FUSED NITROGEN HETEROCYCLIC COMPOUNDS, PROCESS OF PREPARATION AND USES THEREOF

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Abstract: Fused nitrogen heterocyclic compounds, their stereoisomers, tautomers, prodrugs, pharmaceutically acceptable salts, polymorphs, solvates and formulations thereof, useful as Glucokinase activators or modulators, which are beneficial for the prophylaxis, management, treatment, control of progression, or adjunct treatment of diseases and/or medical conditions where the activation of glucokinase would be beneficial, such as diabetes, metabolic syndrome, and/or diabetes-related complications including retinopathy, nephropathy, neuropathy, ischemic heart disease, arteriosclerosis, β-cell dysfunction, and as therapeutic and/or prophylactic agents for obesity are disclosed. The invention also relates to process of preparation of the fused nitrogen heterocyclic compounds.
FUSED NITROGEN HETEROCYCLIC COMPOUNDS, PROCESS OF PREPARATION AND USES THEREOF

Field of the invention

This disclosure relates to a series of fused nitrogen heterocyclic compounds, their stereoisomers, tautomers, prodrugs, pharmaceutically acceptable salts, polymorphs, solvates and formulations thereof. The disclosure also relates to process of preparation of the fused nitrogen heterocyclic compounds. The compounds of the present disclosure are identified as Glucokinase activators or modulators, which are beneficial for the prophylaxis, management, treatment, control of progression, or adjunct treatment of diseases and/or medical conditions where the activation of glucokinase would be beneficial, such as diabetes, metabolic syndrome, and/or diabetes-related complications including retinopathy, nephropathy, neuropathy, ischemic heart disease, arteriosclerosis, β-cell dysfunction, and as therapeutic and/or prophylactic agents for obesity.

Background of the invention

Diabetes mellitus is a metabolic disorder characterized by recurrent or persistent hyperglycemia (high blood glucose) and other signs, as distinct from a single disease or condition. Glucose level abnormalities can result in serious long-term complications, which include beta-cell dysfunction, glucotoxicity, cardiovascular disease, chronic renal failure, retinal damage, nerve damage (of several kinds), microvascular damage, macrovascular damage, adipocyte inflammation, vascular inflammation and obesity.

Type 1 diabetes, also known as Insulin Dependent Diabetes Mellitus (IDDM), is characterized by loss of the insulin-producing β-cells of the islets of Langerhans of the pancreas leading to a deficiency of insulin. Type-2 diabetes previously known as adult-onset diabetes, maturity-onset diabetes, or Non-Insulin Dependent Diabetes Mellitus (NIDDM) - is due to a combination of increased hepatic glucose output, defective insulin secretion, and insulin resistance or reduced insulin sensitivity (defective responsiveness of tissues to insulin).

Glucokinase (GK), also known as hexokinase IV or D, is one of four glucose-phosphorylating enzymes called hexokinases that catalyze the first step of glycolysis, the conversion of glucose to glucose 6-phosphate (G6P), in vertebrate tissues. GK functions in a dual role, with distinct functions in the pancreas and liver; (a) as a molecular glucose sensor in the insulin-producing pancreatic β-cells, and (b) as the high-capacity enzymatic step initiating the storage of glucose in the form of glycogen in the liver and uptake of glucose during hyperglycemia. Therefore,

The physiological concentration of glucose in human plasma is approximately 5.5 mM under fasting conditions, and increases to about 12 mM in the fed state. This concentration is dependent on and maintained by the activity of GK, which senses glucose and controls metabolic flux in key cell types. The glucose concentration, at which GK activity is at half of its maximal velocity or $V_{\text{max}}$, is defined as its $S_{0.5}$. The $S_{0.5}$ of GK for glucose lies in the middle of the physiological glucose concentration range at approximately 8 mM, allowing this enzyme to act as a molecular glucose sensor crucial for glucose homeostasis. The limited tissue distribution and unique kinetic properties of GK allow it to play a critical role in pancreatic β-cell insulin secretion and hepatic glucose utilization. GK differs from the other members of the mammalian hexokinase family in its unique sigmoidal kinetics with respect to glucose, a high $S_{0.5}$ that lies in the physiological glucose concentration range (the other three mammalian hexokinases have $S_{0.5}$ values less than 0.5 mM), the lack of product inhibition by G6P, and its tissue distribution in cell types that are thought to be responsive to changing plasma glucose levels.

Given the role of GK as a molecular glucose sensor, it is not surprising that GK mutations have a profound influence on glucose homeostasis. About 2000 GK mutations that have been identified in humans result in impaired glucose-mediated insulin secretion and maturity-onset diabetes of the young type 2 (MODY-2). Some of these mutations result in decreased accumulation of hepatic glycogen, while others decrease GK activity by reducing the stability of the enzyme or by decreasing its $V_{\text{max}}$. Mutations that result in activation of GK are implicated in the onset of persistent hyperinsulinemic hypoglycemia of infancy (PHHI). Single point mutations (e.g. V62M, D158A, Y2I4A, V455M, and F456V) in regions distinct from the substrate binding site of the enzyme lead to modulation of GK activity (Glaser, B. et al (1998) N. Engl. J. Med. 338: 226-230; Gloyn, A. L. (2003) Hum. Mutat. 22: 353-362; Gloyn, A. L. et al (2003) Diabetes 52: 2433-2440). These observations highlight that GK activity can be regulated through allosteric modulation.

