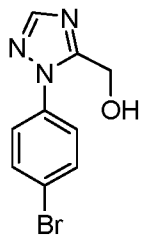
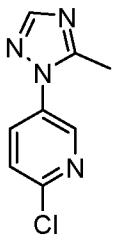
Alternative route:

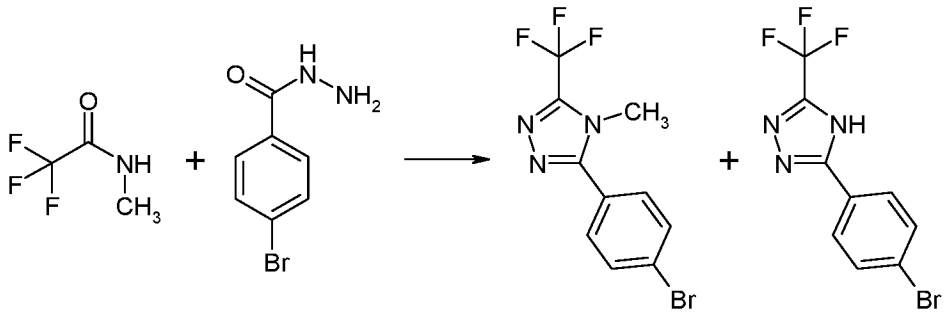


Acid chloride, amidine salt were mixed in DMF, HATU (1.1. eq.) and DIPEA (4 eq.) were added. The mixture was stirred o. n. Then AcOH (10mL/mmol) and hydrazine salt was added. The mixture was stirred at 80°C for 6h, then 2 days at r.t. The reaction mixture was diluted with EtOAc, neutralized with $NaHCO_3$ aq. the washed with water. The organic layer is dried, (Na_2SO_4), filtered and concentrated under reduced pressure. The crude product is purified by gradient flash chromatography.

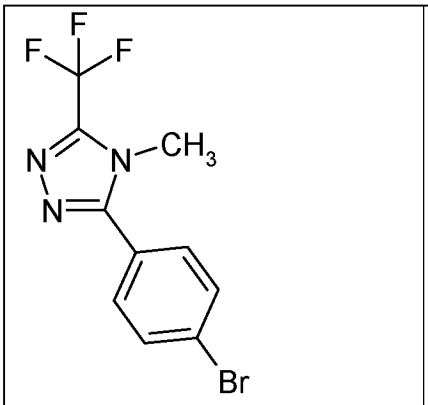
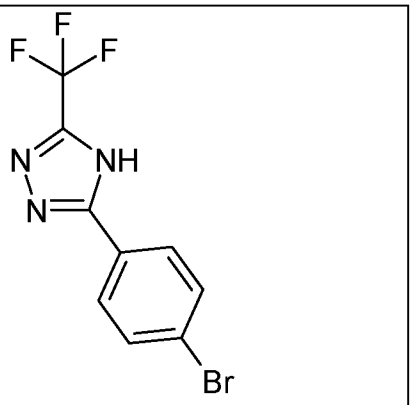
The following intermediates were synthesized following the method mentioned above.

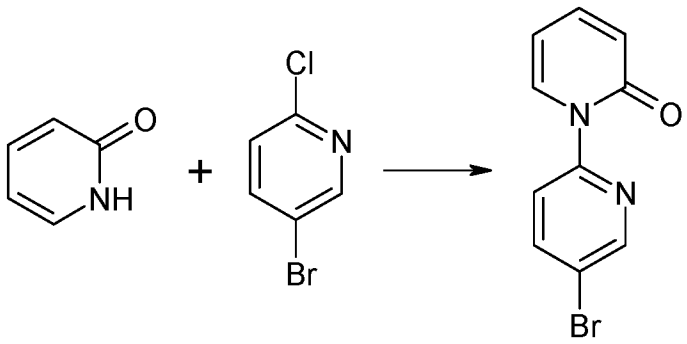
		
		



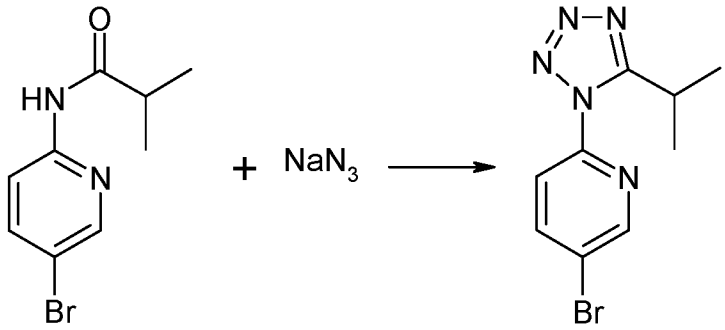
The following intermediates were synthesized as described in Org. Lett. 2015, 17, 1184-1187, the contents of which are incorporated herein by reference.



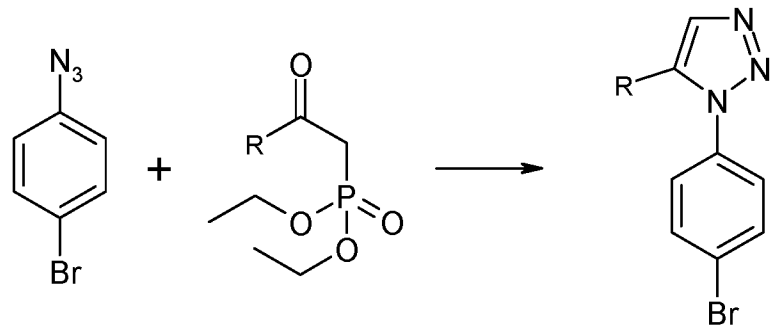
The amide and chloro pyridine were mixed in dry DMSO. The mixture was heated at 100°C for 4h. The mixture was diluted with water, extracted with EtOAc, the organic layer dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude product was purified by gradient flash chromatography.

1 pyridyl, 5- isopropyl tetrazoles



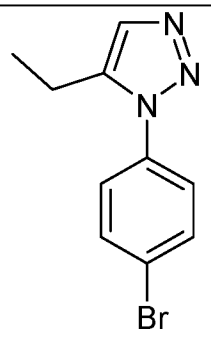
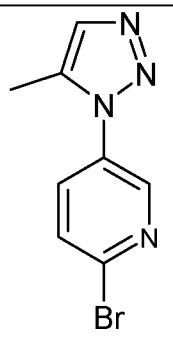
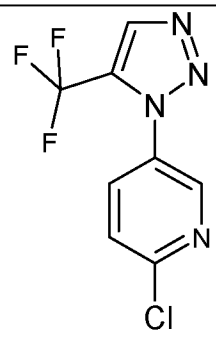
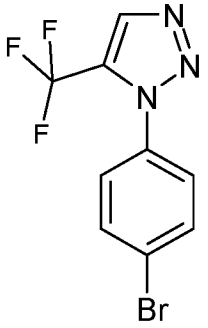
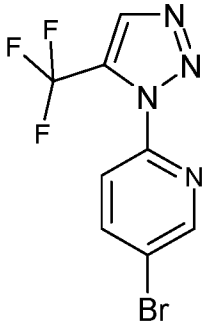
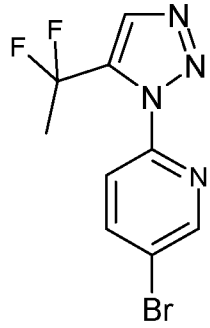
The amide was dissolved in dry THF $SiCl_4$ (2eq.) and NaN_3 (2eq.) were added. The mixture was heated at 90°C for two days. The additional $SiCl_4$ and NaN_3 (2eq. each) were and the mixture hated at 90°C for two additional days. The mixture was diluted with $NaHCO_3$ aq. sat, extracted with DCM/MeOH (9/1), the organic layer washed with brine, dried (Na_2SO_4) filtered and concentrated under reduced pressure. The product was used without further purification.

14: 1-aryl, 5- alky 1,2,3 triazoles

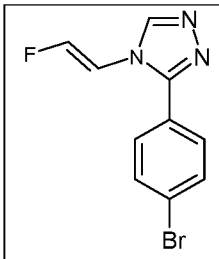


The aryl azide, tetramethylguanidine (3eq) and the corresponding phosphonate were mixed in acetonitrile. The mixture was heated at 80°C o.n. The mixture was diluted with water, extracted with DCM, the organic layer dried (Na_2SO_4) filtered and concentrated under reduced pressure. The crude product was used without further purification.

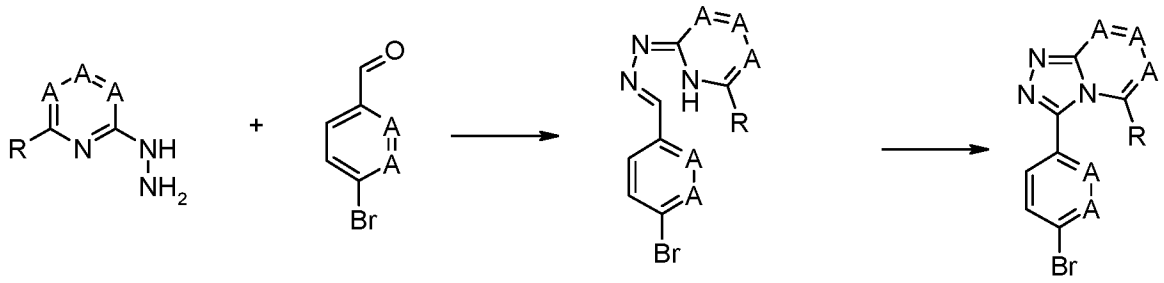
The following intermediated were synthesized using this procedure.

Special examples:


Side product isolated during synthesis of the trifluoro cpd

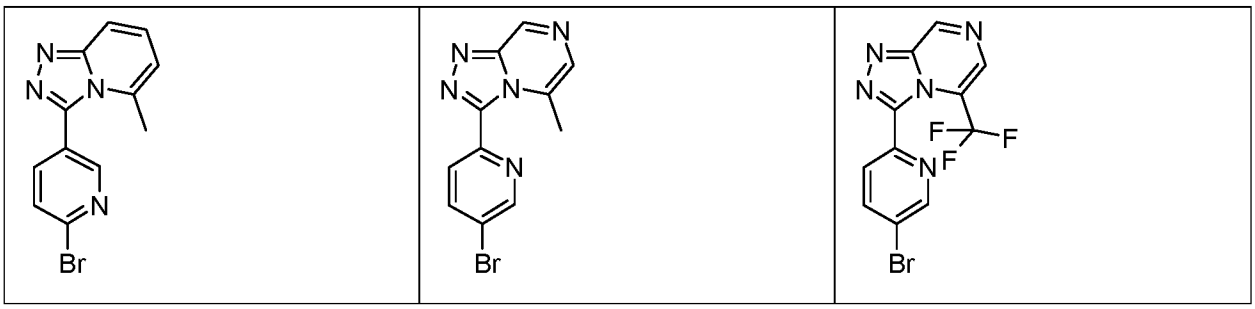
3-(bromo-aryl)-5-substituted-[1,2,4]triazolo[4,3-a]pyridines



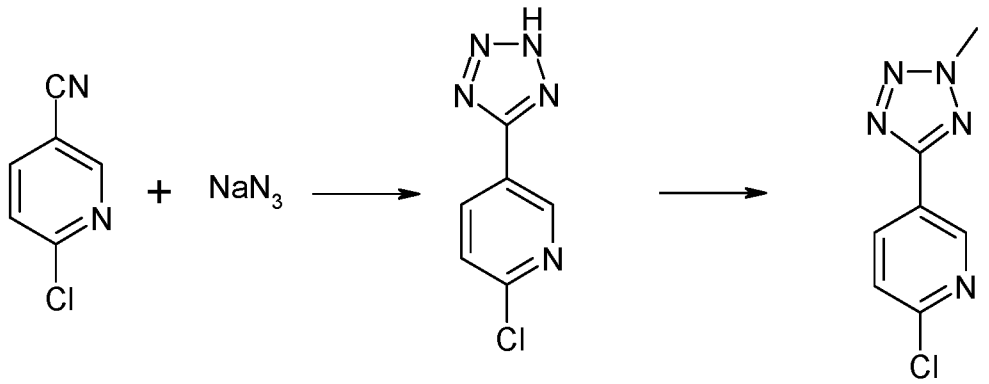
A = CH, N

The hydrazine and aldehyde (1.1 eq.) were mixed in EtOH. The mixtures was heated for 3h at reflux. The mixture was concentrated under reduced presuure and use without purification. The product from step 1 was dissolved in DCM, iodobenzene diacetate (1eq.) was added and the mixture stirred at r.t.

The following intermediates were synthesized using this method:



2-alky-5-aryl tetrazole

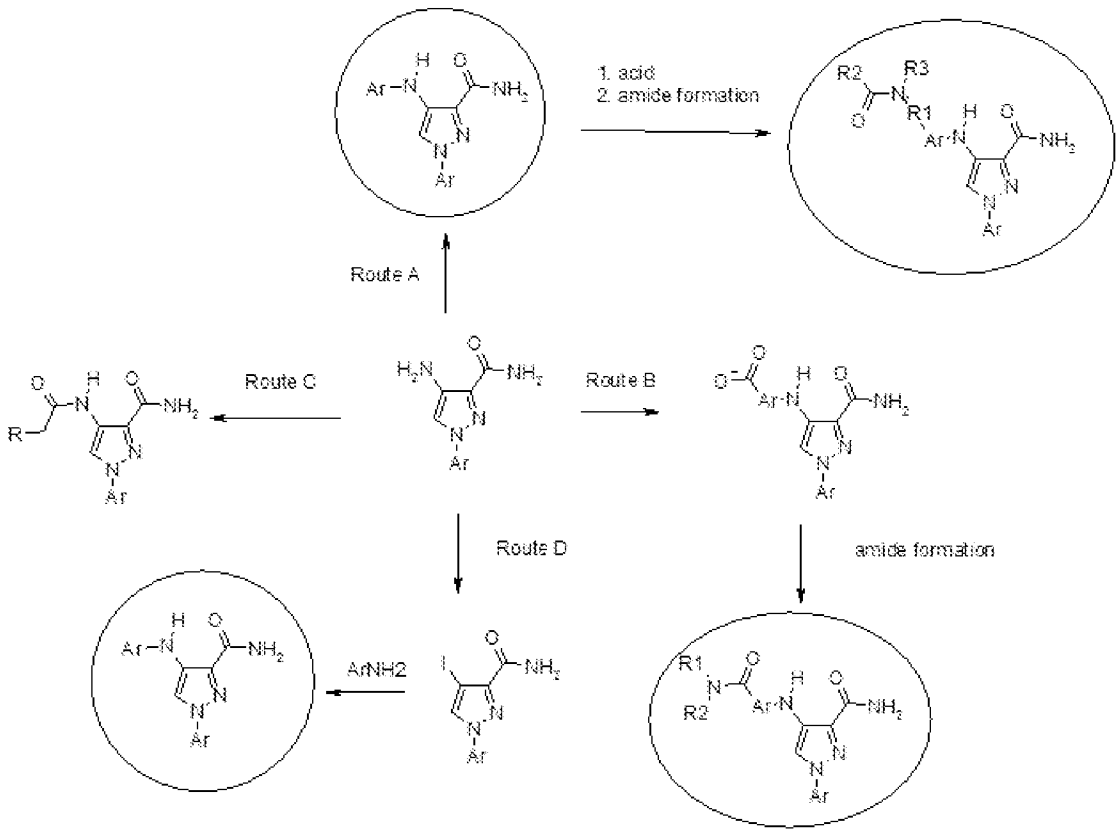


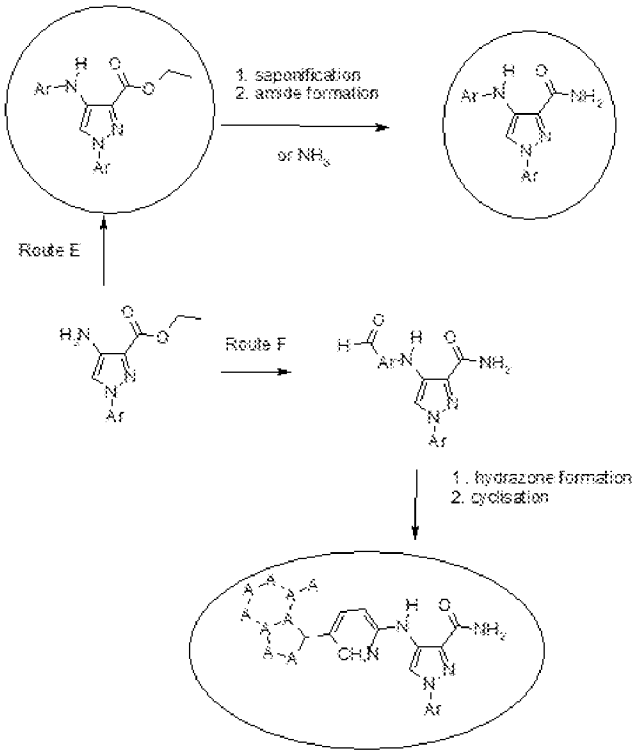
Step 1 was performed as described in J Med Chem 2010, 53, 3814-3830, the contents of which are incorporated herein by reference.

The product from step1 was dissolved in dry DMF, followed by NaH (2,3 eq. (60% suspension in oil) and MeI (1,15 eq.). The mixture was stirred o.n. at r.t., concentrated and purified with gradient flash chromatography.

Example 8

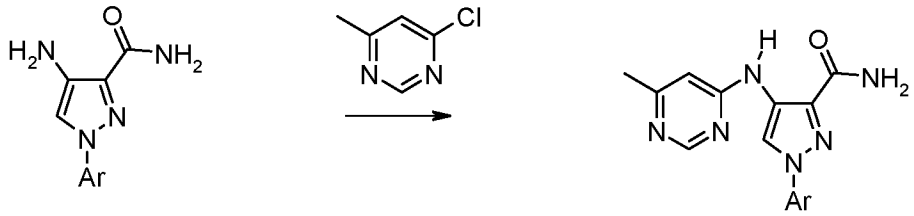
General synthesis scheme to final compounds.





Example 9

Route A.



Example 10

Method A1 - arylation. The arylation were performed by nucleophilic displacement or Buchwald-Hartwig conditions.

Nucleophilic displacements - general method: The pyrazole amine and the corresponding pyrimidine chloride (2eq.) were dissolved in *i*PrOH, followed by some drops of HCl 4M in dioxane. The mixture was irradiated under microwave conditions at 150°C for 15 min. The mixture was diluted with $NaHCO_3$ aq. and water and extracted with ethyl acetate. The organic

layer was concentrated under reduced pressure, and the crude material purified by semipreparative HPLC.

This method was used to synthesize Compound Nos. 4, 5 and 12.

Example 11

Method A2 – Buchwald type coupling:

General method A2.1: The pyrazole amine, the haloarene (2eq.), K_2CO_3 (3 eq.) and $Pd_2(dba)_3$ and X-Phos were dissolved in *iso*-butanol. The mixture was irradiated under microwave conditions for 1h at 110°C. The solvent was removed under reduced pressure. The residue was triturated with diethyl ether, the solids filtered off, the filtrate was concentrated under reduced pressure and purified using semipreparative HPLC.

This method was used to synthesize Compound Nos. 6, 7, 8, 9, 10, 11, 17, 18, 19, 20, 21, 22, 28, and 29.

Example 12

General method A2.2: The pyrazole amine, the haloarene (1.2eq.), NaO*t*Bu (3 eq.) and X-Phos Pd G2 (0.1eq.), X-Phos (0.1.eq.) were dissolved in dioxane. The mixture was degassed with N_2, then heated to 95°C o.n. The mixture was filtered, and the filtrate concentrated under reduced pressure. The residue was purified by chromatography.

This method was used to synthesize Compound Nos. 31, 32, 33, 35, 36, 37, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 56, 60, 61, 67, 74, 82, 83, 84, 85, 86, 89, 90, 91, 92, 93, 94, 95, 204, 246, 247, 248, 313, 314, 315, 316, 323, 324, 325, 331, 332, 354, 355, 356, 358, 362 , 363, 364, 365, 366, 367, 369, 370, 382, 383, 407, 439, 440, 441, 442, 443, and 444.

Example 13

General method A2.3: The pyrazole amine, the haloarene (1.2eq.), NaO*t*Bu (3 eq.) and ^{t}BuBrettPhos Pd G3 (0.25eq.), X-Phos (0.25.eq.) were dissolved in dioxane. The mixture was degassed with N_2, then heated to 95°C for 3h. The mixture was filtered, and the filtrate concentrated under reduced pressure. The residue was purified by chromatography.

This method was used to synthesize Compound Nos. 55, 57, 58, 59, 62, 63, 65, 66, 68, 69, 70, 71, 72, 73, 75, 76, 77, 78, 79, 80, 81, 87, 88, 96, 201, 202, 203, 205, 206, 207, 208 , 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 227, 228, 229, 230,

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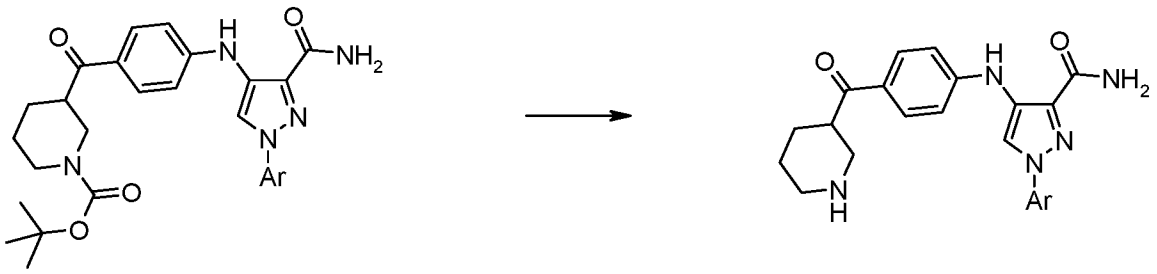
Example 14

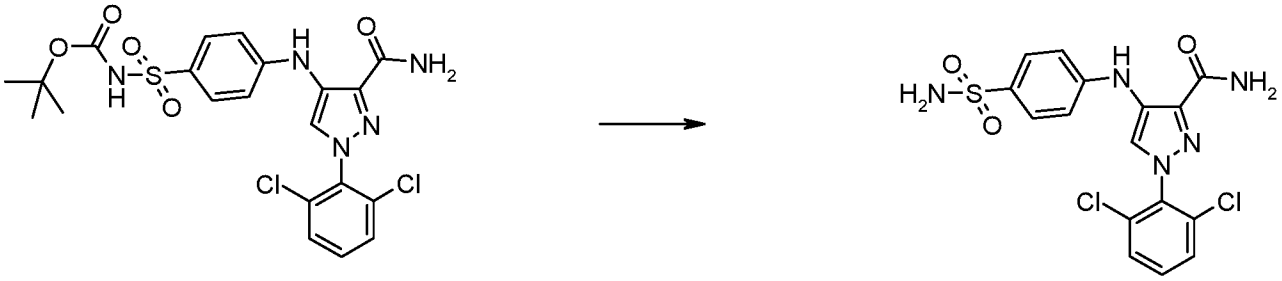
Further extension of Route A: Example of Boc deprotection:



General method: The protected compound was dissolved in DCM. TFA (10%v/v) was added and the mixture stirred for 1h. The mixture was diluted with water, basified with $NaHCO_3$ (pH8), dried over Na_2SO_4, filtered and concentrated und reduced pressure.

This method was used to synthesize Compound Nos. 38 39, 317, 318, 319, 357, and 368.

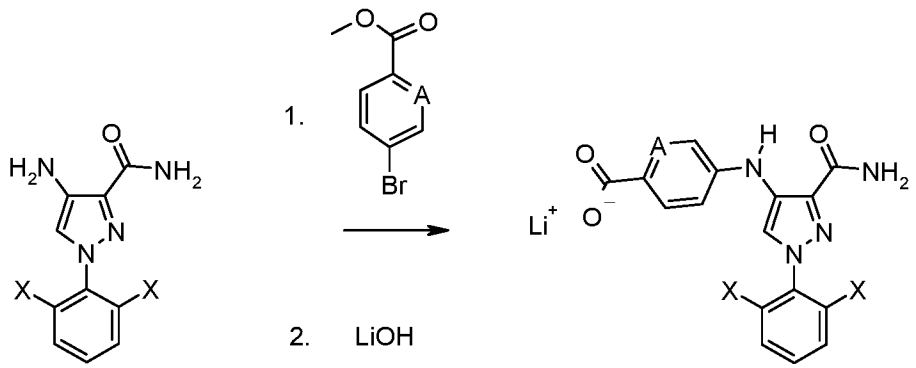
Special example:



The protected compound was dissolved in DCM. TFA (10%v/v) was added and the mixture sirred for 1h. The mixture was diluted with water, basified with $NaHCO_3$ (pH8), dried over Na_2SO_4, filtered and concentrated und reduced pressure and purified by reversed phase HPLC.

Example 15

Route B: The following intermediates was synthesized using a Buchwald type - Method A2:

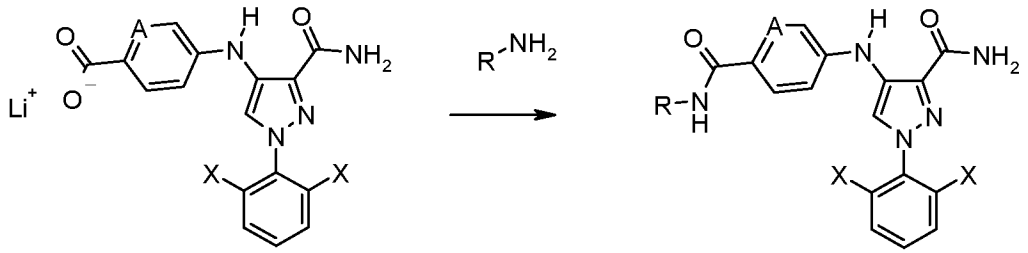


A = CH, N, CF
X = Cl , F

Modified work up: The solvent was removed by concentration under reduced pressure. The residue partitioned in between DCM and water, the aqueous layer was washed with DCM (3x) and 10% MeOH in DCM. The combined organic layers were washed with bine, dried (Na_2SO_4) and concentrated under reduced pressure. The crude product was purified by gradient

flash chromatography. The intermediate ester was saponified with LiOH (10eq) in THF:MeOH (3:1) at 60°C o.n. The mixture was concentrated and used without further purification.

Amination:

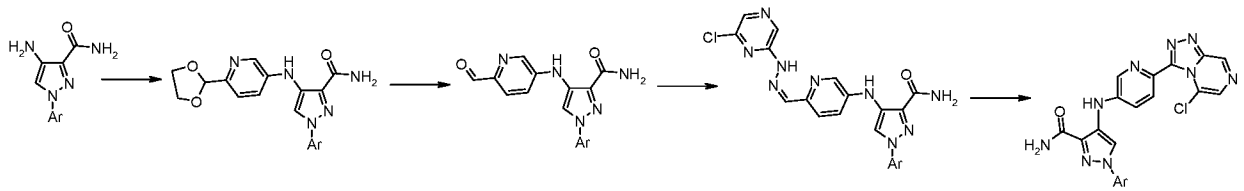


A = CH, N; CF
X = F, Cl

General method: The lithium salt was dissolved in DMF, the corresponding amine (2eq.), HATU (3eq.) and DIPEA (3eq.) were added. The mixture was stirred at 50°C o.n. The reaction mixture was purified without work up with semipreparative HPLC.

This method was used to synthesize Compound Nos. 13, 14, 15, 16, 23, 24, 25, 26, 27, 30, 34, 40, 226, and 472

Special method:

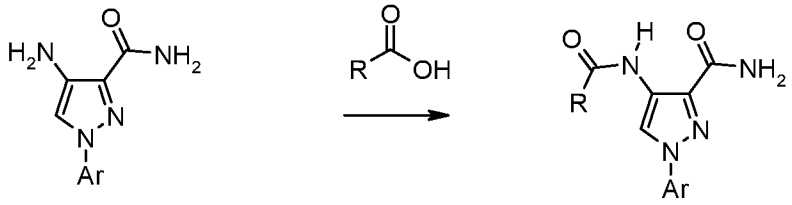


Step1 is performed according to the procedures of A2.3. The deprotection is performed by treating the product of step1 with THF/HCl aq. 2M for 1h at r.t.. The mixture was diluted with water extracted with DCM, the organics dried (Na_2SO_4), filtered and concentrated under reduced pressure. Hydrazone formation and oxidative cyclisation are following the procedures of intermediate 15 synthesis. The final crude product is purified by reversed phase chromatography

This method was used to synthesize Compound Nos. 447, 470, 471, 474, 475, and 476.

Example 16

Route C - Amide formation.



General method: The pyrazole amine and carboxylic acid (1eq.) were dissolved in DMF (dry), followed by HOBt (2eq,), EDCI (2eq.) and DIPEA (3eq.). The mixture was stirred at r.t. for 4h. The mixture was diluted with ethyl acetate, washed with $NaHCO_3$ aq. and brine. The desired compound was purified by semipreparative HPLC.

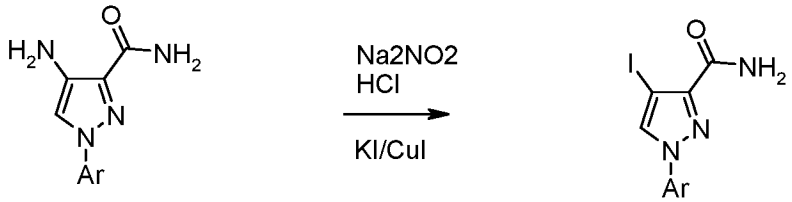
Alternatively the corresponding acid chloride was used with triethyl amine (3 eq.)in DCM.

The following compounds were synthesized according this procedure using an appropriate pyrazole amine and carboxylic acid.

This method was used to synthesize Compound Nos. 1, 2, and 3.

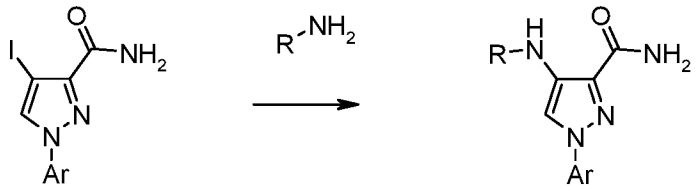
Example 17

Route D - Special final compounds.



A solution of $NaNO_2$ (1.2 eq) was dropped to a cooled (0°C) solution of the aminopyrazole in HCl (37% aq). Subsequently acetone, KI (1.1eq.) and CuI (1.1 eq.) were added. The solution was stirred at r.t. o.n. The reaction mixture was quenched with buffer (pH7). The aqueous layer was extracted with DCM and 5%MeOH in DCM. The combined organic

phases were dried (Na_2SO_4) filtered and evaporated under reduced pressure. The residue was purified by gradient flash chromatography.



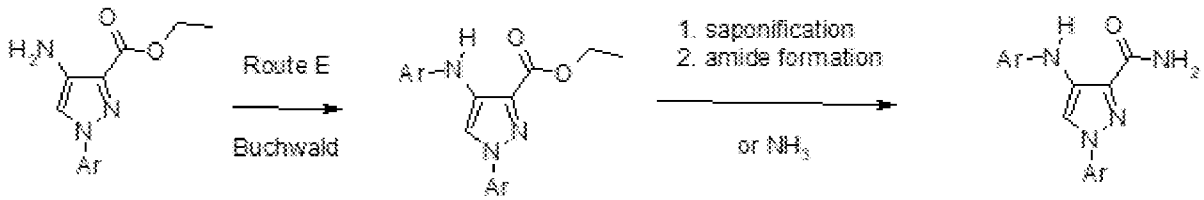
A modified method B was used to synthesize Compound No. 64.

Compound No. 453 was isolated as a byproduct in the corresponding nitril synthesis.

Reductive amination was used to synthesize Compound No. 455.

The aldehyde was dissolved in MeOH, followed by the addition of amine, acetic acid and sodiumcyanoborohydride (5 eq. each). After 30 min the mixture was dilute with water, extracted with DCM, dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude product was purified by reversed phase HPLC.

Route E:



The "Buchwald-type" step was performed, using the conditions A2.1, A2.2 or A2.3 starting from the ester intermediate of the building block synthesis.

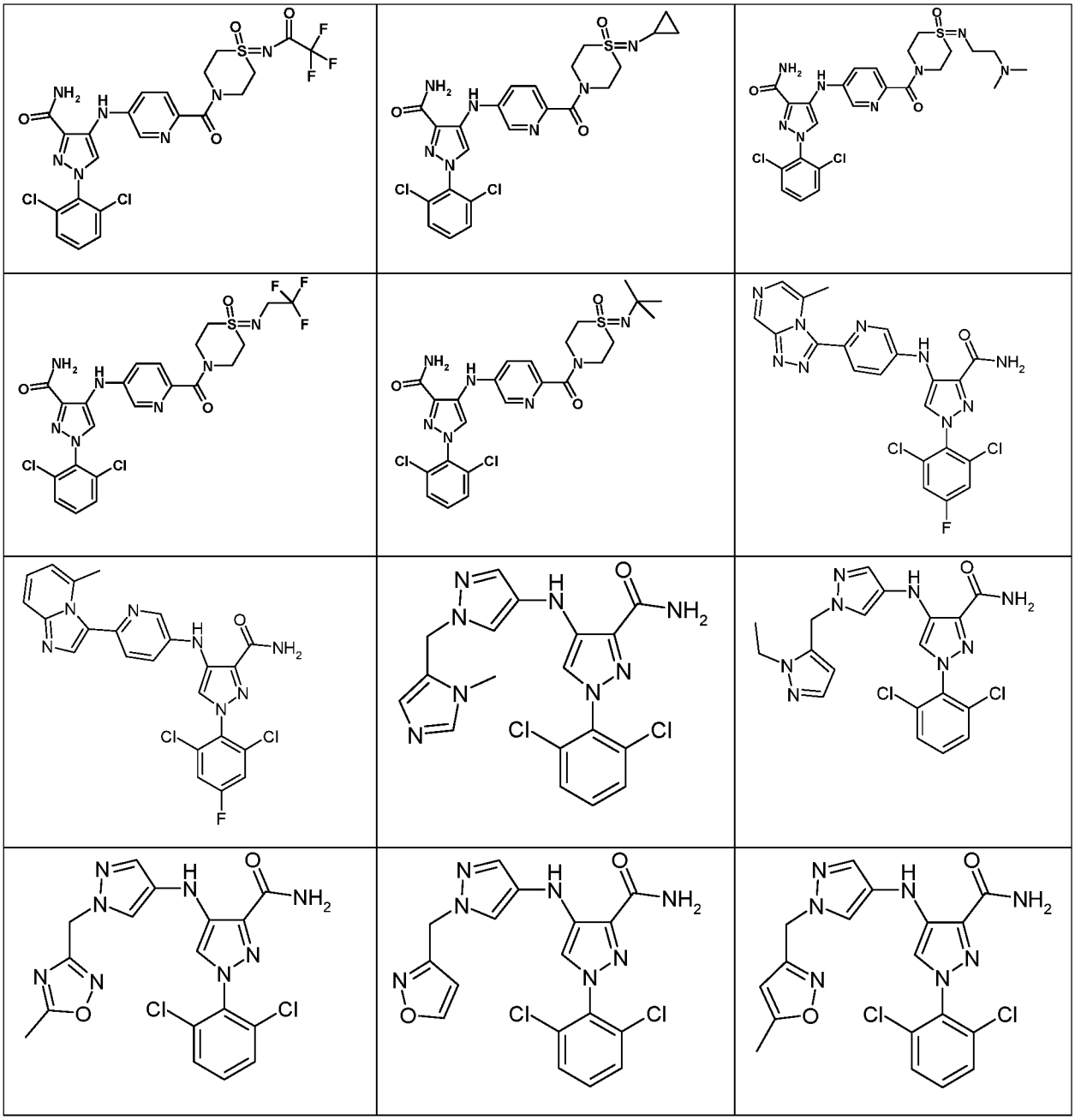
The saponification is performed by treating the corresponding ester by NaOH in MeOH. The amidation was performed by dissolving the acid in DMF, followed by addition of an excess (10-20 eq.) ammonium chloride, HATU (1.2 eq.) and DIPEA (3eq.)

