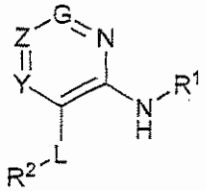
Rev. of Physiol., 1996, *58*, 171-186). Conversely, humans with a glucokinase activation mutation are less prone to hyperglycemia and have increased insulin secretion in response to a glucose challenge (Christesen, H. B., et al., *Diabetes*, 2002, *51*, 1240-1246; Gloyn, A. L, et al., *Diabetes*, 2003, *52*, 2433-2440; Glaser, B., et al., *New England J. Med.*, 1998, *338*, 226-230). Also, NIDDM patients have been reported to have inappropriately low glucokinase activity. Furthermore, over expression of glucokinase in dietary or genetic animal models of diabetes either prevents, ameliorates, or reverses the progress of pathological symptoms in the disease (Caro, J. F., et al., *Hormone & Metabolic Res.*, 1995, *27*, 19-22). For these reasons, compounds that activate glucokinase have been sought by the pharmaceutical industry.

[0013] Substituted benzyl carbamoyl, substituted heterobenzyl carbamoyl, substituted phenyl carbamoyl, and substituted heteroaryl carbamoyl compounds have been disclosed as glucokinase activators. See, for example, WO 03/000267, WO 03/015774, WO 04/045614, WO 04/046139, WO 05/04480, WO 05/054200, WO 05/054233, WO 05/044801, WO 05/056530, WO 03/080585, WO 04/076420, WO 04/081001, WO 04/063194, WO 04/050645, WO 03/055482, WO 04/002481, WO 05/066145, WO 04/072031, WO 04/072066, US 6,610,846, WO 00/058293, WO 03/095438, WO 01/44216, WO 01/083465, WO 01/083478, WO 01/085706, WO 01/085707, WO 02/008209, WO 02/014312, WO 02/046173, WO 02/048106, WO 03/095438, WO 04/031179, and WO 04/052869. These compounds either lower the K_m for glucose and/or increase the V_{max} of glucokinase.

SUMMARY ~~OF THE INVENTION~~

[0014] The present ~~invention~~disclosure relates to novel compounds that are activators of glucokinase which are useful in the treatment of diseases and disorders that would benefit from activation of glucokinase.

[0014a] In one aspect, there is provided a compound selected from the Formula



I

and salts thereof, wherein:

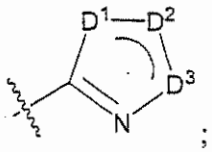
L is O, S, C(=O) or CHR^{14};

Y is CR^4;

Z is CR^3;

G is CR^{11};

R^1 is a heteroaryl ring represented by the formula



;

D^1 is S;

D^2 is N or CR^{12};

D^3 is S, O or CR^{13};

R^2 is aryl, heteroaryl, saturated or partially unsaturated cycloalkyl, or saturated or partially unsaturated heterocyclyl, wherein said aryl, heteroaryl, cycloalkyl and heterocyclyl are monocyclic or bicyclic and are optionally substituted with one or more groups independently selected from C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, saturated and partially unsaturated C_3-C_6 cycloalkyl, saturated and partially unsaturated C_1-C_6 heterocyclyl, aryl, heteroaryl, F, Cl, Br, I, CF_3, CN, NO_2, OR^6, $C(=O)R^6$, $C(=O)OR^6$, $OC(=O)R^6$, $O(CH_2)_nC(=O)OR^6$, $O(CH_2)_nC(=O)NR^6R^7$, $C(=O)NR^6R^7$, NR^6R^7, $NR^6C(=O)R^7$, SR^6, $S(O)R^6$, and $S(O)_2R^6$, and wherein said alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, and heteroaryl are optionally substituted with one or more groups independently selected from oxo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, saturated and partially unsaturated C_3-C_6 V_n-cycloalkyl, saturated and partially unsaturated C_1-C_6 V_n-heterocyclyl, V_n-aryl, V_n-heteroaryl, V_n-F, V_n-Cl, V_n-Br, V_n-I, V_n-CF_3, V_n-CN, V_n-OR^8, V_n-$C(=O)R^8$, V_n-$C(=O)OR^8$, V_n-$OC(=O)R^8$, V_n-$C(=O)NR^8R^9$, V_n-NR^8R^9, V_n-$NR^8C(=O)R^9$, V_n-SR^8, V_n-$S(O)R^8$, and V_n-$S(O)_2R^8$;

R^3 is SR^6, $S(O)R^6$, $S(O)_2R^6$ or $S(O)_2NR^6R^7$;

R^4 is H;

R^6 and R^7 are independently H, C_1-C_{12} alkyl, C_2-C_{12} alkenyl, C_2-C_{12} alkynyl, saturated or partially unsaturated C_3-C_{12} cycloalkyl, saturated or partially unsaturated C_1-C_{12} heterocyclyl, V_n-aryl, or V_n-heteroaryl, wherein said alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl and heteroaryl portions are optionally substituted with one or more groups independently selected from oxo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, saturated and partially unsaturated C_3-C_6 cycloalkyl, saturated and partially unsaturated C_1-C_6 heterocyclyl [optionally substituted with C(O)O(1-6C alkyl), (1-6C)alkyl or (1-6C alkyl)OH], V_n-aryl, V_n-heteroaryl, V_n-F, V_n-Cl, V_n-Br, V_n-I, V_n-CF_3, V_n-CN, V_n-OR^8, V_n-$C(=O)R^8$, V_n-$C(=O)OR^8$, V_n-$OC(=O)R^8$, V_n-$C(=O)NR^8R^9$, V_n-NR^8R^9, V_n-$NR^8C(=O)R^9$, V_n-SR^8, V_n-$S(O)R^8$, V_n-$S(O)_2R^8$, V_n-$S(O)_2NR^8R^9$, and (C_1-C_6 alkyl)OH;

or R^6 and R^7 together with the atoms to which they are attached form a saturated or partially unsaturated heterocyclic ring, wherein said heterocyclic ring optionally comprises one or more additional ring heteroatoms independently selected from N, O or S, wherein said heterocyclic ring is optionally substituted with one or more groups independently selected from oxo, V_n-F, V_n-Cl, V_n-Br, V_n-I, V_n-OR^8, V_n-$C(=O)OR^8$, V_n-$C(=O)NR^8R^9$, V_n-NR^8R^9, V_n-$NR^8C(=O)R^9$, V_n-$NR^8C(=O)NR^9R^{10}$, C_1-C_6 alkyl, C_2-C_6 alkenyl, and C_2-C_6 alkynyl;

R^8, R^9 and R^{10} are independently H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, saturated and partially unsaturated C_3-C_6 cycloalkyl, saturated and partially unsaturated C_1-C_6 heterocyclyl, aryl or heteroaryl, wherein said alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl and heteroaryl are optionally substituted with one or more groups independently selected from oxo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, saturated and partially unsaturated C_3-C_6 cycloalkyl, saturated and partially unsaturated C_1-C_6 heterocyclyl, V_n-aryl, V_n-heteroaryl, V_n-F, V_n-Cl, V_n-Br, V_n-I, V_n-OR^a, V_n-NR^aR^b, V_n-$C(=O)OR^a$, V_n-$C(=O)NR^aR^b$, and V_n-$NR^aC(=O)R^b$,

or R^8 and R^9 together with the atoms to which they are attached form a saturated or partially unsaturated heterocyclic ring, wherein said heterocyclic ring optionally comprises one or more additional ring heteroatoms independently selected from N, O or S, wherein said heterocyclic ring is optionally substituted with one or more groups independently selected from oxo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, V_n-F, V_n-Cl, V_n-Br, V_n-I, V_n-OR^a, and V_n-CN,

or R^9 and R^{10} together with the atoms to which they are attached form a saturated or partially unsaturated heterocyclic ring, wherein said heterocyclic ring optionally comprises one or more additional ring heteroatoms independently selected from N, O or S, wherein said heterocyclic ring is optionally substituted with one or more groups independently selected from oxo,C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, V_n-F, V_n-Cl, V_n-Br, V_n-I, V_n-OR^a, and V_n-CN;

R^{11} is H;