Several patent applications and publications describe the discovery of small-molecule glucokinase activators (GKAs) that allosterically modulate or activate the activity of GK (Kamata, K. et al (2004) Structure 12: 429-438; WO 2003/055482 A1; WO 2005/123132 A2; WO
The present disclosure provides a novel class of fused nitrogen heterocyclic compounds characterized as glucokinase activators or modulators, and their potential use as medicament for the prophylactic or therapeutic treatment of hyperglycemia, diabetes, obesity, dyslipidemia, metabolic syndrome and like.

Summary of the invention

The present disclosure relates to compounds of formula (I), their stereoisomers, tautomers, prodrugs, pharmaceutically acceptable salts, polymorphs, solvates and formulations thereof:

![Formula (I)](image)

wherein

ring A and ring B are independently selected from cycloalkyl, aryl, heterocyclyl or heteroaryl;

ring A and ring B is unsubstiuted or substituted with up to 4 substituents independently selected from alkyl, alkenyl, alkynyl, halogen, mono, di, tri or perhaloalkyl, nitrile, nitro, oxo, -NR^4R^5, -OR^4, -S(0)NR^4R^5, -SR^4S(0), -NR^4C(0)R^5, -OS(0)R^5, -NR^4C(0)OR^5, -SR^4C(0)OR^5, -NR^4C(0)OR^5, -(CR^4R^7)gC(0)OR^4, -(CR^4R^7)gC(0)NR^4R^5, -(CR^4R^7)gC(0)R^4, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl or heteroarylalkyl;

wherein n = 0-4 and p = 0-2;

ring C is a heterocyclyl or a heteroaryl each with at least one N-atom;

X is selected from (CHR^2), NR^2, O, or S(0) wherein n = 1-2 and p = 0-2;

Y is CR or N; wherein R is selected from hydrogen, halogen, alkyl, fluoroalkyl, OR^5 or aryl;
R is selected from hydrogen, alkyl, halogen, haloalkyl or perhaloalkyl;
R₂ is selected from hydrogen or alkyl; or
R¹ and R² taken together form a monocyclic or a bicyclic ring system which is saturated or
partially unsaturated and optionally have additional heteroatoms selected from O, N or S;
R³ and R⁴ are independently selected from the group consisting of hydrogen, halogen, alkyl,
alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocycloalkyl, aryl,
arylalkyl, heteroaryl, heteroarylalkyl, mono, di, tri or perhaloalkyl, nitrile, nitro, -NR₅²⁻,
-R⁻⁵⁻, -OR, -S(0)ₖR₅⁺, -S(0)ₖNR₅⁻R⁺, -NR₅⁺S(0)ₖR⁺, -NR₅⁺C(0)R⁺, -OS(0)ₖR⁺, -
NR₅⁺C(0)OR⁺, -(CR²⁺)ₖC(0)OR⁺, -(CR²⁺)ₖC(0)SₖR⁺, -(CR²⁺)ₖSₖR⁺, -
(CR²⁺)ₖN(0)ₖR⁺C(0)R⁺, -(CR²⁺)ₖN(0)ₖR⁺C(0)ₖR⁺, C(R²⁺)ₖNR₅⁺R⁺ and C(R²⁺)ₖCO(R⁻⁵⁻);
wherein each of R³ and R⁴ is unsubstituted or substituted with one or more substituents selected
from halo, alkyl, alkenyl, alkynyl, cycoalkyl, aryl, heteroaryl, heterocycle, alkylsulphonyl, oxo, nitro, cyano,
-COOR⁺, -C(0)NR₅⁺R⁺, -OR⁺, -SR⁻ or -NR⁻₅⁻R⁺;
wherein n = 0-4 and p = 0-2; or
R³ and R⁴ taken together form a monocyclic or a bicyclic ring system which is saturated or
partially unsaturated and optionally have additional heteroatoms selected from O, N or S;
the said ring system may be unsubstituted or substituted with 1 to 4 substituents independently
selected from halo, alkyl, alkenyl, alkynyl, nito, cyano, -OR⁺, -SR⁻, -NR⁻₅⁻R⁺,
oxo, alkylsulfonyl, -COOR⁺, -C(0)NR₅⁺R⁺, cycoalkyl, cycloalkylalkyl, aryl, arylalkyl,
heterocyclyl, heterocyclylalkyl, heteroaryl or heteroarylalkyl;
R⁵ and R⁶ are independently selected from the group consisting of hydrogen, alkyl,
alkenyl, alkynyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloalkyl, cycloalkylalkyl,
heterocyclyl and heterocyclylalkyl; or
R⁵ and R⁶ taken together form a mononcyclic or a bicyclic ring system which is
saturated or partially unsaturated and optionally have additional heteroatoms
selected from O, N or S; said ring system may be unsubstituted or substituted with 1
to 4 substituents independently selected from halo, alkyl, alkenyl, alkynyl, nito,
cyano, -OR⁺, -SR⁻, -NR⁻₅⁻R⁺, oxo, alkylsulfonyl, -COOR⁺, -C(0)NR₅⁺R⁺, cycoalkyl,
cycloalkylalkyl, aryl, arylalky, heterocyclyl, heterocyclylalkyl, heteroaryl or
heteroarylalkyl;
R⁷ and R⁸ are independently selected from the group consisting of hydrogen,
fluorine, OR⁺, alkyl, and perfluoroalkyl; or
R\textsuperscript{7} and R\textsuperscript{8} taken together form a monocyclic or a bicyclic ring system which is saturated or partially unsaturated and optionally have additional heteroatoms selected from O, N or S; said ring system is unsubstituted or substituted with 1 to 4 substituents independently selected from halo, alkyl, alkenyl, alkynyl, nitro, cyano, oxo, -OR\textsuperscript{5}, -SR\textsuperscript{5}, -NR\textsuperscript{6}R\textsuperscript{6}, alkylsulfonyl, -COOR\textsuperscript{5}, -C(0)NR\textsuperscript{6}R\textsuperscript{6}, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl or heteroarylalkyl.