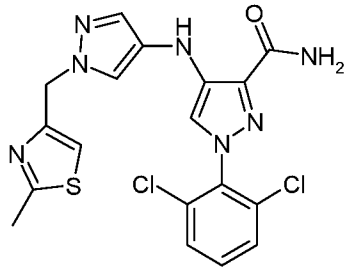
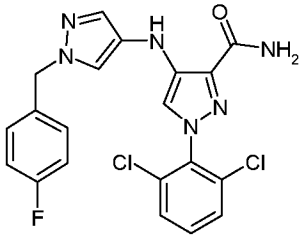
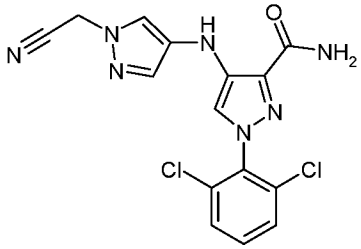
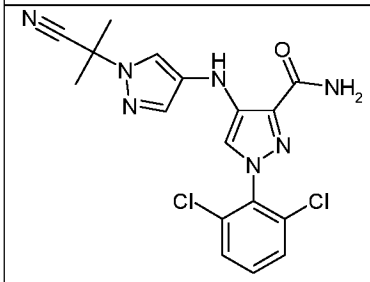
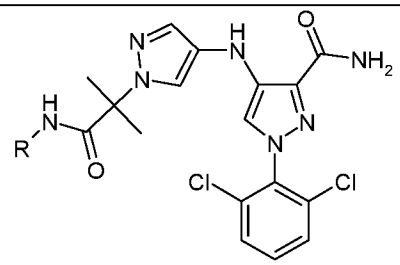
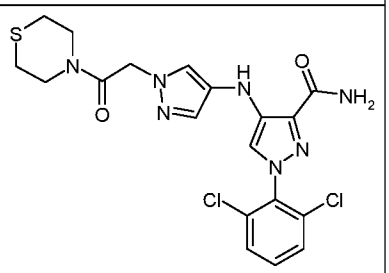
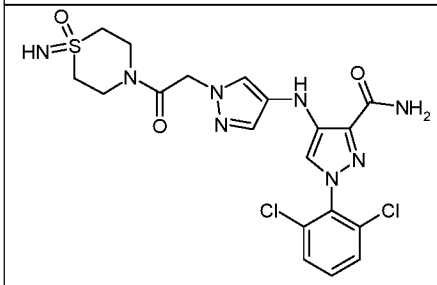
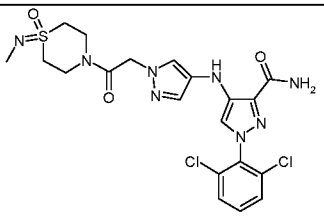
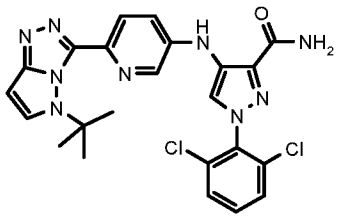
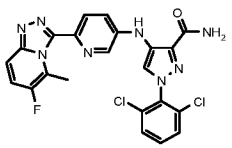
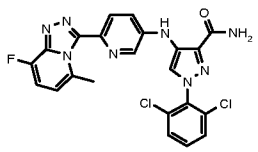
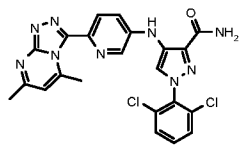
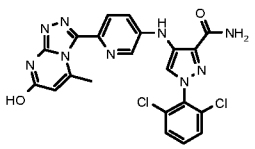
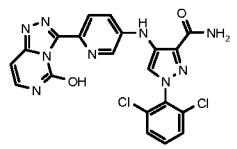
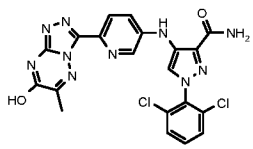
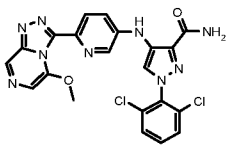
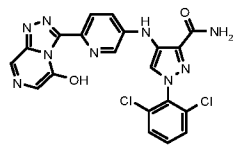
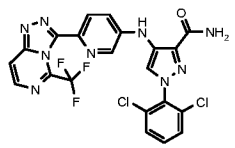
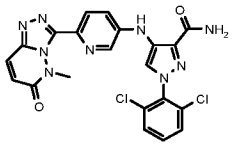
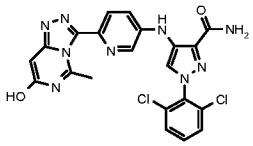
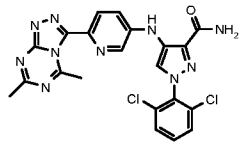
Alternatively the ester intermediate can be treated with NH3 to get directly to the amide.

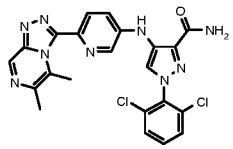
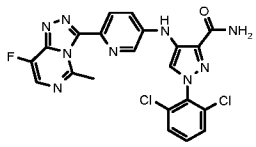
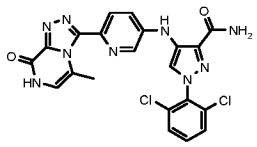
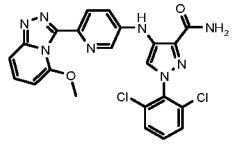
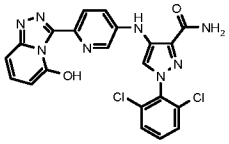
The residue was purified by chromatography.

The method of using A2.3 in the Buchwald step was used to synthesize Compound Nos. 359, 372, 374, 375, 378, 379, 380, 392, 396, 397, 412, 413, 414, 416, 417, 418. and 461

This method can also be used to make the following compounds:



		
	 R = NRR´	
		
		
		
		
		

Example 18

The HPLC Methods used in preparation of the compounds are listed in Table 6.

Table 6.

Method	col	grad	flow (mL/min)	ms
HPLC-MS A	Waters ACQUITY UPLC HSS T3 50x2.1 1.8 μm PN:186003538	2%-4.0min->95%-1.0min->95%-0.1min->2%-2.9min->2%; ACN/H_2O + 0.1% HCOOH	0.6	ESI positive & negative
HPLC-MS B	Waters ACQUITY UPLC CSH C18 50x2.1 1.7 μm PN:186005296	5%-4.0min->95%-1.0min->95%-0.1min->5%-2.9min->5%; ACN/H2O + 0.1% HCOOH	0.6	ESI positive & negative
HPLC-MS C	Waters ACQUITY UPLC CSH C18 50x2.1 1.7 μm PN:186005296	4%-4.0min->96%-1.0min->96%-0.1min->4%-2.9min->4%; ACN/H2O + 100mM NH4Ac-	1.2	ESI positive
HPLC-MS D	Waters CORTECS UPLC C18+ 50x2.1 1.6 μm PN:186007114	5%-4.0min->95%-1.0min->95%-0.1min->5%-2.9min->5%; ACN/H2O + 0.1% HCOOH	0.6	ESI positive & negative
HPLC-MS E	Waters ACQUITY UPLC CSH C18 50x2.1 1.7µm PN:186005296	5%-0.75min->95%-0.5min->95%-0.05min->5%-1.2min->5%; ACN/H2O + 0.1% HCOOH	1.2	ESI positive

Example 19

Chemical analytical data for the compounds listed in Table 1 is summarized in Table 7.

Table 7.

Compound No	HPLC-MS Method	retention time (min)	m+H Found	NMR
1	C	3.047	360.2	1H NMR (400 MHz, MeOD) δ 8.70 (s, 1H), 7.79 – 7.73 (m, 2H), 7.12 – 7.03 (m, 2H), 3.87 (m, 7H), 3.25 (s, 2H), 2.66 (m, 4H).
2	C	2.923	366.2	1H NMR (400 MHz, Methanol-d_4) δ 8.42 (d, J = 1.2 Hz, 1H), 7.43 (tt, J = 8.3, 6.0 Hz, 1H), 7.15 – 7.04 (m, 2H), 3.90 (s, 4H), 3.51 (d, J = 5.0 Hz, 7H), 2.86 (s, 3H).
3	C	3.015	348.1	1H NMR (400 MHz, Methanol-d_4) δ 8.72 (d, J = 2.9 Hz, 1H), 7.92 (dtd, J = 15.8, 7.9, 1.6 Hz, 2H), 7.67 (d, J = 3.0 Hz, 1H), 7.51 – 7.43 (m, 1H), 7.43 – 7.28 (m, 5H), 3.91 – 3.82 (m, 4H), 3.24 (s, 2H), 2.65 (dd, J = 5.5, 3.5 Hz, 4H).
4	C	3.074	331.2	1H NMR (400 MHz, Chloroform-d) δ 9.37 (s, 1H), 8.72 (s, 1H), 8.69 (q, J = 1.0 Hz, 1H), 7.48 (tt, J = 8.6, 6.0 Hz, 1H), 7.21 – 7.09 (m, 2H), 6.85 (s, 1H), 6.63 (s, 1H), 5.56 (s, 1H), 4.14 (q, J = 7.2 Hz, 1H), 2.50 (s, 3H), 2.07 (s, 2H), 1.28 (t, J = 7.2 Hz, 3H).
5	C	3.174	313.2	1H NMR (400 MHz, Chloroform-d) δ 8.93 (d, J = 3.0 Hz, 1H), 8.74 (s, 1H), 7.83 (td, J = 7.8, 2.1 Hz, 1H), 7.47 – 7.35 (m, 1H), 7.35 – 7.25 (m, 3H), 6.60 (s, 1H), 2.48 (s, 3H).
6	C	2.690	331.2	
7	C	3.642	316.2	1H NMR (400 MHz, Methanol-d_4) δ 8.62 (t, J = 1.1 Hz, 1H), 8.20 (ddd, J = 5.1, 1.9, 0.9 Hz, 1H), 7.62 – 7.51 (m, 2H), 7.29 – 7.19 (m, 2H), 6.84 (dt, J = 8.4, 1.0 Hz, 1H), 6.74 (ddd, J = 7.2, 5.1, 0.9 Hz, 1H).
8	C	2.822	346.2	
9	C	4.017	372.3	1H NMR (400 MHz, Methanol-d_4) δ 8.73 (s, 1H), 7.71 (dt, J = 7.6, 1.0 Hz, 1H), 7.65 – 7.56 (m, 2H), 7.37 – 7.22 (m, 3H), 7.16 (td, J = 7.7, 1.2 Hz, 1H).
10	C	3.834	330.3	1H NMR (400 MHz, Methanol-d_4) δ 8.59 (t, J = 1.0 Hz, 1H), 8.05 (dd, J = 5.2, 0.8 Hz, 1H), 7.62 – 7.49 (m, 1H), 7.30 – 7.11 (m, 2H), 6.67 (dt, J = 1.6, 0.9 Hz, 1H), 6.61 (ddd, J = 5.3, 1.5, 0.7 Hz, 1H), 2.29 (s, 3H).
11	C	3.474	355.3	1H NMR (400 MHz, Methanol-d_4) δ 8.52 (d, J = 1.0 Hz, 1H), 7.60 (tt, J = 8.6, 6.1 Hz, 1H), 7.36 – 7.22 (m, 4H), 7.06 (dd, J = 5.9, 3.2 Hz, 2H).

Compound No	HPLC-MS Method	retention time (min)	m+H Found	NMR
12	C	3.118	428.3	1H NMR (400 MHz, Methanol-d_4) δ 8.15 (s, 1H), 7.63 – 7.52 (m, 1H), 7.41 – 7.36 (m, 2H), 7.28 – 7.18 (m, 2H), 7.10 – 7.04 (m, 2H), 3.82 - 3.53 (brs, 8H).
13	C	3.120	442.2	1H NMR (400 MHz, Methanol-d_4) δ 8.19 (s, 1H), 7.83 – 7.75 (m, 2H), 7.59 (ddd, J = 8.6, 6.1, 2.5 Hz, 1H), 7.30 – 7.21 (m, 2H), 7.09 – 7.01 (m, 2H), 4.09 (ddd, J = 11.3, 7.0, 4.3 Hz, 1H), 4.02 – 3.94 (m, 2H), 3.52 (td, J = 11.9, 2.1 Hz, 2H), 1.89 (ddd, J = 12.6, 4.4, 2.0 Hz, 2H), 1.74 – 1.60 (m, 2H).
14	C	3.467	440.2	1H NMR (400 MHz, Methanol-d_4) δ 8.21 (s, 1H), 7.85 – 7.79 (m, 2H), 7.64 - 7.53 (m, 1H), 7.30 – 7.21 (m, 2H), 7.11 – 7.04 (m, 2H), 4.07 (q, J = 9.4 Hz, 1H).
15	C	3.634	414.2	1H NMR (400 MHz, Methanol-d_4) δ 8.17 (s, 1H), 7.74 – 7.68 (m, 2H), 7.63 – 7.54 (m, 1H), 7.30 – 7.20 (m, 2H), 7.07 – 6.98 (m, 2H), 1.45 (s, 9H).
16	C	3.158	386.2	1H NMR (400 MHz, Methanol-d_4) δ 8.19 (s, 1H), 7.81 – 7.74 (m, 2H), 7.61 - 7.57 (m, 1H), 7.25 (t, J = 8.3 Hz, 2H), 7.09 – 7.02 (m, 2H), 3.39 (q, J = 7.3 Hz, 3H), 1.21 (t, J = 7.2 Hz, 4H).
17	C	3.360	460.2	1H NMR (400 MHz, Methanol- d_4) d 8.12 (s, 1H), 7.64 (d, J = 1.5 Hz, 1H), 7.62 (d, J = 0.7 Hz, 1H), 7.55 (dd, J = 9.2, 7.0 Hz, 1H), 7.40 (d, J = 8.6 Hz, 2H), 7.08 (d, J = 8.6 Hz, 2H), 3.68 (bs, 8H).
18	C	3.369	428.2	1H NMR (400 MHz, Methanol- d_4) δ 8.17 (s, 1H), 7.64 - 7.54 (m, 1H), 7.36 (t, J = 7.8 Hz, 1H), 7.30 – 7.19 (m, 2H), 7.16 - 7.09 (m, 1H), 7.08 - 7.04 (m, 1H), 6.87 (dt, J = 7.7, 1.1 Hz, 1H), 3.75 (brs, 5H), 3.62 (brs, 3H).
19	C	3.904	349.3	
20	C	4.208	381.0	1H NMR (400 MHz, Methanol- d_4) d 8.03 (s, 1H), 7.67 – 7.61 (m, 2H), 7.56 (dd, J = 9.2, 7.0 Hz, 1H), 7.30 – 7.21 (m, 2H), 7.05 – 6.98 (m, 2H).
21	C	3.950	347.0	1H NMR (400 MHz, Methanol- d_4) d 8.00 (s, 1H), 7.64 (dd, J = 8.1, 1.1 Hz, 2H), 7.56 (dd, J = 9.2, 7.0 Hz, 1H), 7.32 – 7.23 (m, 2H), 7.07 – 6.99 (m, 3H), 6.85 (tt, J = 7.4, 1.1 Hz, 1H).
22	C	3.335	444.2	1H NMR (400 MHz, Methanol- d_4) d 8.15 (s, 1H), 7.59 (td, J = 8.4, 5.6 Hz, 1H), 7.50 (dt, J = 8.3, 1.4 Hz, 1H), 7.43 – 7.34 (m, 3H), 7.11 – 7.04 (m, 2H), 3.66 (d, J = 14.9 Hz, 8H).
23	C	3.685	416.2	
24	C	3.185	387.2	

Compound No	HPLC-MS Method	retention time (min)	m+H Found	NMR
25	C	3.361	387.2	
26	C	3.801	446.2	1H NMR (400 MHz, Methanol- d_4) d 8.12 (s, 1H), 7.75 – 7.68 (m, 2H), 7.66 – 7.60 (m, 2H), 7.56 (dd, J = 9.2, 7.0 Hz, 1H), 7.08 – 6.99 (m, 2H), 1.44 (s, 9H).
27	C	3.719	430.2	1H NMR (400 MHz, Methanol- d_4) d 8.15 (s, 1H), 7.74 – 7.67 (m, 2H), 7.59 (td, J = 8.3, 5.6 Hz, 1H), 7.50 (dt, J = 8.2, 1.3 Hz, 1H), 7.38 (ddd, J = 9.6, 8.5, 1.4 Hz, 1H), 7.03 (d, J = 8.8 Hz, 2H), 1.44 (s, 9H).
28	C	4.028	464.0	1H NMR (400 MHz, Methanol- d_4) d 8.19 (s, 1H), 7.70 – 7.63 (m, 3H), 7.58 (dd, J = 9.2, 6.9 Hz, 1H), 6.89 (dd, J = 8.6, 2.3 Hz, 1H), 6.80 (dd, J = 14.0, 2.3 Hz, 1H), 1.46 (s, 9H).
29	C	3.939	448.2	1H NMR (400 MHz, Methanol- d_4) d 8.23 (s, 1H), 7.67 (t, J = 8.7 Hz, 1H), 7.61 (td, J = 8.3, 5.6 Hz, 1H), 7.52 (dt, J = 8.3, 1.3 Hz, 1H), 7.40 (ddd, J = 9.6, 8.4, 1.4 Hz, 1H), 6.89 (dd, J = 8.6, 2.3 Hz, 1H), 6.80 (dd, J = 14.0, 2.3 Hz, 1H), 1.46 (s, 9H).
30	C	2.884	429.2	1H NMR (400 MHz, Methanol- d_4) δ 8.34 - 8.32 (m, 1H), 8.28 (s, 1H), 7.65 – 7.50 (m, 3H), 7.26 (t, J = 8.3 Hz, 2H), 3.83 - 3.63 (brs, 8H).
31	C	2.903	487.2	1H NMR (400 MHz, Methanol- d_4) d 8.15 (s, 1H), 7.85 – 7.74 (m, 2H), 7.64 (d, J = 8.8 Hz, 2H), 7.56 (dd, J = 9.2, 6.9 Hz, 1H), 7.12 – 7.03 (m, 2H), 3.99 (tt, J = 11.0, 4.1 Hz, 1H), 3.18 (dd, J = 12.0, 3.6 Hz, 2H), 2.54 (s, 5H), 2.12 – 1.99 (m, 2H), 1.80 (qd, J = 11.6, 6.2 Hz, 2H).
32	C	3.073	473.2	1H NMR (400 MHz, Methanol- d_4) d 8.12 (s, 1H), 7.66 – 7.62 (m, 2H), 7.56 (dd, J = 9.2, 7.0 Hz, 1H), 7.39 (d, J = 8.7 Hz, 2H), 7.08 (d, J = 8.7 Hz, 2H), 3.68 (s, 4H), 2.52 (s, 4H), 2.36 (s, 3H).
33	C	3.968	573.2	1H NMR (400 MHz, Methanol- d_4) d 8.17 (s, 1H), 7.80 (d, J = 8.7 Hz, 2H), 7.68 – 7.63 (m, 2H), 7.58 (dd, J = 9.2, 7.0 Hz, 1H), 7.11 – 7.05 (m, 2H), 3.99 – 3.88 (m, 1H), 2.96 (s, 2H), 2.02 (d, J = 26.7 Hz, 3H), 1.81 (s, 1H), 1.59 (d, J = 9.6 Hz, 2H), 1.46 (s,9H).
34	C	3.355	418.2	1H NMR (400 MHz, Methanol- d_4) d 8.15 (d, J = 4.0 Hz, 1H), 7.81 – 7.76 (m, 2H), 7.68 – 7.63 (m, 2H), 7.61 – 7.55 (m, 1H), 7.09 – 7.05 (m, 2H), 3.41 (q, J = 7.2 Hz, 2H), 1.24 (t, J = 3.6 Hz, 3H).

Compound No	HPLC-MS Method	retention time (min)	m+H Found	NMR
35	C	2.773	471.2	1H NMR (400 MHz, Methanol- d_4) d 8.17 (s, 1H), 7.81 – 7.76 (m, 2H), 7.59 (td, J = 8.3, 5.6 Hz, 1H), 7.50 (dt, J = 8.3, 1.4 Hz, 1H), 7.38 (td, J = 8.8, 1.4 Hz, 1H), 7.08 – 7.02 (m, 2H), 4.02 (tt, J = 11.1, 4.1 Hz, 1H), 3.29 – 3.23 (m, 3H), 2.74 (t, J = 12.3 Hz, 2H), 2.62 (d, J = 1.2 Hz, 3H), 2.08 (dd, J = 14.2, 3.8 Hz, 2H), 1.88 – 1.74 (m, 2H).
36	C	3.013	457.2	1H NMR (400 MHz, Methanol- d_4) d 8.17 (s, 1H), 7.61 (td, J = 8.4, 5.6 Hz, 1H), 7.52 (dt, J = 8.3, 1.3 Hz, 1H), 7.44 – 7.37 (m, 3H), 7.14 – 7.06 (m, 2H), 3.70 (s, 4H), 2.55 (d, J = 4.9 Hz, 4H), 2.38 (s, 3H).
37	C	3.915	557.2	
38	C	2.943	457.2	1H NMR (400 MHz, Methanol- d_4) d 8.20 (s, 1H), 7.81 (d, J = 8.8 Hz, 1H), 7.61 (td, J = 8.3, 5.6 Hz, 1H), 7.52 (dt, J = 8.3, 1.4 Hz, 1H), 7.40 (ddd, J = 9.4, 8.6, 1.3 Hz, 1H), 7.08 (d, J = 8.8 Hz, 2H), 4.12 (td, J = 10.1, 4.7 Hz, 1H), 3.29 (d, J = 4.2 Hz, 1H), 3.12 (d, J = 12.8 Hz, 1H), 2.81 – 2.63 (m, 2H), 2.05 (d, J = 11.9 Hz, 1H), 1.92 (s, 2H), 1.80 – 1.57 (m, 2H).
39	C	3.050	473.2	
40	C	3.261	402.2	
41	C	4.256	431.2	1H NMR (400 MHz, Methanol- d_4) d 8.17 (s, 1H), 7.92 – 7.88 (m, 2H), 7.63 (dd, J = 8.1, 1.1 Hz, 2H), 7.55 (dd, J = 9.2, 7.0 Hz, 1H), 7.06 – 7.00 (m, 2H), 1.37 (s, 9H).
42	C	4.156	415.2	1H NMR (400 MHz, Methanol- d_4) d 8.21 (s, 1H), 7.91 (d, J = 8.8 Hz, 2H), 7.59 (td, J = 8.4, 5.6 Hz, 1H), 7.50 (dt, J = 8.3, 1.4 Hz, 1H), 7.38 (ddd, J = 9.7, 8.5, 1.4 Hz, 1H), 7.03 (d, J = 8.9 Hz, 1H), 1.37 (s, 9H).
43	C	3.258	415.0	1H NMR (400 MHz, Methanol- d_4) d 8.01 (s, 1H), 7.66 (d, J = 1.4 Hz, 1H), 7.64 (d, J = 0.7 Hz, 1H), 7.56 (dd, J = 9.2, 7.0 Hz, 1H), 7.37 (d, J = 8.7 Hz, 1H), 7.23 (d, J = 2.2 Hz, 1H), 7.01 (dd, J = 8.6, 2.2 Hz, 1H), 3.77 (s, 3H), 2.57 (s, 3H).
44	C	3.169	399.2	1H NMR (400 MHz, Methanol- d_4) d 8.04 (s, 1H), 7.60 (td, J = 8.4, 5.6 Hz, 1H), 7.51 (dt, J = 8.3, 1.4 Hz, 1H), 7.43 – 7.34 (m, 2H), 7.23 (d, J = 2.2 Hz, 1H), 7.01 (dd, J = 8.6, 2.1 Hz, 1H), 3.77 (s, 3H), 2.57 (s, 3H).
45	C	3.473	440.3	1H NMR (400 MHz, Methanol- d_4) δ 8.94 (d, J = 5.1 Hz, 1H), 8.13 (s, 1H), 7.67 – 7.59 (m, 3H), 7.59 – 7.50 (m, 3H), 7.22 – 7.15 (m, 2H), 2.43 (s, 3H).

Compound No	HPLC-MS Method	retention time (min)	m+H Found	NMR
46	C	3.860	470.2	1H NMR (400 MHz, Methanol- d_4) d 8.15 (s, 1H), 7.67 – 7.61 (m, 4H), 7.57 (dd, J = 9.2, 7.0 Hz, 1H), 7.12 – 6.99 (m, 2H), 4.39 (s, 2H), 4.12 (s, 2H), 2.25 (t, J = 7.6 Hz, 4H), 1.94 – 1.79 (m, 2H).
47	C	3.480	442.0	1H NMR (400 MHz, Methanol- d_4) d 8.18 (s, 1H), 7.98 (s, 1H), 7.66 (dd, J = 8.1, 1.1 Hz, 2H), 7.61 – 7.57 (m, 3H), 7.24 – 7.19 (m, 2H), 4.32 (q, J = 7.2 Hz, 2H), 1.49 (t, J = 7.2 Hz, 3H).
48	C	3.450	428.0	1H NMR (400 MHz, Methanol- d_4) d 8.14 (s, 1H), 7.75 (s, 1H), 7.65 (dd, J = 8.1, 1.1 Hz, 2H), 7.57 (dd, J = 9.2, 7.0 Hz, 1H), 7.48 (d, J = 8.7 Hz, 2H), 7.25 – 7.15 (m, 2H), 4.11 (s, 3H).
49	C	3.430	425.0	1H NMR (400 MHz, Methanol- d_4) d 9.05 (dd, J = 4.9, 1.5 Hz, 1H), 8.17 (s, 1H), 8.12 (dd, J = 8.8, 1.5 Hz, 1H), 8.06 (d, J = 8.8 Hz, 2H), 7.73 (dd, J = 8.7, 4.9 Hz, 1H), 7.66 (dd, J = 8.2, 1.1 Hz, 2H), 7.57 (dd, J = 9.2, 7.0 Hz, 1H), 7.21 (d, J = 8.8 Hz, 2H).
50	C	3.040	501.2	1H NMR (400 MHz, Methanol- d_4) d 8.13 (s, 1H), 7.65 (dd, J = 8.1, 1.1 Hz, 2H), 7.57 (dd, J = 9.2, 7.0 Hz, 1H), 7.40 (d, J = 8.2 Hz, 2H), 7.12 – 7.07 (m, 2H), 3.33 (s, 3H), 3.26 (bs, 1H), 2.98 (s, 3H), 2.60 (s, 4H), 2.09 (td, J = 12.9, 3.9 Hz, 2H), 1.91 (d, J = 13.1 Hz, 2H).
51	C	3.689	440.2	1H NMR (400 MHz, Methanol- d_4) δ 8.49 – 8.43 (m, 1H), 8.40 (d, J = 2.6 Hz, 1H), 8.12 (s, 1H), 7.63 (dd, J = 8.1, 1.0 Hz, 2H), 7.59 – 7.53 (m, 3H), 7.20 – 7.13 (m, 2H), 2.67 – 2.62 (m, 3H).
52	B	3.739	454.2	1H NMR (400 MHz, Methanol- d_4) δ 8.96 (s, 1H), 8.68 (s, 1H), 8.14 (s, 1H), 7.67 – 7.60 (m, 2H), 7.60 – 7.51 (m, 3H), 7.20 – 7.13 (m, 2H), 2.85 (q, J = 7.6 Hz, 2H), 1.20 (t, J = 7.6 Hz, 3H).
53	C	3.858	441.2	
54	C	3.776	454.2	1H NMR (400 MHz, Methanol- d_4) d 8.18 (s, 1H), 7.66 – 7.56 (m, 3H), 7.52 (dt, J = 8.3, 1.4 Hz, 1H), 7.40 (ddd, J = 9.7, 8.4, 1.4 Hz, 1H), 7.10 – 7.03 (m, 2H), 4.39 (s, 2H), 4.12 (s, 2H), 2.25 (t, J = 7.6 Hz, 5H), 1.88 (td, J = 7.6, 4.8 Hz, 2H).
55	C	3.317	468.2	1H NMR (400 MHz, Chloroform-*d*) d 8.49 (s, 1H), 7.69 (s, 1H), 7.53 – 7.46 (m, 2H), 7.41 (dd, J = 9.0, 7.1 Hz, 1H), 7.10 (d, J = 6.3 Hz, 2H), 6.76 (s, 1H), 5.50 (s, 1H), 4.14 (s, 2H), 3.15 (s, 2H), 2.04 (bs, 4H).
56	C	3.385	423.2	1H NMR (400 MHz, Methanol- d_4) δ 8.95 (d, J = 5.2 Hz, 1H), 8.16 (s, 1H), 7.66 – 7.47 (m, 5H), 7.38 (ddd, J = 9.6, 8.4, 1.4 Hz, 1H), 7.23 – 7.15 (m, 2H), 2.44 (s, 3H).

Compound No	HPLC-MS Method	retention time (min)	m+H Found	NMR
57	C	3.146	471.2	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.15 (s, 1H), 7.71 – 7.60 (m, 4H), 7.56 (dd, *J* = 9.2, 7.0 Hz, 1H), 7.22 – 7.15 (m, 2H), 4.99 (s, 2H), 4.21 (dd, J = 6.0, 4.3 Hz, 2H), 4.06 (dd, J = 6.0, 4.3 Hz, 2H).
58	C	3.250	452.2	1H NMR (400 MHz, Methanol- d_4) d 8.19 (s, 1H), 7.66 – 7.57 (m, 3H), 7.52 (dt, J = 8.3, 1.3 Hz, 1H), 7.40 (ddd, J = 9.6, 8.4, 1.4 Hz, 1H), 7.23 – 7.15 (m, 2H), 4.12 (t, J = 5.6 Hz, 2H), 3.02 (t, J = 6.0 Hz, 2H), 2.02 (dt, J = 6.5, 3.6 Hz, 4H).
59	C	3.855	449.0	1H NMR (400 MHz, Chloroform-*d*) d 8.87 (dd, J = 4.9, 1.8 Hz, 1H), 8.53 (s, 1H), 8.08 (dd, J = 7.8, 1.8 Hz, 1H), 8.04 – 7.97 (m, 2H), 7.76 (s, 1H), 7.53 (dd, J = 8.1, 0.9 Hz, 2H), 7.44 (dd, J = 9.1, 7.1 Hz, 1H), 7.34 (dd, J = 7.8, 4.9 Hz, 1H), 7.21 – 7.14 (m, 2H).
60	C	3.579	450.0	
61	C	3.834	488.2	1H NMR (400 MHz, Methanol- d_4) d 8.20 (s, 1H), 7.87 – 7.67 (m, 4H), 7.66 – 7.56 (m, 2H), 7.11 – 6.98 (m, 2H), 4.38 (s, 2H), 4.12 (s, 2H), 2.24 (t, J = 7.6 Hz, 4H), 1.87 (dq, J = 12.6, 7.4 Hz, 2H).
62	C	3.065	454.2	1H NMR (400 MHz, Methanol- d_4) δ 8.18 (s, 1H), 7.71 – 7.64 (m, 2H), 7.59 (td, *J* = 8.3, 5.6 Hz, 1H), 7.51 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.38 (t, *J* = 8.5 Hz, 1H), 7.22 – 7.16 (m, 2H), 4.99 (s, 2H), 4.21 (dd, *J* = 6.0, 4.3 Hz, 2H), 4.07 (dd, *J* = 6.0, 4.3 Hz, 2H).
63	C	3.450	483.4	1H NMR (400 MHz, Methanol- d_4) δ 8.14 (s, 1H), 7.63 (dd, *J* = 8.1, 1.1 Hz, 2H), 7.56 (dd, *J* = 9.2, 7.0 Hz, 1H), 7.46 (d, *J* = 8.6 Hz, 2H), 7.22 – 7.15 (m, 2H), 4.15 – 4.08 (m, 2H), 3.08 – 3.00 (m, 2H), 1.98-1.90 (m, 2H), 1.83 – 1.76 (m, 4H).
64	C	2.856	391.2	
65	C	4.298	463.2	1H NMR (400 MHz, Chloroform-*d*) d 8.27 (s, 1H), 8.16 (d, J = 1.0 Hz, 1H), 7.78 (dt, J = 8.1, 1.0 Hz, 1H), 7.67 (s, 1H), 7.64 (dq, J = 8.6, 1.0 Hz, 1H), 7.61 – 7.56 (m, 2H), 7.49 (dd, J = 8.1, 0.9 Hz, 2H), 7.41 – 7.35 (m, 2H), 7.18 – 7.14 (m, 2H), 6.75 (s, 1H), 5.42 (s, 1H).
66	C	4.189	463.2	
67	C	3.688	460.2	
68	C	3.232	445.2	

Compound No	HPLC-MS Method	retention time (min)	m+H Found	NMR
69	C	3.806	494.2	1H NMR (400 MHz, Methanol- d_4) δ 9.42 (d, J = 5.3 Hz, 1H), 8.15 (s, 1H), 8.09 (d, J = 5.4 Hz, 1H), 7.67 – 7.60 (m, 2H), 7.60 – 7.50 (m, 3H), 7.22 – 7.15 (m, 2H).
70	C	3.656	469.2	1H NMR (400 MHz, Methanol- d_4) d 8.04 (d, J = 0.8 Hz, 1H), 7.85 (d, J = 0.7 Hz, 1H), 7.64 – 7.59 (m, 2H), 7.54 (dd, J = 9.3, 6.9 Hz, 1H), 7.44 (s, 1H), 7.41 – 7.35 (m, 2H), 7.18 – 7.12 (m, 2H), 4.73 (d, J = 1.3 Hz, 2H), 3.92 (t, J = 5.5 Hz, 2H), 2.81 (dd, J = 6.2, 4.9 Hz, 2H).
71	C	3.706	469.2	1H NMR (400 MHz, Methanol- d_4) d 7.99 (d, J = 0.9 Hz, 1H), 7.76 (s, 1H), 7.64 – 7.58 (m, 2H), 7.56 – 7.50 (m, 3H), 7.15 – 7.07 (m, 2H), 4.75 (d, J = 0.9 Hz, 2H), 3.99 (t, J = 5.7 Hz, 2H), 2.83 (t, J = 5.7 Hz, 2H).
72	C	3.470	455.0	1H NMR (400 MHz, Methanol- d_4) d 8.11 (s, 1H), 7.67 – 7.62 (m, 2H), 7.56 (dd, J = 9.2, 7.0 Hz, 1H), 7.48 – 7.40 (m, 3H), 7.17 – 7.11 (m, 2H), 7.01 (d, J = 9.5 Hz, 1H), 2.40 (s, 3H).
73	C	3.855	468.2	1H NMR (400 MHz, Methanol- d_4) d 8.01 (d, J = 3.0 Hz, 1H), 7.78 (d, J = 2.9 Hz, 1H), 7.61 (d, J = 8.8 Hz, 2H), 7.54 (dd, J = 9.3, 6.8 Hz, 1H), 7.48 – 7.42 (m, 2H), 7.22 – 7.16 (m, 2H), 2.82 – 2.70 (m, 4H), 1.90 (p, J = 3.7 Hz, 4H).
74	C	3.326	461.2	1H NMR (400 MHz, Methanol- d_4) δ 8.61 (s, 1H), 8.36 (dd, J = 2.3, 0.8 Hz, 1H), 7.68 (dd, J = 8.7, 2.3 Hz, 1H), 7.66 – 7.59 (m, 2H), 7.55 (dd, J = 9.2, 6.9 Hz, 1H), 6.93 (dd, J = 8.7, 0.8 Hz, 1H), 3.91-3.49 (m, 8H).
75	C	3.940	427.2	1H NMR (400 MHz, Methanol- d_4) d 8.07 (s, 1H), 7.93 (d, J = 2.4 Hz, 1H), 7.65 (dd, J = 8.1, 1.1 Hz, 2H), 7.56 (dd, J = 9.2, 7.2 Hz, 3H), 7.18 – 7.11 (m, 2H), 6.28 (d, J = 2.4 Hz, 1H), 2.34 (s, 3H).
76	C	4.198	447.0	1H NMR (400 MHz, Methanol- d_4) d 8.09 (s, 1H), 8.08 (d, J = 2.5 Hz, 1H), 7.65 (dd, J = 8.1, 1.1 Hz, 2H), 7.62 – 7.54 (m, 3H), 7.15 (d, J = 9.0 Hz, 2H), 6.44 (d, J = 2.5 Hz, 1H).
77	C	3.719	443.2	1H NMR (400 MHz, Methanol- d_4) d 7.96 (s, 1H), 7.63 (dd, J = 8.1, 1.1 Hz, 2H), 7.55 (dd, J = 9.2, 7.0 Hz, 1H), 7.44 (d, J = 2.4 Hz, 1H), 5.69 (d, J = 2.4 Hz, 1H), 3.77 (s, 3H).
78	C	3.054	443.2	
79	C	3.845	448.0	1H NMR (400 MHz, Chloroform-d) d 8.42 (s, 1H), 8.35 (s, 1H), 7.68 (s, 1H), 7.58 – 7.50 (m, 4H), 7.45 (dd, J = 9.0, 7.1 Hz, 1H), 7.16 – 7.09 (m, 2H), 6.79 (s, 1H), 5.44 (s, 1H).

Compound No	HPLC-MS Method	retention time (min)	m+H Found	NMR
80	C	3.820	427.2	1H NMR (400 MHz, Methanol- d_4) d 8.12 (s, 1H), 7.68 – 7.62 (m, 2H), 7.57 (dd, J = 9.2, 7.0 Hz, 1H), 7.52 (d, J = 1.8 Hz, 2H), 7.36 – 7.30 (m, 2H), 7.20 – 7.13 (m, 2H), 6.25 (s, 1H), 2.30 (s, 3H).
81	C	4.030	465.2	1H NMR (400 MHz, Chloroform-*d*) δ 8.44 (s, 1H), 8.11 (s, 1H), 7.72 (s, 1H), 7.72 – 7.62 (m, 3H), 7.53 (dd, *J* = 8.6, 7.3 Hz, 2H), 7.47 - 7.37 (m, 2H), 7.26 – 7.19 (m, 2H), 6.79 (brs, 1H), 5.45 br (s, 1H).
82	A	3.942	458.2	^{1}H NMR (400 MHz, Methanol- d_4) δ 8.12 (s, 1H), 7.66 (d, *J* = 1.5 Hz, 1H), 7.64 (d, *J* = 0.7 Hz, 1H), 7.59 – 7.56 (m, 1H), 7.39 – 7.35 (m, 2H), 7.11 – 7.06 (m, 2H), 3.61 (m, *J* = 34.7 Hz, 4H), 1.73 (m, *J* = 5.8 Hz, 2H), 1.63 (m, 4H).
83	A	3.428	523.2	^{1}H NMR (400 MHz, Methanol- d_4) δ 8.13 (s, 1H), 7.65 (dd, *J* = 8.1, 1.1 Hz, 2H), 7.57 (dd, *J* = 9.2, 7.0 Hz, 1H), 7.45 – 7.37 (m, 2H), 7.14 – 7.06 (m, 2H), 6.25 – 5.89 (m, 1H), 3.72 (m, *J* = 7.5 Hz, 4H), 2.99 (td, *J* = 15.1, 4.2 Hz, 2H), 2.81 (d, *J* = 5.1 Hz, 4H).
84	C	3.625	499.2	^{1}H NMR (400 MHz, Methanol- d_4) δ 8.13 (s, 1H), 7.65 (dd, *J* = 8.1, 1.1 Hz, 2H), 7.57 (dd, *J* = 9.2, 7.0 Hz, 1H), 7.42 – 7.37 (m, 2H), 7.12 – 7.07 (m, 2H), 3.63 (m, 4H), 2.68 (m, 4H), 1.73 (tt, *J* = 6.6, 3.7 Hz, 1H), 0.56 – 0.49 (m, *J* = 2.8 Hz, 2H), 0.49 – 0.43 (m, 2H).
85	C	3.414	560.2	1H NMR (400 MHz, Methanol- d_4) δ 8.20 (s, 1H), 7.70 – 7.61 (m, 4H), 7.56 (dd, *J* = 9.2, 6.9 Hz, 1H), 7.19 – 7.13 (m, 2H), 3.01 (brs, 4H), 2.52 (brs, 4H), 2.27 (s, 3H).
86	A	2.901	513.2	^{1}H NMR (600 MHz, Methanol- d_4) δ 8.10 (s, 1H), 7.61 (d, *J* = 8.1 Hz, 2H), 7.54 (dd, *J* = 8.9, 7.4 Hz, 1H), 7.39 – 7.35 (m, 2H), 7.08 – 7.04 (m, 2H), 3.67 (m, 4H), 2.60 (m, 4H), 2.32 (d, *J* = 6.7 Hz, 2H), 0.93 – 0.85 (m, 1H), 0.57 – 0.50 (m, 2H), 0.15 (q, *J* = 5.1 Hz, 2H).
87	C	3.234	442.2	1H NMR (400 MHz, Methanol- d_4) d 8.61 (s, 1H), 8.17 (s, 1H), 7.68 – 7.63 (m, 2H), 7.62 – 7.56 (m, 3H), 7.24 – 7.19 (m, 2H), 4.19 (q, J = 7.3 Hz, 2H), 1.42 (t, J = 7.3 Hz, 3H).
88	C	3.103	428.2	1H NMR (400 MHz, Methanol- d_4) d 8.51 (s, 1H), 8.17 (d, J = 0.9 Hz, 1H), 7.68 – 7.61 (m, 4H), 7.57 (ddd, J = 9.2, 7.0, 0.7 Hz, 1H), 7.24 – 7.18 (m, 2H), 3.82 (s, 3H).