R^{12} and R^{13} are independently H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, saturated and partially unsaturated C_3-C_6 cycloalkyl, saturated and partially unsaturated C_1-C_6 heterocyclyl, CH_2-heterocyclyl, aryl, heteroaryl, (1-3C alkyl)heteroaryl, $(CH_2)_n(CR^xR^y)C(O)NR^8R^9$, $(CH_2)_n(CR^xR^y)C(O)NH$-N=$CHNR^8R^9$, F, Cl, Br, I, CF_3, CN, OR^6, $C(=O)R^6$, $C(=O)OR^6$, $OC(=O)R^6$, $C(=O)NR^6R^7$, NR^6R^7, $NR^6C(=O)R^7$, SR^6, $S(O)R^6$, $S(O)_2R^6$, wherein said alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl and heteroaryl are optionally substituted with one or more groups independently selected from oxo, V_n-F, V_n-Cl, V_n-Br, V_n-I, V_n-CF_3, V_n-CN, V_n-OR^8, V_n-$C(=O)OR^8$, V_n-$OC(=O)R^8$, V_n-$C(=O)NR^8R^9$, V_n-NR^8R^9, V_n-$NR^8C(=O)R^9$, $C(O)(C_1$-C_6 alkyl), C(O)-heterocycle [optionally substituted with O-(C_1-C_6 alkyl], SR^a, SO_2R^f, $SO_2NR^cR^e$, $C(O)(C_1$-C_6 alkyl)NR^cR^d, $C(O)(C_1$-C_6 alkyl)OR^c, $C(O)CH_2C(O)(C_1$-C_6 alkyl),

$C(=O)CHR^gNHC(=O)(C_1\text{-}C_6$ alkyl), $C(=O)CH_2OC(=O)(C_1\text{-}C_6$ alkyl), $C_1\text{-}C_6$ alkyl, $C_2\text{-}C_6$ alkenyl, $C_2\text{-}C_6$ alkynyl, saturated and partially unsaturated $C_3\text{-}C_6$ cycloalkyl, saturated and partially unsaturated $C_1\text{-}C_6$ heterocyclyl, V_n-aryl, and V_n-heteroaryl, wherein said heterocyclyl is optionally substituted with one or more oxo,

or R^{12} and R^{13} together with the atoms to which they are attached form a saturated, partially unsaturated or aromatic carbocyclic or heterocyclic ring, wherein said carbocyclic and heterocyclic rings are optionally substituted with one or more groups independently selected from $C_1\text{-}C_6$ alkyl, $C_2\text{-}C_6$ alkenyl, $C_2\text{-}C_6$ alkynyl, saturated and partially unsaturated $C_3\text{-}C_6$ cycloalkyl, saturated and partially unsaturated $C_1\text{-}C_6$ heterocyclyl, aryl, heteroaryl, oxo, F, Cl, Br, I, CF_3, CN, OR^6, $C(=O)R^6$, $C(=O)OR^6$, $OC(=O)R^6$, $C(=O)NR^6R^7$, NR^6R^7, $NR^6C(=O)R^7$, SR^6, $S(O)R^6$, $S(O)_2R^6$ and $SO_2NR^6R^7$, wherein said alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl and heteroaryl are optionally substituted with one or more groups independently selected from oxo, V_n-F, V_n-Cl, V_n-Br, V_n-I, V_n-CF_3, V_n-CN, V_n-OR^8, V_n-$C(=O)OR^8$, V_n-$OC(=O)R^8$, V_n-$C(=O)NR^8R^9$, V_n-NR^8R^9, V_n-$NR^8C(=O)R^9$, $C_1\text{-}C_6$ alkyl, $C_2\text{-}C_6$ alkenyl, $C_2\text{-}C_6$ alkynyl, saturated and partially unsaturated $C_3\text{-}C_6$ cycloalkyl, saturated and partially unsaturated $C_1\text{-}C_6$ heterocyclyl, V_n-aryl, and V_n-heteroaryl;

R^{14} is H, methyl, ethyl or OH;

R^a and R^b are independently H, $C_1\text{-}C_6$ alkyl, $C_2\text{-}C_6$ alkenyl, $C_2\text{-}C_6$ alkynyl, saturated and partially unsaturated $V_n\text{-}C_3\text{-}C_6$ cycloalkyl, saturated and partially unsaturated $V_n\text{-}C_1\text{-}C_6$ heterocyclyl, V_n-aryl, or V_n-heteroaryl, wherein said alkyl, alkenyl, alkynyl, saturated or partially unsaturated V_n-cycloalkyl, saturated or partially unsaturated V_n-heterocyclyl, V_n-aryl, and V_n-heteroaryl are optionally substituted with one or more OH;

each R^c, R^e and R^g is independently H or $C_1\text{-}C_6$ alkyl;

R^d is H, $C_1\text{-}C_6$ alkyl or $C(O)O(C_1\text{-}C_6$ alkyl);

R^f is $C_1\text{-}C_6$ alkyl or $(C_1\text{-}C_6$ alkyl)NH_2;

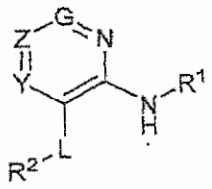
R^x is H or $C_1\text{-}C_6$ alkyl;

R^y is H, $C_1\text{-}C_6$ alkyl, or $-O(C_1\text{-}C_6$ alkyl);

V is alkylene having from 1 to 12 carbons, or alkenylene or alkynylene each having from 2 to 12 carbons, wherein said alkylene, alkenylene, or alkynylene are optionally substituted with one or more groups independently selected from $C_1\text{-}C_6$ alkyl, $C_2\text{-}C_6$ alkenyl, $C_2\text{-}C_6$ alkynyl, saturated and partially unsaturated $C_3\text{-}C_6$ cycloalkyl, saturated and partially unsaturated $C_1\text{-}C_6$ heterocyclyl, aryl, heteroaryl, F, Cl, Br, I, CF_3, cyano, OR^8, $C(=O)OR^8$, $OC(=O)R^8$, $C(=O)NR^8R^9$, NR^8R^9, $(C_1\text{-}C_6$ alkyl$)NR^cR^e$, and $NR^8C(=O)R^9$; and

n is 0 or 1.

[0015] More specifically, one ~~aspect~~embodiment of this ~~invention~~disclosure provides compounds of Formula I



I

[0016] and solvates, metabolites, salts and pharmaceutically acceptable prodrugs thereof, wherein L, Y, Z, G, R^1 and R^2 are as defined below.

[0017] The ~~invention~~disclosure also provides pharmaceutical compositions comprising a compound of Formula I, or a solvate, metabolite, and solvate, metabolite, salt or pharmaceutically acceptable prodrugs thereof, and a pharmaceutically acceptable carrier.

[0017a] In one aspect, there is provided a composition comprising a compound as defined above and a pharmaceutically acceptable diluent or carrier.

[0018] The inventive compounds may be used advantageously in combination with other know therapeutic agents. Accordingly this ~~invention~~disclosure also provides pharmaceutical compositions comprising a compound of Formula I or a solvate, metabolite, or pharmaceutically acceptable salt or prodrug thereof, in combination with a second therapeutic agent.

[0019] This ~~invention~~disclosure also provides methods of preventing or treating a disease or disorder characterized by underactivation of glucokinase or which can be treated by activating glucokinase in a mammal, comprising administrating to said mammal one or more compounds of Formula I, or a metabolite, solvate, or pharmaceutically acceptable salt or prodrug thereof, in an amount effective to treat said disease or disorder. The compounds of the present ~~invention~~disclosure can be used, for example, as prophylactics or therapeutic agents for treating diseases or disorders mediated by deficient levels of glucokinase activity, including, but not limited to, diabetes mellitus (type I and type II), impaired glucose tolerance, IFG (impaired fasting glucose) and IFG (impaired fasting glycemia), as well as other diseases and disorders characterized by underactivation of glucokinase or which can be treated by activation of glucokinase, such as those discussed below.

[0020] This ~~invention~~disclosure also provides compounds of Formula I for use in therapy.

[0021] An additional ~~aspect~~embodiment of the ~~invention~~disclosure is the use of a compound of Formula I for the preparation of a medicament for use as a glucokinase activator.

[0022] This ~~invention~~disclosure further provides kits for the treatment or prevention of a disease or disorder characterized by underactivation of glucokinase, said kit comprising a compound of Formula I, or a solvate, metabolite, or pharmaceutically acceptable salt or prodrug thereof, a container, and optionally a package insert or label indicating a treatment. The kits may further comprise a second compound or formulation comprising a second pharmaceutical agent useful for treating said disease or disorder.

[0023] This ~~invention~~disclosure further includes methods of preparing, methods of separating, and methods of purifying of the compounds of this ~~invention~~disclosure.