The present invention also relates to process of preparation of compounds of formula (I). The compounds of the present invention are useful as glucokinase activators (GKAs), or modulators, and can be used as medicament for prophylactic or therapeutic treatment of hyperglycemia, diabetes, obesity, dyslipidemia, metabolic syndrome and like.

These and other features, aspects, and advantages of the present subject matter will become better understood with reference to the following description. This Summary is provided to introduce a selection of concepts in a simplified form. This Summary is not intended to identify key features or essential features of the claimed subject matter, nor is it intended to be used to limit the scope of the invention.

**Detailed description of the invention**

**Definitions**

In the structural formulae given herein and throughout the present disclosure, the following terms have the indicated meaning, unless specifically stated otherwise.

The term "optionally substituted" as used herein means that the group in question is either unsubstituted or substituted with one or more of the substituents specified. When the group in question is substituted with more than one substituent, the substituent may be same or different.

The term "alkyl" refers to a monoradical branched or unbranched saturated hydrocarbon chain having 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 carbon atoms, preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 carbon atoms, more preferably 1, 2, 3, 4, 5 or 6 carbon atoms. This term is exemplified by groups such as methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, t-butyl, n-hexyl, n-decyl, tetradecyl, and the like.

The term "alkylene" refers to a diradical of a branched or unbranched saturated hydrocarbon chain, having 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 carbon atoms, preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 carbon atoms, more preferably 1, 2, 3, 4, 5 or 6 carbon atoms. This term is exemplified by groups such as methylene (-CH\textsubscript{2}CH\textsubscript{2}), ethylene (-CH\textsubscript{2}CH\textsubscript{2}), the propylene isomers (e.g., -CH\textsubscript{2}CH\textsubscript{2}CH\textsubscript{2} and -CH(CH\textsubscript{3})CH\textsubscript{2}) and the like.
The term "substituted alkyl" or "substituted alkenyl" refers to: 1) an alkyl group or alkenyl group as defined above, having 1, 2, 3, 4 or 5 substituents, preferably 1, 2 or 3 substituents, selected from the group consisting of aikenyl, alkynyl, alkoxy, cycloalkyl, cycloalkenyl, acyl, acylamino, acyloxy, amino, monoalkylamino, dialkylamino, arylamino, heteroarylamino, aminocarbonyl, alkoxy carbonyl amino, azido, cyano, halogen, hydroxy, hydroxyalkyl, keto, thiocarbonyl, carboxy, carboxyalkyl, -SO₂H, aryl, arylxy, heteroaryl, aminocarboxylamino, heteroarylxy, heterocyclic, heterocyclyloxy, hydroxymino, alkoxyamino, nitro, -S(0)₂NR₃⁺R₄⁺, -NR₃S(0)₂R₄⁺ and -S(0)₂R₅⁺, where each R is independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heteroaryl heteroarylalkyl, heterocyclyl and heterocyclylalkyl; heterocyclyloxy where R is hydrogen, alkyl, aryl, heteroaryl or heterocyclyl. Unless otherwise constrained by the definition, all substituents may optionally be further substituted by 1, 2, or 3 substituents selected from alkyl, carboxy, carboxyalkyl, aminocarbonyl, hydroxy, alkoxy, halogen, CF₃, amino, substituted amino, cyano, and -S(0)₂PR₅⁺, where R is alkyl, aryl, or heteroaryl and p is 0, 1 or 2; or, 2) an alkyl group or alkenyl group as defined above that is interrupted by 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 atoms independently selected from oxygen, sulfur and NRd⁺, where Rd is selected from hydrogen, alkyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl and heterocyclic, carbonylalkyl, carboxyester, carboxyamide and sulfonyl. All substituents may be optionally further substituted by alkyl, alkoxy, halogen, CF₃, amino, substituted amino, cyano, or -S(0)₂PR₅⁺, in which R is alkyl, aryl, or heteroaryl and p is 0, 1, or 2; or, 3) an alkyl or alkenyl as defined above that has 1, 2, 3, 4 or 5 substituents as defined above, as well as interrupted by 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 atoms as defined above.