Compound No	HPLC-MS Method	retention time (min)	m+H Found	NMR
89	C	3.080	524.2	1H NMR (400 MHz, Methanol- d_4) δ 8.18 (s, 1H), 7.78 – 7.72 (m, 2H), 7.67 – 7.61 (m, 2H), 7.56 (dd, J = 9.2, 6.9 Hz, 1H), 7.15 – 7.08 (m, 2H), 3.17 - 3.04 (m, 1H), 2.96 - 2.92 (m, 2H), 2.40 - 2.36 (m, 5H), 1.80 - 1.76 (m, 2H), 1.61 – 1.53 (m, 2H).
90	C	3.669	458.2	
91	C	2.947	487.2	^{1}H NMR (400 MHz, Methanol- d_4) δ 8.07 (s, 1H), 7.63 – 7.58 (m, 2H), 7.53 (dd, J = 9.2, 7.0 Hz, 1H), 7.38 (d, J = 8.2 Hz, 2H), 7.09 – 7.01 (m, 2H), 3.72 (m, J = 44.2 Hz, 4H), 3.04 (m, 1H), 2.87 (s, 3H), 2.58 (m, 3H), 2.00 (m, 2H).
92	C	3.363	430.2	
93	C	3.839	541.2	
94	C	3.526	444.2	^{1}H NMR (400 MHz, Methanol- d_4) δ 8.08 (s, 1H), 7.60 (dd, J = 8.1, 1.1 Hz, 2H), 7.55 – 7.52 (m, 1H), 7.49 (dd, J = 8.4, 1.7 Hz, 2H), 7.07 – 7.00 (m, 2H), 3.55 (t, J = 6.7 Hz, 4H), 1.95 (q, J = 6.6 Hz, 2H), 1.88 (q, J = 6.4 Hz, 2H).
95	C	3.897	472.2	^{1}H NMR (400 MHz, Methanol- d_4) δ 8.06 (s, 1H), 7.62 – 7.58 (m, 2H), 7.52 (dd, J = 9.2, 7.0 Hz, 1H), 7.36 – 7.26 (m, 2H), 7.09 – 7.01 (m, 2H), 3.62 (m, 2H), 3.50 (m, 2H), 1.80 (m, 2H), 1.64 (m, 4H), 1.59 (m, 2H).
96	C	3.325	430.2	1H NMR (400 MHz, Methanol- d_4) δ 8.15 (s, 1H), 7.94 (s, 1H), 7.77 – 7.60 (m, 4H), 7.56 (dd, J = 9.2, 7.0 Hz, 1H), 7.31 – 6.96 (m, 2H), 3.99 (s, 3H).
201	C	4.265	496.0	1H NMR (400 MHz, Methanol-d4) d 8.16 (s, 1H), 7.68 – 7.63 (m, 2H), 7.60 – 7.56 (m, 2H), 7.34 – 7.28 (m, 3H), 7.28 – 7.22 (m, 3H), 6.85 (dd, J = 7.9, 1.2 Hz, 1H).
202	C	3.573	482.2	1H NMR (400 MHz, Methanol-d4) d 8.70 (s, 1H), 8.15 (s, 1H), 7.68 – 7.59 (m, 2H), 7.59 – 7.48 (m, 3H), 7.25 – 7.14 (m, 2H), 4.66 (d, J = 7.3 Hz, 1H), 2.30 – 2.12 (m, 2H), 1.89 (d, J = 13.6 Hz, 4H), 1.79 – 1.64 (m, 2H).
203	C	3.500	470.00	1H NMR (400 MHz, Methanol-d4) d 8.56 (s, 1H), 8.16 (s, 1H), 7.63 (dd, J = 8.1, 1.1 Hz, 2H), 7.60 – 7.48 (m, 3H), 7.25 – 7.07 (m, 2H), 3.98 (d, J = 7.5 Hz, 2H), 1.95 (dt, J = 13.7, 6.9 Hz, 1H), 0.81 (d, J = 6.7 Hz, 6H).
204	C	3.38	427.2	

Compound No	HPLC-MS Method	retention time (min)	m+H Found	NMR
205	C	3.354	456.00	1H NMR (400 MHz, Methanol-d_4) δ 8.73 (s, 1H), 8.13 (s, 1H), 7.61 (dd, J = 8.1, 1.0 Hz, 2H), 7.53 (dd, J = 9.2, 7.0 Hz, 1H), 7.50 – 7.45 (m, 2H), 7.20 – 7.15 (m, 2H), 4.54 (h, J = 6.7 Hz, 1H), 1.48 (d, J = 6.7 Hz, 6H).
206	C	3.295	454.00	1H NMR (400 MHz, Methanol-d_4) δ 8.56 (s, 1H), 8.19 (s, 1H), 7.85 – 7.79 (m, 2H), 7.66 (dd, J = 8.1, 1.1 Hz, 2H), 7.58 (dd, J = 9.2, 7.0 Hz, 1H), 7.23 – 7.16 (m, 2H), 3.61 (tt, J = 7.3, 3.8 Hz, 1H), 1.18 – 1.10 (m, 2H), 1.00 – 0.93 (m, 2H).
207	C	3.14	426.2	1H NMR (400 MHz, Methanol-d_4) δ 8.60 (s, 1H), 8.18 (s, 1H), 7.66 – 7.47 (m, 4H), 7.38 (ddd, J = 9.6, 8.4, 1.4 Hz, 1H), 7.26 – 7.13 (m, 2H), 4.18 (q, J = 7.3 Hz, 2H), 1.40 (t, J = 7.3 Hz, 3H).
208	C	3.56	453.2	1H NMR (400 MHz, Methanol-d_4) δ 8.12 (s, 1H), 7.58 (td, J = 8.3, 5.6 Hz, 1H), 7.50 (dt, J = 8.3, 1.3 Hz, 1H), 7.47 – 7.31 (m, 4H), 7.21 – 7.09 (m, 2H), 4.72 (2, 2H), 3.91 (t, J = 5.7 Hz, 2H), 2.81 (t, J = 5.7 Hz, 2H).
209	C	3.61	453.2	1H NMR (400 MHz, Methanol-d_4) δ 8.09 (s, 1H), 7.79 (s, 1H), 7.62 – 7.47 (m, 4H), 7.42 – 7.33 (m, 1H), 7.15 – 7.07 (m, 2H), 4.75 (s, 2H), 3.99 (t, J = 5.7 Hz, 2H), 2.83 (t, J = 5.7 Hz, 2H).
210	C	3.400	496.00	1H NMR (400 MHz, Methanol-d4) d 8.71 (s, 1H), 8.19 (s, 1H), 7.65 (dd, J = 8.1, 1.1 Hz, 2H), 7.60 – 7.52 (m, 3H), 7.27 – 7.19 (m, 2H), 5.00 (q, J = 8.6 Hz, 2H).
211	C	3.570	440.20	1H NMR (400 MHz, Methanol-d4) d 8.20 (s, 1H), 7.99 (d, J = 0.7 Hz, 1H), 7.61 (td, J = 8.3, 5.6 Hz, 1H), 7.56 – 7.49 (m, 3H), 7.40 (td, J = 8.8, 8.4, 1.4 Hz, 1H), 7.25 – 7.18 (m, 2H), 4.80 (p, J = 6.7 Hz, 1H), 1.51 (d, J = 6.6 Hz, 6H).
212	C	3.240	478.00	1H NMR (400 MHz, Methanol-d4) d 8.63 (d, J = 1.1 Hz, 1H), 8.18 (s, 1H), 7.65 (dd, J = 8.1, 1.1 Hz, 2H), 7.60 – 7.52 (m, 3H), 7.25 – 7.18 (m, 2H), 6.22 (tt, J = 54.3, 2.9 Hz, 1H), 4.60 (td, J = 15.5, 2.9 Hz, 2H).
213	C	3.590	453.20	1H NMR (400 MHz, Methanol-d4) d 8.88 (s, 1H), 8.14 (s, 1H), 7.68 – 7.63 (m, 2H), 7.57 (dd, J = 9.2, 7.0 Hz, 1H), 7.51 – 7.46 (m, 2H), 7.23 – 7.17 (m, 2H), 2.43 (s, 3H), 2.36 (s, 3H).
214	C	2.94	485.2	1H NMR (400 MHz, Methanol-d_4) δ 8.16 (s, 1H), 7.71 – 7.50 (m, 6H), 7.20 (d, J = 8.7 Hz, 2H), 4.29 (t, J = 6.6 Hz, 2H), 2.77 (t, J = 6.6 Hz, 2H), 2.30 (s, 6H).
215	C	4.070	496.00	1H NMR (400 MHz, Methanol-d4) d 8.19 (s, 1H), 7.76 – 7.68 (m, 2H), 7.66 (dd, J = 8.1, 1.1 Hz, 2H), 7.58 (dd, J = 9.2, 7.0 Hz, 1H), 7.26 – 7.18 (m, 2H), 4.08 (s, 3H).

Compound No	HPLC-MS Method	retention time (min)	m+H Found	NMR
216	C	3.846	441.20	1H NMR (400 MHz, Methanol-d4) d 8.11 (s, 1H), 7.65 (dd, J = 8.1, 1.1 Hz, 2H), 7.57 (dd, J = 9.2, 7.0 Hz, 1H), 7.34 – 7.28 (m, 2H), 7.19 – 7.13 (m, 2H), 6.03 (s, 1H), 2.31 – 2.15 (m, 6H).
217	C	4.120	441.20	1H NMR (400 MHz, Methanol-d4) d 8.06 (s, 1H), 7.76 (s, 1H), 7.65 (dd, J = 8.1, 1.0 Hz, 2H), 7.56 (dd, J = 9.2, 7.0 Hz, 1H), 7.54 – 7.49 (m, 2H), 7.16 – 7.09 (m, 2H), 2.26 (s, 3H), 2.09 (d, J = 0.9 Hz, 3H).
218	C	3.997	441.20	1H NMR (400 MHz, Methanol-d4) d 8.12 (s, 1H), 7.65 (dd, J = 8.1, 1.1 Hz, 2H), 7.57 (dd, J = 9.2, 7.0 Hz, 1H), 7.39 (s, 1H), 7.35 – 7.27 (m, 2H), 7.19 – 7.12 (m, 2H), 2.20 (s, 3H), 2.08 (s, 3H).
219	C	4.384	475.00	1H NMR (400 MHz, Methanol-d4) d 8.13 (s, 1H), 7.65 (dd, J = 8.1, 1.1 Hz, 2H), 7.57 (dd, J = 9.2, 7.0 Hz, 1H), 7.35 – 7.30 (m, 2H), 7.20 – 7.14 (m, 2H), 2.25 (s, 3H), 2.24 (s, 3H).
220	C	4.421	461.20	1H NMR (400 MHz, Methanol-d4) d 8.12 (s, 1H), 8.08 (s, 1H), 7.65 (dd, J = 8.1, 1.1 Hz, 2H), 7.57 (dt, J = 9.1, 3.6 Hz, 3H), 7.18 – 7.11 (m, 2H), 2.30 (s, 3H).
221	C	4.243	461.20	1H NMR (400 MHz, Methanol-d4) d 8.13 (s, 1H), 7.65 (dd, J = 8.1, 1.1 Hz, 2H), 7.60 – 7.56 (m, 2H), 7.37 – 7.32 (m, 2H), 7.21 – 7.15 (m, 2H), 2.27 (s, 3H).
222	C	4.274	469.20	1H NMR (600 MHz, Methanol-d4) d 8.08 (s, 1H), 7.64 – 7.60 (m, 2H), 7.54 (dd, J = 8.9, 7.4 Hz, 1H), 7.28 – 7.24 (m, 2H), 7.15 – 7.10 (m, 2H), 2.44 (q, J = 7.6 Hz, 2H), 2.20 (s, 3H), 2.16 (s, 3H), 1.11 (t, J = 7.5 Hz, 3H).
223	C	4.329	469.20	1H NMR (600 MHz, Methanol-d4) d 8.10 (s, 1H), 7.64 – 7.59 (m, 2H), 7.54 (dd, J = 8.9, 7.4 Hz, 1H), 7.29 – 7.23 (m, 2H), 7.16 – 7.10 (m, 2H), 6.08 (s, 1H), 2.60 (dq, J = 20.4, 7.6 Hz, 4H), 1.24 (t, J = 7.6 Hz, 3H), 1.16 (t, J = 7.5 Hz, 3H).
224	C	4.105	455.20	1H NMR (600 MHz, Methanol-d4) d 8.08 (s, 1H), 7.65 – 7.58 (m, 2H), 7.54 (dd, J = 8.9, 7.5 Hz, 1H), 7.29 – 7.23 (m, 2H), 7.17 – 7.08 (m, 2H), 2.17 (s, 3H), 2.14 (s, 3H), 1.97 (s, 3H).
225	C	3.09	427.2	1H NMR (400 MHz, Methanol-d_4) δ 8.11 (s, 1H), 7.67 – 7.47 (m, 5H), 7.20 – 7.08 (m, 3H), 6.99 (d, J = 1.4 Hz, 1H), 3.74 (s, 3H).
226	C	3.547	445.20	1H NMR (400 MHz, Methanol-d4) d 8.63 (s, 1H), 8.50 (dd, J = 2.4, 0.8 Hz, 1H), 7.81 (dd, J = 8.7, 2.3 Hz, 1H), 7.65 (dd, J = 8.1, 1.1 Hz, 2H), 7.57 (dd, J = 9.2, 6.9 Hz, 1H), 6.93 (dd, J = 8.7, 0.8 Hz, 1H), 3.62 (q, J = 7.2 Hz, 4H), 2.00 (td, J = 12.1, 11.6, 6.1 Hz, 4H).

Compound No	HPLC-MS Method	retention time (min)	m+H Found	NMR
227	C	3.43	428.2	1H NMR (400 MHz, Methanol-d_4) δ 8.14 (s, 1H), 7.66 – 7.43 (m, 4H), 7.37 (ddd, J = 9.6, 8.4, 1.4 Hz, 1H), 7.13 – 6.99 (m, 2H), 3.57 (t, J = 6.7 Hz, 4H), 2.00-1.88 (m, 4H).
228	C	3.68	442.2	1H NMR (400 MHz, Methanol-d_4) δ 8.13 (s, 1H), 7.57 (dd, J = 8.3, 5.6 Hz, 1H), 7.50 (dt, J = 8.3, 1.4 Hz, 1H), 7.43 – 7.27 (m, 3H), 7.13 – 6.96 (m, 2H), 3.58 (brs, 4H), 1.66 (brs, 6H).
229	C	3.442	441.20	1H NMR (400 MHz, Methanol-d4) d 8.13 (s, 1H), 7.65 (dd, J = 8.1, 1.0 Hz, 2H), 7.57 (dd, J = 9.2, 7.0 Hz, 1H), 7.52 – 7.47 (m, 2H), 7.24 (d, J = 1.5 Hz, 1H), 7.20 – 7.14 (m, 2H), 7.06 (d, J = 1.5 Hz, 1H), 4.11 (q, J = 7.3 Hz, 2H), 1.40 (t, J = 7.3 Hz, 3H).
230	C	3.525	477.20	1H NMR (400 MHz, Methanol-d4) d 8.14 (s, 1H), 7.65 (dd, J = 8.1, 1.1 Hz, 2H), 7.57 (dd, J = 9.2, 7.0 Hz, 1H), 7.51 – 7.45 (m, 2H), 7.29 (d, J = 1.4 Hz, 1H), 7.21 – 7.14 (m, 2H), 7.10 (d, J = 1.5 Hz, 1H), 6.16 (tt, J = 54.8, 3.4 Hz, 1H), 4.47 (td, J = 15.0, 3.4 Hz, 2H).
231	B	3.96	479.2	1H NMR (400 MHz, Methanol-d_4) δ 8.20 (d, J = 0.5 Hz, 1H), 7.71 (d, J = 8.8 Hz, 2H), 7.59 (td, J = 8.3, 5.6 Hz, 1H), 7.54 – 7.48 (m, 1H), 7.38 (ddd, J = 9.2, 8.4, 1.4 Hz, 1H), 7.20 (d, J = 8.9 Hz, 2H), 4.06 (s, 3H).
232	B	3.8	410.2	1H NMR (400 MHz, Methanol-d_4) δ 8.14 (s, 1H), 7.58 (td, J = 8.4, 5.6 Hz, 1H), 7.53 – 7.46 (m, 2H), 7.37 (ddd, J = 9.6, 8.4, 1.4 Hz, 1H), 7.32 (d, J = 8.8 Hz, 2H), 7.15 (d, J = 8.8 Hz, 2H), 6.23 (dd, J = 1.9, 0.9 Hz, 1H), 2.28 (d, J = 0.6 Hz, 3H).
233	B	3.69	410.2	1H NMR (400 MHz, Methanol-d_4) δ 8.14 (d, J = 0.5 Hz, 1H), 7.58 (td, J = 8.3, 5.6 Hz, 1H), 7.53 – 7.46 (m, 2H), 7.42 – 7.33 (m, 1H), 7.32 (d, J = 8.9 Hz, 1H), 7.16 (d, J = 8.9 Hz, 2H), 6.23 (dd, J = 1.9, 0.8 Hz, 1H), 2.28 (t, J = 0.6 Hz, 3H).
234	C	4.11	452.2	
235	C	3.45	446.2	
236	C	4.78	535.2	1H NMR (400 MHz, Methanol-d_4) δ 8.11 (s, 1H), 7.69 – 7.48 (m, 3H), 7.45 – 7.34 (m, 2H), 7.23 – 7.00 (m, 2H), 2.71-2.61 (m, 4H), 1.84-1.81 (m, 4H).

Compound No	HPLC-MS Method	retention time (min)	m+H Found	NMR
237	C	3.165	460.20	1H NMR (400 MHz, Methanol-d4) d 7.87 (s, 1H), 7.63 (dd, J = 8.1, 1.1 Hz, 2H), 7.55 (dd, J = 9.2, 7.0 Hz, 1H), 7.05 – 6.99 (m, 2H), 6.99 – 6.93 (m, 2H), 4.47 (s, 1H), 3.24 – 3.13 (m, 2H), 2.97 (s, 2H), 2.70 (s, 3H), 2.15 – 1.93 (m, 4H).
238	C	3.436	429.20	1H NMR (400 MHz, Methanol-d4) d 8.21 (s, 1H), 7.81 – 7.73 (m, 2H), 7.66 (dd, J = 8.1, 1.1 Hz, 2H), 7.58 (dd, J = 9.2, 7.0 Hz, 1H), 7.29 – 7.19 (m, 2H), 4.22 (s, 3H).
239	C	4.53	441.2	1H NMR (400 MHz, Methanol-d_4) δ 8.04 (s, 1H), 7.70 – 7.46 (m, 7H), 7.17 – 6.99 (m, 4H).
240	C	4.181	441.20	1H NMR (400 MHz, Methanol-d4) d 8.07 (s, 1H), 7.94 (d, J = 2.4 Hz, 1H), 7.65 (dd, J = 8.1, 1.1 Hz, 2H), 7.60 – 7.53 (m, 3H), 7.18 – 7.11 (m, 2H), 6.32 (d, J = 2.4 Hz, 1H), 2.72 (q, J = 7.6 Hz, 2H), 1.30 (t, J = 7.6 Hz, 3H).
241	C	4.012	441.20	1H NMR (400 MHz, Methanol-d4) d 8.13 (s, 1H), 7.65 (dd, J = 8.1, 1.1 Hz, 2H), 7.61 – 7.55 (m, 1H), 7.55 – 7.52 (m, 1H), 7.36 – 7.29 (m, 2H), 7.21 – 7.14 (m, 2H), 6.28 (dd, J = 1.9, 0.9 Hz, 1H), 2.66 (q, J = 7.6 Hz, 2H), 1.21 (t, J = 7.5 Hz, 3H).
242	C	3.67	96.2	
243	C	3.472	429.20	1H NMR (400 MHz, Methanol-d4) d 8.19 (s, 1H), 7.66 (dd, J = 8.1, 1.1 Hz, 2H), 7.58 (dd, J = 9.2, 7.0 Hz, 1H), 7.50 – 7.44 (m, 2H), 7.28 – 7.22 (m, 2H), 2.59 (s, 3H).
244	C	4.551	441.20	1H NMR (400 MHz, Methanol-d4) d 8.07 (s, 1H), 7.65 (dd, J = 8.1, 1.1 Hz, 2H), 7.62 – 7.56 (m, 3H), 7.44 – 7.39 (m, 2H), 7.32 (dt, J = 10.7, 1.9 Hz, 1H), 7.16 – 7.10 (m, 2H), 7.03 – 6.96 (m, 1H).
245	C	4.549	459.00	1H NMR (400 MHz, Methanol-d4) d 8.09 (s, 1H), 7.67 – 7.62 (m, 2H), 7.60 – 7.56 (m, 1H), 7.54 – 7.49 (m, 2H), 7.23 (td, J = 6.2, 3.1 Hz, 1H), 7.15 (d, J = 1.0 Hz, 1H), 7.15 – 7.11 (m, 2H), 7.02 (ddt, J = 9.0, 7.6, 3.4 Hz, 1H).
246	A	3.619	462.2	1H NMR (600 MHz, cd3od) δ 8.12 (s, 1H), 7.64 – 7.60 (m, 2H), 7.57 – 7.50 (m, 3H), 7.09 – 7.05 (m, 2H), 5.28 (t, J = 55.1 Hz, 1H), 3.94 – 3.65 (m, 4H), 2.37 – 2.05 (m, 2H).
247	A	3.835	481.2	1H NMR (600 MHz, cd3od) δ 8.12 (s, 1H), 7.65 – 7.60 (m, 2H), 7.58 – 7.50 (m, 3H), 7.09 – 7.05 (m, 2H), 3.94 (t, J = 12.6 Hz, 2H), 3.88 – 3.78 (m, 2H), 2.43 (s, 2H).

Compound No	HPLC-MS Method	retention time (min)	m+H Found	NMR
248	A	2.774	487.2	1H NMR (600 MHz, cd3od) δ 8.11 (s, 1H), 7.65 – 7.60 (m, 2H), 7.57 – 7.48 (m, 3H), 7.08 – 7.03 (m, 2H), 3.89 – 3.53 (m, 4H), 3.48 – 3.38 (m, 1H), 2.86 (d, J = 72.7 Hz, 1H), 2.34 (s, 3H), 2.25 (s, 3H), 1.84 (dq, J = 28.9, 9.8 Hz, 1H).
249	A	2.822	513.2	1H NMR (600 MHz, cd3od) δ 8.11 (s, 1H), 7.62 (d, J = 8.0 Hz, 2H), 7.57 – 7.49 (m, 3H), 7.06 (d, J = 7.5 Hz, 2H), 3.86 – 3.55 (m, 3H), 3.48 (dd, J = 11.4, 8.0 Hz, 1H), 2.90 (d, J = 76.4 Hz, 1H), 2.61 (d, J = 83.4 Hz, 4H), 2.18 (d, J = 50.1 Hz, 1H), 1.83 (d, J = 38.4 Hz, 5H).
250	C	4.36	455.2	1H NMR (400 MHz, Chloroform-*d*) δ 8.16 (s, 1H), 7.61 (s, 1H), 7.56 – 7.47 (m, 4H), 7.41 (dd, *J* = 9.0, 7.1 Hz, 1H), 7.11 – 7.03 (m, 2H), 2.71 (q, *J* = 7.6 Hz, 2H), 2.09 (s, 3H), 1.29 (t, *J* = 7.6 Hz, 7H).
251	C	3.075	484.20	1H NMR (400 MHz, Methanol-d4) d 8.09 (s, 1H), 7.63 – 7.59 (m, 2H), 7.53 (dd, J = 9.2, 7.0 Hz, 1H), 7.46 (d, J = 8.2 Hz, 2H), 7.22 (s, 1H), 7.13 (d, J = 8.1 Hz, 2H), 6.99 (s, 1H), 4.15 (t, J = 7.1 Hz, 2H), 2.61 (t, J = 7.1 Hz, 2H), 2.16 (s, 6H).
252	C	4.028	452.20	1H NMR (400 MHz, Chloroform-d) d 8.34 (s, 1H), 8.08 (s, 1H), 7.64 (s, 1H), 7.53 – 7.49 (m, 4H), 7.42 (dd, J = 9.0, 7.1 Hz, 1H), 7.12 – 7.06 (m, 2H), 6.76 (s, 1H), 5.41 (s, 1H), 2.47 (s, 3H).
253	C	3.867	452.20	1H NMR (400 MHz, Chloroform-d) d 8.42 (s, 1H), 7.83 (s, 1H), 7.67 (s, 1H), 7.51 (dd, J = 8.1, 1.0 Hz, 2H), 7.42 (dd, J = 9.1, 7.1 Hz, 1H), 7.32 – 7.27 (m, 2H), 7.13 – 7.07 (m, 2H), 6.77 (s, 1H), 5.44 (s, 1H), 2.44 (s, 3H).
254	C	3.959	516.2	1H NMR (400 MHz, cd3od) δ 8.11 (s, 1H), 7.61 (dd, J = 8.1, 1.1 Hz, 2H), 7.57 – 7.49 (m, 3H), 7.10 – 7.04 (m, 2H), 4.18 (t, J = 13.6 Hz, 4H).
255	C	4.51	441.2	1H NMR (600 MHz, Methanol-d_4) δ 8.05 (s, 1H), 7.66 – 7.60 (m, 2H), 7.55 (dd, *J* = 8.9, 7.5 Hz, 1H), 7.51 – 7.43 (m, 3H), 7.31 – 7.24 (m, 1H), 7.22 – 7.17 (m, 1H), 7.16 – 7.07 (m, 3H).
256	C	4.27	448.2	1H NMR (600 MHz, Methanol-d_4) δ 8.10 (s, 1H), 7.78 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.68 (td, *J* = 7.7, 1.4 Hz, 1H), 7.65 – 7.61 (m, 2H), 7.58 – 7.54 (m, 2H), 7.54 – 7.50 (m, 2H), 7.45 (td, *J* = 7.6, 1.2 Hz, 1H), 7.17 – 7.13 (m, 2H).
257	C	4.38	495.2	1H NMR (600 MHz, Chloroform-*d*) δ 8.36 (brs, 1H), 7.66 (s, 1H), 7.52 – 7.48 (m, 2H), 7.42 (dd, *J* = 8.8, 7.5 Hz, 1H), 7.34 – 7.30 (m, 2H), 7.12 – 7.07 (m, 2H), 6.77 (brs, 1H), 6.42 (s, 1H), 5.46 (brs, 1H), 2.30 (s, 3H).

Compound No	HPLC-MS Method	retention time (min)	m+H Found	NMR
258	C	4.35	495.2	1H NMR (600 MHz, Chloroform-*d*) δ 8.36 (brs, 1H), 7.66 (s, 1H), 7.52 – 7.48 (m, 2H), 7.41 (dd, *J* = 8.8, 7.5 Hz, 1H), 7.37 – 7.32 (m, 2H), 7.08 – 7.04 (m, 2H), 6.75 (brs, 1H), 6.55 (s, 1H), 5.39 (brs, 1 H), 2.35 (s, 3H).
259	C	3.629	443.20	1H NMR (600 MHz, Methanol-d4) d 8.17 (s, 1H), 7.65 – 7.61 (m, 2H), 7.55 (dd, J = 8.9, 7.4 Hz, 1H), 7.43 – 7.40 (m, 2H), 7.25 – 7.19 (m, 2H), 2.91 (q, J = 7.6 Hz, 2H), 1.32 (t, J = 7.6 Hz, 3H).
260	C	3.91	438.2	1H NMR (400 MHz, Methanol-d_4) δ 8.31 (t, *J* = 2.6 Hz, 2H), 8.07 (s, 1H), 7.63 (dd, *J* = 8.1, 1.0 Hz, 2H), 7.55 (dd, *J* = 9.2, 7.0 Hz, 1H), 7.33 (d, *J* = 5.1 Hz, 1H), 7.31 – 7.24 (m, 2H), 7.18 – 7.09 (m, 2H), 2.35 (s, 3H).
261	C	4.226	405.20	1H NMR (400 MHz, Methanol-d4) d 7.80 (s, 1H), 7.60 – 7.56 (m, 2H), 7.50 (dd, J = 9.2, 7.0 Hz, 1H), 6.97 – 6.93 (m, 2H), 6.85 – 6.81 (m, 2H), 4.43 (p, J = 6.1 Hz, 1H), 1.26 (s, 3H), 1.24 (s, 3H).
262	C	4.403	455.20	1H NMR (400 MHz, Chloroform-d) d 8.16 (s, 1H), 7.69 (d, J = 2.4 Hz, 1H), 7.60 (s, 1H), 7.57 – 7.51 (m, 2H), 7.51 – 7.45 (m, 2H), 7.39 (dd, J = 9.0, 7.1 Hz, 1H), 7.09 – 7.03 (m, 2H), 6.72 (s, 1H), 6.24 (d, J = 2.4 Hz, 1H), 5.36 (s, 1H), 3.10 (h, J = 6.9 Hz, 1H), 1.31 (s, 3H), 1.30 (s, 3H).
263	C	4.149	455.20	
264	C	3.54	474.2	
265	C	3.28	426.2	
266	C	3.753	372.20	1H NMR (400 MHz, Methanol-d4) d 8.15 (s, 1H), 7.61 (dd, J = 8.1, 1.1 Hz, 2H), 7.58 – 7.52 (m, 3H), 7.11 – 7.05 (m, 2H).
267	C	3.305	354.20	1H NMR (400 MHz, Methanol-d4) d 8.24 (t, J = 1.4 Hz, 1H), 8.16 (dd, J = 6.7, 2.0 Hz, 1H), 8.07 (s, 1H), 7.63 – 7.58 (m, 2H), 7.52 (dd, J = 9.2, 7.0 Hz, 1H), 7.39 (d, J = 6.6 Hz, 1H), 7.36 – 7.32 (m, 2H), 7.15 – 7.10 (m, 2H), 2.34 (s, 3H).
268	C	3.710	495.20	
269	C	3.1	483.2	1H NMR (400 MHz, Methanol-d_4) δ 8.15 (s, 1H), 7.70 – 7.52 (m, 5H), 7.24 – 7.11 (m, 2H), 4.20 (t, *J* = 5.5 Hz, 2H), 3.87 (s, 2H), 2.96 (t, *J* = 5.5 Hz, 2H), 2.57 (s, 2H).
270	C	3.48	454.2	1H NMR (400 MHz, Methanol-d_4) δ 7.97 (s, 1H), 7.62 (dd, *J* = 8.1, 1.1 Hz, 2H), 7.54 (dd, *J* = 9.2, 7.0 Hz, 1H), 7.23 – 7.15 (m, 2H), 7.03 – 6.97 (m, 2H), 3.01 (q, *J* = 7.4 Hz, 2H), 1.31 (t, *J* = 7.4 Hz, 3H).

Compound No	HPLC-MS Method	retention time (min)	m+H Found	NMR
271	C	3.35	440.2	
272	C	3.505	466.20	1H NMR (400 MHz, Methanol-d4) d 8.01 (s, 1H), 7.64 (dd, J = 8.1, 1.1 Hz, 2H), 7.56 (dd, J = 9.2, 7.0 Hz, 1H), 7.29 – 7.22 (m, 2H), 7.10 – 7.02 (m, 2H), 3.74 (t, J = 6.6 Hz, 2H), 3.40 (dd, J = 8.2, 7.0 Hz, 2H), 2.49 (dq, J = 8.3, 6.7 Hz, 2H).
273	C	2.999	486.20	1H NMR (400 MHz, Methanol-d4) d 8.20 (s, 1H), 7.68 – 7.63 (m, 2H), 7.58 (dd, J = 9.2, 7.0 Hz, 1H), 7.49 – 7.44 (m, 2H), 7.28 – 7.23 (m, 2H), 3.13 (t, J = 7.3 Hz, 2H), 2.82 (t, J = 7.4 Hz, 2H), 2.27 (s, 6H).
274	C	4.37	524.2	1H NMR (600 MHz, Methanol-d_4) δ 8.16 (s, 1H), 7.67 – 7.60 (m, 2H), 7.60 – 7.51 (m, 1H), 7.43 – 7.35 (m, 2H), 7.26 – 7.12 (m, 2H), 3.17 (sept, J = 6.9 Hz, 1H), 1.29 (d, J = 6.9 Hz, 5H).
275	C	4.05	496.2	1H NMR (600 MHz, Methanol-d_4) δ 8.15 (s, 1H), 7.69 – 7.60 (m, 2H), 7.56 (dd, J = 8.9, 7.5 Hz, 1H), 7.49 – 7.40 (m, 2H), 7.28 – 7.11 (m, 2H), 2.51 (s, 3H).
276	C	3.32	455.2	1H NMR (600 MHz, Methanol-d_4) δ 8.14 (s, 1H), 7.68 – 7.51 (m, 5H), 7.10 – 7.00 (m, 2H), 4.74 – 4.17 (m, 4H), 3.81-3.73 (m, 1H).
277	C	4.230	510.20	1H NMR (400 MHz, Methanol-d4) d 8.17 (s, 1H), 7.65 (dd, J = 8.0, 1.1 Hz, 2H), 7.57 (dd, J = 9.2, 7.0 Hz, 1H), 7.45 – 7.39 (m, 2H), 7.25 – 7.18 (m, 2H), 2.85 (q, J = 7.6 Hz, 2H), 1.31 (t, J = 7.6 Hz, 3H).
278	C	4.245	510.20	1H NMR (400 MHz, Methanol-d4) d 8.19 (s, 1H), 7.68 – 7.62 (m, 4H), 7.58 (dd, J = 9.2, 7.0 Hz, 1H), 7.25 – 7.20 (m, 2H), 4.39 (q, J = 7.2 Hz, 2H), 1.53 (t, J = 7.2 Hz, 3H).
279	C	4.388	524.20	1H NMR (400 MHz, Methanol-d4) d 8.18 (s, 1H), 7.67 – 7.63 (m, 2H), 7.57 (dd, J = 9.2, 7.0 Hz, 1H), 7.44 – 7.38 (m, 2H), 7.24 – 7.19 (m, 2H), 2.81 (dd, J = 8.0, 7.1 Hz, 2H), 1.77 (h, J = 7.4 Hz, 2H), 0.95 (t, J = 7.4 Hz, 3H).
280	C	4.402	524.20	1H NMR (400 MHz, Methanol-d4) d 8.19 (s, 1H), 7.66 (dd, J = 8.1, 1.1 Hz, 2H), 7.62 – 7.54 (m, 3H), 7.25 – 7.20 (m, 2H), 3.32 (1H under solvent peak), 1.54 (d, J = 6.6 Hz, 6H).
281	C	4.143	526.20	1H NMR (400 MHz, Methanol-d4) d 8.18 (s, 1H), 7.68 – 7.63 (m, 2H), 7.57 (dd, J = 9.2, 7.0 Hz, 1H), 7.55 – 7.51 (m, 2H), 7.24 – 7.18 (m, 2H), 4.58 (s, 2H), 3.42 (s, 3H).
282	C	4.412	524.20	1H NMR (400 MHz, Methanol-d4) d 8.19 (s, 1H), 7.69 – 7.60 (m, 4H), 7.58 (dd, J = 9.2, 7.0 Hz, 1H), 7.26 – 7.18 (m, 2H), 4.35 – 4.27 (m, 2H), 2.01 – 1.86 (m, 2H), 0.91 (t, J = 7.4 Hz, 3H).