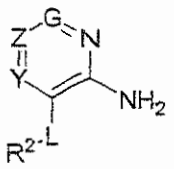
[0023a] In one aspect, there is provided a method of preparing a compound as defined above, said method comprising:

(a) reacting a compound of the formula



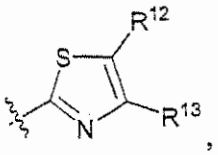
with a compound of the formula R^1NH_2 in the presence of a base catalyst or metal catalyst; or

(b) reacting a compound of the formula

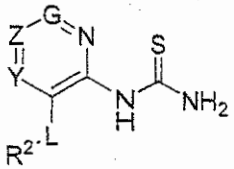


with a compound of the formula R^1-X, wherein X is Cl or Br, in the presence of a base catalyst or metal catalyst; or

(c) for a compound of Formula **I** wherein R^1 is

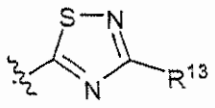


reacting a compound of the formula

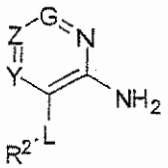


with a compound of the formula $R^{13}COCHR^{12}X$, wherein X is a leaving group, in the presence of a base; or

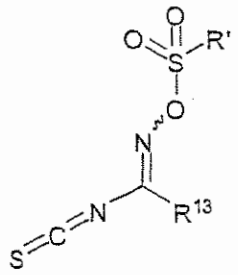
(d) for a compound of Formula I wherein R^1 is



reacting a compound of the formula

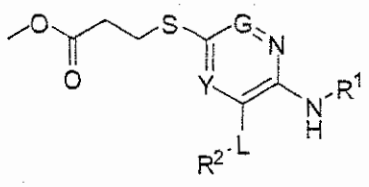


with a compound having the formula



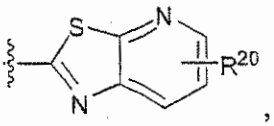
where R' is C_1-C_6 alkyl or aryl optionally substituted with C_1-C_6 alkyl, in the presence of a base; or

(e) for a compound of Formula **I** wherein Z is CR^3 and R^3 is SR^6, reacting a corresponding compound having the formula



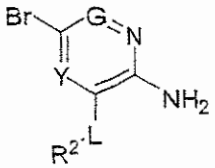
with a compound having the formula R^6X wherein X is a leaving group or atom in the presence of a base; or

(f) for a compound of Formula **I** wherein R^1 is

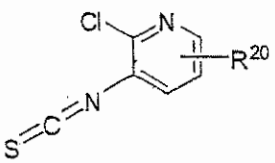


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reacting a corresponding compound having the formula

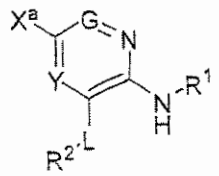


with a compound having the formula



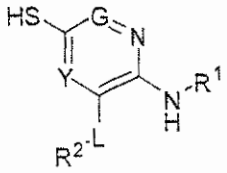
at elevated temperatures; or

g) for a compound of Formula **I** wherein Z is CR^3, reacting a corresponding compound having the formula



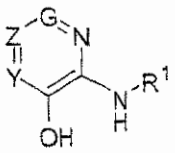
wherein X^a is a leaving group or atom (e.g., a halogen such as Br, Cl or I,) with a compound having the formula R^3-X^b wherein X^b is a leaving group or atom, in the presence of a suitable base; or

h) for a compound of Formula **I** wherein Z is C-SR^6 and R^6 is alkyl, CH_2-aryl, heteroaryl, or aryl and wherein said R^6 groups are optionally substituted, reacting a corresponding compound having the formula



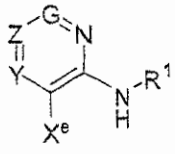
with a compound having the formula R^6-X^c wherein X^c is a leaving group or atom, in the presence of a suitable base; or

i) for a compound of Formula **I** wherein L is O, reacting a corresponding compound having the formula



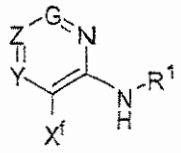
with a compound having the formula R^2-X^d, wherein X^d is a leaving group or atom, in the presence of a base, or in the presence of a copper or palladium catalyst; or

j) for a compound of Formula **I** wherein L is O or S, reacting a corresponding compound having the formula



wherein X^e is a leaving group or atom with a compound having the formula R^2LH wherein L is O or S, respectively; in the presence of a palladium catalyst and a suitable base; or

k) for a compound of Formula **I** wherein **L** is CH_2, reacting a corresponding compound having the formula



wherein X^f is a leaving group or atom (e.g., Cl, Br, I, OTf or acetyloxy) in the presence of an organozinc compound having the formula R^2-Zn-X^g wherein X^g is a halide, and a nickel or palladium catalyst; and

removing any protecting group or groups and, if desired, forming a salt.

[0023b] In one aspect, there is provided a compound selected from the group consisting of:
N-(4-methylthiazol-2-yl)-3-phenoxy-5-(phenylthio)pyridin-2-amine;
methyl 3-(6-(4-methylthiazol-2-ylamino)-5-phenoxypyridin-3-ylthio)propanoate;
N-(5-(cyclohexylthio)-3-phenoxypyridin-2-yl)-4-methylthiazol-2-amine;
N-(5-(benzylthio)-3-phenoxypyridin-2-yl)-4-methylthiazol-2-amine;
4-methyl-N-(3-phenoxy-5-(pyridin-2-ylmethylthio)pyridin-2-yl)thiazol-2-amine;
4-methyl-N-(3-phenoxy-5-(piperidin-4-ylmethylthio)pyridin-2-yl)thiazol-2-amine;
5-(2-methoxybenzylthio)-N-(4-methylthiazol-2-yl)-3-phenoxypyridin-2-amine;
5-(4-methoxybenzylthio)-N-(4-methylthiazol-2-yl)-3-phenoxypyridin-2-amine;
5-(2-chlorobenzylthio)-N-(4-methylthiazol-2-yl)-3-phenoxypyridin-2-amine;
N-(4-methylthiazol-2-yl)-3-phenoxy-5-(1-(pyridin-2-yl)ethylthio)pyridin-2-amine;
5-(3-methoxybenzylthio)-N-(4-methylthiazol-2-yl)-3-phenoxypyridin-2-amine;
5-(3-(dimethylamino)propylthio)-N-(4-methylthiazol-2-yl)-3-phenoxypyridin-2-amine;
N-(3-(2-chlorophenylthio)-5-(phenylthio)pyridin-2-yl)-4-methylthiazol-2-amine;
methyl 3-(5-(2-chlorophenylthio)-6-(4-methylthiazol-2-ylamino)pyridin-3-ylthio)propanoate;
N-(3-(2-chlorophenylthio)-5-(1-(pyridin-2-yl)ethylthio)pyridin-2-yl)-4-methylthiazol-2-amine;
N-(3-(2-chlorophenylthio)-5-(piperidin-4-ylmethylthio)pyridin-2-yl)-4-methylthiazol-2-amine;
N-(3-(2-chlorophenylthio)-5-(3-(dimethylamino)propylthio)pyridin-2-yl)-4-methylthiazol-2-amine;