The term "aikenyl" refers to a monoradical of a branched or unbranched unsaturated hydrocarbon group preferably having from 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 carbon atoms, more preferably 2, 3, 4, 5, 6, 7, 8, 9 or 10 carbon atoms and even more preferably 2, 3, 4, 5 or 6 carbon atoms and having 1, 2, 3, 4, 5 or 6 double bond (vinyl), preferably 1 double bond. Preferred aikenyl groups include ethenyl or vinyl(-CH=CH₂), 1-propylene or allyl (-CH₂CH=CH₂), isopropylene (-C(CH₃)=CH₂), bicyclo [2. 2. 1] heptene, and the like.

The term "alkenylene" refers to a diradical of a branched or unbranched unsaturated hydrocarbon group preferably having from 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 carbon atoms, more preferably 2, 3, 4, 5, 6, 7, 8, 9 or 10 carbon atoms and even more preferably 2, 3, 4, 5 or 6 carbon atoms and having 1, 3, 4, 5 or 6 double bond (vinyl), preferably 1 double bond.
The term "substituted alkenyl" refers to an alkenyl group as defined above having 1, 2, 3, 4 or 5 substituents, and preferably 1, 2, or 3 substituents, selected from the group consisting of alkyl, alkenyl, alkylnyl, alkoxy, cycloalkyl, cycloalkenyl, acyl, acylamino, acyloxy, amino, aminocarboxy, alkoxy carbonylamino, azido, cyano, halogen, thiocarboxy, carboxy, carboxyalkyl, S0, H, aryl, arylxy, heteroaryl, aminocarboxy lamino, heteroaryloxy, heterocyclyl, heterocyclyoxy, hydroxyamino, alkoxyamino, nitro, -S(0)NR*R, -NR*S(0)R and -S(0)Rb where each R is independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, cycloalkylalkyl, aryl, aryalkyl, heteroaryl heteroarylalkyl, heterocyclyl and heterocyclylalkyl; heterocyclyloxy where R is alkyl, aryl, heteroaryl or heterocyclyl and p is 0, 1 or 2. Unless otherwise constrained by the definition, all substituents may optionally be further substituted by 1, 2, or 3 substituents selected from alkyl, carboxy, carboxyalkyl, aminocarboxy, hydroxy, alkoxy, halogen, CF3, amino, substituted amino, cyano, and -S(0)R where R is alkyl, aryl, or heteroaryl and p is 0, 1 or 2.

The term "alkynyl" refers to a monoradical of an unsaturated hydrocarbon, preferably having from 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 carbon atoms, more preferably 2, 3, 4, 5, 6, 7, 8, 9 or 10 carbon atoms and even more preferably 2, 3, 4, 5 or 6 carbon atoms and having 1, 2, 3, 4, 5 or 6 sites of acetylene (triple bond) unsaturation, preferably 1 triple bond. Preferred alkynyl groups include ethynyl, (-C≡CH), propargyl (or prop-1-yn-3-yl), homopropargyl (or but-1-yn-4-yl, -CH2CH2C≡CH) and the like.

The term "alkynylene" refers to a diradical of a branched or unbranched unsaturated hydrocarbon group preferably having from 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 carbon atoms, more preferably 2, 3, 4, 5, 6, 7, 8, 9 or 10 carbon atoms and even more preferably 2, 3, 4, 5 or 6 carbon atoms and having 1, 3, 4, 5 or 6 sites of acetylene (triple bond) unsaturation, preferably 1 triple bond.

The term "substituted alkynyl" refers to an alkynyl group as defined above having 1, 2, 3, 4 or 5 substituents, and preferably 1, 2, or 3 substituents, selected from the group consisting of alkyl, alkenyl, alkylnyl, alkoxy, cycloalkyl, cycloalkenyl, acyl, acylamino, acyloxy, amino, aminocarboxy, alkoxy carbonylamino, azido, cyano, halogen, hydroxy, keto, thiocarboxy, carboxy, carboxyalkyl, -S0,H, aryl, arlyxy, heteroaryl, aminocarboxy lamino, heteroaryloxy, heterocyclyl, heterocyclyoxy, hydroxyamino, alkoxyamino, nitro, -S(0),NR*R, -NR*S(0)R and -S(0)Rb, where each R is independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, cycloalkylalkyl, aryl, aryalkyl, heteroaryl heteroarylalkyl, heterocyclyl and heterocyclylalkyl; heterocyclyloxy where R is alkyl, aryl, heteroaryl or heterocyclyl and p is 0, 1 or 2. Unless otherwise constrained by the definition, all substituents may optionally be further substituted by 1, 2, or 3 substituents selected.
from alky], carboxy, carboxyalkyl, aminocarbonyl, hydroxy, alkoxy, halogen, CF₃, amino, substituted amino, cyano, and-S(O)ₚR² where R² is alkyl, aryl, or heteroaryl and p is 0, 1 or 2.