Compound No	HPLC-MS Method	retention time (min)	m+H Found	NMR
283	C	4.145	494.20	1H NMR (400 MHz, Methanol-d4) d 8.20 (d, J = 0.5 Hz, 1H), 7.61 (td, J = 8.3, 5.6 Hz, 1H), 7.52 (dt, J = 8.3, 1.3 Hz, 1H), 7.47 – 7.35 (m, 3H), 7.25 – 7.17 (m, 2H), 2.85 (q, J = 7.6 Hz, 2H), 1.30 (q, J = 7.3 Hz, 3H).
284	C	4.064	478.20	1H NMR (400 MHz, Methanol-d4) d 8.23 (d, J = 0.9 Hz, 1H), 7.61 (tt, J = 8.4, 6.1 Hz, 1H), 7.49 – 7.40 (m, 2H), 7.34 – 7.24 (m, 2H), 7.24 – 7.16 (m, 2H), 2.85 (q, J = 7.6 Hz, 2H), 1.31 (t, J = 7.6 Hz, 3H).
285	C	3.915	464.20	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.25 (t, *J* = 0.9 Hz, 1H), 7.77 – 7.69 (m, 2H), 7.61 (tt, *J* = 8.6, 6.1 Hz, 1H), 7.33 – 7.23 (m, 2H), 7.26 – 7.18 (m, 2H), 4.08 (s, 3H).
286	C	3.927	425.20	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.16 (d, *J* = 0.5 Hz, 1H), 7.60 (td, *J* = 8.4, 5.6 Hz, 1H), 7.55 – 7.49 (m, 2H), 7.39 (ddd, *J* = 9.2, 8.4, 1.4 Hz, 1H), 7.34 – 7.29 (m, 2H), 7.20 – 7.13 (m, 2H), 6.28 (dd, *J* = 1.8, 0.9 Hz, 1H), 2.70 – 2.61 (m, 2H), 1.22 – 1.16 (m, 3H).
287	C	3.838	409.20	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.19 (d, *J* = 1.0 Hz, 1H), 7.60 (tt, *J* = 8.6, 6.1 Hz, 1H), 7.54 (d, *J* = 1.9 Hz, 1H), 7.36 – 7.30 (m, 2H), 7.30 – 7.23 (m, 2H), 7.20 – 7.13 (m, 2H), 6.28 (dd, *J* = 1.9, 0.9 Hz, 1H), 2.66 (q, *J* = 7.5 Hz, 2H), 1.21 (t, *J* = 7.6 Hz, 3H).
288	C	3.057	428.40	^{1}H NMR (400 MHz, Methanol-d_4) δ 7.94 (d, *J* = 1.0 Hz, 1H), 7.59 (tt, *J* = 8.5, 6.1 Hz, 1H), 7.31 – 7.20 (m, 2H), 7.07 – 6.95 (m, 4H), 4.61 – 4.49 (m, 1H), 3.42-3.32 (m, 2H), 3.28-3.13 (m, 2H), 2.86 (s, 3H), 2.20-2.01 (m, 4H).
289	C	4.166	494.20	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.22 (s, 1H), 7.67 – 7.63 (m, 2H), 7.60 (dd, *J* = 8.4, 5.6 Hz, 1H), 7.53 (dt, *J* = 8.3, 1.3 Hz, 1H), 7.40 (ddd, *J* = 9.6, 8.4, 1.4 Hz, 1H), 7.26 – 7.19 (m, 2H), 4.39 (q, *J* = 7.2 Hz, 2H), 1.53 (t, *J* = 7.3 Hz, 3H).
290	C	2.75	427.2	
291	C	3.520	442.20	1H NMR (400 MHz, Methanol-d4) d 8.16 (s, 1H), 8.00 (s, 1H), 7.68 – 7.63 (m, 2H), 7.57 (dd, J = 9.2, 7.0 Hz, 1H), 7.41 – 7.34 (m, 2H), 7.23 – 7.17 (m, 2H), 2.82 (q, J = 7.6 Hz, 2H), 1.29 (t, J = 7.6 Hz, 3H).
292	C	4.043	525.20	1H NMR (400 MHz, Methanol-d4) d 8.15 (d, J = 1.0 Hz, 1H), 7.87 (q, J = 1.4 Hz, 1H), 7.71 – 7.67 (m, 2H), 7.66 – 7.62 (m, 2H), 7.60 – 7.54 (m, 1H), 7.20 – 7.14 (m, 2H), 5.34 (s, 2H), 3.41 (s, 3H).

Compound No	HPLC-MS Method	retention time (min)	m+H Found	NMR
293	C	4.096	509.20	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.15 (s, 1H), 7.74 (q, J = 1.3 Hz, 1H), 7.65 (dd, J = 8.1, 1.1 Hz, 2H), 7.57 (dd, J = 9.2, 7.0 Hz, 1H), 7.56 – 7.47 (m, 2H), 7.22 – 7.14 (m, 2H), 4.13 (q, J = 7.3 Hz, 2H), 1.41 (t, J = 7.3 Hz, 3H).
294	C	3.95	495.2	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.13 (s, 1H), 7.66 – 7.59 (m, 3H), 7.59 – 7.50 (m, 3H), 7.20 – 7.09 (m, 2H), 3.77 (s, 3H).
295	C	3.122	444.20	^{1}H NMR (400 MHz, Methanol-d_4) δ 7.90 (s, 1H), 7.58 (td, J = 8.3, 5.6 Hz, 1H), 7.49 (dt, J = 8.3, 1.4 Hz, 1H), 7.37 (td, J = 8.9, 8.3, 1.4 Hz, 1H), 7.03 – 6.98 (m, 2H), 6.98 – 6.91 (m, 2H), 4.46 – 4.39 (m, 1H), 3.07 (ddd, J = 12.2, 8.5, 3.7 Hz, 2H), 2.77 (d, J = 37.0 Hz, 2H), 2.60 (s, 3H), 2.07 (ddt, J = 12.4, 7.9, 3.5 Hz, 2H).
296	C	3.317	407.20	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.97 (d, J = 5.1 Hz, 1H), 8.22 (d, J = 0.9 Hz, 1H), 7.65 (dd, J = 5.2, 0.9 Hz, 1H), 7.60 (ddt, J = 8.1, 6.3, 2.3 Hz, 1H), 7.58 – 7.53 (m, 2H), 7.31 – 7.24 (m, 2H), 7.24 – 7.17 (m, 2H), 2.46 (d, J = 0.9 Hz, 3H).
297	C	4.168	539.20	1H NMR (400 MHz, Methanol-d4) d 8.18 (s, 1H), 7.70 – 7.62 (m, 2H), 7.61 – 7.50 (m, 3H), 7.24 – 7.14 (m, 2H), 3.66 (s, 2H), 2.30 (s, 6H).
298	C	4.056	510.20	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.22 – 8.18 (m, 1H), 7.61 (td, J = 8.4, 5.6 Hz, 1H), 7.56 – 7.49 (m, 3H), 7.40 (ddd, J = 9.3, 8.4, 1.4 Hz, 1H), 7.24 – 7.18 (m, 2H), 4.58 (s, 2H), 3.42 (s, 3H).
299	C	3.973	494.20	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.23 (d, J = 0.9 Hz, 1H), 7.61 (tt, J = 8.6, 6.1 Hz, 1H), 7.56 – 7.51 (m, 2H), 7.31 – 7.24 (m, 2H), 7.24 – 7.18 (m, 2H), 4.61, 4.58 (s, 2H), 3.42 (s, 3H).
300	C	3.426	458.20	
301	C	3.84	537.2	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.22 (s, 1H), 8.14 (s, 1H), 7.67 – 7.60 (m, 2H), 7.56 (dd, J = 9.1, 7.0 Hz, 1H), 7.43 – 7.34 (m, 2H), 7.20 – 7.11 (m, 2H), 5.57 (ddd, J = 7.5, 6.1, 1.4 Hz, 1H), 5.01 (t, J = 7.3 Hz, 2H), 4.85 (t, J = 7.3 Hz, 2H).
302	C	4.084	478.20	1H NMR (400 MHz, Methanol-d4) d 8.25 (d, J = 1.0 Hz, 1H), 7.68 – 7.63 (m, 2H), 7.60 (dt, J = 8.6, 6.1 Hz, 1H), 7.32 – 7.25 (m, 2H), 7.25 – 7.20 (m, 2H), 4.39 (q, J = 7.2 Hz, 2H), 1.53 (t, J = 7.2 Hz, 3H).

Compound No	HPLC-MS Method	retention time (min)	m+H Found	NMR
303	C	4.008	493.20	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.18 (d, J = 0.5 Hz, 1H), 7.74 (q, J = 1.2 Hz, 1H), 7.61 (td, J = 8.4, 5.6 Hz, 1H), 7.55 – 7.48 (m, 3H), 7.40 (ddd, J = 9.3, 8.4, 1.4 Hz, 1H), 7.22 – 7.15 (m, 2H), 4.14 (q, J = 7.3 Hz, 2H), 1.41 (t, J = 7.3 Hz, 3H).
304	C	3.928	477.20	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.21 (d, J = 0.9 Hz, 1H), 7.74 (q, J = 1.2 Hz, 1H), 7.61 (tt, J = 8.6, 6.1 Hz, 1H), 7.55 – 7.49 (m, 2H), 7.31 – 7.24 (m, 2H), 7.22 – 7.16 (m, 2H), 4.14 (q, J = 7.3 Hz, 2H), 1.41 (t, J = 7.3 Hz, 3H).
305	C	3.867	479.20	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.18 (d, J = 0.5 Hz, 1H), 7.65 (q, J = 1.3 Hz, 1H), 7.64 – 7.55 (m, 3H), 7.52 (dt, J = 8.3, 1.3 Hz, 1H), 7.40 (ddd, J = 9.2, 8.4, 1.4 Hz, 1H), 7.21 – 7.15 (m, 2H), 3.79 (s, 3H).
306	C	3.652	552.20	1H NMR (400 MHz, Methanol-d4) d 8.16 (s, 1H), 7.79 (q, J = 1.3 Hz, 1H), 7.65 (dd, J = 8.1, 1.0 Hz, 2H), 7.57 (dd, J = 9.2, 7.0 Hz, 1H), 7.55 – 7.51 (m, 2H), 7.21 – 7.16 (m, 2H), 4.21 (t, J = 6.8 Hz, 2H), 2.66 (t, J = 6.8 Hz, 2H), 2.19 (s, 6H).
307	C	4.01	539.2	1H NMR (400 MHz, Methanol-d_4) δ 8.13 (s, 1H), 7.72 (q, J = 1.3 Hz, 1H), 7.66 – 7.59 (m, 2H), 7.59 – 7.47 (m, 3H), 7.21 – 7.10 (m, 2H), 4.22 (t, J = 5.2 Hz, 2H), 3.67 (t, J = 5.2 Hz, 2H), 3.30 (s, , 3H).
308	C	3.786	463.20	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.21 (t, J = 0.9 Hz, 1H), 7.65 (p, J = 1.1 Hz, 1H), 7.59 – 7.56 (m, 2H), 7.31 – 7.23 (m, 2H), 7.21 – 7.14 (m, 2H), 3.79 (s, 3H).
309	C	3.495	424.20	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.23 (s, 1H), 7.99 (s, 1H), 7.66 – 7.56 (m, 1H), 7.53 (d, J = 8.2 Hz, 2H), 7.27 (td, J = 8.7, 7.4, 1.7 Hz, 2H), 7.21 (d, J = 8.4 Hz, 2H), 4.80 (s, 1H), 1.51 (d, J = 6.6 Hz, 6H).
310	C	3.740	466.20	1H NMR (400 MHz, Methanol-d4) d 8.11 (d, J = 0.9 Hz, 1H), 7.99 (d, J = 0.9 Hz, 1H), 7.63 – 7.58 (m, 2H), 7.56 – 7.50 (m, 1H), 7.50 – 7.44 (m, 2H), 7.16 – 7.11 (m, 2H), 4.12 (q, J = 7.3 Hz, 2H), 1.42 – 1.30 (m, 3H).
311	C	4.23	523.2	^{1}H NMR (400 MHz, Methanol-d_4) δ 7.69 (s, 1H), 7.62 (dd, J = 8.1, 1.1 Hz, 2H), 7.57 – 7.48 (m, 2H), 7.38 (s, 1H), 6.97 (d, J = 1.7 Hz, 1H), 2.65 (s, 3H).
312	C	4.39	537.2	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.14 (s, 1H), 7.74 – 7.52 (m, 3H), 7.52 – 7.41 (m, 2H), 7.21 – 7.09 (m, 2H), 4.09 (t, J = 7.4 Hz, 2H), 1.71 (dd, J = 8.5, 7.4 Hz, 2H), 1.38 – 1.14 (m, 2H), 0.86 (t, J = 7.4 Hz, 3H).

Compound No	HPLC-MS Method	retention time (min)	m+H Found	NMR
313	A	2.785	487.2	1H NMR (400 MHz, cd3od) δ 8.09 (s, 1H), 7.60 (d, J = 7.2 Hz, 2H), 7.51 (dd, J = 18.2, 7.8 Hz, 3H), 7.04 (d, J = 8.4 Hz, 2H), 3.90 – 3.51 (m, 4H), 3.43 (t, J = 10.0 Hz, 1H), 2.92 (d, J = 42.3 Hz, 1H), 2.30 (d, J = 39.3 Hz, 6H), 1.83 (s, 1H).
314	C	2.894	487.2	1H NMR (400 MHz, cd3od) δ 8.09 (s, 1H), 7.64 – 7.58 (m, 2H), 7.51 (dd, J = 17.9, 7.8 Hz, 3H), 7.06 (s, 2H), 3.90 – 3.51 (m, 4H), 3.45 (t, J = 10.0 Hz, 1H), 2.96 (d, J = 45.5 Hz, 1H), 2.33 (d, J = 22.3 Hz, 6H), 1.83 (s, 1H).
315	B	3.419	462.2	1H NMR (400 MHz, cd3od) δ 8.09 (s, 1H), 7.61 (d, J = 8.6 Hz, 2H), 7.56 – 7.46 (m, 3H), 7.05 (d, J = 8.7 Hz, 2H), 5.44 – 5.07 (m, 1H), 3.73 (d, J = 14.0 Hz, 4H), 2.20 (s, 2H).
316	B	3.420	462.2	1H NMR (400 MHz, cd3od) δ 8.09 (s, 1H), 7.64 – 7.57 (m, 2H), 7.53 (dd, J = 9.2, 6.9 Hz, 3H), 7.05 (d, J = 8.7 Hz, 2H), 5.43 – 5.08 (m, 1H), 3.75 (t, J = 20.5 Hz, 4H), 2.08 (d, J = 47.0 Hz, 2H).
317	C	2.741	459.2	1H NMR (400 MHz, cd3od) δ 8.08 (s, 1H), 7.63 – 7.61 (m, 1H), 7.60 (s, 1H), 7.52 (d, J = 8.9 Hz, 3H), 7.06 (d, J = 8.6 Hz, 2H), 3.93 (s, 3H), 3.83 – 3.77 (m, 1H), 3.76 – 3.60 (m, 3H), 2.37 (d, J = 10.1 Hz, 1H), 2.05 (s, 1H).
318	C	2.808	459.2	1H NMR (400 MHz, cd3od) δ 8.08 (s, 1H), 7.61 (d, J = 8.7 Hz, 2H), 7.52 (dd, J = 9.2, 3.0 Hz, 3H), 7.05 (d, J = 8.6 Hz, 2H), 3.90 – 3.59 (m, 5H), 3.51 (s, 2H), 2.33 (s, 1H), 1.98 – 1.93 (m, 1H).
319	C	2.787	459.2	1H NMR (400 MHz, cd3od) δ 8.08 (s, 1H), 7.60 (d, J = 7.4 Hz, 2H), 7.54 – 7.48 (m, 3H), 7.05 (d, J = 8.6 Hz, 2H), 3.88 – 3.73 (m, 3H), 3.69 – 3.61 (m, 2H), 3.49 (s, 2H), 2.25 (s, 1H), 1.95 (t, J = 6.7 Hz, 1H).
320	C	3.68	434.2	1H NMR (400 MHz, Methanol-d_4) δ 7.69 (s, 1H), 7.62 (dd, J = 8.1, 1.1 Hz, 2H), 7.57 – 7.48 (m, 2H), 7.38 (s, 1H), 6.97 (d, J = 1.7 Hz, 1H), 2.65 (s, 3H).
321	C	3.4	425.2	1H NMR (400 MHz, Methanol-d_4) δ 9.56 (s, 1H), 9.12 (d, J = 5.7 Hz, 1H), 8.17 (s, 1H), 8.05 (dd, J = 5.8, 2.5 Hz, 1H), 7.96 – 7.82 (m, 2H), 7.64 (dd, J = 8.1, 1.1 Hz, 2H), 7.56 (dd, J = 9.2, 7.0 Hz, 1H), 7.30 – 7.10 (m, 2H).
322	C	3.67	453.2	1H NMR (400 MHz, Methanol-d_4) δ 9.09 (s, 1H), 8.97 (s, 1H), 8.13 (s, 1H), 7.69 – 7.45 (m, 3H), 7.45 – 7.29 (m, 2H), 7.25 – 7.00 (m, 2H), 2.84 (q, J = 5.2 Hz, 2H), 1.22 (t, J = 5.2 Hz, 3H)
323	C	3.717	559.2	
324	C	3.718	559.2	
325	C	3.717	559.2	

Compound No	HPLC-MS Method	retention time (min)	m+H Found	NMR
326	C	3.363	428.20	1H NMR (400 MHz, Methanol-d4) d 8.10 (s, 1H), 7.94 (s, 1H), 7.63 – 7.57 (m, 2H), 7.53 (dd, J = 9.2, 7.0 Hz, 1H), 7.37 (d, J = 8.6 Hz, 2H), 7.20 – 7.13 (m, 2H), 2.44 (s, 3H).
327	C	3.401	472.20	1H NMR (400 MHz, Methanol-d4) d 8.11 (s, 1H), 7.99 (s, 1H), 7.61 (d, J = 7.5 Hz, 2H), 7.53 (dd, J = 9.2, 7.0 Hz, 1H), 7.40 – 7.35 (m, 2H), 7.18 – 7.13 (m, 2H), 3.70 (t, J = 6.3 Hz, 2H), 3.24 (s, 3H), 3.01 (t, J = 6.3 Hz, 2H).
328	C	4.066	527.20	1H NMR (400 MHz, Methanol-d4) d 8.28 (d, J = 2.9 Hz, 1H), 8.19 (s, 1H), 7.74 (d, J = 8.9 Hz, 1H), 7.67 – 7.59 (m, 3H), 7.54 (dd, J = 9.2, 7.0 Hz, 1H), 4.99 (s, 2H), 3.42 (s, 3H).
329	C	4.253	511.20	1H NMR (400 MHz, Methanol-d4) d 8.30 – 8.27 (m, 1H), 8.19 (s, 1H), 7.70 – 7.63 (m, 2H), 7.63 – 7.59 (m, 2H), 7.54 (dd, J = 9.2, 7.0 Hz, 1H), 3.15 (q, J = 7.5 Hz, 2H), 1.32 (t, J = 7.5 Hz, 3H).
330	C	4.116	540.20	1H NMR (400 MHz, Methanol-d4) d 8.12 (s, 1H), 7.63 – 7.58 (m, 2H), 7.53 (dd, J = 9.2, 7.0 Hz, 1H), 7.46 – 7.36 (m, 2H), 7.20 – 7.12 (m, 2H), 3.72 (t, J = 6.2 Hz, 2H), 3.25 (s, 3H), 3.04 (t, J = 6.2 Hz, 2H).
331	A	2.806	513.2	
332	A	2.803	513.2	
333	B	3.22	464.2	1H NMR (400 MHz, Methanol-d4) δ 8.50 (dd, J = 7.1, 1.2 Hz, 1H), 8.18 (s, 1H), 7.81 – 7.73 (m, 3H), 7.68 – 7.60 (m, 2H), 7.56 (dd, J = 9.2, 7.0 Hz, 1H), 7.48 (ddd, J = 9.3, 6.6, 1.1 Hz, 1H), 7.31 – 7.23 (m, 2H), 7.05 (td, J = 6.8, 1.1 Hz, 1H).
334	E	0.78	482	----
335	C	4.065	528.20	1H NMR (400 MHz, Methanol-d4) d 8.67 (s, 1H), 7.92 (d, J = 9.5 Hz, 1H), 7.65 – 7.59 (m, 2H), 7.54 (dd, J = 9.3, 7.1 Hz, 2H), 5.03 (s, 2H), 3.42 (s, 3H).
336	C	4.297	512.20	1H NMR (400 MHz, Methanol-d4) d 8.66 (d, J = 0.9 Hz, 1H), 7.87 (d, J = 9.5 Hz, 1H), 7.64 – 7.59 (m, 2H), 7.57 – 7.51 (m, 2H), 3.21 (q, J = 7.5 Hz, 2H), 1.36 (t, J = 7.5 Hz, 3H).
337	C	3.355	415.20	1H NMR (400 MHz, Methanol-d4) d 9.16 (s, 1H), 8.25 (dd, J = 2.9, 0.7 Hz, 1H), 8.15 (s, 1H), 8.11 (s, 1H), 7.80 (dd, J = 8.9, 0.7 Hz, 1H), 7.65 (d, J = 2.9 Hz, 1H), 7.64 – 7.59 (m, 2H), 7.54 (dd, J = 9.2, 7.0 Hz, 1H).
338	C	3.639	525.20	1H NMR (400 MHz, Methanol-d4) d 8.09 (s, 1H), 7.72 (q, J = 1.3 Hz, 1H), 7.64 – 7.58 (m, 2H), 7.57 – 7.48 (m, 3H), 7.18 – 7.08 (m, 2H), 4.13 (t, J = 5.3 Hz, 2H), 3.79 (dd, J = 5.8, 4.9 Hz, 2H).

Compound No	HPLC-MS Method	retention time (min)	m+H Found	NMR
339	C	4.198	510.20	1H NMR (400 MHz, Methanol-d4) d 8.45 (dd, J = 3.0, 0.7 Hz, 1H), 8.23 (s, 1H), 7.95 – 7.91 (m, 1H), 7.72 (q, J = 1.2 Hz, 1H), 7.66 (dd, J = 8.1, 1.1 Hz, 2H), 7.62 – 7.54 (m, 2H), 4.59 (q, J = 7.2 Hz, 2H), 1.44 (t, J = 7.1 Hz, 3H).
340	C	3.5	439.2	
341	C	3.65	456.2	1H NMR (400 MHz, Methanol-d_4) δ 8.14 (s, 1H), 7.98 (d, J = 0.6 Hz, 1H), 7.66 – 7.60 (m, 2H), 7.56 (dd, J = 9.2, 6.9 Hz, 1H), 7.36 – 7.30 (m, 2H), 7.26 – 7.11 (m, 2H), 3.13 (sept, J = 6.8 Hz, 1H), 1.27 (d, J = 6.8 Hz, 6H).
342	C	3.1	483.2	1H NMR (400 MHz, Methanol-d_4) δ 8.19 – 8.15 (m, 1H), 8.13 (s, 1H), 7.65 (d, J = 1.5 Hz, 1H), 7.63 (d, J = 0.7 Hz, 1H), 7.56 (dd, J = 9.2, 7.0 Hz, 1H), 7.46 – 7.40 (m, 2H), 7.20 – 7.14 (m, 2H), 5.32-5.24 (m, 1H), 4.67-4.60 (m, 1H), 4.49 – 4.40 (m, 2H), 4.23-4.16 (m, 1H), 1.90 (s, 3H).
343	C	3.47	443.2	1H NMR (400 MHz, Methanol-d_4) δ 8.30 (dd, J = 2.3, 1.3 Hz, 1H), 8.20 (s, 1H), 7.96 (s, 1H), 7.68 – 7.64 (m, 2H), 7.63 (d, J = 0.7 Hz, 1H), 7.56 (dd, J = 9.2, 6.9 Hz, 2H), 3.13 (q, J = 7.5 Hz, 2H), 1.31 (t, J = 7.5 Hz, 3H).
344	D	2.96	454.2	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.35 (dd, J = 2.9, 0.7 Hz, 1H), 8.14 (s, 1H), 7.71 (dd, J = 8.7, 0.7 Hz, 1H), 7.66 – 7.61 (m, 2H), 7.58 – 7.53 (m, 3H), 7.51 (dd, J = 8.7, 2.9 Hz, 1H), 7.35 (ddd, J = 8.3, 7.4, 1.8 Hz, 1H), 7.09 (dd, J = 8.4, 1.0 Hz, 1H), 7.03 (td, J = 7.5, 1.1 Hz, 1H), 3.84 (s, 3H).
345	D	3.32	431.2	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.15 (s, 1H), 8.13 (dd, J = 5.6, 0.7 Hz, 1H), 8.05 (s, 1H), 7.63 (d, J = 1.5 Hz, 1H), 7.61 (d, J = 0.7 Hz, 1H), 7.59 – 7.48 (m, 2H), 4.10 – 4.04 (m, 2H), 2.63 (dd, J = 8.5, 7.6 Hz, 2H), 2.19 – 2.09 (m, 2H).
346	D	3.57	428.2	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.23 (s, 1H), 8.09 (dd, J = 2.9, 0.6 Hz, 1H), 7.97 (dd, J = 2.4, 0.7 Hz, 1H), 7.72 (dd, J = 1.9, 0.7 Hz, 1H), 7.65 (d, J = 1.5 Hz, 1H), 7.63 (d, J = 0.7 Hz, 1H), 7.56 (dd, J = 9.2, 7.0 Hz, 1H), 7.48 (dd, J = 2.8, 0.8 Hz, 1H), 6.51 (dd, J = 2.5, 1.9 Hz, 1H), 2.25 (t, J = 0.6 Hz, 3H).
347	C	3.296	470.20	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.13 – 8.08 (m, 1H), 8.05 (q, J = 0.7 Hz, 1H), 7.63 – 7.58 (m, 2H), 7.57 – 7.48 (m, 1H), 7.24 (dd, J = 8.9, 1.8 Hz, 2H), 7.18 – 7.10 (m, 2H), 4.88 (dqd, J = 6.8, 5.8, 1.2 Hz, 4H), 4.60 – 4.41 (m, 1H).
348	C	3.136	444.20	

Compound No	HPLC-MS Method	retention time (min)	m+H Found	NMR
349	C	3.523	494.20	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.47 (s, 1H), 8.11 (s, 1H), 7.61 (dd, J = 8.1, 1.1 Hz, 2H), 7.53 (dd, J = 9.2, 7.0 Hz, 1H), 7.41 – 7.33 (m, 2H), 7.18 – 7.04 (m, 2H), 5.56 (ddd, J = 13.4, 7.4, 6.1 Hz, 1H), 5.02 – 4.94 (m, 2H), 4.80 (under MeOD signal, m, 2H).
350	C	3.23	440.2	1H NMR (400 MHz, Methanol-d_4) δ 9.21 (s, 1H), 9.09 (s, 1H), 8.57 – 8.48 (m, 1H), 8.22 (s, 1H), 7.74 – 7.48 (m, 5H), 2.54 (s, 3H).
351	C	3.39	454.2	^{1}H NMR (400 MHz, Methanol-d_4) δ 9.18 (s, 1H), 8.52 (s, 1H), 8.22 (s, 1H), 7.73 – 7.49 (m, 6H), 2.96 (q, J = 7.6 Hz, 2H), 1.22 (t, J = 7.6 Hz, 3H).
352	C	3.2	426.2	1H NMR (400 MHz, Methanol-d_4) δ 9.81 (s, 1H), 9.19 (s, 2H), 8.57 – 8.49 (m, 1H), 8.24 (s, 1H), 8.11 – 8.02 (m, 1H), 7.65 (dd, J = 8.1, 1.1 Hz, 2H), 7.61 – 7.48 (m, 2H).
353	C	2.81	364.2	
354	A	2.723	490.2	
355	C	3.335	463.2	1H NMR (400 MHz, MeOD) δ 8.37 (d, J = 2.6 Hz, 1H), 8.24 (s, 1H), 7.83 (dd, J = 12.5, 8.7 Hz, 1H), 7.67 (d, J = 1.5 Hz, 1H), 7.65 (d, J = 0.7 Hz, 1H), 7.61 – 7.49 (m, 2H), 5.40 (d, J = 10.3 Hz, 1H), 5.26 (d, J = 10.3 Hz, 1H), 4.22 – 3.65 (m, 5H), 2.35 – 2.03 (m, 2H).
356	A	2.776	515.2	
357	A	2.714	460.2	
358	A	3.507	447.2	1H NMR (400 MHz, MeOD) δ 8.35 (d, J = 2.8 Hz, 1H), 8.23 (s, 1H), 7.75 (d, J = 8.7 Hz, 1H), 7.68 – 7.62 (m, 2H), 7.61 – 7.48 (m, 2H), 3.84 – 3.77 (m, 2H), 3.67 – 3.60 (m, 2H), 2.01 – 1.92 (m, 4H).
359	C	3.008	335.20	1H NMR (400 MHz, Methanol-d4) d 7.59 (s, 1H), 7.49 (d, J = 0.9 Hz, 1H), 7.45 (t, J = 1.3 Hz, 1H), 7.43 (dd, J = 2.7, 1.4 Hz, 1H), 7.35 (d, J = 0.9 Hz, 1H), 7.35 – 7.28 (m, 1H), 3.80 (s, 3H).
360	C	3.057	429.20	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.51 (s, 1H), 8.25 (s, 1H), 8.02 (d, J = 8.7 Hz, 1H), 7.70 – 7.64 (m, 2H), 7.64 – 7.53 (m, 3H), 4.08 (s, 3H).
361	C	3.334	482.20	1H NMR (400 MHz, Methanol-d4) d 8.15 (s, 1H), 8.05 (s, 1H), 7.70 – 7.61 (m, 2H), 7.64 – 7.51 (m, 3H), 7.21 – 7.13 (m, 2H), 4.20 (dd, J = 5.7, 4.8 Hz, 2H), 3.82 (dd, J = 5.8, 4.8 Hz, 2H) .

Compound No	HPLC-MS Method	retention time (min)	m+H Found	NMR
362	A	4.108 & 4.167	518.2	
363	A	2.686	475.4	
364	A	2.742	502.2	1H NMR (400 MHz, MeOD) δ 8.34 (dd, J = 2.8, 0.8 Hz, 1H), 8.22 (s, 1H), 7.67 (d, J = 1.6 Hz, 1H), 7.65 (d, J = 0.7 Hz, 1H), 7.61 – 7.52 (m, 3H), 3.69 (d, J = 40.4 Hz, 4H), 2.70 (d, J = 28.8 Hz, 4H), 1.74 (tt, J = 6.6, 3.7 Hz, 1H), 0.58 – 0.40 (m, 4H).
365	A	3.263	461.2	
366	A	2.759	490.3	
367	A	3.632	465.2	
368	A	2.753	460.2	
369	A	4.107 & 4.162	517.2	
370	A	2.779	476.2	
371	C	3.796	512.20	1H NMR (400 MHz, Methanol-d4) d 8.17 (s, 1H), 7.69 – 7.62 (m, 2H), 7.61 – 7.52 (m, 3H), 7.25 – 7.17 (m, 2H), 4.70 (s, 2H).
372	C	3.201	361.20	1H NMR (400 MHz, Methanol-d4) d 7.55 (d, J = 1.0 Hz, 1H), 7.51 (s, 1H), 7.51 – 7.41 (m, 2H), 7.17 (ddd, J = 8.5, 6.1, 1.2 Hz, 2H), 4.11 (q, J = 7.0 Hz, 2H), 3.85 (s, 3H), 1.29 (t, J = 7.0 Hz, 3H).
373	C	3.700	526.20	1H NMR (400 MHz, Methanol-d4) d 8.42 (dd, J = 3.0, 0.6 Hz, 1H), 8.23 (s, 1H), 7.95 (dd, J = 8.8, 0.6 Hz, 1H), 7.72 (q, J = 1.2 Hz, 1H), 7.66 (dd, J = 8.1, 1.1 Hz, 2H), 7.58 (ddd, J = 9.2, 5.2, 2.2 Hz, 2H), 4.65 (t, J = 5.3 Hz, 2H), 3.91 (t, J = 5.3 Hz, 2H).
374	C	3.718	443.20	1H NMR (400 MHz, Methanol-d4) d 8.31 (s, 1H), 8.22 (d, J = 1.0 Hz, 1H), 7.84 (s, 1H), 7.79 (d, J = 1.0 Hz, 1H), 7.67 – 7.61 (m, 2H), 7.56 (dd, J = 9.2, 7.0 Hz, 1H), 2.78 (s, 3H), 2.54 (t, J = 0.7 Hz, 3H).
375	C	3.478	430.2	
376	B	3.276	478	---

Compound No	HPLC-MS Method	retention time (min)	m+H Found	NMR
377	C	3.11	351.2	1H NMR (400 MHz, Methanol-d_4) δ 7.64 – 7.56 (m, 3H), 7.55 – 7.49 (m, 2H), 7.37 (d, J = 0.9 Hz, 1H), 3.82 (s, 3H).
378	C	3.48	379.2	1H NMR (400 MHz, Methanol-d_4) δ 7.64 – 7.46 (m, 5H), 7.39 (d, J = 1.0 Hz, 1H), 4.44 (sept, J = 6.7 Hz, 1H), 1.46 (d, J = 6.7 Hz, 6H).
379	C	3.45	352.2	1H NMR (400 MHz, Methanol-d_4) δ 8.10 (s, 1H), 7.67 – 7.47 (m, 3H), 7.27 (s, 1H), 4.03 (s, 3H).
380	C	3.07	3352.2	1H NMR (400 MHz, Methanol-d_4) δ 7.95 (s, 1H), 7.68 – 7.43 (m, 5H), 4.05 (s, 3H).
381	C	2.84	378.2	1H NMR (400 MHz, Methanol-d_4) δ 8.15 (d, J = 0.8 Hz, 1H), 7.64 (dd, J = 8.1, 1.2 Hz, 2H), 7.56 (dd, J = 9.2, 6.9 Hz, 2H), 7.49 (d, J = 7.4 Hz, 1H), 6.22 (dd, J = 7.4, 1.4 Hz, 1H), 3.49 (s, 3H).
382	C	2.963	514.2	
383	C	3.664	500.2	
384	C	3.26	445.2	1H NMR (400 MHz, Methanol-d_4) δ 8.22 (d, J = 3.0 Hz, 1H), 8.11 (s, 1H), 7.64 (d, J = 1.5 Hz, 1H), 7.62 (d, J = 0.7 Hz, 1H), 7.56 – 7.50 (m, 2H), 7.35 (dd, J = 8.8, 0.7 Hz, 1H), 3.76 (t, J = 5.8 Hz, 2H), 2.53 (t, J = 5.8 Hz, 2H), 2.01-1.89 (m, 4H).
385	C	3.847	513.20	1H NMR (400 MHz, Methanol-d4) d 8.30 (dd, J = 2.9, 0.7 Hz, 1H), 8.19 (s, 1H), 7.80 (dd, J = 8.9, 0.7 Hz, 1H), 7.67 (dd, J = 8.9, 2.9 Hz, 1H), 7.64 – 7.59 (m, 2H), 7.54 (dd, J = 9.2, 7.0 Hz, 1H), 5.00 (s, 2H).
386	C	3.544	432.20	no nmr
387	C	3.362	483.20	1H NMR (400 MHz, Methanol-d4) d 8.37 (dd, J = 2.9, 0.7 Hz, 1H), 8.18 (s, 1H), 7.93 (s, 1H), 7.91 (dd, J = 8.7, 0.7 Hz, 1H), 7.64 – 7.57 (m, 2H), 7.56 – 7.50 (m, 2H), 4.64 (t, J = 5.3 Hz, 2H), 3.86 (t, J = 5.3 Hz, 2H).
388	B	3.21	479.2	^{1}H NMR (600 MHz, Methanol-d_4) δ 8.50 (d, J = 2.8 Hz, 1H), 8.28 (s, 1H), 7.76 (d, J = 8.5 Hz, 1H), 7.69 (d, J = 9.2 Hz, 1H), 7.64 (d, J = 7.7 Hz, 2H), 7.63 – 7.61 (m, 1H), 7.57 (dd, J = 8.9, 7.4 Hz, 1H), 7.43 (dd, J = 9.2, 6.7 Hz, 1H), 6.83 (d, J = 6.7 Hz, 1H), 2.35 (s, 3H).
389	C	2.93	378.2	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.25 (d, J = 2.8 Hz, 1H), 7.72 (dd, J = 9.6, 2.8 Hz, 1H), 7.63 – 7.56 (m, 3H), 7.56 – 7.46 (m, 1H), 6.56 (d, J = 9.6 Hz, 1H), 3.60 (s, 3H).
390	C	3.19	441.2	

Compound No	HPLC-MS Method	retention time (min)	m+H Found	NMR
391	C	3.51	428.2	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.17 (s, 1H), 7.68 – 7.51 (m, 4H), 7.46 – 7.33 (m, 2H), 7.27 – 7.13 (m, 2H), 2.34 (d, J = 0.8 Hz, 3H).
392	C	3.71	457.2	
393	C	3.76	458.2	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.37 (dd, J = 2.9, 0.8 Hz, 1H), 8.26 (s, 1H), 7.78 – 7.61 (m, 4H), 7.57 (dd, J = 9.2, 7.0 Hz, 1H), 3.77 (sept, J = 6.9 Hz, 1H), 1.38 (d, J = 6.9 Hz, 6H).
394	C	3.496	439.20	1H NMR (400 MHz, Methanol-d4) d 8.50 (s, 1H), 8.46 (d, J = 2.9 Hz, 1H), 8.41 (d, J = 5.2 Hz, 1H), 8.22 (d, J = 1.9 Hz, 1H), 7.69 – 7.64 (m, 2H), 7.64 – 7.54 (m, 2H), 7.50 (dd, J = 8.5, 1.8 Hz, 1H), 7.40 (d, J = 5.2 Hz, 1H), 2.43 (s, 3H).
395	C	3.646	439.20	1H NMR (400 MHz, Methanol-d4) d 8.46 – 8.41 (m, 2H), 8.24 (s, 1H), 7.80 (ddd, J = 7.6, 1.7, 0.8 Hz, 1H), 7.69 – 7.61 (m, 4H), 7.58 (dd, J = 9.2, 7.0 Hz, 1H), 7.37 (dd, J = 7.7, 4.8 Hz, 1H), 2.43 (s, 3H).
396	C	4.002	448.20	
397	C	3.785	414.20	1H NMR (400 MHz, Methanol-d4) d 8.42 – 8.37 (m, 2H), 7.96 – 7.92 (m, 2H), 7.84 (s, 1H), 7.76 (d, J = 1.0 Hz, 1H), 7.67 – 7.62 (m, 2H), 7.57 (dd, J = 9.2, 7.0 Hz, 1H), 7.27 (td, J = 5.1, 3.3 Hz, 1H).
398	C	3.908	442.20	1H NMR (400 MHz, Methanol-d4) d 8.26 (dd, J = 3.1, 0.6 Hz, 1H), 8.18 (s, 1H), 7.68 – 7.61 (m, 3H), 7.60 – 7.54 (m, 1H), 7.52 (dd, J = 8.8, 0.7 Hz, 1H), 6.06 (s, 1H), 2.44 (d, J = 0.8 Hz, 3H), 2.26 (s, 3H).
399	C	3.500	414.20	
400	C	3.355	457.20	1H NMR (400 MHz, Methanol-d4) d 8.72 (s, 1H), 8.45 (d, J = 2.9 Hz, 1H), 8.21 (d, J = 0.5 Hz, 1H), 7.92 (dd, J = 8.7, 0.7 Hz, 1H), 7.65 – 7.58 (m, 2H), 7.58 – 7.49 (m, 2H), 5.52 (p, J = 6.8 Hz, 1H), 1.51 (d, J = 6.7 Hz, 6H).
401	C	3.273	462.20	1H NMR (400 MHz, Methanol-d4) d 8.59 (d, J = 0.6 Hz, 1H), 8.52 (d, J = 1.4 Hz, 1H), 8.27 (t, J = 1.1 Hz, 1H), 7.62 – 7.57 (m, 2H), 7.52 (dd, J = 9.4, 6.9 Hz, 1H), 3.74 (s, 8H).
402	C	3.300	475.20	1H NMR (400 MHz, Methanol-d4) d 8.60 (s, 1H), 8.51 (d, J = 1.4 Hz, 1H), 8.28 (d, J = 1.4 Hz, 1H), 7.64 – 7.57 (m, 2H), 7.53 (dd, J = 9.2, 6.9 Hz, 1H), 3.80 – 3.73 (m, 4H), 2.54 (bs, 4H), 2.34 (s, 3H).
403	C	3.46	464.2	