N-(5-(2-chlorophenylthio)-3-phenoxypyridin-2-yl)-4-methylthiazol-2-amine;
N-(5-(3-chlorophenylthio)-3-phenoxypyridin-2-yl)-4-methylthiazol-2-amine;
N-(5-(2-methoxyphenylthio)-3-phenoxypyridin-2-yl)-4-methylthiazol-2-amine;
N-(5-(3-methoxyphenylthio)-3-phenoxypyridin-2-yl)-4-methylthiazol-2-amine;
3-(6-(4-methylthiazol-2-ylamino)-5-phenoxypyridin-3-ylthio)phenol;
2-(3-(6-(4-methylthiazol-2-ylamino)-5-phenoxypyridin-3-ylthio)phenoxy)acetic acid;
4-methyl-N-(3-phenoxy-5-(3-(2-(piperidin-1-yl)ethoxy)phenylthio)pyridin-2-yl)thiazol-2-amine;
N-(5-(3-(3-(dimethylamino)propoxy)phenylthio)-3-phenoxypyridin-2-yl)-4-methylthiazol-2-amine;
5-(2-fluorobenzylthio)-N-(4-methylthiazol-2-yl)-3-phenoxypyridin-2-amine;
N-(4-methylthiazol-2-yl)-3-phenoxy-5-(1-(pyridin-2-yl)propylthio)pyridin-2-amine;
2-((6-(4-methylthiazol-2-ylamino)-5-phenoxypyridin-3-ylthio)methyl)pyridin-3-ol;
3-(2-(3-phenoxy-5-(1-(pyridin-2-yl)ethylthio)pyridin-2-ylamino)thiazol-4-yl)propanoic acid;
4-chloro-3-(2-(4-methylthiazol-2-ylamino)-5-(phenylthio)pyridin-3-yloxy)benzoic acid;
4-chloro-N-(2-(dimethylamino)ethyl)-3-(2-(4-methylthiazol-2-ylamino)-5-(phenylthio)pyridin-3-yloxy)benzamide;
4-chloro-3-(2-(4-methylthiazol-2-ylamino)-5-(1-(pyridin-2-yl)ethylthio)pyridin-3-yloxy)benzoic acid;
4-chloro-N-(2-(dimethylamino)ethyl)-3-(2-(4-methylthiazol-2-ylamino)-5-(1-(pyridin-2-yl)ethylthio)pyridin-3-yloxy)benzamide;
N-(5-(2-chlorophenylthio)-3-phenoxypyridin-2-yl)-4-methylthiazol-2-amine;
N-(5-(3-chlorophenylthio)-3-phenoxypyridin-2-yl)-4-methylthiazol-2-amine;
N-(5-(2-methoxyphenylthio)-3-phenoxypyridin-2-yl)-4-methylthiazol-2-amine;
N-(5-(3-methoxyphenylthio)-3-phenoxypyridin-2-yl)-4-methylthiazol-2-amine;
methyl 3-(5-(2-chlorophenylthio)-6-(4-methylthiazol-2-ylamino)pyridin-3-ylthio)propanoate;
N-(5-(2,5-dimethoxyphenylthio)-3-phenoxypyridin-2-yl)-4-methylthiazol-2-amine;
N-(5-(2,5-dichlorophenylthio)-3-phenoxypyridin-2-yl)-4-methylthiazol-2-amine;
N-(5-(2,5-dimethylphenylthio)-3-phenoxypyridin-2-yl)-4-methylthiazol-2-amine;
N-(5-(1-(2-(dimethylamino)ethyl)-1H-tetrazol-5-ylthio)-3-phenoxypyridin-2-yl)-4-methylthiazol-2-amine;
4-methyl-N-(5-(4-methyl-4H-1,2,4-triazol-3-ylthio)-3-phenoxypyridin-2-yl)thiazol-2-amine;
3-(2-chlorophenylthio)-N-(4-methylthiazol-2-yl)-5-(phenylthio)pyridin-2-amine;
N-(5-([1,2,4]triazolo[4,3-a]pyridin-3-ylthio)-3-phenoxypyridin-2-yl)-4-methylthiazol-2-amine;
2-(4-methyl-5-(6-(4-methylthiazol-2-ylamino)-5-phenoxypyridin-3-ylthio)-4H-1,2,4-triazol-3-yl)acetonitrile;

methyl 3-(6-(4-phenethylthiazol-2-ylamino)-5-phenoxypyridin-3-ylthio)propanoate;
methyl 3-(6-(4-(1-methylpiperidin-4-yl)thiazol-2-ylamino)-5-phenoxypyridin-3-ylthio)propanoate;
methyl 3-(5-(4-fluorophenoxy)-6-(4-phenethylthiazol-2-ylamino)pyridin-3-ylthio)propanoate;
methyl 3-(5-(2-chlorophenylthio)-6-(4-methylthiazol-2-ylamino)pyridin-3-ylthio)propanoate;
methyl 3-(6-(4-methylthiazol-2-ylamino)-5-(phenylthio)pyridin-3-ylthio)propanoate;
tert-butyl 4-(5-(3-(4-fluorophenoxy)-5-(3-methoxy-3-oxopropylthio)pyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)piperidine-1-carboxylate;
tert-butyl 4-((5-(3-(4-fluorophenoxy)-5-(3-methoxy-3-oxopropylthio)pyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)methyl)piperidine-1-carboxylate;
N-(3-(2-chlorophenylthio)-5-(1-(pyridin-2-yl)ethylthio)pyridin-2-yl)-4-methylthiazol-2-amine;
N-(3-(2-chlorophenylthio)-5-(piperidin-4-ylmethylthio)pyridin-2-yl)-4-methylthiazol-2-amine;
N-(3-(2-chlorophenylthio)-5-(3-(dimethylamino)propylthio)pyridin-2-yl)-4-methylthiazol-2-amine;
4-phenethyl-N-(3-phenoxy-5-(piperidin-4-ylmethylthio)pyridin-2-yl)thiazol-2-amine;
3-(6-(4-methylthiazol-2-ylamino)-5-phenoxypyridin-3-ylthio)phenol;
4-methyl-N-(3-phenoxy-5-(3-(2-(piperidin-1-yl)ethoxy)phenylthio)pyridin-2-yl)thiazol-2-amine;
2-(3-(6-(4-methylthiazol-2-ylamino)-5-phenoxypyridin-3-ylthio)phenoxy)acetic acid;
N-(5-(3-(3-(dimethylamino)propoxy)phenylthio)-3-phenoxypyridin-2-yl)-4-methylthiazol-2-amine;
4-methyl-N-(3-phenoxy-5-(pyridin-2-ylthio)pyridin-2-yl)thiazol-2-amine;
4-methyl-N-(3-phenoxy-5-(pyridin-4-ylthio)pyridin-2-yl)thiazol-2-amine;
4-methyl-N-(3-phenoxy-5-(pyrimidin-2-ylthio)pyridin-2-yl)thiazol-2-amine;
4-methyl-N-(5-(6-methylpyridin-2-ylthio)-3-phenoxypyridin-2-yl)thiazol-2-amine;
4-methyl-N-(5-(4-methylthiazol-2-ylthio)-3-phenoxypyridin-2-yl)thiazol-2-amine;
N-(3-(2-chlorophenylthio)-5-(pyridin-4-ylthio)pyridin-2-yl)-4-methylthiazol-2-amine;
4-(1-methylpiperidin-4-yl)-N-(3-phenoxy-5-(phenylthio)pyridin-2-yl)thiazol-2-amine;
N-(3,5-bis(phenylthio)pyridin-2-yl)-4-methylthiazol-2-amine;
4-methyl-N-(3-(phenylthio)-5-(pyridin-2-ylthio)pyridin-2-yl)thiazol-2-amine;
3-methyl-N-(3-phenoxy-5-(pyridin-2-ylthio)pyridin-2-yl)-1,2,4-thiadiazol-5-amine;
N-(5-(4-methoxyphenylthio)-3-phenoxypyridin-2-yl)-3-methyl-1,2,4-thiadiazol-5-amine;
N-(3-(4-fluorophenoxy)-5-(pyridin-2-ylthio)pyridin-2-yl)-3-isobutyl-1,2,4-thiadiazol-5-amine;
5-(2-chloropyridin-4-ylthio)-N-(4-methylthiazol-2-yl)-3-phenoxypyridin-2-amine;
N-(5-(2-chloropyrimidin-4-ylthio)-3-phenoxypyridin-2-yl)-4-methylthiazol-2-amine;