The term "cycloalkyi" refers to unless otherwise mentioned, carbocyclic groups of from 3 to 20 carbon atoms having a single cyclic ring, multiple condensed rings or spirocyclic rings which may be saturated or partially unsaturated. Such cycloalkyi groups include, by way of example, single ring structures such as cyclopropyl, cyclobutyl, cyclopentyl, cyclopentenyl, cyclohexyl, cyclohexenyl, cyclooctyl, and the like, or multiple ring structures such as adamantyl, bicyclo[2.2.1]heptane, bicyclo[2.2.2]octane, 1,3,3-trimethylbicyclo[2.2.1]hept-2-yl, (2,3,3-trimethyl)bicyclo[2.2.1]hept-2-yl, spiro[4.5]decan, spiro[4.4]nonane or cycloalkyi groups to which is fused an aryl group, for example indane, and the like.

The term "substituted cycloalkyi" refers to cycloalkyi groups having 1, 2, 3, 4 or 5 substituents, and preferably 1, 2, or 3 substituents, selected from the group consisting of alkyl, alkoxy, cycloalkyi, cycloalkenyl, acyl, acylamino, acyloxy, amino, aminocarbonyl, alkoxy carbonylamino, azido, cyano, halogen, hydroxy, oxo, thiocarbonyl, aryl, arloxy, heteroaryl, aminosulfonyl, aminocarbonylamino, heteroaryloxy, heterocyclyl, heterocyclyloxy, hydroxyamino, alkoxyamino, nitro, -C(0)R and -S(0)ₚR², where R is hydrogen, hydroxyl, alkoxy, alkyl and cycloalkyi, heterocyclyloxywhere R² is alkyl, aryl, heteroaryl or heterocyclyl and p is 0, 1 or 2. Unless otherwise constrained by the definition, all substituents may optionally be further substituted by 1, 2, or 3 substituents selected from alkyl, alkoxy, carboxyalkyl, aminocarbonyl, hydroxy, alkoxy, halogen, CF₃, amino, substituted amino, cyano, and-S(O)ₚR², where R² is alkyl, aryl, or heteroaryl and p is 0, 1 or 2.

"Halo" or "Halogen", alone or in combination with any other term means halogens such as chloro (Cl), fluoro (F), bromo (Br) and iodo (I).

"Haloalkyl" refers to a straight chain or branched chain haloalkyl group with 1 to 6 carbon atoms. The alkyl group may be partly or totally halogenated. Representative examples of haloalkyl groups include but are not limited to fluoromethyl, chloromethyl, bromomethyl, difluoromethyl, dichloromethyl, dibromomethyl, trifluoromethyl, trichloromethyl, 2-fluoroethyl, 2-chloroethyl, 2-bromoethyl, 2,2,2-trifluoroethyl, 3-fluoropropyl, 3-chloropropyl, 3-bromopropyl and the like.

The term "alkoxy" refers to the group R""0-, where R"" is optionally substituted alkyl or optionally substituted cycloalkyi, or optionally substituted alkenyl or optionally substituted alkynyl; or optionally substituted cycloalkenyl, where alkyl, alkenyl, alkynyl, cycloalkyi and cycloalkenyl are as defined herein. Representative examples of alkoxy groups include but are not limited to methoxy, ethoxy, n-propoxy, iso-propoxy, n-butoxy, tert-butoxy, sec-butoxy, n-pentoxy, n-hexoxy, 1,2-dimethylbutoxy, trifluoromethoxy, and the like.
The term "aminocarbonyl" refers to the group -C(0)NR' R' where each R' is independently hydrogen, alkyl, aryl, heteroaryl, heterocyclyl or both R' groups are joined to form a heterocyclic group (e.g. morpholino). Unless otherwise constrained by the definition, all substituents may optionally be further substituted by 1-3 substituents selected from alkyl, carboxy, carboxyalkyl, aminocarbonyl, hydroxy, alkoxy, halogen, CF₃, amino, substituted amino, cyano, and -S(0)ₚR⁶, where R⁶ is alkyl, aryl, or heteroaryl and p is 0, 1 or 2.

The term "acylamino" refers to the group -NR'C(0)R" where each R" is independently hydrogen, alkyl, aryl, heteroaryl, or heterocyclyl. Unless otherwise constrained by the definition, all substituents may optionally be further substituted by 1-3 substituents selected from alkyl, carboxy, carboxyalkyl, aminocarbonyl, hydroxy, alkoxy, halogen, CF₃, amino, substituted amino, cyano, and -S(0)ₚR⁶, where R⁶ is alkyl, aryl, or heteroaryl and p is 0, 1 or 2.

The term "acyloxy" refers to the groups -OC(0)-alkyl, -OC(0)-cycloalkyl, -OC(0)-aryl, -OC(0)-heteroaryl, and -OC(0)-heterocyclyl. Unless otherwise constrained by the definition, all substituents may be optionally further substituted by alkyl, carboxy, carboxyalkyl, aminocarbonyl, hydroxy, alkoxy, halogen, CF₃, amino, substituted amino, cyano, or -S(0)ₚR⁶, where R⁶ is alkyl, aryl, or heteroaryl and p is 0, 1 or 2.