Compound No	HPLC-MS Method	retention time (min)	m+H Found	NMR
404	C	3.04	336.2	1H NMR (400 MHz, Methanol-d_4) δ 8.24 (s, 1H), 7.64 – 7.54 (m, 2H), 7.49 (dt, J = 8.3, 1.3 Hz, 1H), 7.37 (ddd, J = 9.5, 8.5, 1.4 Hz, 1H), 3.76 (s, 3H).
405	C	3.075	461.20	
406	C	3.16	352.2	
407	C	2.9	337.2	
408	C	3.229	388.20	1H NMR (400 MHz, Methanol-d4) d 8.51 (dd, J = 4.4, 1.4 Hz, 1H), 8.06 (s, 1H), 7.95 (d, J = 9.2 Hz, 1H), 7.65 (dd, J = 8.1, 1.1 Hz, 2H), 7.57 (dd, J = 9.2, 7.0 Hz, 1H), 7.54 (bs, 1H), 7.14 (dd, J = 9.2, 4.4 Hz, 1H).
409	C	3.215	388.20	1H NMR (400 MHz, Methanol-d4) d 8.76 (dd, J = 7.1, 1.7 Hz, 1H), 8.41 (dd, J = 4.0, 1.6 Hz, 1H), 8.19 (s, 1H), 7.76 (s, 1H), 7.62 (dd, J = 8.1, 1.1 Hz, 2H), 7.54 (dd, J = 9.2, 7.0 Hz, 1H), 6.93 (dd, J = 7.1, 3.9 Hz, 1H).
410	C	2.821	461.40	
411	C	3.7	442.2	1H NMR (400 MHz, Methanol-d_4) δ 8.15 (s, 1H), 7.69 – 7.50 (m, 4H), 7.43 – 7.27 (m, 2H), 7.27 – 7.07 (m, 2H), 2.71 (q, J = 7.6, 2H), 1.22 (m, J = 7.6, 3H).
412	A	3.6	478.2	1H NMR (400 MHz, Methanol-d_4) δ 8.12 (s, 1H), 7.55 (d, J = 8.1 Hz, 2H), 7.43 – 7.37 (m, 2H), 7.10 – 7.05 (m, 2H), 3.67 (d, J = 15.0 Hz, 9H).
413	A	2.910	519.2	
414	A	3.22	460.2	1H NMR (400 MHz, Methanol-d_4) δ 8.63 (s, 1H), 8.17 (s, 1H), 7.56 (dd, J = 8.5, 6.9 Hz, 4H), 7.23 – 7.17 (m, 2H), 4.19 (q, J = 7.3 Hz, 2H), 1.41 (t, J = 7.3 Hz, 3H).
415	C	3.342	458.20	
416	A	3.66	478.2	1H NMR (400 MHz, Methanol-d_4) δ 8.15 (s, 1H), 7.67 (dd, J = 9.2, 5.0 Hz, 1H), 7.55 (dd, J = 9.2, 8.4 Hz, 1H), 7.43 – 7.37 (m, 2H), 7.11 – 7.05 (m, 2H), 3.67 (m, 8H).
417	A	2.93	519.2	1H NMR (400 MHz, Methanol-d_4) δ 8.17 (s, 1H), 7.69 (dd, J = 9.1, 5.0 Hz, 1H), 7.57 (dd, J = 9.2, 8.3 Hz, 1H), 7.40 (d, J = 8.2 Hz, 2H), 7.14 – 7.07 (m, 2H), 3.33 (p, J = 1.6 Hz, 1H), 2.98 (s, 3H), 2.58 (m, 4H), 2.13 – 2.00 (m, 2H), 1.98 (s, 3H), 1.91 (m, 2H).
418	A	3.42	460.2	

Compound No	HPLC-MS Method	retention time (min)	m+H Found	NMR
419	C	3.37	448.2	1H NMR (400 MHz, Methanol-d_4) δ 8.13 (d, J = 0.5 Hz, 1H), 7.81 – 7.71 (m, 2H), 7.66 – 7.59 (m, 2H), 7.55 (ddd, J = 9.2, 7.0, 0.5 Hz, 1H), 7.09 – 7.00 (m, 2H), 3.58 – 3.49 (m, 4H), 3.38 (s, 3H).
420	C	3.47	462.2	1H NMR (600 MHz, Methanol-d_4) δ 8.13 (s, 1H), 7.80 – 7.70 (m, 2H), 7.67 – 7.59 (m, 2H), 7.55 (dd, J = 8.9, 7.4 Hz, 1H), 7.11 – 6.95 (m, 2H), 3.48 (t, J = 6.5 Hz, 2H), 3.43 (t, J = 6.5 Hz, 2H), 3.34 (s, 3H), 1.86 (q, J = 6.5 Hz, 2H).
421	C	3.33	436.2	1H NMR (400 MHz, Methanol-d_4) δ 8.15 (s, 1H), 7.85 – 7.70 (m, 2H), 7.70 – 7.46 (m, 3H), 7.12 – 6.97 (m, 2H), 4.60 (t, J = 5.1 Hz, 1H), 4.48 (t, J = 5.1 Hz, 1H), 3.68 (t, J = 5.1 Hz, 1H), 3.62 (t, J = 5.1 Hz, 1H).
422	C	3.18	489.2	1H NMR (400 MHz, Methanol-d_4) δ 8.14 (s, 1H), 7.82 – 7.72 (m, 2H), 7.67 – 7.49 (m, 3H), 7.11 – 7.00 (m, 2H), 3.55 (t, J = 6.8 Hz, 2H), 2.96 – 2.71 (m, 6H), 1.17 (t, J = 7.2 Hz, 6H).
423	C	2.91	501.2	1H NMR (400 MHz, Methanol-d_4) δ 8.10 (s, 1H), 7.70 – 7.59 (m, 2H), 7.55 (dd, J = 9.2, 7.0 Hz, 1H), 7.45 – 7.32 (m, 2H), 7.14 – 6.99 (m, 2H), 3.20 – 2.86 (m, 3H), 2.57 (s, 6H), 2.05-2.01 (m, 4H), 1.61-1.51 (m, 2H).
424	C	3.13	446.2	1H NMR (400 MHz, Methanol-d_4) δ 7.85 (s, 1H), 7.61 (dd, J = 8.1, 1.1 Hz, 2H), 7.53 (dd, J = 9.2, 7.0 Hz, 1H), 7.05 – 6.88 (m, 4H), 4.48 (dt, J = 6.9, 3.5 Hz, 1H), 3.31 – 3.20 (m, 2H), 3.08 - 2.93 (m, 2H), 2.10 - 1.99 (m, 2H), 1.96 – 1.79 (m, 2H).
425	C	3.43	448.2	1H NMR (400 MHz, Methanol-d_4) δ 8.14 (s, 1H), 7.74 – 7.41 (m, 5H), 7.24 – 6.92 (m, 2H), 5.31 (dt, J = 6.1, 2.9 Hz, 1H), 4.79 - 3.99 (m, 4H).
426	C	3.04	446.2	1H NMR (400 MHz, Methanol-d_4) δ 8.13 (s, 1H), 7.70 – 7.47 (m, 5H), 7.14 – 6.96 (m, 2H), 4.71 – 4.51 (m, 2H), 4.38 (brs, 1H), 4.19 (brs, 1H), 3.94 (brs, 1H).
427	B	3.415	478.2	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.80 – 8.74 (m, 1H), 8.44 – 8.36 (m, 1H), 8.29 (s, 1H), 7.98 – 7.86 (m, 2H), 7.66 (dd, J = 8.2, 1.1 Hz, 1H), 7.58 (dd, J = 9.2, 7.0 Hz, 1H), 7.45 (d, J = 8.4 Hz, 1H), 7.39 – 7.32 (m, 1H), 7.02 (d, J = 7.0 Hz, 1H), 2.46 (s, 3H).
428	C	3.69	433.2	^{1}H NMR (400 MHz, Chloroform-d) δ 8.87 (brs, 1H), 8.51 (s, 1H), 7.94 (d, J = 3.0 Hz, 1H), 7.57 – 7.29 (m, 4H), 6.78 (d, J = 8.7 Hz, 2H), 5.41 (brs, 1H), 4.02 – 3.78 (m, 4H), 3.20 – 2.97 (m, 4H).

Compound No	HPLC-MS Method	retention time (min)	m+H Found	NMR
429	B	3.298	479.2	1H NMR (400 MHz, Methanol-d4) δ 8.65 (s, 1H), 8.45 (dd, J = 2.4, 0.8 Hz, 1H), 7.82 (dd, J = 8.6, 2.4 Hz, 1H), 7.69 – 7.61 (m, 3H), 7.55 (dd, J = 9.2, 7.0 Hz, 1H), 7.40 (dd, J = 9.3, 6.7 Hz, 1H), 7.05 (dd, J = 8.6, 0.8 Hz, 1H), 6.79 (dt, J = 6.7, 1.1 Hz, 1H), 2.36 (s, 3H).
430	C	3.385	429.20	^{1}H NMR (600 MHz, Methanol-d_4) δ 8.63 (d, J = 1.1 Hz, 1H), 8.36 (d, J = 2.6 Hz, 1H), 8.00 (s, 1H), 7.72 (ddd, J = 9.0, 2.9, 1.9 Hz, 1H), 7.64 – 7.60 (m, 2H), 7.54 (ddt, J = 9.1, 7.6, 1.4 Hz, 1H), 7.05 (dd, J = 9.0, 2.6 Hz, 1H), 2.48 (d, J = 1.5 Hz, 3H).
431	C	3.541	443.20	1H NMR (600 MHz, Methanol-d4) d 8.65 (s, 1H), 8.52 (d, J = 2.1 Hz, 1H), 8.02 (s, 1H), 7.85 (dd, J = 8.7, 2.2 Hz, 1H), 7.64 – 7.59 (m, 2H), 7.55 (dd, J = 8.9, 7.5 Hz, 1H), 7.05 (d, J = 8.6 Hz, 1H), 4.30 (q, J = 7.2 Hz, 2H), 1.48 (t, J = 7.2 Hz, 3H).
432	C	3.545	429.20	1H NMR (600 MHz, Methanol-d4) d 8.64 (d, J = 1.2 Hz, 1H), 8.37 (t, J = 2.4 Hz, 1H), 7.74 (dt, J = 8.9, 2.4 Hz, 1H), 7.65 – 7.60 (m, 3H), 7.55 (ddd, J = 9.0, 7.4, 2.1 Hz, 1H), 7.08 (dd, J = 8.9, 2.2 Hz, 1H), 2.35 (s, 3H).
433	C	3.97	496.2	1H NMR (600 MHz, Methanol-d_4) δ 8.64 (s, 1H), 8.51 (d, J = 2.4 Hz, 1H), 7.85 (dd, J = 8.7, 2.4 Hz, 1H), 7.71 – 7.59 (m, 3H), 7.55 (dd, J = 8.9, 7.4 Hz, 1H), 7.01 (d, J = 8.7 Hz, 1H), 3.79 (s, 3H).
434	C	3.79	430.2	1H NMR (400 MHz, Methanol-d_4) δ 8.95 (d, J = 2.2 Hz, 1H), 8.63 (s, 1H), 8.21 (dd, J = 8.7, 2.3 Hz, 1H), 7.71 – 7.47 (m, 3H), 7.01 (d, J = 8.7 Hz, 1H), 4.40 (s, 3H).
435	C	3.51	430.2	1H NMR (600 MHz, Methanol-d_4) δ 8.65 (d, J = 1.0 Hz, 1H), 8.42 (dd, J = 2.7, 0.7 Hz, 1H), 7.79 (dd, J = 8.9, 2.7 Hz, 1H), 7.68 – 7.59 (m, 2H), 7.59 – 7.48 (m, 1H), 7.11 (dd, J = 8.9, 0.8 Hz, 1H), 2.58 (s, 3H).
436	B	3.098	480.2	1H NMR (400 MHz, Methanol-d4) δ 9.25 (s, 1H), 8.54 (d, J = 2.8 Hz, 1H), 8.28 (s, 1H), 7.82 (d, J = 8.6 Hz, 1H), 7.76 (s, 1H), 7.66 – 7.61 (m, 3H), 7.59 – 7.54 (m, 2H), 2.41 (d, J = 1.0 Hz, 3H).
437	C	4.070	483.20	^{1}H NMR (400 MHz, Chloroform-d) δ 9.34 (s, 1H), 8.58 (s, 1H), 8.33 (d, J = 2.6 Hz, 1H), 8.10 (d, J = 0.9 Hz, 1H), 7.58 (dd, J = 8.9, 2.6 Hz, 1H), 7.48 (dd, J = 8.1, 0.9 Hz, 2H), 7.39 (dd, J = 9.0, 7.2 Hz, 1H), 6.89 (dd, J = 8.9, 0.7 Hz, 1H), 6.80 (s, 1H), 5.44 (s, 1H).
438	C	4.01	482.2	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.32 (q, J = 0.9 Hz, 1H), 8.18 (s, 1H), 7.63 (dd, J = 8.1, 1.1 Hz, 2H), 7.55 (dd, J = 9.2, 7.0 Hz, 1H), 7.49 – 7.35 (m, 2H), 7.27 – 7.11 (m, 2H).

Compound No	HPLC-MS Method	retention time (min)	m+H Found	NMR
439	C	2.992	447.2	
440	A	2.780	475.2	1H NMR (600 MHz, cdcl3) δ 8.32 (d, J = 2.8 Hz, 1H), 8.18 (s, 1H), 7.58 (s, 1H), 7.51 (d, J = 0.9 Hz, 1H), 7.49 (s, 1H), 7.42 (dd, J = 8.8, 7.4 Hz, 1H), 7.31 (dd, J = 8.5, 2.9 Hz, 1H), 7.26 (s, 1H), 6.75 (s, 1H), 5.42 (s, 1H), 3.85 (s, 2H), 3.62 (d, J = 4.1 Hz, 6H), 3.57 – 3.52 (m, 2H).
441	C	3.131	463.2	1H NMR (600 MHz, cdcl3) δ 8.34 (d, J = 2.8 Hz, 1H), 8.16 (s, 1H), 7.58 (s, 1H), 7.52 – 7.43 (m, 2H), 7.41 (dd, J = 8.8, 7.5 Hz, 1H), 7.32 – 7.24 (m, 3H), 6.75 (s, 1H), 5.28 (dtt, J = 56.5, 6.3, 3.5 Hz, 1H), 4.51 (dddd, J = 19.4, 10.4, 6.1, 1.7 Hz, 1H), 4.37 – 4.22 (m, 2H), 4.17 – 4.07 (m, 1H), 3.66 – 3.57 (m, 2H).
442	A	2.796	502.2	1H NMR (400 MHz, CDCl3) δ 9.13 (s, 1H), 8.62 (s, 1H), 8.35 (d, J = 2.4 Hz, 1H), 7.66 – 7.60 (m, 1H), 7.52 (dd, J = 8.0, 0.9 Hz, 2H), 7.43 (dd, J = 9.0, 7.2 Hz, 1H), 7.28 (s, 1H), 6.87 – 6.77 (m, 2H), 5.56 (s, 1H), 2.99 (s, 2H), 2.73 – 2.50 (m, 2H), 2.36 (s, 6H), 1.99 (s, 2H), 1.61 – 1.45 (m, 2H).
443	A	3.620	465.2	1H NMR (400 MHz, CDCl3) δ 9.24 (s, 1H), 8.55 (d, J = 36.2 Hz, 2H), 7.80 (d, J = 8.6 Hz, 1H), 7.52 (dd, J = 8.1, 0.9 Hz, 2H), 7.43 (dd, J = 9.0, 7.1 Hz, 1H), 6.81 (dd, J = 8.7, 0.8 Hz, 2H), 5.52 (s, 1H), 5.34 (d, J = 53.0 Hz, 2H), 4.08 – 3.58 (m, 4H).
444	A	3.519	456.2	1H NMR (400 MHz, CDCl3) δ 8.63 – 8.54 (m, 1H), 8.45 (dd, J = 8.7, 0.8 Hz, 1H), 8.02 (dd, J = 8.7, 2.4 Hz, 1H), 7.60 – 7.33 (m, 4H), 7.28 (s, 1H), 7.19 (s, 1H), 6.82 (d, J = 8.6 Hz, 1H), 4.68 – 4.45 (m, 4H), 3.62 (ddd, J = 15.4, 9.0, 6.4 Hz, 1H).
445	C	3.35	430.2	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.75 – 8.60 (m, 2H), 8.02 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.64 (dd, *J* = 8.1, 1.1 Hz, 2H), 7.56 (dd, *J* = 9.2, 7.0 Hz, 1H), 7.09 (dd, *J* = 8.8, 0.8 Hz, 1H), 4.22 (s, 3H).
446	C	3.62	483.2	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.38 – 8.29 (m, 2H), 8.25 (s, 1H), 7.76 (dd, *J* = 8.8, 0.7 Hz, 1H), 7.73 – 7.61 (m, 3H), 7.56 (dd, *J* = 9.2, 7.0 Hz, 1H).
447	B	3.182	500	--
448	A	2.668	488.2	1H NMR (600 MHz, cdcl3) δ 9.08 (s, 1H), 8.57 (s, 1H), 8.32 (s, 1H), 7.60 (d, J = 8.6 Hz, 1H), 7.48 (d, J = 8.3 Hz, 2H), 7.39 (dd, J = 8.8, 7.5 Hz, 1H), 6.86 – 6.68 (m, 2H), 5.51 (s, 1H), 3.69 (dd, J = 87.7, 30.2 Hz, 4H), 2.78 (s, 1H), 2.60 (s, 3H), 2.37 (d, J = 23.7 Hz, 3H), 2.01 (d, J = 24.7 Hz, 2H).

Compound No	HPLC-MS Method	retention time (min)	m+H Found	NMR
449	A	3.622	449.2	
450	C	3.169	437.20	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.35 (s, 1H), 7.97 (d, *J* = 3.0 Hz, 1H), 7.72 – 7.67 (m, 1H), 7.65 – 7.49 (m, 4H), 7.08 – 7.03 (m, 2H), 6.87 (s, 1H), 5.50 (s, 1H), 5.45 – 5.08 (m, 1H), 4.02 – 3.61 (m, 5H), 2.18 (d, *J* = 98.0 Hz, 2H).
451	C	3.246	508.00	1H NMR (400 MHz, Chloroform-d) d 8.51 (s, 1H), 7.69 (s, 1H), 7.56 – 7.50 (m, 2H), 7.48 – 7.39 (m, 3H), 7.08 – 7.02 (m, 2H), 6.79 (s, 1H), 5.49 (s, 1H), 4.14 (t, J = 5.1 Hz, 4H), 3.09 (s, 4H).
452	C	3.246	483.20	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (s, 1H), 7.93 (d, *J* = 2.8 Hz, 1H), 7.68 – 7.63 (m, 1H), 7.59 – 7.46 (m, 2H), 7.45 – 7.37 (m, 2H), 7.08 – 6.99 (m, 2H), 6.84 (s, 1H), 5.52 (s, 1H), 4.17 – 3.97 (m, 4H), 3.05 (t, *J* = 5.4 Hz, 4H).
453	E	0.834	473.2	
454	C	3.031	435.20	1H NMR (400 MHz, Chloroform-d) d 8.29 (s, 1H), 7.92 (d, J = 3.0 Hz, 1H), 7.68 – 7.62 (m, 1H), 7.58 – 7.44 (m, 2H), 7.43 – 7.35 (m, 2H), 7.06 – 6.98 (m, 2H), 6.82 (s, 1H), 5.45 (s, 1H), 3.66 (d, J = 17.2 Hz, 6H).
455	B	2.485	495.18	1H NMR (400 MHz, Methanol-d4) δ 8.28 (d, J = 2.2 Hz, 1H), 8.10 (s, 1H), 7.63 (dd, J = 8.1, 1.1 Hz, 2H), 7.55 (dd, J = 9.2, 7.0 Hz, 1H), 7.50 (dd, J = 8.5, 2.8 Hz, 1H), 7.42 (dd, J = 8.5, 0.7 Hz, 1H), 3.73 (s, 2H), 3.16 – 2.96 (m, 8H).
456	C	3.75	458.2	1H NMR (400 MHz, Methanol-d_4) δ 8.12 (s, 1H), 7.68 – 7.48 (m, 5H), 7.05 (d, *J* = 8.8 Hz, 2H), 4.10 (s, 2H), 3.83 (s, 2H), 1.31 (s, 6H).
457	C	3.030	499.20	1H NMR (400 MHz, Methanol-d4) d 8.27 (s, 1H), 7.96 (dd, J = 8.3, 1.4 Hz, 1H), 7.91 (dd, J = 7.8, 1.3 Hz, 1H), 7.69 (t, J = 8.1 Hz, 1H), 7.48 – 7.40 (m, 2H), 7.14 – 7.06 (m, 2H), 4.05 (d, J = 6.0 Hz, 4H), 3.17 (t, J = 5.5 Hz, 4H).
458	C	3.094	451.20	1H NMR (400 MHz, Methanol-d4) d 8.26 (s, 1H), 7.96 (dd, J = 8.2, 1.4 Hz, 1H), 7.91 (dd, J = 7.8, 1.4 Hz, 1H), 7.69 (t, J = 8.1 Hz, 1H), 7.43 – 7.31 (m, 2H), 7.12 – 7.04 (m, 2H), 3.64 (d, J = 14.6 Hz, 8H).
459	C	3.234	453.20	

Compound No	HPLC-MS Method	retention time (min)	m+H Found	NMR
460	C	3.8	480.2	1H NMR (400 MHz, Methanol-d_4) δ 8.35 (dd, J = 2.9, 0.7 Hz, 1H), 8.26 (s, 1H), 7.69 – 7.54 (m, 5H), 2.24 (t, J = 19.0 Hz, 3H).
461	C	2.958	464.2	1H NMR (600 MHz, cdcl3) δ 7.46 (d, J = 8.4 Hz, 2H), 7.43 (d, J = 0.9 Hz, 1H), 7.39 – 7.36 (m, 1H), 7.35 (d, J = 11.0 Hz, 2H), 7.21 (s, 1H), 6.67 (s, 1H), 5.34 (s, 1H), 4.91 (s, 2H), 3.69 – 3.63 (m, 2H), 3.60 (q, J = 4.6 Hz, 4H), 3.55 (q, J = 4.5, 4.1 Hz, 2H).
462	C	3.183	409.2	
463	B	3.05	509.2	^{1}H NMR (600 MHz, Methanol-d_4) δ 8.34 (d, J = 2.8 Hz, 1H), 8.22 (s, 1H), 7.70 (d, J = 8.6 Hz, 1H), 7.66 – 7.61 (m, 2H), 7.56 (dd, J = 8.9, 7.4 Hz, 1H), 7.52 (dd, J = 8.6, 2.9 Hz, 1H), 4.18 (s, 4H), 3.26 (s, 4H).
464	C	3.697	459.20	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.35 (d, J = 2.9 Hz, 1H), 8.23 (s, 1H), 7.94 (d, J = 8.7 Hz, 1H), 7.72 – 7.62 (m, 2H), 7.58 (dd, J = 9.2, 6.9 Hz, 1H), 7.49 (dd, J = 8.7, 2.9 Hz, 1H), 4.39 (d, J = 1.1 Hz, 2H), 3.86 (d, J = 1.0 Hz, 2H), 1.34 (s, 6H).
465	C	3.796	459.20	^{1}H NMR (400 MHz, Methanol-d_4) δ 8.64 (s, 1H), 8.58 (dd, J = 2.4, 0.8 Hz, 1H), 7.89 (dd, J = 8.7, 2.4 Hz, 1H), 7.71 – 7.62 (m, 2H), 7.62 – 7.50 (m, 1H), 6.93 (dd, J = 8.8, 0.8 Hz, 1H), 4.15 (s, 2H), 3.86 (s, 2H), 1.33 (s, 6H).
466	C	3.092	521.2	1H NMR (400 MHz, Methanol-d4) δ 8.14 (s, 1H), 7.67 – 7.62 (m, 2H), 7.57 (dd, J = 9.2, 7.0 Hz, 1H), 7.51 – 7.44 (m, 2H), 7.15 – 7.06 (m, 2H), 4.29 – 4.12 (m, 2H), 3.88 (ddd, J = 14.5, 8.6, 3.2 Hz, 2H), 3.31 – 3.20 (m, 4H), 2.81 (s, 3H).
467	C	3.670	476.2	1H NMR (400 MHz, Methanol-d4) δ 8.13 (s, 1H), 7.68 – 7.62 (m, 2H), 7.57 (dd, J = 9.2, 6.9 Hz, 1H), 7.45 – 7.32 (m, 2H), 7.15 – 7.06 (m, 2H), 3.89 (s, 4H), 2.68 (d, J = 5.8 Hz, 4H)
468	C	2.97	507.2	1H NMR (400 MHz, Methanol-d4) δ 8.14 (s, 1H), 7.67 – 7.62 (m, 2H), 7.57 (dd, J = 9.2, 7.0 Hz, 1H), 7.50 – 7.44 (m, 2H), 7.14 – 7.08 (m, 2H), 4.27 – 4.12 (m, 2H), 3.94 (ddd, J = 14.5, 8.3, 3.2 Hz, 2H), 3.25 (d, J = 13.3 Hz, 4H).
469	C	2.921	512.0	1H NMR (400 MHz, CDCl3) δ 7.54 – 7.38 (m, 5H), 7.36 (s, 1H), 7.28 (s, 1H), 6.72 (s, 1H), 5.43 (s, 1H), 4.98 (s, 2H), 4.25 – 4.04 (m, 4H), 2.98 (d, J = 35.0 Hz, 4H).
470	B	3.326	494.2	

Compound No	HPLC-MS Method	retention time (min)	m+H Found	NMR
471	B	3.338	533	
472	E	0.92	534.0	
473	HPLC MS-C	3.47	478.2	
474	D	3.11	480.2	
475	A	3.59	485.2	
476	B	3.16	490.2	
477	D	3.12	497.2	
478		1.75	473.1	^{1}H NMR (CD_3OD) δ 3.51 (m, 1H), δ 4.25 (m, 2H), δ 4.52 (d, 2H), δ 7.06 (d, 2H), δ 7.55 (m, 1H), δ 7.63 (m, 4H), δ 8.14 (s, 1H).

Example 20

The compounds listed in Table 1 were tested for their ability to inhibit a set of kinases according to the following procedures.

Biochemical assays:

The basic protocol for TR-FRET LanthaScreen Eu Kinase Binding Assay inhibitor studies were performed as follows. LanthaScreen Kinase Binding Assays (ThermoFisher/USA) to evaluate inhibitors were performed by addition of 5 μL of test compound in corresponding DMSO dilutions/ 5 µl of kinase/antibody mixture, 5 μL of tracer into 384 well small volume plates. After incubation for 1 hour at room temperature, plates were read. Data analysis of emission ratios was according LanthaScreen Eu Kinase Binding Assay protocol.

Kinase and assay components were adjusted to final concentrations according to kit protocol. For LRRK2: 5 nM wt human LRRK2, catalytic site, or G2019S human LRRK2, catalytic site (ThermoFisher/USA), 2 nM Eu-Anti-GST Antibody, 10 nM Kinase Tracer 236 in 1X Kinase Buffer A. For NUAK1: 8 nM wt human NUAK1, full length (ThermoFisher/USA), 2 nM Eu-Anti-His Antibody, 5 nM Kinase Tracer 236 in 1X Kinase Buffer A.

Basic protocol for Z´-LYTE Assays (ThermoFisher/USA) inhibitor studies involved two steps:

Kinase reaction: Addition of 2 μL of test compound in corresponding DMSO dilutions, 5 µL of kinase/substrate mixture, 3 μL of ATP into 384 well small volume plates. Incubation for at least 1 hour at room temperature.

Development reaction: Addition of 5 μL development reagent, incubation for 1 hour at room temperature, addition of 5 μL stop reagent, read plate. Data analysis of emission ratios according to Z'-LYTE assay protocol.

Kinase and assay components were adjusted to final concentrations according to kit protocol. For JAK2: 5 nM wt human JAK2, catalytic site (ThermoFisher/USA), 2 μM Z´-LYTE Tyr 06 Peptide, 36 μM ATP in Kinase Buffer.

Basic protocol for HTRF KinEASE assay (Cisbio/FRA) inhibitor studies involved two steps:

Enzymatic step: Addition of 4 μL of test compound in corresponding DMSO dilutions, 4 μL of kinase/substrate mixture, 2 μL of ATP into 384 well small volume plates. Incubation for at least 30 minutes at room temperature.

Detection step: Addition of 5 μL antibody and 5 µL streptavidin-XL665, read plate after 60 minutes. Data analysis of emission ratios according KinEASE assay protocol.

Kinase and assay components were adjusted to final concentrations according to kit protocol. For TYK2: 2 nM wt human TYK2, catalytic site (SignalChem/CAN), 1 μM HTRF KinEASE-TK Substrate-biotin, 1 μM ATP in 1x Kinase Buffer. For JAK1: 4 nM wt human JAK1, catalytic site (ThermoFisher/USA), 1 μM HTRF KinEASE-TK Substrate-biotin, 2.5 μM ATP in 1x Kinase Buffer. For JAK2: 1 nM wt human JAK2, catalytic site (SignalChem/CAN), 1 μM HTRF KinEASE-TK Substrate-biotin, 100 μM ATP in 1x Kinase Buffer.

Results for from biochemical tests were as follows:

Activity toward TYK2

The following compounds had an IC_{50} lower than 10 nM: Compound Nos. 17, 22, 32, 36, 42, 45, 46, 57, 58, 62, 83, 84, 85, 86, 87, 88, 89, 91, 95, 203, 207, 212, 214, 215, 227, 230, 231, 237, 238, 243, 247, 249, 254, 259, 275, 276, 277, 281, 283, 292, 294, 297, 299, 301, 302, 305, 314, 315, 316, 332, 333, 338, 342, 347, 348, 349, 361, 371, 411, 413, 414, 415, 416, 425, 426, 450, 451, 452, 453, 454, 456, 457, 458, 459, 463, 466, 467, and 468.

The following compounds had an IC_{50} between 10 nM and 100 nM: Compound Nos. 12, 13, 14, 15, 16, 26, 27, 28, 29, 30, 31, 34, 35, 38, 40, 44, 47, 48, 49, 50, 51, 52, 54, 55, 56, 60, 61, 63, 68, 69, 70, 72, 73, 74, 78, 79, 80, 82, 90, 92, 93, 94, 96, 202, 204, 205, 206, 208, 209, 210, 211, 213, 216, 225, 226, 228, 229, 232, 233, 241, 242, 246, 248, 251, 267, 268, 269, 270, 271, 273, 284, 285, 286, 288, 291, 293, 295, 296, 298, 300, 303, 304, 306, 307, 308, 310, 313, 317, 318, 319, 321, 322, 323, 325, 326, 327, 330, 331, 340, 341, 351, 354, 355, 356, 357, 358, 359, 360, 362, 363, 364, 365, 366, 367, 370, 373, 375, 376, 378, 383, 385, 386, 387, 388, 391, 400, 412, 417, 418, 419, 421, 422, 423, 424, 429, 433, 435, 436, 438, 443, 444, 445, 447, 455, 461, 464, 469, 472, and 473.

The following compounds had an IC_{50} between 100 nM and 1000 nM: Compound Nos. 4, 5, 6, 7, 8, 10, 11, 18, 21, 23, 24, 25, 33, 37, 39, 41, 43, 53, 59, 64, 67, 71, 75, 77, 81, 201, 218, 224, 236, 240, 253, 257, 260, 261, 263, 266, 272, 274, 278, 279, 280, 287, 289, 309, 311, 324, 328, 329, 334, 337, 339, 343, 344, 345, 346, 350, 352, 368, 369, 372, 374, 377, 379, 380, 381, 383, 384, 390, 392, 393, 394, 395, 397, 398, 401, 402, 403, 405, 407, 420, 427, 428, 430, 431, 432, 434, 439, 440, 441, 442, 448, 449, 460, 462, 465, 470, 471, 475, and 476.

Activity toward LRRK2(wt) and LRRK2(G2019)

The following compounds had an IC_{50} between 10 nM and 100 nM: Compound Nos. 12, 35, 36, 45, 56, 58, 62, 63, 208, 211, 304, and 309.

The following compounds had an IC_{50} between 100 nM and 1000 nM: Compound Nos. 4, 7, 8, 10, 11, 13, 14, 15, 16, 17, 18, 22, 23, 26, 27, 30, 31, 32, 34, 37, 38, 40, 42, 46, 47, 48, 49, 50, 51, 52, 53, 54, 57, 59, 60, 61, 64, 68, 70, 71, 80, 82, 83, 84, 85, 86, 87, 88, 89, 202, 205, 206, 207, 212, 225, 227, 228, 229, 230, 231, 232, 233, 246, 247, 248, 249, 259, 260, 267, 268, 272, 276, 283, 284, 285, 286, 287, 288, 295, 296, 299, 302, 303, 305, 308, 310, 313, 315, 316, 317, 318, 321, 322, 323, 326, 331, 333, 342, 344, 347, 349, 355, 359, 361, 376, 386, 387, 388, 391, 394, 395, 400, 414, 415, 416, 417, 418, 421, 422, 423, 425, 426, 436, 450, 452, 453, 454, 456, 466, and 472.

Activity toward NUAK1

The following compounds had an IC_{50} between 10 nM and 100 nM: Compound Nos. 8, 13, 14, 22, 38, 227, 287, 288, and 295.

The following compounds had an IC_{50} between 100 nM and 1000 nM: Compound Nos. 4, 7, 12, 15, 16, 27, 30, 31, 35, 36, 44, 48, 54, 56, 58, 61, 62, 68, 82, 86, 87, 88, 91, 202, 203, 205, 206, 207, 208, 211, 212, 214, 225, 228, 229, 230, 232, 237, 248, 249, 251, 284, 285, 286, 296, 308, 309, 313, 314, 317, 318, 319, 323, 327, 331, 332, 333, 338, 342, 349, 359, 361, 403, 407, 416, 417, 422, 423, 424, 452, 453, and 454.

Activity toward JAK1

The following compounds had an IC_{50} lower than 10 nM: Compound Nos. 42, 46, 229, 231, 241, 291, 436, 451, 452, 453, 467, and 468.

The following compounds had an IC_{50} between 10 nM and 100 nM: Compound Nos. 17, 22, 26, 31, 32, 34, 35, 36, 38, 39, 40, 49, 51, 53, 58, 59, 60, 74, 80, 82, 84, 85, 86, 87, 88, 91, 92, 94, 96, 203, 205, 206, 207, 208, 212, 214, 215, 216, 225, 227, 228, 230, 232, 233, 238, 242, 243, 246, 247, 248, 254, 259, 260, 266, 267, 268, 269, 270, 271, 272, 273, 275, 276, 285, 292, 293, 294, 295, 302, 303, 305, 308, 310, 313, 314, 315, 316, 317, 318, 319, 321, 322, 326, 327, 330, 333, 347, 348, 359, 361, 365, 376, 377, 386, 387, 388, 391, 411, 412, 413, 414, 415, 416, 417,

418, 419, 421, 422, 423, 425, 426, 431, 432, 433, 435, 439, 440, 443, 444, 445, 447, 448, 450, 454, 456, 457, 458, 459, 461, 462, 463, 466, 469, 472, 473, and 476.