5-(4,6-dimethylpyrimidin-2-ylthio)-N-(4-methylthiazol-2-yl)-3-phenoxypyridin-2-amine;
N-(5-(4,6-dimethoxypyrimidin-2-ylthio)-3-phenoxypyridin-2-yl)-4-methylthiazol-2-amine;
5-(4-methoxypyrimidin-2-ylthio)-N-(4-methylthiazol-2-yl)-3-phenoxypyridin-2-amine;
N-(4-methylthiazol-2-yl)-3-phenoxy-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-amine;
4-methyl-N-(5-(3-methylisoxazolo[5,4-b]pyridin-4-ylthio)-3-phenoxypyridin-2-yl)thiazol-2-amine;
N-(5-(2-(methoxymethyl)pyrimidin-4-ylthio)-3-phenoxypyridin-2-yl)-4-methylthiazol-2-amine;
4-phenethyl-N-(3-phenoxy-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-yl)thiazol-2-amine;
N-(5-(3-methylisoxazolo[5,4-b]pyridin-4-ylthio)-3-phenoxypyridin-2-yl)-4-phenethylthiazol-2-amine;
N-(5-(5-methylpyrazolo[1,5-a]pyrimidin-7-ylthio)-3-phenoxypyridin-2-yl)-4-phenethylthiazol-2-amine;
4-phenethyl-N-(3-phenoxy-5-(thieno[3,2-d]pyrimidin-4-ylthio)pyridin-2-yl)thiazol-2-amine;
4-methyl-N-(5-(5-methylpyrazolo[1,5-a]pyrimidin-7-ylthio)-3-phenoxypyridin-2-yl)thiazol-2-amine;
4-methyl-N-(3-phenoxy-5-(thieno[3,2-d]pyrimidin-4-ylthio)pyridin-2-yl)thiazol-2-amine;
4-(1-methylpiperidin-4-yl)-N-(3-phenoxy-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-yl)thiazol-2-amine;
N-(5-(3-methylisoxazolo[5,4-b]pyridin-4-ylthio)-3-phenoxypyridin-2-yl)-4-(1-methylpiperidin-4-yl)thiazol-2-amine;
N-(5-(2-iodothieno[3,2-b]pyridin-7-ylthio)-3-phenoxypyridin-2-yl)-4-methylthiazol-2-amine;
4-methyl-N-(5-(2-methylthieno[3,2-b]pyridin-7-ylthio)-3-phenoxypyridin-2-yl)thiazol-2-amine;
N-(5-(2-methylthieno[3,2-b]pyridin-7-ylthio)-3-phenoxypyridin-2-yl)-4-phenethylthiazol-2-amine;
N-(5-(2,5-dimethylpyrazolo[1,5-a]pyrimidin-7-ylthio)-3-phenoxypyridin-2-yl)-4-phenethylthiazol-2-amine;
N-(3-(4-fluorophenoxy)-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-yl)-4-phenethylthiazol-2-amine;
N-(3-(4-fluorophenoxy)-5-(3-methylisoxazolo[5,4-b]pyridin-4-ylthio)pyridin-2-yl)-4-phenethylthiazol-2-amine;
N-(3-(4-fluorophenoxy)-5-(5-methylpyrazolo[1,5-a]pyrimidin-7-ylthio)pyridin-2-yl)-4-phenethylthiazol-2-amine;

N-(5-(2,5-dimethylpyrazolo[1,5-a]pyrimidin-7-ylthio)-3-(4-fluorophenoxy)pyridin-2-yl)-4-phenethylthiazol-2-amine;

N-(3-(4-fluorophenoxy)-5-(2-methylthieno[3,2-b]pyridin-7-ylthio)pyridin-2-yl)-4-phenethylthiazol-2-amine;

4-(6-(4-methylthiazol-2-ylamino)-5-phenoxypyridin-3-ylthio)benzonitrile;

N-(3-(2-chlorophenylthio)-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-yl)-4-methylthiazol-2-amine;

4-(5-phenoxy-6-(4-(piperidin-4-yl)thiazol-2-ylamino)pyridin-3-ylthio)benzonitrile;

N-(5-(furo[3,2-c]pyridin-4-ylthio)-3-phenoxypyridin-2-yl)-4-methylthiazol-2-amine;

N-(5-(2-iodothieno[3,2-b]pyridin-7-ylthio)-3-phenoxypyridin-2-yl)-4-(piperidin-4-yl)thiazol-2-amine;

4-methyl-N-(3-(phenylthio)-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-yl)thiazol-2-amine;

4-methyl-N-(5-(3-methylisoxazolo[5,4-b]pyridin-4-ylthio)-3-(phenylthio)pyridin-2-yl)thiazol-2-amine;

4-(6-(4-methylthiazol-2-ylamino)-5-(phenylthio)pyridin-3-ylthio)benzonitrile;

4-methyl-N-(3-(phenylthio)-5-(5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-ylthio)pyridin-2-yl)thiazol-2-amine;

tert-butyl 4-(5-(3-(4-fluorophenoxy)-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)piperidine-1-carboxylate;

N-(4-cyclopropylthiazol-2-yl)-3-phenoxy-5-(pyridin-4-ylthio)pyridin-2-amine;

4-isobutyl-N-(3-phenoxy-5-(pyridin-4-ylthio)pyridin-2-yl)thiazol-2-amine;

4-cyclohexyl-N-(3-phenoxy-5-(pyridin-4-ylthio)pyridin-2-yl)thiazol-2-amine;

N-(3-phenoxy-5-(pyridin-4-ylthio)pyridin-2-yl)-4-(trifluoromethyl) thiazol-2-amine;

methyl 3-(2-(3-phenoxy-5-(pyridin-4-ylthio)pyridin-2-ylamino)thiazol-4-yl)propanoate;

N-(3-phenoxy-5-(pyridin-4-ylthio)pyridin-2-yl)-4-(pyridin-2-yl)thiazol-2-amine;

N-(3-phenoxy-5-(pyridin-4-ylthio)pyridin-2-yl)-4-phenylthiazol-2-amine;

N-(3-phenoxy-5-(pyridin-4-ylthio)pyridin-2-yl)-4-(thiophen-3-yl)thiazol-2-amine;

4-phenethyl-N-(3-phenoxy-5-(pyridin-4-ylthio)pyridin-2-yl)thiazol-2-amine;

4-ethyl-N-(3-phenoxy-5-(pyridin-4-ylthio)pyridin-2-yl)thiazol-2-amine;

N-(3-phenoxy-5-(pyridin-4-ylthio)pyridin-2-yl)thiazol-2-amine;

4-isopropyl-N-(3-phenoxy-5-(pyridin-4-ylthio)pyridin-2-yl)thiazol-2-amine;

N-(5-(2-chloro-5-methoxyphenylthio)-3-phenoxypyridin-2-yl)-4-methylthiazol-2-amine;

(R)-4-methyl-N-(5-(5-methyl-6,7-dihydro-5H-cyclopenta[d]pyrimidin-4-ylthio)-3-phenoxypyridin-2-yl)thiazol-2-amine;

3-(2-(3-phenoxy-5-(pyridin-4-ylthio)pyridin-2-ylamino)thiazol-4-yl)propanoic acid;
N-(5-(3,5-dimethylisoxazolo[4,5-b]pyridin-7-ylthio)-3-phenoxypyridin-2-yl)-4-methylthiazol-2-amine;
1-(4-(2-(3-phenoxy-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-ylamino)thiazol-4-yl)piperidin-1-yl)ethanone;
1-(4-(5-(3-phenoxy-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)piperidin-1-yl)ethanone;
1-(4-(5-(3-(phenylthio)-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)piperidin-1-yl)ethanone;
1-(4-(2-(3-(phenylthio)-5-(pyridin-2-ylthio)pyridin-2-ylamino)thiazol-4-yl)piperidin-1-yl)ethanone;
methyl 4-(2-(3-(phenylthio)-5-(pyridin-2-ylthio)pyridin-2-ylamino)thiazol-4-yl)piperidine-1-carboxylate;
1-(4-(2-(3-(phenylthio)-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-ylamino)thiazol-4-yl)piperidin-1-yl)ethanone;
4-(1-(methylsulfonyl)piperidin-4-yl)-N-(3-(phenylthio)-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-yl)thiazol-2-amine;
2-(dimethylamino)-1-(4-(2-(3-(phenylthio)-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-ylamino)thiazol-4-yl)piperidin-1-yl)ethanone;
1-(4-(5-(3-(4-fluorophenoxy)-5-(5-methylpyrazolo[1,5-a]pyrimidin-7-ylthio)pyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)piperidin-1-yl)ethanone;
1-(4-(5-(3-(4-fluorophenoxy)-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)piperidin-1-yl)ethanone;
N-(3-(4-fluorophenoxy)-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-yl)-3-(1-(methylsulfonyl)piperidin-4-yl)-1,2,4-thiadiazol-5-amine;
2-(dimethylamino)-1-(4-(5-(3-(4-fluorophenoxy)-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)piperidin-1-yl)ethanone;
3-(phenylthio)-N-(3-(piperidin-4-yl)-1,2,4-thiadiazol-5-yl)-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-amine;
N-(3-(phenylthio)-5-(pyridin-2-ylthio)pyridin-2-yl)-4-(piperidin-4-yl)thiazol-2-amine;
tert-butyl 4-(2-(3-(phenylthio)-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-ylamino)thiazol-4-yl)piperidine-1-carboxylate;

tert-butyl 4-(5-(3-(4-fluorophenoxy)-5-(5-methylpyrazolo[1,5-a]pyrimidin-7-ylthio)pyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)piperidine-1-carboxylate;

sodium 4-(6-(4-methylthiazol-2-ylamino)-5-phenoxypyridin-3-ylthio)benzoate;

3-methyl-7-(6-(4-phenethylthiazol-2-ylamino)-5-phenoxypyridin-3-ylthio)thieno[3,2-b]pyridine-6-carboxylic acid;