"Alkoxyalkyl" refers to alkyl groups as defined above wherein at least one of the hydrogen atoms of the alkyl group is replaced by an alkoxy group as defined above. Representative examples of alkoxyalkyl groups include but are not limited to methoxymethyl, methoxyethyl, ethoxymethyl and the like.

"Aryloxyalkyl" refers to the group -alkyl-O-aryl. Representative examples of aryloxyalkyl include but are not limited to phenoxymethyl, naphthoxyethyl, phenoxyethyl, naphthoxyethy1 and the like.

"Di alkylamino" refers to an amino group, to which two same or different straight chain or branched chain alkyl groups with 1 to 6 carbon atoms are bound. Representative examples of di alkylamino include but are not limited to dimethylamino, diethylamino, methylethylamino, dipropylamino, dibutylamino and the like.

"Cycloalkylalkyl" refers to an alkyl radical as defined above which is substituted by a cycloalkyl radical as defined above. Representative examples of cycloalkylalkyl include but are not limited to cyclopropylmethyl, cyclobutylmethyl, cyclopentylmethyl, cyclohexylmethyl, 1-cyclopetylethyl, 1-cyclohexylethyl, 2-cyclopentylethyl, 2-cyclohexylethyl, cyclobutylpropyl, cyclopentylpropyl, cyclohexylbutyl and the like.
"Aminoalkyl" refers to an amino group that is attached to \((\text{C}_{1-4})\text{alkylene}\) as defined herein. Representative examples of aminoalkyl include but are not limited to aminomethyl, aminooethyl, 1-aminopropyl, 2-aminopropyl, and the like. The amino moiety of aminoalkyl may be substituted once or twice with alkyl to provide alkylaminooalkyl and dialkylaminooalkyl respectively. Representative examples of alkylaminooalkyl include but are not limited to methylaminomethyl, methylaminooethyl, methylaminopropyl, ethylaminooethyl and the like. Representative examples of dialkylaminooalkyl include but are not limited to dimethylaminomethyl, dimethylaminooethyl, dimethylaminopropyl, \(N\)-methyl-N-ethylaminooethyl and the like.

The term "aryl" refers to an aromatic carbocyclic group of 6 to 20 carbon atoms having a single ring (e.g. phenyl) or multiple rings (e.g. biphenyl), or multiple condensed (fused) rings (e.g. naphthyl or anthranyl). Preferred aryls include phenyl, naphthyl and the like.

The term "arylene" refers to a diradical of an aryl group as defined above. This term is exemplified by groups such as 1,4-phenylene, 1,3-phenylene, 1,2-phenylene, 1,4'-biphenylene, and the like.

Unless otherwise constrained the aryl or arylene groups may optionally be substituted with 1, 2, 3, 4 or 5 substituents, preferably 1, 2 or 3 substituents, selected from the group consisting of alkyl, alkoxy, cycloalkyl, cycloalkenyl, acyl, acylamino, acyloxy, amino, aminocarbonyl, alkoxy carbonylamino, azido, cyano, halogen, hydroxy, carboxy, carboxyalkyl, \(-\text{SO}_n\)H, aryl, arloxy, heteroaryl, aminosulfonyl, aminocarbonylamino, heteroaryloxy, heterocyclyl, heterocyclyoxy, hydroxamino, alkoxyamino, nitro, \(-\text{S}(0)\) \(_2\)NR*R*, \(-\text{NR}^*\text{S(0)}\) \(_2\)R* and \(-\text{S(0)}\)R\(^b\) where each \(R^*\) is independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, cycloalkylkyl, aryl, aralkyl, heteroaryl, heteroaryalkyl, heterocyclyl and heterocyclyalkyl; where \(R^b\) is hydrogen, alkyl, aryl, heterocyclyl or heteroaryl and \(p\) is 0, 1 or 2. Unless otherwise constrained by the definition, all substituents may optionally be further substituted by 1, 2 or 3 substituents selected from alkyl, carboxy, carboxyalkyl, aminocarbonyl, hydroxy, alkoxy, halogen, CF\(_3\), amino, substituted amino, cyano, and \(-\text{S(0)}\) \(_p\)R\(^c\) where \(R^c\) is hydrogen, alkyl, aryl or heteroaryl and \(p\) is 0, 1 or 2.

The term "aryalkyl" refers to an aryl group covalently linked to an alkyene group, where aryl and alkyene are defined herein.

"Optionally substituted aryalkyl" refers to an optionally substituted aryl group covalently linked to an optionally substituted alkyene group. Such aryalkyl groups are exemplified by benzyl, phenethyl, naphthylmethyl, and the like.

The term "aryloxy" refers to the group aryl-O- wherein the aryl group is as defined above, and includes optionally substituted aryl groups as also defined above.
The term "arylthio" refers to the group -S-aryl, where aryl is as defined herein including optionally substituted aryl groups as also defined above.