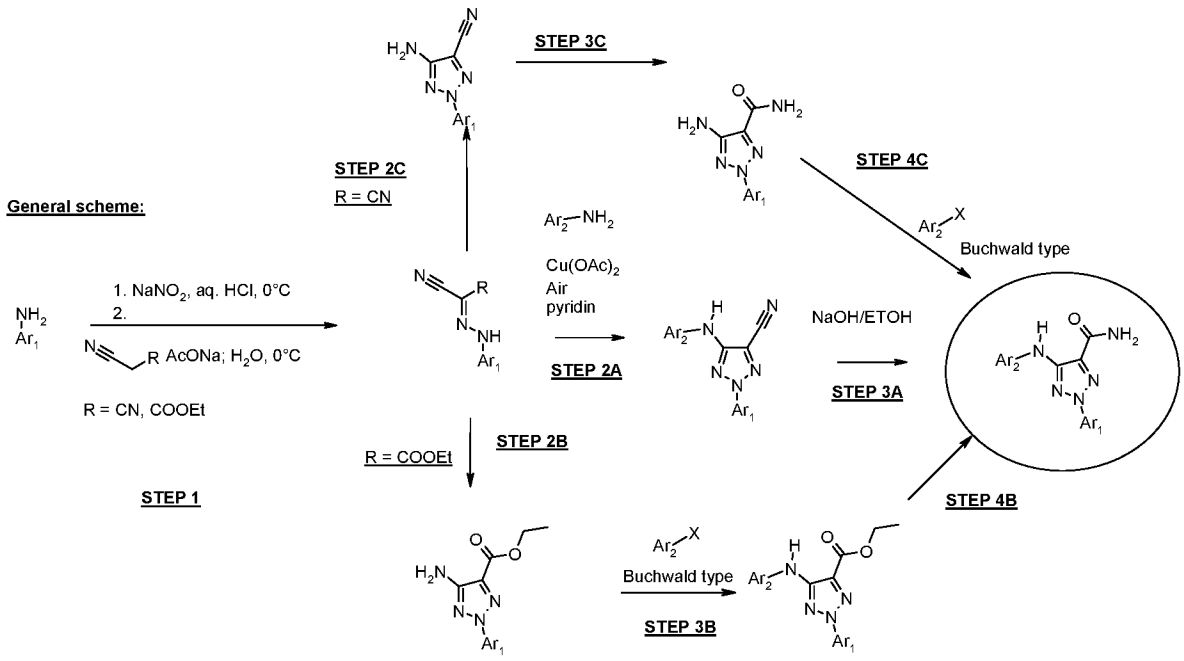
The following compounds had an IC_{50} between 100 nM and 1000 nM: Compound Nos. 8, 11, 12, 13, 14, 15, 16, 18, 27, 28, 29, 30, 33, 37, 41, 43, 44, 45, 47, 48, 50, 52, 54, 55, 56, 57, 61, 62, 63, 64, 67, 68, 69, 70, 71, 72, 73, 75, 76, 77, 78, 79, 83, 89, 90, 93, 95, 202, 204, 209, 210, 211, 213, 217, 218, 222, 224, 226, 234, 237, 240, 249, 251, 253, 261, 263, 277, 281, 283, 284, 286, 287, 288, 296, 297, 298, 299, 300, 304, 307, 309, 323, 324, 325, 331, 332, 334, 338, 340, 341, 342, 349, 350, 351, 352, 354, 355, 356, 357, 358, 360, 362, 363, 364, 366, 367, 370, 371, 373, 374, 375, 378, 379, 380, 381, 383, 383, 384, 385, 390, 392, 393, 394, 395, 397, 398, 400, 401, 402, 405, 407, 420, 424, 428, 429, 430, 437, 438, 441, 442, 449, 455, 460, 464, 470, 471, and 475.

Activity toward JAK2

The following compounds had an IC_{50} between 100 nM and 1000 nM: Compound Nos. 12, 13, 17, 22, 32, 36, 57, 58, 62, 87, 88, 90, 94, 96, 202, 203, 205, 206, 207, 210, 211, 212, 227, 229, 238, 322, 333, 347, 414, 416, 425, 451, 452, 454, and 457.

Example 21

Certain compounds that were used as reagents in synthesis schemes described herein were prepared by the following schemes.



General procedure:

Step 1:

In a round bottom flask, equipped with a magnetic stirrer, aniline (1 eq) was dissolved in aq. 6M HCl (1 mL/mmol). The reaction was cooled to -10 °C in an ice-salt bath. Aq. 1M $NaNO_2$ (1 mL/mmol) was added with a dropping funnel in 20 min at -10 °C. The reaction was stirred at -10 °C for 90 min and then added at once to a solution of the Malone component (1.5 eq) and NaOAc (1 eq.) in MeOH (139 mL) kept at -10 °C in an ice-salt bath. The reaction was stirred at -10 °C until a precipitate formed. The solid was collected by suction filtration. The resulting solution was kept overnight at 5 °C and the filtration repeated. After concentration under reduced pressure and cooling overnight at 5 °C, the filtration was repeated. All the solids from the filtrations were assembled and dried in vacuum.

The desired products were obtained as yellow solid for R= CN or red solids for R= COOEt.

Route A:

Step 2A:

Product of step 1 and the amine (1.5 eq.) are dissolved in pyridine (0.2 mL/mmol). The mixture is stirred at 80 °C. After 20 min, Cu(OAc)2 (1eq.) is added. Then the mixture is stirred

at 80 °C overnight. The mixture is evaporated, then the residue is dissolved in (5 -10 mL/mmol) acetonitrile and add cold water (~50-100 mL/mmol). The precipitated crude product is collected by filtration and purified by gradient flash chromatography.

Step 3A:

The product of step 2A is dissolved in water/ethanol 1:1 (1.5 mL/mmol) and 5 eq. NaOH (5eq.) was added . The mixture is stirred at rt overnight. The mixture is evaporated, dissolve in water and extracted with DCM. The organic layer is dried over Na_2SO_4, filtered and concentrated under reduced pressure to get the crude product. The crude product is purified by semi preparative HPLC (acetonitrile / water). After evaporation and Lyophilization a colourless solid compound is obtained

Route B

Step 2B:

In a 20 mL microwave vial, equipped with a magnetic stirrer, product of Step1 (1 eq) was dissolved in 24 mL/g of dry Pyridine. NH4Cl (1.3 eq) was added. The reaction was stirred at 80 °C for 20 min. Cu(OAc)2H2O (2 eq.) was added and the reaction was stirred at 80 °C overnight and monitored by HPLC MS. After completion, the solvent was removed under reduced pressure. The residue was suspended in EtOAc and filtered through a celite pad. The filtrate was concentrated under reduced pressure till dryness and the final product purified by gradient silica gel column chromatography (EtOAc:Cyc, 0 to 100%). The desired product was obtained as yellow solid

Step 3B:

The product of step 2B, bromo-aryl/heteroaryl compound (1.2 eq.), XPhos (0.25 eq.), 3rd Generation t-BuBrett Pd precatalyst (0.25 eq.), and t-BuONa (1.5 eq.) were mixed in a microwave vial. The vial was sealed and purged with nitrogen. Then, anhydrous 1 ,4-dioxane (3 mL) was added to the mixture. The mixture was bubbled with N2 for 15 min, then it was stirred at 95 °C for 1 to 3 h. The reaction was controlled by LC-MS. When the reaction was finished, the crude was cooled down till room temperature, filtered through a HPLC filter using abundant

methanol, and then concentrated until dryness under reduced pressure. The compound was purified by gradient silica gel column chromatography

Step 4B:

The product of step 3B(1 eq.) was dissolved in THF (5 mL/1 mmol) and then ammonium hydroxide solution was added (33% in water, 30 mL/ mmol). The reaction was stirred at room temperature overnight. After completion, the product was extracted from the water using ethyl acetate (3x100 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The product was then purified by preparative reversed phase HPLC chromatography. After that purification, the tubes containing the product were combined, dried under reduced pressure, re-dissolved in t-Butanol/water, freeze and lyophilized.

Route C

Step 2C:

In a 20 mL microwave vial, equipped with a magnetic stirrer, product of Step1 (1 eq) was dissolved in 24 mL/g of dry Pyridine. NH4Cl (1.3 eq) was added. The reaction was stirred at 80 ^{o}C for 20 min. Cu(OAc)2H2O (2 eq.) was added and the reaction was stirred at 80 ^{o}C overnight and monitored by HPLC MS. After completion, the solvent was removed under reduced pressure. The residue was suspended in EtOAc and filtered through a celite pad. The filtrate was concentrated under reduced pressure till dryness and the final product purified by gradient silica gel column chromatography (EtOAc:Cyc-hexane, 0 to 100%).
The desired product was obtained as a yellow solid

Step 3C:

In a round bottom flask equipped with a magnetic stirrer, the product of Step 2C (1 eq) was dissolved in EtOH:H2O, (1:1). NaOH (5 eq) was added and the reaction was stirred at 40 ^{o}C overnight and monitored by HPLC MS. After completion, the solvent was removed under reduced pressure. The residue was partitioned between DCM-H2O (1:1) and extracted with DCM (3x). The organic layers were assembled, washed with brine and dried ($MgSO_4$). The solvent was removed under reduced pressure to afford the desired product as a yellow solid.

Step 4C:

In a 20 mL microwave vial, equipped with a magnetic stirrer, the product of Step3C (1 eq), the bromide (1.5 eq.) and NaOtBu (3 eq) were dissolved in 2 mL of dry dioxane. The resulting solution was degassed for 5 min in an ultrasound bath. tBuBrettphos Pd G3 (0.25 eq) and XPhos (0.25 eq) were added and the reaction further degassed as before. The reaction was stirred at 100 ^{0}C in an oil bath and monitored by HPLC MS. After completion, the solution was cooled down to room temperature, diluted with MeOH and filtered through a celite pad. The resulting solution was concentrated under reduced pressure and the product pre purified on an by gradient silica gel column chromatography. The final product was further purified using an Agilent semi preparative reverse phase machine. The product was obtained as a white powder after lyophilization from tBuOH-H_2O.

Route D

The intermediate from Step 2C was treated as described in Step 4C to produce the corresponding nitrile from Step 2A, which was then hydrolyze according to Step 3A.

Example 22

Chemical analytical data for the compounds listed in Table 1a is summarized in Table 8.

Table 8.

Compound No	Synthesis Route	HPLC-MS Method	retention time (min)	m+H Found	NMR
101	A	C	3.450	461.2	1H NMR (400 MHz, Chloroform-d) δ 8.64 (s, 1H), 7.59 (d, J = 8.4 Hz, 2H), 7.56 – 7.46 (m, 3H), 7.43 (d, J = 8.5 Hz, 2H), 6.68 (s, 1H), 5.80 – 5.60 (m, 1H), 3.71 (s, 8H).
102	A	C	3.080	474.2	1H NMR (400 MHz, Chloroform-d) δ 8.65 (s, 1H), 7.64 – 7.56 (m, 2H), 7.58 – 7.50 (m, 2H), 7.48 (dd, J = 9.4, 6.5 Hz, 1H), 7.47 – 7.39 (m, 2H), 6.67 (s, 1H), 5.74 (s, 1H), 3.83 (s, 4H), 2.67 (s, 4H), 2.49 (s, 3H).
103	A	C	2.980	416.2	
104	A	C	3.580	430.2	
105	A	C	3.020	488.2	
106	A	C	4.000	463.0	
107	A	C	3.440	456.2	1H NMR (800 MHz, Chloroform-d) δ 8.74 (s, 1H), 7.65 (s, 1H), 7.66 – 7.60 (m, 3H), 7.62 – 7.53 (m, 2H), 7.54 – 7.46 (m, 1H), 6.66 (s, 1H), 5.61 (s, 1H), 4.57 – 4.53 (m, 2H), 4.50 (s, 2H), 3.56 (ddt, J = 15.5, 9.0, 5.6 Hz, 1H).
108	A	C	3.040	474.2	
109	A	C	3.430	469.2	
110	A	C	3.820	470.2	
111	A	C	3.870	470.2	
112	C	B	3.731	526.2	1H NMR (600 MHz, Methanol-d4) d 7.75 (d, J = 1.4 Hz, 1H), 7.72 – 7.69 (m, 2H), 7.67 – 7.65 (m, 2H), 7.63 – 7.60 (m, 2H), 7.59 (s, 1H), 4.15 (t, J = 5.3 Hz, 2H), 3.80 (t, J = 5.3 Hz, 2H).

Compound No	Synthesis Route	HPLC-MS Method	retention time (min)	m+H Found	NMR
113	C	B	3.317	479.2	1H NMR (400 MHz, Methanol-d4) d 8.60 (s, 1H), 7.77 – 7.72 (m, 2H), 7.66-7.58 (dd, J = 2.7. 25 Hz, 1H), 7.64 – 7.60 (m, 2H), 7.58 – 7.54 (m, 2H), 6.16 (tt, J = 54.3, 2.8 Hz, 1H), 4.56 (td, J = 15.6, 2.9 Hz, 3H).
114	C	C	3.170	461.2	1H NMR (400 MHz, Methanol-d4) δ 7.70 – 7.51 (m, 3H), 7.51 – 7.37 (m, 2H), 6.97 – 6.81 (m, 2H), 4.42 (brs, 1H), 2.99 (brs, 2H), 2.74 (brs, 2H), 2.54 (s, 3H), 2.13 – 1.76 (m, 4H).
115	C	C	4.080	496.2	1H NMR (400 MHz, Methanol-d4) δ 7.76 – 7.52 (m, 8H), 3.78 (s, 3H).
116	B	B	3.337	457.2	
117	C	B	3.061	429.2	1H NMR (400 MHz, Chloroform-d) δ 8.64 (s, 1H), 7.59 (d, J = 8.4 Hz, 2H), 7.56 – 7.46 (m, 3H), 7.43 (d, J = 8.5 Hz, 2H), 6.68 (s, 1H), 5.80 – 5.60 (m, 1H), 3.71 (s, 8H).
118		C	4.140	540.2	1H NMR (400 MHz, Chloroform-d) δ 8.66 (s, 1H), 7.69 – 7.62 (m, 2H), 7.60 – 7.51 (m, 4H), 7.53 – 7.44 (m, 2H), 6.66 (s, 1H), 5.64 (s, 1H), 4.17 (t, J = 5.1 Hz, 2H), 3.65 (t, J = 5.1 Hz, 2H), 3.37 (s, 3H).
119	A	C	3.502	463.2	1H NMR (400 MHz, Chloroform-d) δ 8.68 (s, 1H), 7.76 (d, J = 8.7 Hz, 2H), 7.63 – 7.51 (m, 4H), 7.48 (ddd, J = 9.3, 6.5, 0.7 Hz, 1H), 6.80 (d, J = 5.4 Hz, 1H), 6.66 (s, 1H), 5.62 (s, 1H), 3.59 (q, J = 5.9 Hz, 4H), 3.40 (d, J = 0.7 Hz, 3H), 1.90 (p, J = 5.8 Hz, 2H).
120	A	C	3.250	447.2	1H NMR (400 MHz, Chloroform-d) δ 8.27 (s, 1H), 7.58 – 7.39 (m, 5H), 6.90 (d, J = 8.8 Hz, 2H), 6.63 (s, 1H), 6.09 (broad s, NH), 5.76 (s, 1H), 4.46 (s, 1H), 3.27 (s, 2H), 3.03 (s, 2H), 2.13 (d, J = 14.8 Hz, 2H), 2.00 – 1.86 (m, 2H).
121	B	C	4.399	511.2	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.70 (s, 1H), 7.73 – 7.63 (m, 2H), 7.55 – 7.46 (m, 2H), 7.45 (dd, *J* = 9.4, 6.5 Hz, 1H), 7.39 – 7.30 (m, 2H), 6.63 (s, 1H), 5.62 (s, 1H), 2.79 (q, *J* = 7.6 Hz, 2H), 1.30 (t, *J* = 7.6 Hz, 3H).
122	A	C	3.020	502.3	1H NMR (400 MHz, Chloroform-d) δ 8.62 (s, 1H), 7.65 – 7.45 (m, 5H), 7.45 – 7.37 (m, 2H), 6.66 (s, 1H), 5.68 (s, 1H), 3.20 (s, 2H), 2.91 (s, 2H), 2.56 (td, J = 11.4, 5.8 Hz, 1H), 2.36 (s, 6H), 1.90 (s, 2H), 1.51 (d, J = 12.5 Hz, 2H).

Compound No	Synthesis Route	HPLC-MS Method	retention time (min)	m+H Found	NMR
123	A	C	3.410	449.2	1H NMR (400 MHz, Chloroform-d) δ 8.68 (s, 1H), 7.83 – 7.74 (m, 2H), 7.65 – 7.57 (m, 2H), 7.58 – 7.44 (m, 3H), 6.65 (s, 1H), 6.48 (d, J = 5.3 Hz, 1H), 5.62 (s, 1H), 3.67 (td, J = 5.6, 4.3 Hz, 2H), 3.58 (dd, J = 5.4, 4.2 Hz, 2H), 3.41 (s, 3H).
124	A	C	3.150	447.2	1H NMR (400 MHz, Methanol-d4) δ 7.72 – 7.59 (m, 7H), 4.68 – 4.59 (m, 2H), 4.40 (s, 1H), 4.20 (s, 1H), 3.95 (d, J = 10.5 Hz, 1H).
125	B	C	3.470	457.2	^{1}H NMR (400 MHz, Methanol-d_4) δ 7.82 – 7.74 (m, 2H), 7.70 – 7.60 (m, 3H), 7.59-7.51 (m, 3H), 4.58 (sept, J = 6.8 Hz, 1H), 1.50 (d, J = 6.7 Hz, 6H).
126	B	C	3.850	443.2	^{1}H NMR (400 MHz, Methanol-d_4) δ 7.85 – 7.72 (m, 2H), 7.72 – 7.54 (m, 4H), 7.49 – 7.36 (m, 2H), 2.72 (q, J = 7.5 Hz, 2H), 1.22 (t, J = 7.5 Hz, 3H).
127	C	B	2.419	475.2	1H NMR (600 MHz, cdcl3) δ 9.22 (s, 1H), 8.40 (t, J = 2.5 Hz, 1H), 7.97 (dd, J = 8.6, 0.9 Hz, 1H), 7.75 (dd, J = 8.7, 2.3 Hz, 1H), 7.53 (d, J = 8.6 Hz, 2H), 7.48 (dd, J = 9.8, 2.7 Hz, 1H), 6.64 (s, 1H), 5.82 (s, 1H), 4.15 – 3.29 (m, 8H), 2.35 (s, 3H).
128	A	C	3.460	437.2	1H NMR (400 MHz, Chloroform-d) δ 8.71 (s, 1H), 7.83 – 7.73 (m, 2H), 7.65 – 7.57 (m, 2H), 7.55 (d, J = 6.8 Hz, 2H), 7.49 (dd, J = 9.4, 6.5 Hz, 1H), 6.66 (s, 1H), 6.43 (t, J = 5.9 Hz, 1H), 5.63 (s, 1H), 4.68 (t, J = 4.7 Hz, 1H), 4.56 (t, J = 4.7 Hz, 1H), 3.83 (q, J = 5.1 Hz, 1H), 3.76 (q, J = 5.1 Hz, 1H).
129	A	C	3.560	449.0	1H NMR (400 MHz, Chloroform-d) δ 8.71 (s, 1H), 7.74 – 7.58 (m, 4H), 7.58 – 7.42 (m, 3H), 6.65 (s, 1H), 5.58 (s, 1H), 5.37 (dtt, J = 56.8, 6.3, 3.5 Hz, 1H), 4.53 (ddd, J = 19.1, 11.4, 6.4 Hz, 2H), 4.38 (s, 2H).
130	C	A	3.583	466.2	1H NMR (600 MHz, cdcl3) δ 9.25 (s, 1H), 8.53 (d, J = 37.7 Hz, 1H), 8.00 – 7.94 (m, 1H), 7.90 (d, J = 9.8 Hz, 1H), 7.56 – 7.42 (m, 3H), 6.63 (s, 1H), 5.68 (s, 1H), 5.28 (t, J = 55.2 Hz, 1H), 3.90 (d, J = 36.2 Hz, 4H), 3.75 – 3.52 (m, 2H).
131	B	C	3.660	429.2	^{1}H NMR (400 MHz, Methanol-d_4) δ 7.86 – 7.73 (m, 2H), 7.72 – 7.56 (m, 4H), 7.51 – 7.39 (m, 2H), 2.34 (s, 3H).

Compound No	Synthesis Route	HPLC-MS Method	retention time (min)	m+H Found	NMR
132	B	A	4.108	518.2	
133	A	C	2.900	489.2	1H NMR (600 MHz, Chloroform-d) δ 9.24 (s, 1H), 8.52 (d, J = 11.4 Hz, 1H), 7.96 (d, J = 8.8 Hz, 1H), 7.87 (dd, J = 8.7, 2.3 Hz, 1H), 7.55 – 7.50 (m, 2H), 7.47 (dd, J = 9.2, 7.1 Hz, 1H), 6.64 (s, 1H), 5.82 (s, 1H), 4.04 – 3.34 (m, 4H), 2.77 (d, J = 72.3 Hz, 1H), 2.33 (s, 3H), 2.24 (s, 3H), 2.11 (s, 1H), 1.89 (d, J = 11.9 Hz, 1H).
134	C	C	3.470	431.2	1H NMR (600 MHz, Chloroform-d) δ 9.40 (s, 1H), 8.40 (d, J = 2.6 Hz, 1H), 8.17 (d, J = 9.0 Hz, 1H), 7.74 (dd, J = 9.0, 2.7 Hz, 1H), 7.57 – 7.52 (m, 2H), 7.49 (dd, J = 9.2, 7.0 Hz, 1H), 6.66 (s, 1H), 5.75 (s, 1H), 2.60 (s, 3H).
135	C	C	3.420	450.2	1H NMR (400 MHz, Chloroform-d) δ 9.37 (s, 1H), 8.55 (s, 1H), 7.98 (s, 2H), 7.55 – 7.41 (m, 3H), 6.61 (s, 1H), 5.67 (s, 1H), 5.35 (d, J = 56.7 Hz, 1H), 4.50 (d, J = 15.9 Hz, 2H), 4.36 (s, 2H).
136	C	C	3.429	464.2	1H NMR (600 MHz, cdcl3) δ 9.28 (s, 1H), 8.53 (d, J = 37.5 Hz, 1H), 7.98 (d, J = 8.8 Hz, 1H), 7.91 (d, J = 10.6 Hz, 1H), 7.57 – 7.43 (m, 3H), 6.63 (s, 1H), 5.73 (s, 1H), 5.19 (s, 1H), 3.97 – 3.65 (m, 4H), 2.30 (t, J = 15.8 Hz, 1H), 2.16 – 1.93 (m, 1H).
137	C	C	3.500	446.2	1H NMR (600 MHz, cd3od) δ 8.47 (dd, J = 2.3, 0.9 Hz, 1H), 8.00 – 7.94 (m, 2H), 7.69 – 7.60 (m, 3H), 3.58 (q, J = 7.1 Hz, 4H), 1.95 (dp, J = 36.3, 6.9 Hz, 4H).
138		A	3.680	479.2	^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.62 (s, 1H), 7.58 – 7.54 (m, 2H), 7.50 (dd, *J* = 9.1, 4.8 Hz, 1H), 7.43 – 7.39 (m, 2H), 7.37 (dd, *J* = 9.1, 7.8 Hz, 1H), 6.62 (s, 1H), 5.55 (s, 1H), 3.78 – 3.57 (m, 8H).
139	C	B	3.289	480.2	1H NMR (400 MHz, Methanol-d4) δ 8.97 (d, J = 2.7 Hz, 1H), 8.32 (dd, J = 8.6, 2.7 Hz, 1H), 7.83 (d, J = 8.6 Hz, 1H), 7.73 – 7.59 (m, 4H), 7.44 (dd, J = 9.3, 6.7 Hz, 1H), 6.83 (d, J = 6.9 Hz, 1H), 2.34 (s, 3H).
140	C	A	3.450	462.2	

Compound No	Synthesis Route	HPLC-MS Method	retention time (min)	m+H Found	NMR
141	C	C	3.505	430.2	^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.31 (s, 1H), 8.39 (dd, *J* = 2.6, 0.8 Hz, 1H), 8.11 (dd, *J* = 8.9, 0.8 Hz, 1H), 7.74 (dd, *J* = 8.9, 2.6 Hz, 1H), 7.57 (q, *J* = 0.8 Hz, 1H), 7.54 – 7.50 (m, 2H), 7.46 (dd, *J* = 9.5, 6.4 Hz, 1H), 6.62 (s, 1H), 5.63 (s, 1H), 2.32 (d, *J* = 0.8 Hz, 3H).
142	C	C	3.497	444.2	1H NMR (400 MHz, Chloroform-d) d 9.28 (s, 1H), 8.60 – 8.52 (m, 1H), 8.06 (d, J = 8.7 Hz, 1H), 7.99 – 7.89 (m, 2H), 7.52 (dd, J = 7.9, 1.5 Hz, 2H), 7.46 (dd, J = 9.5, 6.4 Hz, 1H), 6.61 (s, 1H), 5.59 (s, 1H), 4.25 (q, J = 7.2 Hz, 2H), 1.50 (t, J = 7.2 Hz, 3H).
143	C	C	3.630	434.2	^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.84 (brs, 1H), 8.00 (d, *J* = 2.9 Hz, 1H), 7.85 (d, *J* = 9.0 Hz, 1H), 7.59 – 7.36 (m, 3H), 7.26 (s, 1H), 6.58 (brs, 1H), 5.55 (brs, 1H), 3.88-3.85 (m, 4H), 3.09-3.05 (m, 4H).
144	C	C	3.920	497.2	^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.25 (brs, 1H), 8.59 – 8.50 (m, 1H), 8.09 – 7.99 (m, 1H), 7.94 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.57 – 7.43 (m, 3H), 7.32 (s, 1H), 6.62 (brs, 1H), 5.60 (brs, 1H), 3.76 (s, 3H).
145	A	A	3.800	481.2	^{1}H NMR (600 MHz, Methanol-d_4) δ 7.71 (dd, *J* = 9.2, 4.9 Hz, 1H), 7.66 – 7.63 (m, 2H), 7.61 (d, *J* = 8.8 Hz, 1H), 7.56 (dd, *J* = 16.2, 8.4 Hz, 2H), 5.29 (dd, *J* = 61.6, 52.8 Hz, 1H), 3.90 – 3.66 (m, 4H), 2.33 – 2.17 (m, 1H), 2.17 – 2.02 (m, 1H).
146	A	A	3.830	481.2	^{1}H NMR (600 MHz, Methanol-d_4) δ 7.65 – 7.61 (m, 2H), 7.59 (d, *J* = 8.1 Hz, 2H), 7.55 (dd, *J* = 16.1, 8.4 Hz, 2H), 5.29 (dd, *J* = 61.6, 52.7 Hz, 1H), 3.91 – 3.65 (m, 4H), 2.33 – 2.17 (m, 1H), 2.17 – 1.95 (m, 1H).
147	A	A	3.720	465.2	^{1}H NMR (600 MHz, Methanol-d_4) δ 7.65 – 7.62 (m, 2H), 7.61 – 7.58 (m, 1H), 7.54 (dd, *J* = 16.1, 8.4 Hz, 2H), 7.46 (td, *J* = 9.1, 4.3 Hz, 1H), 5.38 – 5.15 (m, 1H), 3.91 – 3.63 (m, 4H), 2.32 – 2.17 (m, 1H), 2.16 – 2.02 (m, 1H).
148	A	A	3.710	488.2	^{1}H NMR (600 MHz, Methanol-d_4) δ 8.15 (s, 2H), 7.64 – 7.60 (m, 2H), 7.54 (dd, *J* = 16.2, 8.4 Hz, 2H), 5.27 (dd, *J* = 61.9, 52.8 Hz, 1H), 3.89 – 3.63 (m, 4H), 2.31 – 2.16 (m, 1H), 2.15 – 1.99 (m, 1H).

Compound No	Synthesis Route	HPLC-MS Method	retention time (min)	m+H Found	NMR
149	A	C	3.000	503.2	1H NMR (600 MHz, Chloroform-d) δ 9.22 (s, 1H), 8.39 (dd, J = 2.3, 0.8 Hz, 1H), 7.97 (dd, J = 8.7, 0.9 Hz, 1H), 7.75 (dd, J = 8.7, 2.3 Hz, 1H), 7.55 – 7.50 (m, 2H), 7.47 (dd, J = 9.1, 7.0 Hz, 1H), 6.65 (s, 1H), 6.03 (s, 1H), 2.94 (broad s, 2H), 2.80 (t, J = 11.8 Hz, 1H), 2.41 (s, 6H), 2.04 (s, 4H), 1.96 (s, 2H).
150	A	C	2.940	489.2	1H NMR (400 MHz, Chloroform-d) δ 9.24 (s, 1H), 8.43 (s, 1H), 7.99 (dd, J = 8.7, 0.9 Hz, 1H), 7.82 – 7.70 (m, 1H), 7.57 – 7.46 (m, 3H), 6.67 (s, 1H), 5.94 (s, 1H), 3.98 – 3.50 (m, 4H), 2.92 –2.45 (m,6H), 2.05 (d, J = 10.3 Hz, 3H).
151	D	C	3190.000	476.2	1H NMR (600 MHz, Chloroform-d) δ 8.68 (s, 1H), 8.51 (s, 1H), 8.02 (dd, J = 8.7, 2.8 Hz, 1H), 7.52 (d, J = 7.4 Hz, 2H), 7.47 (dd, J = 9.2, 7.0 Hz, 1H), 7.34 (s, 1H), 6.64 (s, 1H), 5.64 (s, 1H), 3.93 (s, 2H), 3.62 (s, 6H), 3.56 (t, J = 4.6 Hz, 2H).
152	C	C	3.240	464.2	1H NMR (600 MHz, Chloroform-d) δ 8.64 (d, J = 2.8 Hz, 1H), 8.44 (s, 1H), 8.00 (dd, J = 8.5, 2.8 Hz, 1H), 7.54 – 7.49 (m, 2H), 7.46 (dd, J = 9.1, 7.1 Hz, 1H), 7.30 (d, J = 8.5 Hz, 1H), 6.64 (s, 1H), 5.63 (s, 1H), 5.27 (dtt, J = 56.6, 6.4, 3.5 Hz, 1H), 4.51 (dddd, J = 19.7, 10.6, 6.1, 1.7 Hz, 1H), 4.36 – 4.23 (m, 2H), 4.12 (dddd, J = 24.4, 11.6, 3.5, 1.7 Hz, 1H), 3.68 – 3.59 (m, 2H).
153	A	C	3.300	457.2	1H NMR (600 MHz, Chloroform-d) δ 9.34 (s, 1H), 8.55 (dd, J = 2.3, 0.9 Hz, 1H), 7.99 (dd, J = 8.8, 0.9 Hz, 1H), 7.95 (dd, J = 8.8, 2.3 Hz, 1H), 7.56 – 7.50 (m, 2H), 7.48 (dd, J = 9.2, 6.9 Hz, 1H), 6.64 (s, 1H), 5.72 (s, 1H), 4.55 (t, J = 8.6 Hz, 2H), 4.50 (s, 2H), 3.58 (tt, J = 9.1, 6.3 Hz, 1H).
154	A	C	3.030	448.2	1H NMR (600 MHz, Chloroform-d) δ 9.27 (s, 1H), 8.58 (dd, J = 2.2, 1.0 Hz, 1H), 8.02 – 7.94 (m, 2H), 7.53 (d, J = 8.7 Hz, 2H), 7.48 (dd, J = 9.2, 7.0 Hz, 1H), 6.63 (s, 1H), 5.76 (s, 1H), 4.75 (ddt, J = 10.6, 8.2, 4.1 Hz, 1H), 4.51 (s, 2H), 4.22 (s, 1H), 4.08 (s, 1H).
155	C	C	4.170	483.2	^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.77 (brs, 1H), 8.09 (s, 1H), 7.76 – 7.68 (m, 2H), 7.56 – 7.50 (m, 2H), 7.50 – 7.39 (m, 3H), 6.65 (brs, 1H), 5.60 (brs, 1H).

Compound No	Synthesis Route	HPLC-MS Method	retention time (min)	m+H Found	NMR
156	C	C	3.340	430.2	1H NMR (600 MHz, Chloroform-d) d 9.30 (s, 1H), 8.40 (d, J = 2.6 Hz, 1H), 8.10 (d, J = 8.8 Hz, 1H), 7.95 (s, 1H), 7.73 (dd, J = 8.9, 2.7 Hz, 1H), 7.57 – 7.51 (m, 2H), 7.48 (dd, J = 9.1, 7.0 Hz, 1H), 6.64 (s, 1H), 5.61 (s, 1H), 2.51 (s, 3H).
157	C	C	4.030	484.2	^{1}H NMR (600 MHz, Chloroform-*d*) δ 9.41 (s, 1H), 8.45 (d, *J* = 2.6 Hz, 1H), 8.18 – 8.11 (m, 2H), 7.76 (dd, *J* = 9.0, 2.7 Hz, 1H), 7.54 (d, *J* = 8.6 Hz, 2H), 7.49 (dd, *J* = 9.1, 7.0 Hz, 1H), 6.64 (s, 1H), 5.63 (s, 1H).
158	C	C	3.410	431.2	^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.39 (brs, 1H), 8.69 (dd, *J* = 2.3, 0.9 Hz, 1H), 8.20 – 7.98 (m, 2H), 7.63 – 7.40 (m, 3H), 6.65 (s, 1H), 5.63 (brs, 1H), 4.20 (brs, 3H).
159	C	C	4.130	484.2	
160	C	C	3.220	510.0	1H NMR (400 MHz, Chloroform-d) δ 9.38 (s, 1H), 8.47 (s, 1H), 8.04 (s, 1H), 7.81 (d, J = 7.5 Hz, 1H), 7.63 – 7.46 (m, 3H), 6.67 (s, 1H), 5.85 (s, 1H), 4.16 (s, 4H), 3.12 (s, 4H).
161	C	B	3.229	481.2	
162	A	A	3.510	454.2	1H NMR (600 MHz, Methanol-d_4) δ 8.03 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.98 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.78 (t, *J* = 8.1 Hz, 1H), 7.69 – 7.66 (m, 2H), 7.57 (dd, *J* = 16.1, 8.4 Hz, 2H), 5.29 (dd, *J* = 61.6, 52.8 Hz, 1H), 3.90 – 3.67 (m, 4H), 2.33 – 2.17 (m, 1H), 2.17 – 2.01 (m, 1H).
163	A	C	3.350	509.0	1H NMR (400 MHz, Chloroform-d) δ 8.67 (s, 1H), 7.62 – 7.55 (m, 2H), 7.54 – 7.48 (m, 2H), 7.48 – 7.43 (m, 1H), 7.43 – 7.38 (m, 2H), 6.63 (s, 1H), 5.67 (s, 1H), 4.08 (d, J = 5.4 Hz, 4H), 3.04 (s, 4H).
164	A	A	3.440	438.2	
165	A	C	3.750	460.2	1H NMR (400 MHz, Chloroform-d) δ 9.32 (s, 1H), 8.58 (d, J = 2.1 Hz, 1H), 8.02 (dd, J = 8.8, 2.0 Hz, 1H), 7.97 (d, J = 8.7 Hz, 1H), 7.58 – 7.49 (m, 2H), 7.51 – 7.43 (m, 1H), 6.63 (s, 1H), 5.73 (s, 1H), 4.01 (s, 2H), 3.89 (s, 2H), 1.31 (s, 6H).
166	A	C	4.060	459.0	1H NMR (400 MHz, Chloroform-d) δ 8.63 (s, 1H), 7.68 – 7.60 (m, 2H), 7.58 – 7.43 (m, 5H), 6.65 (s, 1H), 5.75 (s, 1H), 3.98 (s, 2H), 3.88 (s, 2H), 1.29 (s, 6H).

Compound No	Synthesis Route	HPLC-MS Method	retention time (min)	m+H Found	NMR
167	A	A	3.730	465.2	
168	C	C	3.020	465.2	1H NMR (600 MHz, cdcl3) δ 7.87 – 7.82 (m, 2H), 7.54 (d, J = 0.8 Hz, 1H), 7.50 (d, J = 1.3 Hz, 1H), 7.49 (d, J = 0.6 Hz, 1H), 7.44 (dd, J = 9.1, 7.2 Hz, 1H), 6.56 (s, 1H), 5.54 (s, 1H), 4.93 (s, 2H), 3.65 – 3.50 (m, 8H).
169	D	C	3.060	508.0	1H NMR (400 MHz, Methanol-d4) δ 7.69 – 7.55 (m, 5H), 7.52 – 7.44 (m, 2H), 4.42 (s, 2H), 3.87 – 3.76 (m, 2H), 3.74 – 3.64 (m, 4H).
170	A	C	3.800	477.2	1H NMR (400 MHz, Methanol-d4) δ 7.67 – 7.54 (m, 5H), 7.40 – 7.30 (m, 2H), 3.84 (s, 4H), 2.64 (s, 4H).
171	A	C	3.190	522.2	1H NMR (400 MHz, Methanol-d4) δ 7.68 – 7.57 (m, 5H), 7.50 – 7.44 (m, 2H), 4.21 (s, 2H), 3.83 (ddd, J = 13.1, 8.6, 3.1 Hz, 2H), 3.52 – 3.32 (m, 4H), 2.80 (s, 3H).
172	C	B	3.051	416.0	
173	C	C	2.472	430.0	
174	C	C	2.986	513.0	1H NMR (400 MHz, CDCl3) δ 7.97 – 7.84 (m, 1H), 7.72 – 7.32 (m, 4H), 6.60 (s, 1H), 5.64 (s, 1H), 5.01 (s, 2H), 4.11 (t, J = 5.5 Hz, 3H), 2.92 (d, J = 62.5 Hz, 3H).
175	A	C	3.440	527.1	1H NMR (400 MHz, Chloroform-d) δ 8.72 (s, 1H), 7.66 – 7.58 (m, 2H), 7.49 – 7.42 (m, 2H), 7.32 (d, J = 7.7 Hz, 2H), 6.65 (s, 1H), 5.61 (s, 1H), 4.14 (s, 4H), 3.09 (d, J = 6.5 Hz, 4H).
176	A	C	3.920	507.0	1H NMR (400 MHz, Chloroform-d) δ 8.61 (s, 1H), 7.63 – 7.55 (m, 2H), 7.43 – 7.35 (m, 2H), 7.04 (s, 2H), 6.65 (s, 1H), 5.62 (s, 1H), 3.91 (s, 4H), 2.67 (s, 4H).
177	A	C	3.440	527.1	1H NMR (400 MHz, Chloroform-d) δ 8.72 (s, 1H), 7.66 – 7.58 (m, 2H), 7.49 – 7.42 (m, 2H), 7.32 (d, J = 7.7 Hz, 2H), 6.65 (s, 1H), 5.61 (s, 1H), 4.14 (s, 4H), 3.09 (d, J = 6.5 Hz, 4H).

Example 23

The compounds listed in Table 1a were tested for their ability to inhibit a set of kinases according to the following procedures.