3-methyl-7-(6-(4-methylthiazol-2-ylamino)-5-phenoxypyridin-3-ylthio)thieno[3,2-b]pyridine-6-carboxylic acid;

N-(5-(6,7-dihydro-5H-pyrrolo[3,4-b]pyridin-4-ylthio)-3-phenoxypyridin-2-yl)-4-methylthiazol-2-amine;

N-(4-methylthiazol-2-yl)-3-phenoxy-5-(5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-ylthio)pyridin-2-amine;

1-(4-((5-(3-(4-fluorophenoxy)-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)methyl)piperidin-1-yl)ethanone;

1-(4-(5-(3-(4-fluorophenoxy)-5-(3-methylisoxazolo [5,4-b]pyridin-4-ylthio)pyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)piperidin-1-yl)ethanone;

2-(dimethylamino)-1-(4-(5-(3-(4-fluorophenoxy)-5-(3-methylisoxazolo [5,4-b]pyridin-4-ylthio)pyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)piperidin-1-yl)ethanone;

tert-butyl 4-(5-(3-phenoxy-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)piperidine-1-carboxylate;

N-(5-((3-methoxypyridin-2-yl)methylthio)-3-phenoxypyridin-2-yl)-4-methylthiazol-2-amine;

4-methyl-N-(3-phenoxy-5-(piperidin-4-yl(pyridin-2-yl)methylthio)pyridin-2-yl)thiazol-2-amine;

4-methyl-N-(3-phenoxy-5-(piperidin-4-yl(pyrazin-2-yl)methylthio)pyridin-2-yl)thiazol-2-amine;

4-methyl-N-(3-phenoxy-5-(piperidin-4-yl(pyrimidin-2-yl)methylthio)pyridin-2-yl)thiazol-2-amine;

N-(5-((3-chloropyridin-2-yl)(piperidin-4-yl)methylthio)-3-phenoxypyridin-2-yl)-4-methylthiazol-2-amine;

N-(2-(dimethylamino)ethyl)-3-(2-(4-isobutylthiazol-2-ylamino)-5-(pyrimidin-2-ylthio)pyridin-3-yloxy)benzamide;

2-(4-((6-(4-methylthiazol-2-ylamino)-5-phenoxypyridin-3-ylthio)(pyridin-2-yl)methyl)piperidin-1-yl)ethanol;

4-methyl-N-(5-((1-methylpiperidin-4-yl)(pyridin-2-yl)methylthio)-3-phenoxypyridin-2-yl)thiazol-2-amine;

N-(5-((1-isopropyl piperidin-4-yl)(pyridine -2-yl)methylthio)-3-phenoxypyridin-2-yl)-4-methylthiazol-2-amine;

1-((6-(4-methylthiazol-2-ylamino)-5-phenoxypyridin-3-ylthio)methyl)pyrrolidin-2-one;
Ethyl 2-(1-methylpiperidin-4-yl)-2-(6-(4-methylthiazol-2-ylamino)-5-phenoxypyridin-3-ylthio)acetate;
2-(1-methylpiperidin-4-yl)-2-(6-(4-methylthiazol-2-ylamino)-5-phenoxypyridin-3-ylthio)ethanol;
N-ethyl-2-(6-(4-methylthiazol-2-ylamino)-5-phenoxypyridin-3-ylthio)-2-(piperidin-4-yl)acetamide;
2-(6-(4-methylthiazol-2-ylamino)-5-phenoxypyridin-3-ylthio)-2-(piperidin-4-yl)-1-(pyrrolidin-1-yl)ethanone;
1-(indolin-1-yl)-2-(6-(4-methylthiazol-2-ylamino)-5-phenoxypyridin-3-ylthio)-2-(piperidin-4-yl)ethanone;
1-(7-azabicyclo[2.2.1]heptan-7-yl)-2-(6-(4-methylthiazol-2-ylamino)-5-phenoxypyridin-3-ylthio)-2-(piperidin-4-yl)ethanone;
1-(2-methylpiperidin-1-yl)-2-(6-(4-methylthiazol-2-ylamino)-5-phenoxypyridin-3-ylthio)-2-(piperidine-4-yl)ethanone *mixture of diastereomers;
2-(4-((6-(4-phenethylthiazol-2-ylamino)-5-phenoxypyridin-3-ylthio)(pyridin-2-yl)methyl)piperidin-1-yl)ethanol;
4-methyl-N-(3-phenoxy-5-(1-(pyridin-2-yl)ethylthio)pyridin-2-yl)thiazol-2-amine;
N-(5-(3-(dimethylamino)-1-phenylpropylthio)-3-phenoxypyridin-2-yl)-4-methylthiazol-2-amine;
5-((5-cyclopropyl-1,3,4-thiadiazol-2-yl)methylthio)-N-(4-methylthiazol-2-yl)-3-phenoxypyridin-2-amine;
5-((1,2,4-oxadiazol-3-yl)methylthio)-N-(4-methylthiazol-2-yl)-3-phenoxypyridin-2-amine;
5-((5-methylisoxazol-3-yl)methylthio)-N-(4-methylthiazol-2-yl)-3-phenoxypyridin-2-amine;
5-((3,5-dimethylisoxazol-4-yl)methylthio)-N-(4-methylthiazol-2-yl)-3-phenoxypyridin-2-amine;
5-((5-chloro-1,2,4-thiadiazol-3-yl)methylthio)-N-(4-methylthiazol-2-yl)-3-phenoxypyridin-2-amine;
N-(5-(isoquinolin-1-ylmethylthio)-3-phenoxypyridin-2-yl)-4-methylthiazol-2-amine;
N-(4-((6-(4-methylthiazol-2-ylamino)-5-phenoxypyridin-3-ylthio)methyl)thiazol-2-yl)acetamide;
N-(5-((5-cyclopropyl-1,3,4-thiadiazol-2-yl)methylthio)-3-(phenylthio)pyridin-2-yl)-4-methylthiazol-2-amine;
4-methyl-N-(5-((5-methylisoxazol-3-yl)methylthio)-3-(phenylthio)pyridin-2-yl)thiazol-2-amine;
N-(5-((3,5-dimethylisoxazol-4-yl)methylthio)-3-(phenylthio)pyridin-2-yl)-4-methylthiazol-2-amine;
2-(6-(4-methylthiazol-2-ylamino)-5-phenoxypyridin-3-ylthio)-1-(pyrrolidin-1-yl)ethanone;
N-(2-(dimethylamino) ethyl)-N-methyl-2-(6-(4-methylthiazol-2-ylamino)-5-phenoxypyridin-3-ylthio)acetamide;

1-(4-methylpiperazin-1-yl)-2-(6-(4-methylthiazol-2-ylamino)-5-phenoxypyridin-3-ylthio)ethanone;

2-(6-(4-methylthiazol-2-ylamino)-5-phenoxypyridin-3-ylthio)-N-(2-(pyrrolidin-1-yl)ethyl)acetamide;

{5-[(1,1-dioxo-hexahydro-1λ^6-thiopyran-4-yl)-pyridin-2-yl-methylsulfanyl]-3-phenoxy-pyridin-2-yl}-(4-methyl-thiazol-2-yl)-amine;

4-methyl-N-(3-phenoxy-5-(1-(piperidin-4-yl)ethylthio)pyridin-2-yl)thiazol-2-amine;

2,2-dimethyl-3-(2-(3-phenoxy-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-ylamino)thiazol-4-yl)propanoic acid;

tert-butyl 4-(5-(3-phenoxy-5-(pyridin-2-ylthio)pyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)piperidine-1-carboxylate;

3-isobutyl-N-(3-phenoxy-5-(pyridin-2-ylthio)pyridin-2-yl)-1,2,4-thiadiazol-5-amine;

3-isopropyl-N-(3-phenoxy-5-(pyridin-2-ylthio)pyridin-2-yl)-1,2,4-thiadiazol-5-amine;

N-(3-phenoxy-5-(pyridin-2-ylthio)pyridin-2-yl)-3-(tetrahydrofuran-2-yl)-1,2,4-thiadiazol-5-amine;

N-(3-phenoxy-5-(pyridin-2-ylthio)pyridin-2-yl)-3-(piperidin-4-yl)-1,2,4-thiadiazol-5-amine;

1-(4-(5-(3-phenoxy-5-(pyridin-2-ylthio)pyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)piperidin-1-yl)ethanone;