The term "substituted amino" refers to the group -NR'R where each R' is independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, carboxyalkyl, alkoxy carbonyl, aryl, heteroaryl and heterocyclyl. Unless otherwise constrained by the definition, all substituents may optionally be further substituted by 1, 2 or 3 substituents selected from alkyl, carboxy, carboxyalkyl, aminocarbonyl, hydroxy, alkoxy, halogen, CF₃, amino, substituted amino, cyano, and -S(0)ₖRₜ, where Rₜ is alkyl, aryl, or heteroaryl and p is 0, 1 or 2.

The term "carboxyalkyl" refers to the groups -alkylene-C(0)OH.

The term "alkylcarboxyalkyl" refers to the groups -alkylene-C(0)OR where Rₖ is alkyl, cycloalkyl, where alkyl, cycloalkyl are as defined herein, and may be optionally further substituted by alkyl, halogen, CF₃, amino, substituted amino, cyano, or -S(0)ₖRₜ in which Rₜ is alkyl, aryl, or heteroaryl and p is 0, 1 or 2.

The term "heteroaryl" refers to an aromatic cyclic group having 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 carbon atoms and 1, 2, 3 or 4 heteroatoms selected from oxygen, nitrogen and sulfur within at least one ring. Such heteroaryl groups can have a single ring (e.g. pyridyl or furyl) or multiple condensed rings (e.g. indolizyl, benzothiazolyl, or benzothienyl). Examples of heteroaryl include, but are not limited to, [1,2,4] oxadiazone, [1,3,4] oxadiazone, [1,2,4] thiadiazone, [1,3,4] thiadiazone, pyrrole, imidazole, pyrazole, pyridine, pyrazine, pyrimidine, pyridazine, indolizine, isoindole, indole, indazole, purine, quinolizine, isoquinoline, quinoline, phthalazine, quinoxaline, quinazoline, cinnoline, pteridine, carbazole, carboline, phenanthridine, acridine, phenanthroline, isothiazole, phenazine, isoaxazole, phenoaxine, phenothiazine, fural, thiophene, oxazole, thiazole, triazole, and the like.

The term "heteroarylene" refers to a diradical of a heteroaryl group as defined above. Unless otherwise constrained the heteroaryl or heterarylene groups can be optionally substituted with 1, 2, 3, 4 or 5 substituents, preferably 1, 2 or 3 substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, cycloalkenyl, acyl, acylamino, acyloxy, amino, aminocarboxyl, alkoxy carbamylaminio, azido, cyano, halogen, hydroxy, thiocarbonyl, carboxy, carboxyalkyl, -SO₃H, aryl, aryloxy, heteroaryl, aminocarboxylamino, heteroaryloxy, heterocyclyl, heterocyclyl, hydroxyamino, alkoxyamino, nitro, -S(0)₂NR'Rₜ, -NR'S(0)₂Rₜ and -S(0)ₖRₜ, where each Rₜ is independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, cycloalkylalkyl, aryl, aryalkyl, heteroaryl heteroarylalkyl, heterocyclyl and heterocyclylalkyl; where Rₜ is hydrogen, alkyl, aryl, heterocyclyl or heteroaryl, and p is 0, 1 or 2. Unless otherwise constrained by the
definition, all substituents may optionally be further substituted by 1-3 substituents selected from alkyl, carboxy, carboxyalkyl, aminocarbonyl, hydroxy, alkoxy, halogen, CF3, amino, substituted amino, cyano, and -S(0)nR\textsuperscript{e}, where R\textsuperscript{e} is alkyl, aryl, or heteroaryl and n is 0, 1 or 2.

The term "heteroaryllalkyl" refers to a heteroaryl group covalently linked to an alkylene group, where heteroaryl and alkylene are defined herein.

"Optionally substituted heteroaryllalkyl" refers to an optionally substituted heteroaryl group covalently linked to an optionally substituted alkylene group. Such heteroaryllalkyl groups are exemplified by 3-pyridylmethyl, quinolin-8-ylethyl, 4-methoxythiazol-2-ylpropyl, and the like.

The term "heterocyclyl" refers to a saturated or partially unsaturated group having a single ring, multiple condensed rings or spirocyclic rings, unless otherwise mentioned, having from 1 to 40 carbon atoms and from 1 to 10 hetero atoms, preferably 1, 2, 3 or 4 heteroatoms, selected from nitrogen, sulfur, phosphorus, and/or oxygen within the ring. Heterocyclic groups can have a single ring or multiple condensed rings, and include tetrahydrofuranyl, morpholinyl, piperidinyl, piperazinyl, dihydropyridinyl, tetrahydroquinolinyl, 7-oxa-spiro[4.5]decane, 7-aza-spiro[4.5]decane and the like. Unless otherwise constrained by the definition for the heterocyclic substituent, such heterocyclic groups can be optionally substituted with 1, 2, 3, 4 or 5, and preferably 1, 2 or 3 substituents, selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, cycloalkenyl, acyl, acylamino, acyloxy, amino, aminocarbonyl, alkoxy carbonylamino, azido, cyano, halogen, hydroxy, oxo, -C(0)R where R is hydrogen, hydroxyl, alkoxy, alkyl and cycloalkyl, thiocarbonyl, carboxy, carboxyalkyl, aryl, aryloxy, heteroaryl, aminosulfonyl, aminocarbonylamino, heteroaryloxy, heterocyclyl, heterocyclyloxy, hydroxyamino, alkoxyamino, nitro, and -S(0)pR\textsuperscript{b}, where R\textsuperscript{b} is hydrogen, alkyl, aryl, heterocyclyl or heteroaryl and p is 0, 1 or 2. Unless otherwise constrained by the definition, all substituents may optionally be further substituted by 1-3 substituents selected from alkyl, carboxy, carboxyalkyl, aminocarbonyl, hydroxy, alkoxy, halogen, CF3, amino, substituted amino, cyano, and -S(0)R\textsuperscript{c}, where R\textsuperscript{c} is alkyl, aryl, or heteroaryl and n is 0, 1 or 2.