Biochemical assays:

The basic protocol for TR-FRET LanthaScreen Eu Kinase Binding Assay inhibitor studies were performed as follows. LanthaScreen Kinase Binding Assays (ThermoFisher/USA) to evaluate inhibitors were performed by addition of 5 μL of test compound in corresponding DMSO dilutions/ 5 µl of kinase/antibody mixture, 5 μL of tracer into 384 well small volume plates. After incubation for 1 hour at room temperature, plates were read. Data analysis of emission ratios was according LanthaScreen Eu Kinase Binding Assay protocol.

Kinase and assay components were adjusted to final concentrations according to kit protocol. For LRRK2: 5 nM wt human LRRK2, catalytic site, or G2019S human LRRK2, catalytic site (ThermoFisher/USA), 2 nM Eu-Anti-GST Antibody, 10 nM Kinase Tracer 236 in 1X Kinase Buffer A. For NUAK1: 8 nM wt human NUAK1, full length (ThermoFisher/USA), 2 nM Eu-Anti-His Antibody, 5 nM Kinase Tracer 236 in 1X Kinase Buffer A.

Basic protocol for Z´-LYTE Assays (ThermoFisher/USA) inhibitor studies involved two steps:

Kinase reaction: Addition of 2 μL of test compound in corresponding DMSO dilutions, 5 µL of kinase/substrate mixture, 3 μL of ATP into 384 well small volume plates. Incubation for at least 1 hour at room temperature.

Development reaction: Addition of 5 μL development reagent, incubation for 1 hour at room temperature, addition of 5 μL stop reagent, read plate. Data analysis of emission ratios according to Z'-LYTE assay protocol.

Kinase and assay components were adjusted to final concentrations according to kit protocol. For JAK2: 5 nM wt human JAK2, catalytic site (ThermoFisher/USA), 2 μM Z´-LYTE Tyr 06 Peptide, 36 μM ATP in Kinase Buffer.

Basic protocol for HTRF KinEASE assay (Cisbio/FRA) inhibitor studies involved two steps:

Enzymatic step: Addition of 4 μL of test compound in corresponding DMSO dilutions, 4 μL of kinase/substrate mixture, 2 μL of ATP into 384 well small volume plates. Incubation for at least 30 minutes at room temperature.

Detection step: Addition of 5 μL antibody and 5 µL streptavidin-XL665, read plate after 60 minutes. Data analysis of emission ratios according KinEASE assay protocol.

Kinase and assay components were adjusted to final concentrations according to kit protocol. For TYK2: 2 nM wt human TYK2, catalytic site (SignalChem/CAN), 1 μM HTRF KinEASE-TK Substrate-biotin, 1 μM ATP in 1x Kinase Buffer. For JAK1: 4 nM wt human JAK1, catalytic site (ThermoFisher/USA), 1 μM HTRF KinEASE-TK Substrate-biotin, 2.5 μM ATP in 1x Kinase Buffer. For JAK2: 1 nM wt human JAK2, catalytic site (SignalChem/CAN), 1 μM HTRF KinEASE-TK Substrate-biotin, 100 μM ATP in 1x Kinase Buffer.

Results for from biochemical tests were as follows:

Activity toward TYK2

The following compounds had an IC_{50} lower than 10 nM: Compound Nos. 101, 102, 104, 105, 106, 107, 108, 109, 112, 114, 116, 122, 124, 128, 129, 131, 160, 162, 163, 169, 170, 171, and 175.

The following compounds had an IC_{50} between 10 nM and 100 nM: Compound Nos. 103, 110, 113, 115, 117, 119, 120, 123, 125, 126, 130, 134, 135, 137, 138, 140, 141, 144, 145, 146, 147, 148, 149, 150, 153, 154, 156, 158, 161, 164, 165, 166, 167, 168, 174, 177 and 477.

The following compounds had an IC_{50} between 100 nM and 1000 nM: Compound Nos. 111, 118, 127, 132, 133, 139, 142, 143, 151, 152, 157, and 176.

Activity toward LRRK2(wt) and LRRK2(G2019)

The following compounds had an IC_{50} between 100 nM and 1000 nM: Compound Nos. 108, 113, 116, 122 , 129, 129, and 131.

Activity toward NUAK1

The following compounds had an IC_{50} between 100 nM and 1000 nM: Compound Nos. 101, 102, 103, 104, 105, and 106.

Activity toward JAK1

The following compounds had an IC_{50} lower than 10 nM: Compound Nos. 101, 102, 105, 108, 112, 113, 114, 123, 126, 128, 129, 138, 145, 146, 147, 149, 163, 166, 169, 170, 171, 174, 175, and 177.

The following compounds had an IC_{50} between 10 nM and 100 nM: Compound Nos. 103, 104, 106, 109, 110, 116, 117, 118, 119, 120, 122, 124, 125, 131, 133, 134, 135, 137, 139, 141, 142, 144, 150, 151, 152, 153, 154, 155, 156, 157, 158, 160, 161, 162, 164, 167, 168, and 176.

The following compounds had an IC_{50} between 100 nM and 1000 nM: Compound Nos. 107, 111, 115, 121, 127, 130, 132, 136, 140, 143, 148, 165, and 172.

Activity toward JAK2

The following compounds had an IC_{50} between 100 nM and 1000 nM: Compound Nos. 101, 102, 103, 104, 105, 106, 107, 108, 109, 113, 114, 116, 117, 119, 120, 122, 124, 125, 129, 131, 138, 145, 147, 162, 163, 164, 167, 169, and 171.

Incorporation by Reference

References and citations to other documents, such as patents, patent applications, patent publications, journals, books, papers, web contents, have been made throughout this disclosure. All such documents are hereby incorporated herein by reference in their entirety for all purposes.

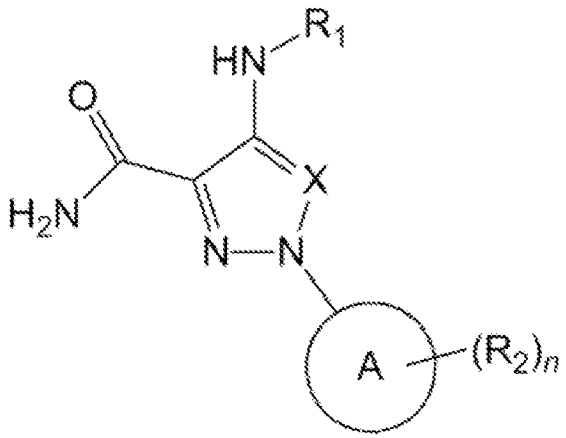
Equivalents

Various modifications of the invention and many further embodiments thereof, in addition to those shown and described herein, will become apparent to those skilled in the art from the full contents of this document, including references to the scientific and patent literature cited herein. The subject matter herein contains important information, exemplification, and guidance that can be adapted to the practice of this invention in its various embodiments and equivalents thereof.

Claims

What is claimed is:

1. A compound of Formula (II):



(II),

wherein:

X is N or CH;

R_1 is $C(O)CH_2R_3$, optionally substituted cycloalkyl, optionally substituted cycloheteroalkyl, optionally substituted cycloalkenyl, optionally substituted cycloheteroalkenyl, optionally substituted aryl, or optionally substituted heteroaryl;

each instance of R_2 is independently halo, haloalkyl, cyano, optionally substituted alkoxyl, optionally substituted alkyl, optionally substituted heteroalkyl, optionally substituted alkenyl, optionally substituted heteroalkenyl;

R_3 is optionally substituted cycloalkyl, optionally substituted cycloheteroalkyl, optionally substituted cycloalkenyl, optionally substituted cycloheteroalkenyl, optionally substituted aryl, or optionally substituted heteroaryl;

A is cycloalkyl, cycloheteroalkyl, cycloalkenyl, cycloheteroalkenyl, aryl, or heteroaryl; and

n is 0-5.

2. The compound of claim 1, wherein X is N.

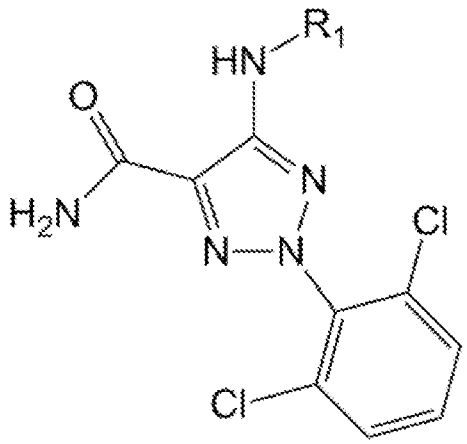
3. The compound of claim 1, wherein X is CH.

4. The compound of claim 1, wherein A is aryl or heteroaryl.

5. The compound of claim 4, wherein each instance of R_2 is halo or cyano.

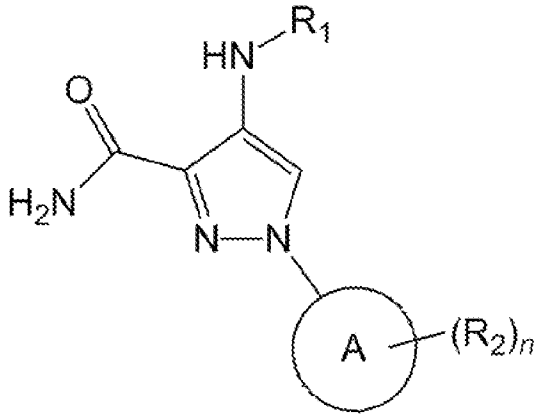
6. The compound of claim 5, wherein *n* is 2 or 3.

7. The compound of claim 6, wherein the compound is represented by Formula (IIa):



(IIa).

8. The compound of claim 6, wherein the compound is represented by Formula (I):



(I).

9. The compound of claim 1, wherein R_1 is an optionally substituted aryl.

10. The compound of claim 9, wherein R_1 is a substituted phenyl.

11. The compound of claim 1, wherein R_1 is optionally substituted aryl or optionally substituted heteroaryl;

12. The compound of claim 11, wherein R_1 is an optionally substituted aryl other than phenyl.

13. The compound of claim 11, wherein R_1 is an optionally substituted heteroaryl.

14. The compound of claim 11, wherein A is aryl or heteroaryl.

15. The compound of claim 14, wherein A is aryl.

16. The compound of claim 14, wherein A is heteroaryl.

17. The compound of claim 14, wherein each instance of R_2 is halo or cyano.

18. The compound of claim 17, wherein *n* is 2 or 3.

19. The compound of claim 1, wherein the compound is selected from the group consisting of 1-(4-methoxyphenyl)-4-(2-morpholinoacetamido)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-(2-morpholinoacetamido)-1H-pyrazole-3-carboxamide; 1-(2-fluorophenyl)-4-(2-morpholinoacetamido)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((6-methylpyrimidin-4-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2-fluorophenyl)-4-((6-methylpyrimidin-4-yl)amino)-1H-pyrazole-3-carboxamide; 4-((5-aminopyridin-2-yl)amino)-1-(2,6-difluorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-(pyridin-2-ylamino)-1H-pyrazole-3-carboxamide; 4-((2-amino-6-methylpyrimidin-4-yl)amino)-1-(2,6-difluorophenyl)-1H-pyrazole-3-carboxamide; 4-(benzo[d]thiazol-2-ylamino)-1-(2,6-difluorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((4-methylpyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 4-((1H-benzo[d]imidazol-2-yl)amino)-1-(2,6-difluorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((4-(morpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((4-((tetrahydro-2H-pyran-4-yl)carbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((4-((2,2,2-trifluoroethyl)carbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(tert-butylcarbamoyl)phenyl)amino)-1-(2,6-difluorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((4-(ethylcarbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(morpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((3-(morpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-chlorophenyl)amino)-1-(2,6-difluorophenyl)-1H-pyrazole-3-carboxamide; 4-((4-chlorophenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-(phenylamino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(morpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; N-(tert-butyl)-5-((3-carbamoyl-1-(2,6-difluorophenyl)-1H-pyrazol-4-yl)amino)picolinamide; 5-((3-carbamoyl-1-(2,6-difluorophenyl)-1H-pyrazol-4-yl)amino)-N-ethylpicolinamide; 5-((3-carbamoyl-1-(2-fluoro-6-methoxyphenyl)-1H-pyrazol-4-yl)amino)-N-ethylpicolinamide; 4-((4-(tert-butylcarbamoyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 4-((4-(tert-butylcarbamoyl)phenyl)amino)-1-(2-chloro-6-fluorophenyl)-1H-pyrazole-3-carboxamide; 4-((4-(tert-butylcarbamoyl)-3-fluorophenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 4-((4-(tert-butylcarbamoyl)-3-fluorophenyl)amino)-1-(2-chloro-6-fluorophenyl)-

1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((6-(morpholine-4-carbonyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-((1-methylpiperidin-4-yl)carbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4-methylpiperazine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; tert-butyl_3-(4-((3-carbamoyl-1-(2,6-dichlorophenyl)-1H-pyrazol-4-yl)amino)benzamido)piperidine-1-carboxylate; 1-(2,6-dichlorophenyl)-4-((4-(ethylcarbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-((1-methylpiperidin-4-yl)carbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(4-methylpiperazine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; tert-butyl_3-(4-((3-carbamoyl-1-(2-chloro-6-fluorophenyl)-1H-pyrazol-4-yl)amino)benzamido)piperidine-1-carboxylate; 1-(2-chloro-6-fluorophenyl)-4-((4-(piperidin-3-ylcarbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(piperidin-3-ylcarbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(ethylcarbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-pivaloylphenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-pivaloylphenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((1,2-dimethyl-1H-benzo[d]imidazol-5-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((1,2-dimethyl-1H-benzo[d]imidazol-5-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4-methylpyridazin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(2-azaspiro[3.3]heptane-2-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-ethyl-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-methyl-1H-1,2,3-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(pyridazin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(methyl(1-methylpiperidin-4-yl)carbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-methylpyrimidin-4-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-ethylpyrimidin-4-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1,4-dimethyl-1H-imidazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(2-azaspiro[3.3]heptane-2-carbonyl)phenyl)amino)-1-(2-chloro-6-fluorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(4-methylpyridazin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-

dichlorophenyl)-4-((4-(6,8-dihydro-5H-[1,2,4]triazolo[3,4-c][1,4]oxazin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(3-cyanopyridin-2-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 4-((4-(4-cyanopyridazin-3-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 4-((4-(2-azaspiro[3.3]heptane-2-carbonyl)phenyl)amino)-1-(2-fluoro-6-(trifluoromethyl)phenyl)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(6,8-dihydro-5H-[1,2,4]triazolo[3,4-c][1,4]oxazin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[4,3-a]azepin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((4-(dimethylphosphoryl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(1H-indazol-1-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 4-((4-(2H-indazol-2-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 4-((4-(4-chloropyridazin-3-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((5-(morpholine-4-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4-(trifluoromethyl)pyridazin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(6,7-dihydropyrano[4,3-c]pyrazol-1(4H)-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(6,7-dihydropyrano[4,3-c]pyrazol-2(4H)-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(3-methyl-6-oxopyridazin-1(6H)-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4,5,6,7-tetrahydro-1H-benzo[d][1,2,3]triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(morpholine-4-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(3-methyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(3-chloro-1H-pyrazol-1-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(2-methyl-5-oxo-2,5-dihydro-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-((1-methyl-1H-pyrazol-3-yl)oxy)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(3-chloro-1H-1,2,4-triazol-1-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-methyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(1H-benzo[d][1,2,3]triazol-1-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(piperidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-

carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4-(2,2-difluoroethyl)piperazine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(4-cyclopropylpiperazine-1-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-((4-methylpiperazin-1-yl)sulfonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(4-(cyclopropylmethyl)piperazine-1-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4-ethyl-4H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4-methyl-4H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(N-(1-methylpiperidin-4-yl)sulfamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-isopropyl-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4-methyl-1,4-diazepane-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(azetidine-1-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4-(2,2,2-trifluoroethyl)piperazine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(pyrrolidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(azepane-1-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-methyl-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(2-oxobenzo[d]thiazol-3(2H)-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(4-cyclopentyl-4H-1,2,4-triazol-3-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4-isobutyl-4H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-methyl-1H-imidazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4-isopropyl-4H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(4-cyclopropyl-4H-1,2,4-triazol-3-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(4-ethyl-4H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(6,7-dihydropyrano[4,3-c]pyrazol-1(4H)-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(6,7-dihydropyrano[4,3-c]pyrazol-2(4H)-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4-(2,2,2-trifluoroethyl)-4H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(1-isopropyl-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4-(2,2-

difluoroethyl)-4H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4,5-dimethylpyridazin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4-(2-(dimethylamino)ethyl)-4H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-methyl-3-(trifluoromethyl)-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(3,5-dimethyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(3,4-dimethyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4,5-dimethyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(4-chloro-3,5-dimethyl-1H-pyrazol-1-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 4-((4-(4-chloro-5-methyl-1H-pyrazol-1-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 4-((4-(4-chloro-3-methyl-1H-pyrazol-1-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4-ethyl-3,5-dimethyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(3,5-diethyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(3,4,5-trimethyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-methyl-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(pyrrolidine-1-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(pyrrolidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(piperidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-ethyl-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-(2,2-difluoroethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(1-methyl-3-(trifluoromethyl)-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(3-methyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(5-methyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(3-ethylpyridin-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(pyrrolidine-1-carbonyl)pyrimidin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(3-(trifluoromethyl)-4,5,6,7-tetrahydro-2H-indazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-((1-methylpiperidin-4-yl)oxy)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-

((4-(1-methyl-1H-tetrazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4'-fluoro-[1,1'-biphenyl]-4-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(3-ethyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-ethyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4-methyl-5-(trifluoromethyl)-4H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-methyl-1H-tetrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((3'-fluoro-[1,1'-biphenyl]-4-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((2',5'-difluoro-[1,1'-biphenyl]-4-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(3-fluoropyrrolidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(3,3-difluoropyrrolidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(3-(dimethylamino)pyrrolidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-([1,3'-bipyrrolidine]-1'-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-ethyl-4-methyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-(2-(dimethylamino)ethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(4-cyano-3-methyl-1H-pyrazol-1-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 4-((4-(4-cyano-5-methyl-1H-pyrazol-1-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(3,3,4,4-tetrafluoropyrrolidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((2'-fluoro-[1,1'-biphenyl]-4-yl)amino)-1H-pyrazole-3-carboxamide; 4-((2'-cyano-[1,1'-biphenyl]-4-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(3-methyl-5-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-ethyl-1H-tetrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(3-methylpyridin-4-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-isopropoxyphenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-isopropyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(3-isopropyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-N-methyl-4-((4-(morpholine-4-carbonyl)phenyl)amino)-

1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-sulfamoylphenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-cyanophenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 4-(4-((3-carbamoyl-1-(2,6-dichlorophenyl)-1H-pyrazol-4-yl)amino)phenyl)-3-methylpyridine_1-oxide; 1-(2,6-dichlorophenyl)-4-((4-(1-(2,2,2-trifluoroethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(7-methyl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(ethylsulfonamido)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(methylsulfonamido)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1,1-dioxidoisothiazolidin-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-(2-(dimethylamino)ethyl)-1H-tetrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-isopropyl-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-methyl-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(3-cyanoazetidine-1-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-ethyl-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-ethyl-3-(trifluoromethyl)-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-propyl-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-isopropyl-3-(trifluoromethyl)-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-(methoxymethyl)-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-propyl-3-(trifluoromethyl)-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(5-ethyl-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((4-(5-ethyl-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((4-(1-methyl-3-(trifluoromethyl)-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(5-ethyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((4-(5-ethyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((4-((1-methylpiperidin-4-yl)oxy)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(1-ethyl-

3-(trifluoromethyl)-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((3-carbamoyl-1-(2,6-dichlorophenyl)-1H-pyrazol-4-yl)amino)benzenesulfonic_acid; 1-(2,6-dichlorophenyl)-4-((4-(5-ethyl-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-(methoxymethyl)-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-ethyl-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-((1-methylpiperidin-4-yl)oxy)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((4-(4-methylpyridazin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-((dimethylamino)methyl)-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(5-(methoxymethyl)-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((4-(5-(methoxymethyl)-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-(methoxymethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-(oxetan-3-yl)-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((4-(1-ethyl-3-(trifluoromethyl)-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(1-ethyl-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((4-(1-ethyl-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-(2-(dimethylamino)ethyl)-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-(2-methoxyethyl)-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((4-(1-isopropyl-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(4-cyano-1-ethyl-1H-imidazol-2-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-propyl-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(1-butyl-4-(trifluoromethyl)-

1H-imidazol-2-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; (R)-1-(2,6-dichlorophenyl)-4-((4-(3-(dimethylamino)pyrrolidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; (S)-1-(2,6-dichlorophenyl)-4-((4-(3-(dimethylamino)pyrrolidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; (R)-1-(2,6-dichlorophenyl)-4-((4-(3-fluoropyrrolidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; (S)-1-(2,6-dichlorophenyl)-4-((4-(3-fluoropyrrolidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(3-aminopyrrolidine-1-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; (R)-4-((4-(3-aminopyrrolidine-1-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; (S)-4-((4-(3-aminopyrrolidine-1-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((2-(2-methyl-1H-imidazol-1-yl)thiazol-4-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(pyridazin-4-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-ethylpyridazin-4-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; tert-butyl_(1-(4-((3-carbamoyl-1-(2,6-dichlorophenyl)-1H-pyrazol-4-yl)amino)benzoyl)pyrrolidin-3-yl)carbamate; (R)-tert-butyl_(1-(4-((3-carbamoyl-1-(2,6-dichlorophenyl)-1H-pyrazol-4-yl)amino)benzoyl)pyrrolidin-3-yl)carbamate; (S)-tert-butyl_(1-(4-((3-carbamoyl-1-(2,6-dichlorophenyl)-1H-pyrazol-4-yl)amino)benzoyl)pyrrolidin-3-yl)carbamate; 1-(2,6-dichlorophenyl)-4-((4-(5-methyl-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-(2-methoxyethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(5-(methoxymethyl)-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(5-ethyl-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-(2-methoxyethyl)-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; (R)-4-((4-([1,3'-bipyrrolidine]-1'-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; (S)-4-((4-([1,3'-bipyrrolidine]-1'-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 4-((4-([1,2,4]triazolo[4,3-a]pyridin-3-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-(trifluoromethyl)-1H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(5-(methoxymethyl)-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)pyridazin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(5-ethyl-3-

(trifluoromethyl)-1H-1,2,4-triazol-1-yl)pyridazin-3-yl)amino)-1H-pyrazole-3-carboxamide; 4-((6-(1H-1,2,4-triazol-1-yl)pyridin-3-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-(2-hydroxyethyl)-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(1-ethyl-4-(trifluoromethyl)-1H-imidazol-2-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-methylpyridazin-4-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-isopropyl-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(1-(1-acetylazetidin-3-yl)-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(5-ethyl-1H-1,2,4-triazol-1-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(2-methoxyphenyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-methyl-6-(1H-pyrazol-1-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-(oxetan-3-yl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-(hydroxymethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(4-cyano-1-(oxetan-3-yl)-1H-imidazol-2-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(5-methylpyridazin-4-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(5-ethylpyridazin-4-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(pyridazin-4-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-oxo-1,6-dihydropyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; (S)-1-(2,6-dichlorophenyl)-4-((6-(3-(dimethylamino)pyrrolidine-1-carbonyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; (S)-1-(2,6-dichlorophenyl)-4-((6-(3-fluoropyrrolidine-1-carbonyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; (R)-4-((6-([1,3'-bipyrrolidine]-1'-carbonyl)pyridin-3-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; (S)-4-((6-(3-aminopyrrolidine-1-carbonyl)pyridin-3-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(pyrrolidine-1-carbonyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((1-methyl-1H-pyrazol-4-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(4-methyl-4H-1,2,4-triazol-3-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(4-cyano-1-(2-hydroxyethyl)-1H-imidazol-2-yl)phenyl)amino)-1-(2,6-

dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(3,3,4,4-tetrafluoropyrrolidine-1-carbonyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(4-methylpiperazine-1-carbonyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 4-((6-(4-cyclopropylpiperazine-1-carbonyl)pyridin-3-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(morpholine-4-carbonyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; (S)-1-(2,6-dichlorophenyl)-4-((5-(3-(dimethylamino)pyrrolidine-1-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; (S)-1-(2,6-dichlorophenyl)-4-((5-(3-fluoropyrrolidine-1-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; (S)-4-((5-(3-aminopyrrolidine-1-carbonyl)pyridin-2-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(3,3,4,4-tetrafluoropyrrolidine-1-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(4-methylpiperazine-1-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-(hydroxymethyl)-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-ethoxyphenyl)-4-((1-methyl-1H-pyrazol-4-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(1-(2-hydroxyethyl)-4-(trifluoromethyl)-1H-imidazol-2-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((1-(3,6-dimethylpyrazin-2-yl)-1H-pyrazol-4-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(1-methyl-1H-tetrazol-5-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-methyl-[1,2,4]triazolo[4,3-a]pyridin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((1-methyl-1H-pyrazol-4-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((1-isopropyl-1H-pyrazol-4-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((2-methyl-2H-1,2,3-triazol-4-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((1-methyl-1H-1,2,3-triazol-4-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)amino)-1H-pyrazole-3-carboxamide; (R)-4-((5-([1,3'-bipyrrolidine]-1'-carbonyl)pyridin-2-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 4-((5-(4-cyclopropylpiperazine-1-carbonyl)pyridin-2-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(2-oxopiperidin-1-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(5-(hydroxymethyl)-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((1-(3-

fluoropyridin-2-yl)-1H-pyrazol-4-yl)amino)-1H-pyrazole-3-carboxamide; 4-((6-(4-cyano-1-(2-hydroxyethyl)-1H-imidazol-2-yl)pyridin-3-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(5-methyl-[1,2,4]triazolo[4,3-a]pyridin-3-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((1-methyl-6-oxo-1,6-dihydropyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((2-oxo-2H-[1,2'-bipyridin]-5'-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-methyl-1H-1,2,3-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((1-(4-methoxybenzyl)-1H-pyrazol-4-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(5-isopropyl-1H-tetrazol-1-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4'-methyl-[2,3'-bipyridin]-5-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((3'-methyl-[2,2'-bipyridin]-5-yl)amino)-1H-pyrazole-3-carboxamide; 4-((1-(3-chloropyridin-2-yl)-1H-pyrazol-3-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((1-(pyridin-2-yl)-1H-pyrazol-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(3,5-dimethyl-1H-pyrazol-1-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((1-(pyridin-2-yl)-1H-imidazol-4-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(4-isopropyl-4H-1,2,4-triazol-3-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(morpholine-4-carbonyl)pyrazin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(4-methylpiperazine-1-carbonyl)pyrazin-2-yl)amino)-1H-pyrazole-3-carboxamide; (R)-1-(2,6-dichlorophenyl)-4-((5-(3-fluoropyrrolidine-1-carbonyl)pyrazin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((1-methyl-1H-1,2,4-triazol-5-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-((1-methylpiperidin-4-yl)oxy)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((1-methyl-1H-1,2,4-triazol-5-yl)amino)-1H-pyrazole-3-carboxamide; 4-((1H-pyrazol-4-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-(imidazo[1,2-b]pyridazin-3-ylamino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-(pyrazolo[1,5-a]pyrimidin-3-ylamino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((2-((1-methylpiperidin-4-yl)amino)pyrimidin-5-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-ethyl-1H-1,2,3-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichloro-4-fluorophenyl)-4-((4-(morpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichloro-4-fluorophenyl)-4-((4-

(methyl(1-methylpiperidin-4-yl)carbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichloro-4-fluorophenyl)-4-((4-(4-ethyl-4H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; (E)-1-(2,6-dichlorophenyl)-4-((4-(4-(2-fluorovinyl)-4H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichloro-3-fluorophenyl)-4-((4-(morpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichloro-3-fluorophenyl)-4-((4-(methyl(1-methylpiperidin-4-yl)carbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichloro-3-fluorophenyl)-4-((4-(4-ethyl-4H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-((2-methoxyethyl)carbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-((3-methoxypropyl)carbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-((2-fluoroethyl)carbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-((2-(diethylamino)ethyl)carbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4-(dimethylamino)piperidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(piperidin-4-yloxy)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(3-fluoroazetidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(3-hydroxyazetidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(4-methyl-3H-indazol-3-ylidene)-1,6-dihydropyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-morpholinopyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(5-methyl-[1,2,4]triazolo[4,3-a]pyridin-3-yl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(5-methyl-1H-1,2,4-triazol-1-yl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(1-ethyl-1H-1,2,4-triazol-5-yl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(5-methyl-1H-1,2,3-triazol-1-yl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(2-methyl-2H-tetrazol-5-yl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(5-methyl-1H-tetrazol-1-yl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(5-methyl-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(5-(trifluoromethyl)-1H-1,2,3-triazol-1-yl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-

(trifluoromethyl)-1H-1,2,3-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(3-hydroxyazetidine-1-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(2-morpholino-2-oxoethyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(2-(3-fluoroazetidin-1-yl)-2-oxoethyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(4-(dimethylamino)piperidine-1-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; (R)-1-(2,6-dichlorophenyl)-4-((5-(3-fluoropyrrolidine-1-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 4-((5-(3-cyanoazetidine-1-carbonyl)pyridin-2-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(1-methyl-1H-tetrazol-5-yl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(5-(trifluoromethyl)-1H-1,2,3-triazol-1-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 4-((6-(5-chloro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)pyridin-3-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(4-methyl-1,4-diazepane-1-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(3-fluoroazetidine-1-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; (R)-1-(2-cyano-6-fluorophenyl)-4-((4-(3-fluoropyrrolidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1,1-dioxidothiomorpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-cyano-6-fluorophenyl)-4-((4-(1,1-dioxidothiomorpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-[4-(3-Carbamoyl-azetidine-1-carbonyl)-phenylamino]-1-(2,6-dichloro-phenyl)-1H-pyrazole-3-carboxylic acid amide; 1-(2-cyano-6-fluorophenyl)-4-((4-(morpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-((1,1-dioxidothiomorpholino)methyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(3,3-dimethylazetidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-cyanophenyl)-4-((4-(1,1-dioxidothiomorpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-cyanophenyl)-4-((4-(morpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-Chloro-6-cyano-phenyl)-4-[4-((R)-3-fluoro-pyrrolidine-1-carbonyl)-phenylamino]-1H-pyrazole-3-carboxylic acid amide; 1-(2,6-dichlorophenyl)-4-((6-(5-(1,1-difluoroethyl)-1H-tetrazol-1-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((1-(2-morpholino-2-oxoethyl)-1H-pyrazol-4-yl)amino)-1H-pyrazole-3-carboxamide; methyl_2-(4-((3-carbamoyl-1-(2,6-dichlorophenyl)-1H-pyrazol-4-yl)amino)-1H-pyrazol-1-yl)acetate; 1-(2,6-dichlorophenyl)-4-((6-

(1,1-dioxidothiomorpholine-4-carbonyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(3,3-dimethylazetidine-1-carbonyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(3,3-dimethylazetidine-1-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-(methylimino)-1-oxidothiomorpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(thiomorpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-imino-1-oxidothiomorpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((1-(2-(1,1-dioxidothiomorpholino)-2-oxoethyl)-1H-pyrazol-4-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(5,7-dimethyl-[1,2,4]triazolo[4,3-c]pyrimidin-3-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(5-(trifluoromethyl)-[1,2,4]triazolo[4,3-a]pyridin-3-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(5-(trifluoromethyl)-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(5-methylimidazo[1,2-a]pyridin-3-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(5-methyl-[1,2,4]triazolo[4,3-c]pyrimidin-3-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(5-methylthiazolo[2,3-c][1,2,4]triazol-3-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 4-((6-(5-cyano-[1,2,4]triazolo[4,3-a]pyridin-3-yl)pyridin-3-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichloro-4-fluorophenyl)-4-((6-(5-methyl-[1,2,4]triazolo[4,3-a]pyridin-3-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; and 4-((4-(3-carbamoylazetidine-1-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide.

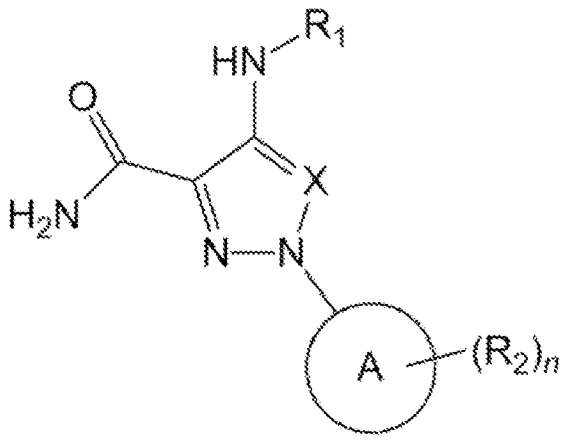
20. The compound of claim 1, wherein the compound is selected from the group consisting of 2-(2,6-Dichloro-phenyl)-5-[4-(morpholine-4-carbonyl)-phenylamino]-2H-[1,2,3]triazole-4-carboxylic acid amide; 2-(2,6-Dichloro-phenyl)-5-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-2H-[1,2,3]triazole-4-carboxylic acid amide; 2-(2,6-Dichloro-phenyl)-5-[4-(1H-tetrazol-5-yl)-phenylamino]-2H-[1,2,3]triazole-4-carboxylic acid amide; 2-(2,6-Dichloro-phenyl)-5-[4-(1-methyl-1H-tetrazol-5-yl)-phenylamino]-2H-[1,2,3]triazole-4-carboxylic acid amide; 2-(2,6-Dichloro-phenyl)-5-[4-((S)-3-dimethylamino-pyrrolidine-1-carbonyl)-phenylamino]-2H-[1,2,3]triazole-4-carboxylic acid amide; 2-(2,6-Dichloro-phenyl)-5-[4-((R)-3-

fluoro-pyrrolidine-1-carbonyl)-phenylamino]-2H-[1,2,3]triazole-4-carboxylic acid amide; 5-[4-(3-Cyano-azetidine-1-carbonyl)-phenylamino]-2-(2,6-dichloro-phenyl)-2H-[1,2,3]triazole-4-carboxylic acid amide; 2-(2,6-dichlorophenyl)-5-((4-(1-(2-hydroxyethyl)-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-Dichloro-phenyl)-5-[4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-3-yl)-phenylamino]-2H-[1,2,3]triazole-4-carboxylic acid amide; 2-(2,6-Dichloro-phenyl)-5-[4-(6,7-dihydro-4H-pyrano[4,3-c]pyrazol-1-yl)-phenylamino]-2H-[1,2,3]triazole-4-carboxylic acid amide; 2-(2,6-Dichloro-phenyl)-5-[4-(6,7-dihydro-4H-pyrano[4,3-c]pyrazol-2-yl)-phenylamino]-2H-[1,2,3]triazole-4-carboxylic acid amide; 2-(2,6-dichlorophenyl)-5-((4-(1-(2-hydroxyethyl)-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(4-(2,2-difluoroethyl)-4H-1,2,4-triazol-3-yl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-((1-methylpiperidin-4-yl)oxy)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(4-isopropyl-4H-1,2,4-triazol-3-yl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(4-methyl-4H-1,2,4-triazol-3-yl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(1-(2-methoxyethyl)-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-((3-methoxypropyl)carbamoyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(piperidin-4-yloxy)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(5-ethyl-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(4-(dimethylamino)piperidine-1-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-((2-methoxyethyl)carbamoyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(3-hydroxyazetidine-1-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(4-isopropyl-4H-1,2,4-triazol-3-yl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(5-ethyl-1H-1,2,3-triazol-1-yl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((5-(4-methylpiperazine-1-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-((2-fluoroethyl)carbamoyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(3-fluoroazetidine-1-carbonyl)phenyl)amino)-2H-

1,2,3-triazole-4-carboxamide; (S)-2-(2,6-dichlorophenyl)-5-((5-(3-fluoropyrrolidine-1-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(5-methyl-1H-1,2,3-triazol-1-yl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((5-(3,3,4,4-tetrafluoropyrrolidine-1-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; (R)-2-(2,6-dichlorophenyl)-5-((5-(3-(dimethylamino)pyrrolidine-1-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((5-(5-methyl-1H-tetrazol-1-yl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((5-(3-fluoroazetidine-1-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; (R)-2-(2,6-dichlorophenyl)-5-((5-(3-fluoropyrrolidine-1-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((5-(pyrrolidine-1-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichloro-3-fluorophenyl)-5-((4-(morpholine-4-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((6-(5-methyl-[1,2,4]triazolo[4,3-a]pyridin-3-yl)pyridin-3-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((5-(morpholine-4-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((5-(5-methyl-1H-1,2,3-triazol-1-yl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((5-(1-ethyl-1H-1,2,4-triazol-5-yl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((5-morpholinopyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((5-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; (R)-2-(2,6-dichloro-3-fluorophenyl)-5-((4-(3-fluoropyrrolidine-1-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; (R)-2-(2,6-dichloro-4-fluorophenyl)-5-((4-(3-fluoropyrrolidine-1-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; (R)-2-(2-chloro-3,6-difluorophenyl)-5-((4-(3-fluoropyrrolidine-1-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; (R)-2-(2,6-dichloro-4-cyanophenyl)-5-((4-(3-fluoropyrrolidine-1-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((5-(4-(dimethylamino)piperidine-1-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((5-(4-methyl-1,4-diazepane-1-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((6-(2-morpholino-2-oxoethyl)pyridin-3-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((6-(2-(3-fluoroazetidin-1-yl)-2-oxoethyl)pyridin-3-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 5-((5-(3-cyanoazetidine-1-carbonyl)pyridin-2-yl)amino)-2-(2,6-dichlorophenyl)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-

dichlorophenyl)-5-((5-(3-hydroxyazetidine-1-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(5-(trifluoromethyl)-1H-1,2,3-triazol-1-yl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((5-(5-methyl-1H-1,2,4-triazol-1-yl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((5-(5-(trifluoromethyl)-1H-1,2,3-triazol-1-yl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((5-(1-methyl-1H-tetrazol-5-yl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((6-(5-(trifluoromethyl)-1H-1,2,3-triazol-1-yl)pyridin-3-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((5-(1,1-dioxidothiomorpholine-4-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((6-(5-methyl-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)pyridin-3-yl)amino)-2H-1,2,3-triazole-4-carboxamide; (R)-2-(2-chloro-6-cyanophenyl)-5-((4-(3-fluoropyrrolidine-1-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(1,1-dioxidothiomorpholine-4-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; (R)-2-(2-cyano-6-fluorophenyl)-5-((4-(3-fluoropyrrolidine-1-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((5-(3,3-dimethylazetidine-1-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(3,3-dimethylazetidine-1-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; (R)-2-(6-chloro-2,3-difluorophenyl)-5-((4-(3-fluoropyrrolidine-1-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((1-(2-morpholino-2-oxoethyl)-1H-pyrazol-4-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(1-imino-1-oxidothiomorpholine-4-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(thiomorpholine-4-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(1-(methylimino)-1-oxidothiomorpholine-4-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((1-(methylsulfonyl)-1H-pyrazol-4-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((1-(ethylsulfonyl)-1H-pyrazol-4-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((1-(2-(1,1-dioxidothiomorpholino)-2-oxoethyl)-1H-pyrazol-4-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichloro-4-fluorophenyl)-5-((4-(1,1-dioxidothiomorpholine-4-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichloro-4-methoxyphenyl)-5-((4-(thiomorpholine-4-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; and 2-(2,6-dichloro-4-fluorophenyl)-5-((4-(thiomorpholine-4-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide.