2-methoxy-1-(4-(5-(3-phenoxy-5-(piperidi-2-ylthio)piperidi-2-ylamino)-1,2,4-thiadiazol-3-yl)piperidine-1-yl)ethanone;

2-(dimethylamino)-1-(4-(5-(3-phenoxy-5-(pyridin-2-ylthio)pyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)piperidin-1-yl)ethanone;

N,N-dimethyl-4-(5-(3-phenoxy-5-(pyridin-2-ylthio)pyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)piperidine-1-carboxamide;

N,N-dimethyl-4-(5-(3-phenoxy-5-(pyridin-2-ylthio)pyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)piperidine-1-sulfonamide;

2-methyl-1-(4-(5-(3-phenoxy-5-(pyridin-2-ylthio)pyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)piperidin-1-yl)propan-1-one;

3-(1-(methylsulfonyl)piperidin-4-yl)-N-(3-phenoxy-5-(pyridin-2-ylthio)pyridin-2-yl)-1,2,4-thiadiazol-5-amine;

2-oxo-2-(4-(5-(3-phenoxy-5-(pyridin-2-ylthio)pyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)piperidin-1-yl)ethyl acetate;

4-(5-(3-phenoxy-5-(pyridin-2-ylthio)pyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)piperidine-1-carboxamide;

2-hydroxy-1-(4-(5-(3-phenoxy-5-(pyridin-2-ylthio)pyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)piperidin-1-yl)ethanone;

tert-butyl 2-oxo-2-(4-(5-(3-phenoxy-5-(pyridin-2-ylthio)pyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)piperidin-1-yl)ethylcarbamate;

(R)-2-hydroxy-1-(4-(5-(3-phenoxy-5-(pyridin-2-ylthio)pyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)piperidin-1-yl)propan-1-one;

2-methyl-1-(4-(5-(3-phenoxy-5-(pyridin-2-ylthio)pyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)piperidin-1-yl)propan-1-one;

2-amino-1-(4-(5-(3-phenoxy-5-(pyridin-2-ylthio)pyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)piperidin-1-yl)ethanone;

2-(4-(5-(3-phenoxy-5-(pyridin-2-ylthio)pyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)piperidin-1-yl)ethanol;

4-(5-(3-Phenoxy-5-(pyridin-2-ylthio)pyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)piperidine-1-sulfonamide;

3-(1-(2-aminoethylsulfonyl)piperidin-4-yl)-N-(3-phenoxy-5-(pyridin-2-ylthio)pyridin-2-yl)-1,2,4-thiadiazol-5-amine;

tert-butyl 3-methyl-4-(2-(3-phenoxy-5-(pyridin-2-ylthio)pyridin-2-ylamino)thiazol-4-yl)piperidine-1-carboxylate;

1-(3-methyl-4-(2-(3-phenoxy-5-(pyridin-2-ylthio)pyridin-2-ylamino)thiazol-4-yl)piperidin-1-yl)ethanone;

1-(4-(2-(3-phenoxy-5-(pyridin-2-ylthio)pyridin-2-ylamino)thiazol-4-yl)piperidin-1-yl)ethanone;

Methyl 3-(5-phenoxy-6-(thiazolo[5,4-b]pyridin-2-ylamino)pyridin-3-ylthio)propanoate;

N-(3-phenoxy-5-(pyridin-4-ylthio)pyridin-2-yl)thiazolo[5,4-b]pyridin-2-amine;

4-(5-phenoxy-6-(thiazolo[5,4-b]pyridin-2-ylamino)pyridin-3-ylthio)benzonitrile;

N-(3-phenoxy-5-(pyrimidin-2-ylthio)pyridin-2-yl)thiazolo[5,4-b]pyridin-2-amine;

N-(3-phenoxy-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-yl)thiazolo[5,4-b]pyridin-2-amine;

N-(5-(pyridin-2-ylthio)-3-(4-(trifluoromethyl)phenoxy)pyridin-2-yl)-3-(tetrahydrofuran-2-yl)-1,2,4-thiadiazol-5-amine;

N-(4-(2-(5-methyloxazol-2-yl)ethyl)thiazol-2-yl)-3-phenoxy-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-amine;

4-(2-(5-methyloxazol-2-yl)ethyl)-N-(3-phenoxy-5-(piperidin-4-ylmethylthio)pyridin-2-yl)thiazol-2-amine;

2-(dimethylamino)-1-(4-(5-(3-(4-fluorophenoxy)-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)piperidin-1-yl)ethanone;

1-(4-((5-(3-(4-fluorophenoxy)-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)methyl)piperidin-1-yl)ethanone;

1-(4-(5-(3-(4-fluorophenoxy)-5-(3-methylisoxazolo[5,4-b]pyridin-4-ylthio)pyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)piperidin-1-yl)ethanone;

2-(dimethylamino)-1-(4-(5-(3-(4-fluorophenoxy)-5-(3-methylisoxazolo[5,4-b]pyridin-4-ylthio)pyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)piperidin-1-yl)ethanone;

3-(2-bromo-4-fluorophenoxy)-5-(3-methoxyphenylthio)-N-(4-(piperidin-4-yl)thiazol-2-yl)pyridin-2-amine;

4-(2-(3-(4-fluorophenoxy)-5-(3-methoxyphenylthio)pyridin-2-ylamino)thiazol-4-yl)piperidine-1-carboxylate trifluoroacetate;

1-(4-(2-(3-(4-fluoro-2-methylphenoxy)-5-(3-methoxyphenylthio)pyridin-2-ylamino)thiazol-4-yl)piperidin-1-yl)ethanone;

1-(4-(2-(3-(4-fluorophenoxy)-5-(3-methoxyphenylthio)pyridin-2-ylamino)thiazol-4-yl)piperidin-1-yl)ethanone;

1-(4-(2-(3-(2-bromo-4-fluorophenoxy)-5-(3-methoxyphenylthio)pyridin-2-ylamino)thiazol-4-yl)piperidin-1-yl)ethanone;

1-(4-(2-(3-(2-bromo-4-fluorophenoxy)-5-(3-methoxyphenylthio)pyridin-2-ylamino)thiazol-4-yl)piperidin-1-yl)-2-(dimethylamino)ethanone;

1-(4-(2-(5-(thieno[3,2-b]pyridin-7-ylthio)-3-(4-(trifluoromethyl)phenoxy)pyridin-2-ylamino)thiazol-4-yl)piperidin-1-yl)ethanone;

1-(4-(2-(5-(thieno[3,2-b]pyridin-7-ylthio)-3-(2-(trifluoromethyl)phenoxy)pyridin-2-ylamino)thiazol-4-yl)piperidin-1-yl)ethanone;

1-(4-(2-(5-(2-methylthieno[3,2-b]pyridin-7-ylthio)-3-phenoxypyridin-2-ylamino)thiazol-4-yl)piperidin-1-yl)ethanone;

1-(4-(2-(5-(4-methoxypyrimidin-2-ylthio)-3-phenoxypyridin-2-ylamino)thiazol-4-yl)piperidin-1-yl)ethanone;

4-(6-(4-(1-acetylpiperidin-4-yl)thiazol-2-ylamino)-5-phenoxypyridin-3-ylthio)benzonitrile;

4-(6-(4-(1-acetylpiperidin-4-yl)thiazol-2-ylamino)-5-phenoxypyridin-3-ylthio)-3-(trifluoromethyl)benzonitrile;

4-(6-(4-(1-acetylpiperidin-4-yl)thiazol-2-ylamino)-5-phenoxypyridin-3-ylthio)-2-(trifluoromethyl)benzonitrile;

6-(6-(4-(1-acetylpiperidin-4-yl)thiazol-2-ylamino)-5-phenoxypyridin-3-ylthio)nicotinonitrile;

5-(6-(4-(1-acetylpiperidin-4-yl)thiazol-2-ylamino)-5-phenoxypyridin-3-ylthio)-3-methoxypicolinonitrile;

Ethyl 6-(6-(4-(1-acetylpiperidin-4-yl)thiazol-2-ylamino)-5-phenoxypyridin-3-ylthio)picolinate;

1-(4-(2-(3-phenoxy-5-(6-(trifluoromethyl)pyridin-3-ylthio)pyridin-2-ylamino)thiazol-4-yl)piperidin-1-yl)ethanone;

1-(4-(2-(5-(6-bromothieno[3,2-b]pyridin-7-ylthio)-3-phenoxypyridin-2-ylamino)thiazol-4-yl)piperidin-1-yl)ethanone;

1-(4-(5-(5-(thieno[3,2-b]pyridin-7-ylthio)-3-(2-(trifluoromethyl)phenoxy)pyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)piperidin-1-yl)ethanone;

tert-butyl 4-(2-(3-(4-fluorophenoxy)-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-ylamino)thiazol-4-yl)piperidine-1-carboxylate;

N-(3-(4-fluorophenoxy)-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-yl)-4-(piperidin-4-yl)thiazol-2-amine;

1-(4-(2-(3-(4-fluorophenoxy)-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-ylamino)thiazol-4-yl)piperidin-1-yl)ethanone;

2-(4-(2-(3-(4-fluorophenoxy)-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-ylamino)thiazol-4-yl)piperidin-1-yl)-2-oxoethyl acetate;

Isopropyl 4-(2-(3-(4-fluorophenoxy)-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-ylamino)thiazol-4-yl)piperidine-1-carboxylate;

2-(dimethylamino)-1-(4-(2-(3-(4-fluorophenoxy)-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-ylamino)thiazol-4-yl)piperidin-1-yl)ethanone;

N-(3-(4-fluorophenoxy)-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-yl)-4-(1-(methylsulfonyl)piperidin-4-yl)thiazol-2-amine;

N-(1-(4-(2-(3-(4-fluorophenoxy)-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-ylamino)thiazol-4-yl)piperidin-1-yl)-1-oxopropan-2-yl)acetamide;

N-(2-(4-(2-(3-(4-fluorophenoxy)-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-ylamino)thiazol-4-yl)piperidin-1-yl)-2-oxoethyl)acetamide;

4-(1-(2-aminoethylsulfonyl)piperidin-4-yl)-N-(3-(4-fluorophenoxy)-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-yl)thiazol-2-amine;

4-(2-(3-(4-fluorophenoxy)-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-ylamino)thiazol-4-yl)piperidine-1-sulfonamide 2,2,2-trifluoroacetate;

4-(2-(3-(4-fluorophenoxy)-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-ylamino)thiazol-4-yl)piperidine-1-carboxamide;

tert-butyl 4-(2-(3-(4-fluorophenoxy)-5-(3-methylisoxazolo[5,4-b]pyridin-4-ylthio)pyridin-2-ylamino)thiazol-4-yl)piperidine-1-carboxylate;

N-(3-(4-fluorophenoxy)-5-(3-methylisoxazolo[5,4-b]pyridin-4-ylthio)pyridin-2-yl)-4-(piperidin-4-yl)thiazol-2-amine;

1-(4-(2-(3-(4-fluorophenoxy)-5-(3-methylisoxazolo[5,4-b]pyridin-4-ylthio)pyridin-2-ylamino)thiazol-4-yl)piperidin-1-yl)ethanone;

2-(dimethylamino)-1-(4-(2-(3-(4-fluorophenoxy)-5-(3-methylisoxazolo[5,4-b]pyridin-4-ylthio)pyridin-2-ylamino)thiazol-4-yl)piperidin-1-yl)ethanone;

Methyl 4-(5-(3-phenoxy-5-(pyridin-2-ylthio)pyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)piperidine-1-carboxylate;

1-(4-(2-(5-(3-methylthieno[3,2-b]pyridin-7-ylthio)-3-phenoxypyridin-2-ylamino)thiazol-4-yl)piperidin-1-yl)ethanone;

1-(4-(2-(5-(5-chlorothieno[3,2-b]pyridin-7-ylthio)-3-phenoxypyridin-2-ylamino)thiazol-4-yl)piperidin-1-yl)ethanone;

1-(4-(2-(3-phenoxy-5-(thieno[2,3-d]pyrimidin-4-ylthio)pyridin-2-ylamino)thiazol-4-yl)piperidin-1-yl)ethanone;

tert-butyl 4-((2-(5-(3-methoxy-3-oxopropylthio)-3-phenoxypyridin-2-ylamino)thiazol-4-yl)methyl)piperidine-1-carboxylate;

tert-butyl 4-(2-(3-(4-cyanophenoxy)-5-(3-methoxy-3-oxopropylthio)pyridin-2-ylamino)thiazol-4-yl)piperidine-1-carboxylate;

tert-butyl 3-(5-(5-(3-methoxy-3-oxopropylthio)-3-phenoxypyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)pyrrolidine-1-carboxylate;

tert-butyl 3-(2-(5-(3-methoxy-3-oxopropylthio)-3-phenoxypyridin-2-ylamino)thiazol-4-yl)piperidine-1-carboxylate;

tert-butyl 3-(2-(5-(3-methoxy-3-oxopropylthio)-3-phenoxypyridin-2-ylamino)thiazol-4-yl)pyrrolidine-1-carboxylate;

tert-butyl 4-((2-(3-phenoxy-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-ylamino)thiazol-4-yl)methyl)piperidine-1-carboxylate;

tert-butyl 4-((2-(5-(4-cyanophenylthio)-3-phenoxypyridin-2-ylamino)thiazol-4-yl)methyl)piperidine-1-carboxylate;

tert-butyl 3-((2-(3-phenoxy-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-ylamino)thiazol-4-yl)methyl)piperidine-1-carboxylate;

tert-butyl 3-(5-(3-phenoxy-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)pyrrolidine-1-carboxylate;

tert-butyl 3-(2-(3-phenoxy-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-ylamino)thiazol-4-yl)pyrrolidine-1-carboxylate;

tert-butyl 3-(2-(5-(4-cyanophenylthio)-3-phenoxypyridin-2-ylamino)thiazol-4-yl)piperidine-1-carboxylate;

tert-butyl 3-(5-(5-(4-cyanophenylthio)-3-phenoxypyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)pyrrolidine-1-carboxylate;

N-(3-phenoxy-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-yl)-4-(piperidin-4-ylmethyl)thiazol-2-amine;

N-(3-phenoxy-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-yl)-4-(piperidin-3-yl)thiazol-2-amine;

N-(3-phenoxy-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-yl)-3-(pyrrolidin-3-yl)-1,2,4-thiadiazol-5-amine;

N-(3-phenoxy-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-yl)-4-(pyrrolidin-3-yl)thiazol-2-amine;

4-(5-phenoxy-6-(4-(piperidin-4-ylmethyl)thiazol-2-ylamino)pyridin-3-ylthio)benzonitrile;

4-(5-phenoxy-6-(3-(pyrrolidin-3-yl)-1,2,4-thiadiazol-5-ylamino)pyridin-3-ylthio)benzonitrile;

4-(5-phenoxy-6-(3-(piperidin-3-yl)-1,2,4-thiadiazol-5-ylamino)pyridin-3-ylthio)benzonitrile;

1-(4-((2-(3-phenoxy-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-ylamino)thiazol-4-yl)methyl)piperidin-1-yl)ethanone;

1-(3-(2-(3-phenoxy-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-ylamino)thiazol-4-yl)piperidin-1-yl)ethanone;

1-(3-(5-(3-phenoxy-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-ylamino)-1,2,4-thiadiazol-3-yl)pyrrolidin-1-yl)ethanone;

1-(3-(2-(3-phenoxy-5-(thieno[3,2-b]pyridin-7-ylthio)pyridin-2-ylamino)thiazol-4-yl)pyrrolidin-1-yl)ethanone;

4-(6-(4-(1-acetylpiperidin-3-yl)thiazol-2-ylamino)-5-phenoxypyridin-3-ylthio)benzonitrile;

4-(6-(3-(1-acetylpyrrolidin-3-yl)-1,2,4-thiadiazol-5-ylamino)-5-phenoxypyridin-3-ylthio)benzonitrile;

4-(6-(4-((1-acetylpiperidin-4-yl)methyl)thiazol-2-ylamino)-5-phenoxypyridin-3-ylthio)benzonitrile; and

1-(4-(2-(5-(2-chloropyridin-4-ylthio)-3-phenoxypyridin-2-ylamino)thiazol-4-yl)piperidin-1-yl)ethanone;

or a pharmaceutically acceptable salt thereof.

[0024] Additional advantages and novel features of this ~~invention~~disclosure shall be set forth in part in the description that follows, and in part will become apparent to those skilled in the art upon examination of the following specification or may be learned by the practice of the ~~invention~~disclosure. The advantages of the invention may be realized and attained by means of the instrumentalities, combinations, compositions, and methods particularly pointed out in the appended claims.

DETAILED DESCRIPTION OF THE INVENTION

[0025] Reference will now be made in detail to certain embodiments of the invention, examples of which are illustrated in the accompanying structures and formulas. While the invention will be described in conjunction with the enumerated embodiments, it will be understood that they