21. A method of modulating the activity of a kinase, the method comprising contacting cells containing a kinase with a compound of Formula (II):



(II),

wherein:

X is N or CH;

R_1 is $C(O)CH_2R_3$, optionally substituted cycloalkyl, optionally substituted cycloheteroalkyl, optionally substituted cycloalkenyl, optionally substituted cycloheteroalkenyl, optionally substituted aryl, or optionally substituted heteroaryl;

each instance of R_2 is independently halo, haloalkyl, cyano, optionally substituted alkoxyl, optionally substituted alkyl, optionally substituted heteroalkyl, optionally substituted alkenyl, optionally substituted heteroalkenyl;

R_3 is optionally substituted cycloalkyl, optionally substituted cycloheteroalkyl, optionally substituted cycloalkenyl, optionally substituted cycloheteroalkenyl, optionally substituted aryl, or optionally substituted heteroaryl;

A is cycloalkyl, cycloheteroalkyl, cycloalkenyl, cycloheteroalkenyl, aryl, or heteroaryl; and

n is 0-5.

22. The method of claim 21, wherein X is N.

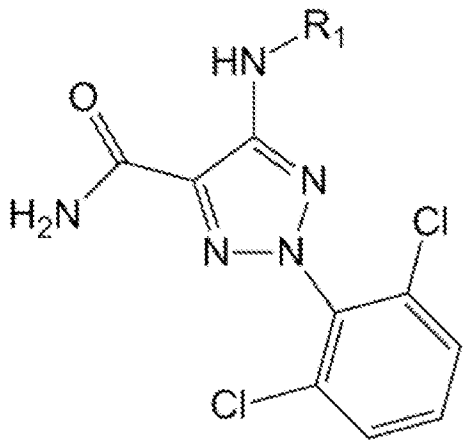
23. The method of claim 21, wherein X is CH.

24. The method of claim 21, wherein A is aryl or heteroaryl.

25. The method of claim 24, wherein each instance of R_2 is halo or cyano.

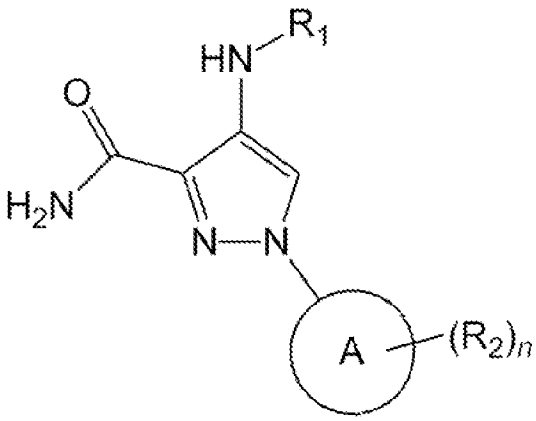
26. The method of claim 25, wherein *n* is 2 or 3.

27. The compound of claim 26, wherein the compound is represented by Formula (IIa):



(IIa).

28. The method of claim 26, wherein the compound is represented by Formula (I):



(I).

29. The method of claim 21, wherein R_1 is an optionally substituted aryl.

30. The method of claim 29, wherein R_1 is a substituted phenyl.

31. The method of claim 21, wherein R_1 is optionally substituted aryl or optionally substituted heteroaryl;

32. The method of claim 31, wherein R_1 is an optionally substituted aryl other than phenyl.

33. The method of claim 31, wherein R_1 is an optionally substituted heteroaryl.

34. The method of claim 31, wherein A is aryl or heteroaryl.

35. The method of claim 34, wherein A is aryl.

36. The method of claim 34, wherein A is heteroaryl.

37. The method of claim 34, wherein each instance of R_2 is halo or cyano.

38. The method of claim 37, wherein *n* is 2 or 3.

39. The method of claim 21, wherein the compound is selected from the group consisting of 1-(4-methoxyphenyl)-4-(2-morpholinoacetamido)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-(2-morpholinoacetamido)-1H-pyrazole-3-carboxamide; 1-(2-fluorophenyl)-4-(2-morpholinoacetamido)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((6-methylpyrimidin-4-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2-fluorophenyl)-4-((6-methylpyrimidin-4-yl)amino)-1H-pyrazole-3-carboxamide; 4-((5-aminopyridin-2-yl)amino)-1-(2,6-difluorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-(pyridin-2-ylamino)-1H-pyrazole-3-carboxamide; 4-((2-amino-6-methylpyrimidin-4-yl)amino)-1-(2,6-difluorophenyl)-1H-pyrazole-3-carboxamide; 4-(benzo[d]thiazol-2-ylamino)-1-(2,6-

difluorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((4-methylpyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 4-((1H-benzo[d]imidazol-2-yl)amino)-1-(2,6-difluorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((4-(morpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((4-((tetrahydro-2H-pyran-4-yl)carbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((4-((2,2,2-trifluoroethyl)carbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(tert-butylcarbamoyl)phenyl)amino)-1-(2,6-difluorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((4-(ethylcarbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(morpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((3-(morpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-chlorophenyl)amino)-1-(2,6-difluorophenyl)-1H-pyrazole-3-carboxamide; 4-((4-chlorophenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-(phenylamino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(morpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; N-(tert-butyl)-5-((3-carbamoyl-1-(2,6-difluorophenyl)-1H-pyrazol-4-yl)amino)picolinamide; 5-((3-carbamoyl-1-(2,6-difluorophenyl)-1H-pyrazol-4-yl)amino)-N-ethylpicolinamide; 5-((3-carbamoyl-1-(2-fluoro-6-methoxyphenyl)-1H-pyrazol-4-yl)amino)-N-ethylpicolinamide; 4-((4-(tert-butylcarbamoyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 4-((4-(tert-butylcarbamoyl)phenyl)amino)-1-(2-chloro-6-fluorophenyl)-1H-pyrazole-3-carboxamide; 4-((4-(tert-butylcarbamoyl)-3-fluorophenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 4-((4-(tert-butylcarbamoyl)-3-fluorophenyl)amino)-1-(2-chloro-6-fluorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((6-(morpholine-4-carbonyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-((1-methylpiperidin-4-yl)carbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4-methylpiperazine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; tert-butyl_3-(4-((3-carbamoyl-1-(2,6-dichlorophenyl)-1H-pyrazol-4-yl)amino)benzamido)piperidine-1-carboxylate; 1-(2,6-dichlorophenyl)-4-((4-(ethylcarbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-((1-methylpiperidin-4-yl)carbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(4-methylpiperazine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; tert-butyl_3-(4-((3-carbamoyl-1-(2-chloro-6-fluorophenyl)-1H-pyrazol-4-yl)amino)benzamido)piperidine-1-carboxylate; 1-(2-chloro-6-fluorophenyl)-4-((4-

(piperidin-3-ylcarbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(piperidin-3-ylcarbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(ethylcarbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-pivaloylphenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-pivaloylphenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((1,2-dimethyl-1H-benzo[d]imidazol-5-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((1,2-dimethyl-1H-benzo[d]imidazol-5-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4-methylpyridazin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(2-azaspiro[3.3]heptane-2-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-ethyl-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-methyl-1H-1,2,3-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(pyridazin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(methyl(1-methylpiperidin-4-yl)carbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-methylpyrimidin-4-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-ethylpyrimidin-4-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1,4-dimethyl-1H-imidazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(2-azaspiro[3.3]heptane-2-carbonyl)phenyl)amino)-1-(2-chloro-6-fluorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(4-methylpyridazin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(6,8-dihydro-5H-[1,2,4]triazolo[3,4-c][1,4]oxazin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(3-cyanopyridin-2-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 4-((4-(4-cyanopyridazin-3-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 4-((4-(2-azaspiro[3.3]heptane-2-carbonyl)phenyl)amino)-1-(2-fluoro-6-(trifluoromethyl)phenyl)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(6,8-dihydro-5H-[1,2,4]triazolo[3,4-c][1,4]oxazin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[4,3-a]azepin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((4-(dimethylphosphoryl)phenyl)amino)-1H-pyrazole-3-

carboxamide; 4-((4-(1H-indazol-1-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 4-((4-(2H-indazol-2-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 4-((4-(4-chloropyridazin-3-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((5-(morpholine-4-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4-(trifluoromethyl)pyridazin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(6,7-dihydropyrano[4,3-c]pyrazol-1(4H)-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(6,7-dihydropyrano[4,3-c]pyrazol-2(4H)-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(3-methyl-6-oxopyridazin-1(6H)-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4,5,6,7-tetrahydro-1H-benzo[d][1,2,3]triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(morpholine-4-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(3-methyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(3-chloro-1H-pyrazol-1-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(2-methyl-5-oxo-2,5-dihydro-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-((1-methyl-1H-pyrazol-3-yl)oxy)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(3-chloro-1H-1,2,4-triazol-1-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-methyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(1H-benzo[d][1,2,3]triazol-1-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(piperidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4-(2,2-difluoroethyl)piperazine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(4-cyclopropylpiperazine-1-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-((4-methylpiperazin-1-yl)sulfonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(4-(cyclopropylmethyl)piperazine-1-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4-ethyl-4H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4-methyl-4H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(N-(1-methylpiperidin-4-yl)sulfamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-isopropyl-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-

carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4-methyl-1,4-diazepane-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(azetidine-1-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4-(2,2,2-trifluoroethyl)piperazine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(pyrrolidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(azepane-1-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-methyl-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(2-oxobenzo[d]thiazol-3(2H)-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(4-cyclopentyl-4H-1,2,4-triazol-3-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4-isobutyl-4H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-methyl-1H-imidazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4-isopropyl-4H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(4-cyclopropyl-4H-1,2,4-triazol-3-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(4-ethyl-4H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(6,7-dihydropyrano[4,3-c]pyrazol-1(4H)-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(6,7-dihydropyrano[4,3-c]pyrazol-2(4H)-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4-(2,2,2-trifluoroethyl)-4H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(1-isopropyl-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4-(2,2-difluoroethyl)-4H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4,5-dimethylpyridazin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4-(2-(dimethylamino)ethyl)-4H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-methyl-3-(trifluoromethyl)-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(3,5-dimethyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(3,4-dimethyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4,5-dimethyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(4-chloro-3,5-dimethyl-1H-pyrazol-1-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 4-((4-(4-chloro-5-methyl-1H-pyrazol-1-

yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 4-((4-(4-chloro-3-methyl-1H-pyrazol-1-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4-ethyl-3,5-dimethyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(3,5-diethyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(3,4,5-trimethyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-methyl-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(pyrrolidine-1-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(pyrrolidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(piperidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-ethyl-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-(2,2-difluoroethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(1-methyl-3-(trifluoromethyl)-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(3-methyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(5-methyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(3-ethylpyridin-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(pyrrolidine-1-carbonyl)pyrimidin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(3-(trifluoromethyl)-4,5,6,7-tetrahydro-2H-indazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-((1-methylpiperidin-4-yl)oxy)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-methyl-1H-tetrazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4'-fluoro-[1,1'-biphenyl]-4-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(3-ethyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-ethyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4-methyl-5-(trifluoromethyl)-4H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-methyl-1H-tetrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((3'-fluoro-[1,1'-biphenyl]-4-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((2',5'-difluoro-[1,1'-biphenyl]-4-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(3-fluoropyrrolidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-

dichlorophenyl)-4-((4-(3,3-difluoropyrrolidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(3-(dimethylamino)pyrrolidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-([1,3'-bipyrrolidine]-1'-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-ethyl-4-methyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-(2-(dimethylamino)ethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(4-cyano-3-methyl-1H-pyrazol-1-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 4-((4-(4-cyano-5-methyl-1H-pyrazol-1-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(3,3,4,4-tetrafluoropyrrolidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((2'-fluoro-[1,1'-biphenyl]-4-yl)amino)-1H-pyrazole-3-carboxamide; 4-((2'-cyano-[1,1'-biphenyl]-4-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(3-methyl-5-(trifluoromethyl)-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-ethyl-1H-tetrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(3-methylpyridin-4-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-isopropoxyphenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-isopropyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(3-isopropyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-N-methyl-4-((4-(morpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-sulfamoylphenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-cyanophenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 4-(4-((3-carbamoyl-1-(2,6-dichlorophenyl)-1H-pyrazol-4-yl)amino)phenyl)-3-methylpyridine_1-oxide; 1-(2,6-dichlorophenyl)-4-((4-(1-(2,2,2-trifluoroethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(7-methyl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(ethylsulfonamido)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(methylsulfonamido)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1,1-dioxidoisothiazolidin-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-(2-(dimethylamino)ethyl)-1H-tetrazol-1-

yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-isopropyl-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-methyl-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(3-cyanoazetidine-1-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-ethyl-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-ethyl-3-(trifluoromethyl)-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-propyl-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-isopropyl-3-(trifluoromethyl)-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-(methoxymethyl)-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-propyl-3-(trifluoromethyl)-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(5-ethyl-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((4-(5-ethyl-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((4-(1-methyl-3-(trifluoromethyl)-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(5-ethyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((4-(5-ethyl-1H-pyrazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((4-((1-methylpiperidin-4-yl)oxy)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(1-ethyl-3-(trifluoromethyl)-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((3-carbamoyl-1-(2,6-dichlorophenyl)-1H-pyrazol-4-yl)amino)benzenesulfonic_acid; 1-(2,6-dichlorophenyl)-4-((4-(5-ethyl-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-(methoxymethyl)-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-ethyl-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-((1-methylpiperidin-4-yl)oxy)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((4-(4-methylpyridazin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-

(5-((dimethylamino)methyl)-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(5-(methoxymethyl)-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((4-(5-(methoxymethyl)-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-(methoxymethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-(oxetan-3-yl)-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((4-(1-ethyl-3-(trifluoromethyl)-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(1-ethyl-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((4-(1-ethyl-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-(2-(dimethylamino)ethyl)-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-(2-methoxyethyl)-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-difluorophenyl)-4-((4-(1-isopropyl-1H-1,2,4-triazol-5-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(4-cyano-1-ethyl-1H-imidazol-2-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-propyl-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(1-butyl-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; (R)-1-(2,6-dichlorophenyl)-4-((4-(3-(dimethylamino)pyrrolidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; (S)-1-(2,6-dichlorophenyl)-4-((4-(3-(dimethylamino)pyrrolidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; (R)-1-(2,6-dichlorophenyl)-4-((4-(3-fluoropyrrolidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; (S)-1-(2,6-dichlorophenyl)-4-((4-(3-fluoropyrrolidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(3-aminopyrrolidine-1-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; (R)-4-((4-(3-aminopyrrolidine-1-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; (S)-4-((4-(3-aminopyrrolidine-1-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-

dichlorophenyl)-4-((2-(2-methyl-1H-imidazol-1-yl)thiazol-4-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(pyridazin-4-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-ethylpyridazin-4-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; tert-butyl_(1-(4-((3-carbamoyl-1-(2,6-dichlorophenyl)-1H-pyrazol-4-yl)amino)benzoyl)pyrrolidin-3-yl)carbamate; (R)-tert-butyl_(1-(4-((3-carbamoyl-1-(2,6-dichlorophenyl)-1H-pyrazol-4-yl)amino)benzoyl)pyrrolidin-3-yl)carbamate; (S)-tert-butyl_(1-(4-((3-carbamoyl-1-(2,6-dichlorophenyl)-1H-pyrazol-4-yl)amino)benzoyl)pyrrolidin-3-yl)carbamate; 1-(2,6-dichlorophenyl)-4-((4-(5-methyl-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-(2-methoxyethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(5-(methoxymethyl)-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(5-ethyl-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-(2-methoxyethyl)-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; (R)-4-((4-([1,3'-bipyrrolidine]-1'-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; (S)-4-((4-([1,3'-bipyrrolidine]-1'-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 4-((4-([1,2,4]triazolo[4,3-a]pyridin-3-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-(trifluoromethyl)-1H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(5-(methoxymethyl)-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)pyridazin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(5-ethyl-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)pyridazin-3-yl)amino)-1H-pyrazole-3-carboxamide; 4-((6-(1H-1,2,4-triazol-1-yl)pyridin-3-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-(2-hydroxyethyl)-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(1-ethyl-4-(trifluoromethyl)-1H-imidazol-2-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-methylpyridazin-4-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-isopropyl-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(1-(1-acetylazetidin-3-yl)-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(5-ethyl-1H-1,2,4-triazol-1-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-

dichlorophenyl)-4-((6-(2-methoxyphenyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(2-oxopyrrolidin-1-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-methyl-6-(1H-pyrazol-1-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-(oxetan-3-yl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-(hydroxymethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(4-cyano-1-(oxetan-3-yl)-1H-imidazol-2-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(5-methylpyridazin-4-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(5-ethylpyridazin-4-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(pyridazin-4-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-oxo-1,6-dihydropyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; (S)-1-(2,6-dichlorophenyl)-4-((6-(3-(dimethylamino)pyrrolidine-1-carbonyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; (S)-1-(2,6-dichlorophenyl)-4-((6-(3-fluoropyrrolidine-1-carbonyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; (R)-4-((6-([1,3'-bipyrrolidine]-1'-carbonyl)pyridin-3-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; (S)-4-((6-(3-aminopyrrolidine-1-carbonyl)pyridin-3-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(pyrrolidine-1-carbonyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((1-methyl-1H-pyrazol-4-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(4-methyl-4H-1,2,4-triazol-3-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 4-((4-(4-cyano-1-(2-hydroxyethyl)-1H-imidazol-2-yl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(3,3,4,4-tetrafluoropyrrolidine-1-carbonyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(4-methylpiperazine-1-carbonyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 4-((6-(4-cyclopropylpiperazine-1-carbonyl)pyridin-3-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(morpholine-4-carbonyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; (S)-1-(2,6-dichlorophenyl)-4-((5-(3-(dimethylamino)pyrrolidine-1-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; (S)-1-(2,6-dichlorophenyl)-4-((5-(3-fluoropyrrolidine-1-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; (S)-4-((5-(3-aminopyrrolidine-1-carbonyl)pyridin-2-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(3,3,4,4-

tetrafluoropyrrolidine-1-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(4-methylpiperazine-1-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-(hydroxymethyl)-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-ethoxyphenyl)-4-((1-methyl-1H-pyrazol-4-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(1-(2-hydroxyethyl)-4-(trifluoromethyl)-1H-imidazol-2-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((1-(3,6-dimethylpyrazin-2-yl)-1H-pyrazol-4-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(1-methyl-1H-tetrazol-5-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-methyl-[1,2,4]triazolo[4,3-a]pyridin-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((1-methyl-1H-pyrazol-4-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((1-isopropyl-1H-pyrazol-4-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((2-methyl-2H-1,2,3-triazol-4-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((1-methyl-1H-1,2,3-triazol-4-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)amino)-1H-pyrazole-3-carboxamide; (R)-4-((5-([1,3'-bipyrrolidine]-1'-carbonyl)pyridin-2-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 4-((5-(4-cyclopropylpiperazine-1-carbonyl)pyridin-2-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(2-oxopiperidin-1-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(5-(hydroxymethyl)-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((1-(3-fluoropyridin-2-yl)-1H-pyrazol-4-yl)amino)-1H-pyrazole-3-carboxamide; 4-((6-(4-cyano-1-(2-hydroxyethyl)-1H-imidazol-2-yl)pyridin-3-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(5-methyl-[1,2,4]triazolo[4,3-a]pyridin-3-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((1-methyl-6-oxo-1,6-dihydropyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((2-oxo-2H-[1,2'-bipyridin]-5'-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-methyl-1H-1,2,3-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((1-(4-methoxybenzyl)-1H-pyrazol-4-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(5-isopropyl-1H-tetrazol-1-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4'-methyl-[2,3'-bipyridin]-5-yl)amino)-1H-pyrazole-3-

carboxamide; 1-(2,6-dichlorophenyl)-4-((3'-methyl-[2,2'-bipyridin]-5-yl)amino)-1H-pyrazole-3-carboxamide; 4-((1-(3-chloropyridin-2-yl)-1H-pyrazol-3-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((1-(pyridin-2-yl)-1H-pyrazol-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(3,5-dimethyl-1H-pyrazol-1-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((1-(pyridin-2-yl)-1H-imidazol-4-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(4-isopropyl-4H-1,2,4-triazol-3-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(morpholine-4-carbonyl)pyrazin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(4-methylpiperazine-1-carbonyl)pyrazin-2-yl)amino)-1H-pyrazole-3-carboxamide; (R)-1-(2,6-dichlorophenyl)-4-((5-(3-fluoropyrrolidine-1-carbonyl)pyrazin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-fluorophenyl)-4-((1-methyl-1H-1,2,4-triazol-5-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-((1-methylpiperidin-4-yl)oxy)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((1-methyl-1H-1,2,4-triazol-5-yl)amino)-1H-pyrazole-3-carboxamide; 4-((1H-pyrazol-4-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-(imidazo[1,2-b]pyridazin-3-ylamino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-(pyrazolo[1,5-a]pyrimidin-3-ylamino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((2-((1-methylpiperidin-4-yl)amino)pyrimidin-5-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-ethyl-1H-1,2,3-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichloro-4-fluorophenyl)-4-((4-(morpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichloro-4-fluorophenyl)-4-((4-(methyl(1-methylpiperidin-4-yl)carbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichloro-4-fluorophenyl)-4-((4-(4-ethyl-4H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; (E)-1-(2,6-dichlorophenyl)-4-((4-(4-(2-fluorovinyl)-4H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichloro-3-fluorophenyl)-4-((4-(morpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichloro-3-fluorophenyl)-4-((4-(methyl(1-methylpiperidin-4-yl)carbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichloro-3-fluorophenyl)-4-((4-(4-ethyl-4H-1,2,4-triazol-3-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-((2-methoxyethyl)carbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-((3-methoxypropyl)carbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-

dichlorophenyl)-4-((4-((2-fluoroethyl)carbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-((2-(diethylamino)ethyl)carbamoyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(4-(dimethylamino)piperidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(piperidin-4-yloxy)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(3-fluoroazetidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(3-hydroxyazetidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(4-methyl-3H-indazol-3-ylidene)-1,6-dihydropyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-morpholinopyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(5-methyl-[1,2,4]triazolo[4,3-a]pyridin-3-yl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(5-methyl-1H-1,2,4-triazol-1-yl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(1-ethyl-1H-1,2,4-triazol-5-yl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(5-methyl-1H-1,2,3-triazol-1-yl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(2-methyl-2H-tetrazol-5-yl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(5-methyl-1H-tetrazol-1-yl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(5-methyl-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(5-(trifluoromethyl)-1H-1,2,3-triazol-1-yl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(5-(trifluoromethyl)-1H-1,2,3-triazol-1-yl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(3-hydroxyazetidine-1-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(2-morpholino-2-oxoethyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(2-(3-fluoroazetidin-1-yl)-2-oxoethyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(4-(dimethylamino)piperidine-1-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; (R)-1-(2,6-dichlorophenyl)-4-((5-(3-fluoropyrrolidine-1-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 4-((5-(3-cyanoazetidine-1-carbonyl)pyridin-2-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(1-methyl-1H-tetrazol-5-yl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(5-(trifluoromethyl)-1H-

1,2,3-triazol-1-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 4-((6-(5-chloro-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)pyridin-3-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(4-methyl-1,4-diazepane-1-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(3-fluoroazetidine-1-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; (R)-1-(2-cyano-6-fluorophenyl)-4-((4-(3-fluoropyrrolidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1,1-dioxidothiomorpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-cyano-6-fluorophenyl)-4-((4-(1,1-dioxidothiomorpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 4-[4-(3-Carbamoyl-azetidine-1-carbonyl)-phenylamino]-1-(2,6-dichloro-phenyl)-1H-pyrazole-3-carboxylic acid amide; 1-(2-cyano-6-fluorophenyl)-4-((4-(morpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-((1,1-dioxidothiomorpholino)methyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(3,3-dimethylazetidine-1-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-cyanophenyl)-4-((4-(1,1-dioxidothiomorpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-chloro-6-cyanophenyl)-4-((4-(morpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2-Chloro-6-cyano-phenyl)-4-[4-((R)-3-fluoro-pyrrolidine-1-carbonyl)-phenylamino]-1H-pyrazole-3-carboxylic acid amide; 1-(2,6-dichlorophenyl)-4-((6-(5-(1,1-difluoroethyl)-1H-tetrazol-1-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((1-(2-morpholino-2-oxoethyl)-1H-pyrazol-4-yl)amino)-1H-pyrazole-3-carboxamide; methyl_2-(4-((3-carbamoyl-1-(2,6-dichlorophenyl)-1H-pyrazol-4-yl)amino)-1H-pyrazol-1-yl)acetate; 1-(2,6-dichlorophenyl)-4-((6-(1,1-dioxidothiomorpholine-4-carbonyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(3,3-dimethylazetidine-1-carbonyl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((5-(3,3-dimethylazetidine-1-carbonyl)pyridin-2-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-(methylimino)-1-oxidothiomorpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(thiomorpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((4-(1-imino-1-oxidothiomorpholine-4-carbonyl)phenyl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((1-(2-(1,1-dioxidothiomorpholino)-2-oxoethyl)-1H-pyrazol-4-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(5,7-dimethyl-[1,2,4]triazolo[4,3-c]pyrimidin-3-yl)pyridin-3-yl)amino)-1H-pyrazole-3-

carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(5-(trifluoromethyl)-[1,2,4]triazolo[4,3-a]pyridin-3-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(5-(trifluoromethyl)-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(5-methylimidazo[1,2-a]pyridin-3-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(5-methyl-[1,2,4]triazolo[4,3-c]pyrimidin-3-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 1-(2,6-dichlorophenyl)-4-((6-(5-methylthiazolo[2,3-c][1,2,4]triazol-3-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; 4-((6-(5-cyano-[1,2,4]triazolo[4,3-a]pyridin-3-yl)pyridin-3-yl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide; 1-(2,6-dichloro-4-fluorophenyl)-4-((6-(5-methyl-[1,2,4]triazolo[4,3-a]pyridin-3-yl)pyridin-3-yl)amino)-1H-pyrazole-3-carboxamide; and 4-((4-(3-carbamoylazetidine-1-carbonyl)phenyl)amino)-1-(2,6-dichlorophenyl)-1H-pyrazole-3-carboxamide.

40. The method of claim 21, wherein the compound is selected from the group consisting of 2-(2,6-Dichloro-phenyl)-5-[4-(morpholine-4-carbonyl)-phenylamino]-2H-[1,2,3]triazole-4-carboxylic acid amide; 2-(2,6-Dichloro-phenyl)-5-[4-(4-methyl-piperazine-1-carbonyl)-phenylamino]-2H-[1,2,3]triazole-4-carboxylic acid amide; 2-(2,6-Dichloro-phenyl)-5-[4-(1H-tetrazol-5-yl)-phenylamino]-2H-[1,2,3]triazole-4-carboxylic acid amide; 2-(2,6-Dichloro-phenyl)-5-[4-(1-methyl-1H-tetrazol-5-yl)-phenylamino]-2H-[1,2,3]triazole-4-carboxylic acid amide; 2-(2,6-Dichloro-phenyl)-5-[4-((S)-3-dimethylamino-pyrrolidine-1-carbonyl)-phenylamino]-2H-[1,2,3]triazole-4-carboxylic acid amide; 2-(2,6-Dichloro-phenyl)-5-[4-((R)-3-fluoro-pyrrolidine-1-carbonyl)-phenylamino]-2H-[1,2,3]triazole-4-carboxylic acid amide; 5-[4-(3-Cyano-azetidine-1-carbonyl)-phenylamino]-2-(2,6-dichloro-phenyl)-2H-[1,2,3]triazole-4-carboxylic acid amide; 2-(2,6-dichlorophenyl)-5-((4-(1-(2-hydroxyethyl)-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-Dichloro-phenyl)-5-[4-(5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-3-yl)-phenylamino]-2H-[1,2,3]triazole-4-carboxylic acid amide; 2-(2,6-Dichloro-phenyl)-5-[4-(6,7-dihydro-4H-pyrano[4,3-c]pyrazol-1-yl)-phenylamino]-2H-[1,2,3]triazole-4-carboxylic acid amide; 2-(2,6-Dichloro-phenyl)-5-[4-(6,7-dihydro-4H-pyrano[4,3-c]pyrazol-2-yl)-phenylamino]-2H-[1,2,3]triazole-4-carboxylic acid amide; 2-(2,6-dichlorophenyl)-5-((4-(1-(2-hydroxyethyl)-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(4-(2,2-

difluoroethyl)-4H-1,2,4-triazol-3-yl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-((1-methylpiperidin-4-yl)oxy)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(4-isopropyl-4H-1,2,4-triazol-3-yl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(4-methyl-4H-1,2,4-triazol-3-yl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(1-(2-methoxyethyl)-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-((3-methoxypropyl)carbamoyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(piperidin-4-yloxy)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(5-ethyl-3-(trifluoromethyl)-1H-1,2,4-triazol-1-yl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(4-(dimethylamino)piperidine-1-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-((2-methoxyethyl)carbamoyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(3-hydroxyazetidine-1-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(4-isopropyl-4H-1,2,4-triazol-3-yl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(5-ethyl-1H-1,2,3-triazol-1-yl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((5-(4-methylpiperazine-1-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-((2-fluoroethyl)carbamoyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(3-fluoroazetidine-1-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; (S)-2-(2,6-dichlorophenyl)-5-((5-(3-fluoropyrrolidine-1-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(5-methyl-1H-1,2,3-triazol-1-yl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((5-(3,3,4,4-tetrafluoropyrrolidine-1-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; (R)-2-(2,6-dichlorophenyl)-5-((5-(3-(dimethylamino)pyrrolidine-1-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((5-(5-methyl-1H-tetrazol-1-yl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((5-(3-fluoroazetidine-1-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; (R)-2-(2,6-dichlorophenyl)-5-((5-(3-fluoropyrrolidine-1-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((5-(pyrrolidine-1-

carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichloro-3-fluorophenyl)-5-((4-(morpholine-4-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((6-(5-methyl-[1,2,4]triazolo[4,3-a]pyridin-3-yl)pyridin-3-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((5-(morpholine-4-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((5-(5-methyl-1H-1,2,3-triazol-1-yl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((5-(1-ethyl-1H-1,2,4-triazol-5-yl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((5-morpholinopyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((5-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; (R)-2-(2,6-dichloro-3-fluorophenyl)-5-((4-(3-fluoropyrrolidine-1-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; (R)-2-(2,6-dichloro-4-fluorophenyl)-5-((4-(3-fluoropyrrolidine-1-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; (R)-2-(2-chloro-3,6-difluorophenyl)-5-((4-(3-fluoropyrrolidine-1-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; (R)-2-(2,6-dichloro-4-cyanophenyl)-5-((4-(3-fluoropyrrolidine-1-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((5-(4-(dimethylamino)piperidine-1-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((5-(4-methyl-1,4-diazepane-1-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((6-(2-morpholino-2-oxoethyl)pyridin-3-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((6-(2-(3-fluoroazetidin-1-yl)-2-oxoethyl)pyridin-3-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 5-((5-(3-cyanoazetidine-1-carbonyl)pyridin-2-yl)amino)-2-(2,6-dichlorophenyl)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((5-(3-hydroxyazetidine-1-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(5-(trifluoromethyl)-1H-1,2,3-triazol-1-yl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((5-(5-methyl-1H-1,2,4-triazol-1-yl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((5-(5-(trifluoromethyl)-1H-1,2,3-triazol-1-yl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((5-(1-methyl-1H-tetrazol-5-yl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((6-(5-(trifluoromethyl)-1H-1,2,3-triazol-1-yl)pyridin-3-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((5-(1,1-dioxidothiomorpholine-4-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((6-(5-methyl-[1,2,4]triazolo[4,3-a]pyrazin-3-yl)pyridin-3-yl)amino)-

2H-1,2,3-triazole-4-carboxamide; (R)-2-(2-chloro-6-cyanophenyl)-5-((4-(3-fluoropyrrolidine-1-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(1,1-dioxidothiomorpholine-4-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; (R)-2-(2-cyano-6-fluorophenyl)-5-((4-(3-fluoropyrrolidine-1-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((5-(3,3-dimethylazetidine-1-carbonyl)pyridin-2-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(3,3-dimethylazetidine-1-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; (R)-2-(6-chloro-2,3-difluorophenyl)-5-((4-(3-fluoropyrrolidine-1-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((1-(2-morpholino-2-oxoethyl)-1H-pyrazol-4-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(1-imino-1-oxidothiomorpholine-4-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(thiomorpholine-4-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((4-(1-(methylimino)-1-oxidothiomorpholine-4-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((1-(methylsulfonyl)-1H-pyrazol-4-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((1-(ethylsulfonyl)-1H-pyrazol-4-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichlorophenyl)-5-((1-(2-(1,1-dioxidothiomorpholino)-2-oxoethyl)-1H-pyrazol-4-yl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichloro-4-fluorophenyl)-5-((4-(1,1-dioxidothiomorpholine-4-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; 2-(2,6-dichloro-4-methoxyphenyl)-5-((4-(thiomorpholine-4-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide; and 2-(2,6-dichloro-4-fluorophenyl)-5-((4-(thiomorpholine-4-carbonyl)phenyl)amino)-2H-1,2,3-triazole-4-carboxamide.

41. The method of claim 21, wherein the kinase is LRRK2, NUAK1, JAK1, JAK2, or TYK2.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 21/41270

A. CLASSIFICATION OF SUBJECT MATTER

IPC - A61K 31/506; A61K 31/517; A61K 31/519 (2021.01)

CPC - A61K 31/506; A61K 31/517; A61K 31/519

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)
See Search History document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
See Search History document

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2016/135163 A1 (F HOFFMANN LA ROCHE AG) 1 September 2016 (01.09.2016), especially: para [0213] scheme, product.	1-2
A	FRANCHETTI et al. "8-Azaxanthine Derivatives as Antagonists of Adenosine Receptors", J. Med. Chem. 1994. 37, pp 2970-2975, especially: pg 2971, Table 1, compound 2.	1-2
A	PubChem-SID-131879496, Modify Date: 31 May 2019 (31.05.2019), pg 2, figure, this is a purchasable chemical	1-2

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"D" document cited by the applicant in the international application
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"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
16 November 2021 (16.11.2021)	DEC 14 2021
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 Kari Rodriquez Telephone No. PCT Helpdesk: 571-272-4300

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 21/41270

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
(see extra sheet)

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims:

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-2

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

--BOX III - LACK OF UNITY--

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I+: Claims 1-20, directed to a compound of Formula (II). The compound of Formula (II) will be searched to the extent that it encompasses the first species of claim 1, wherein X is N; R1 is C(O)CH2R3; R3 is unsubstituted cycloalkyl; A is cycloalkyl; and n is 0. It is believed that claims 1-2 encompass this first named invention, and thus these claims will be searched without fee to the extent that they encompass the first species of claim 1. Applicant is invited to elect additional compounds of Formula (II), wherein each additional compound elected will require one additional invention fee. Applicants must specify the claims that encompass any additionally elected compound. Applicants must further indicate, if applicable, the claims which encompass the first named invention, if different than what was indicated above for this group. Failure to clearly identify how any paid additional invention fees are to be applied to the "+" group(s) will result in only the first claimed invention to be searched. Additionally, an exemplary election wherein different actual variables are selected is suggested. An exemplary election would be a compound of claim 1, wherein X is CH; R1 is C(O)CH2R3; R3 is unsubstituted cycloalkyl; A is cycloalkyl; and n is 0 (i.e. claims 1 and 3).

Group II: Claims 21-41, directed to a method of modulating the activity of a kinase, the method comprising contacting cells containing a kinase with a compound of Formula (II).

The groups of inventions listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Special Technical Features:

Group I+ includes the technical feature of a unique compound of Formula (II), which is not required by any other invention of Group I+.

Group II requires a method of modulating the activity of a kinase, the method comprising contacting cells containing a kinase with a compound, which is not required by Group I+.

Common technical features:

The inventions of Groups I+ share the technical feature of a compound having the structure of Formula (II).

The inventions of Group I+ and Group II share the technical feature of a compound having the structure of Formula (II).

These shared technical features, however, do not provide a contribution over the prior art, as being anticipated by WO 2016/135163 A1 to F Hoffmann-La Roche AG (hereinafter 'HOFFMANN').

Hoffmann teaches a compound of Formula (II) wherein X is CH; R1 is substituted heteroaryl; R2 is unsubstituted alkoxyl; A is aryl; n is 1 (para [0213] scheme, product).

As said compound was known in the art at the time of the invention, this cannot be considered a special technical feature that would otherwise unify the inventions of Group I+ and Group II.

The inventions of Group I+ and Group II thus lack unity under PCT Rule 13.