The term "heterocyclylalkyl" refers to a heterocyclyl group covalently linked to an alkylene group, where heterocyclyl and alkylene are defined herein.

"Optionally substituted heterocyclylalkyl" refers to an optionally substituted heterocyclyl group covalently linked to an optionally substituted alkylene group.

The term "heteroaryloxy" refers to the group heteroaryl-O-.

The term "thiol" refers to the group -SH.

The term "substituted alkylthio" refers to the group -S-substituted alkyl.
The term "heteroarylthio" refers to the group -S-heteroaryl wherein the heteroaryl group is as defined above including optionally substituted heteroaryl groups as also defined above. The term "sulfoxide" refers to a group -S(O).

"Substituted sulfoxide" refers to a group -S(0)R, in which R is substituted alkyl, substituted aryl, or substituted heteroaryl, as defined herein.

The term "sulfone" refers to a group -S(O)₂R.

The term "substituted sulfone" refers to a group -S(0)₂R, in which R is alkyl, aryl, or heteroaryl.

The compounds of the present invention may have the ability to crystallize in more than one form, a characteristic known as polymorphism, and all such polymorphic forms ("polymorphs") are encompassed within the scope of the invention. Polymorphism generally can occur as a response to changes in temperature or pressure or both, and can also result from variations in the crystallization process. Polymorphs can be distinguished by various physical characteristics, and typically the x-ray diffraction patterns, solubility behavior, and melting point of the compound are used to distinguish polymorphs.

The compounds described herein may contain one or more chiral centers and/or double bonds and therefore, may exist as stereoisomers, such as double-bond isomers (i.e., geometric isomers), regioisomers, enantiomers or diastereomers. Accordingly, the chemical structures depicted herein encompass all possible enantiomers and stereoisomers of the illustrated or identified compounds including the stereoisomerically pure form (e.g., geometrically pure, enantiomerically pure or diastereomerically pure) and enantiomeric and stereoisomeric mixtures. Enantiomeric and stereoisomeric mixtures can be resolved into their component enantiomers or stereoisomers using separation techniques or chiral synthesis techniques well known to the person skilled in the art. The compounds may also exist in several tautomeric forms including the enol form, the keto form and mixtures thereof. Accordingly, the chemical structures depicted herein encompass all possible tautomeric forms of the illustrated or identified compounds.

Compounds may exist in unsolvated forms as well as solvated forms, including hydrated forms and as N-oxides. In general, compounds may be hydrated, solvated or N-oxides. Certain compounds may exist in multiple crystalline or amorphous forms. Also contemplated within the scope of the invention are congeners, analogs, hydrolysis products, metabolites and precursor or prodrugs of the compound. In general, unless otherwise indicated, all physical forms are equivalent for the uses contemplated herein and are intended to be within the scope of the present invention.

"Prodrug" refers to a derivative of a drug molecule as, for example, esters, carbonates, carbamates, ureas, amides or phosphates that requires a transformation within the body to release the active drug.
Prodrugs are frequently, although not necessarily, pharmacologically inactive until converted to the parent drug. Prodrugs may be obtained by bonding a promoiety (defined herein) typically via a functional group, to a drug.

"Promoiety" refers to a group bonded to a drug, typically to a functional group of the drug, via bond(s) that are cleavable under specified conditions of use. The bond(s) between the drug and promoiety may be cleaved by enzymatic or non-enzymatic means. Under the conditions of use, for example following administration to a patient, the bond(s) between the drug and promoiety may be cleaved to release the parent drug. The cleavage of the promoiety may proceed spontaneously, such as via a hydrolysis reaction, or it may be catalyzed or induced by another agent, such as by an enzyme, by light, by acid, or by a change of or exposure to a physical or environmental parameter, such as a change of temperature, pH, etc. The agent may be endogenous to the conditions of use, such as an enzyme present in the systemic circulation to which the prodrug is administered or the acidic conditions of the stomach or the agent may be supplied exogenously.

"Pharmacetically acceptable salt" embraces salts with a pharmaceutically acceptable acid or base. Pharmaceutically acceptable acids include both inorganic acids, for example hydrochloric, sulphuric, phosphoric, diphosphoric, hydrobromic, hydroiodic and nitric acid and organic acids, for example citric, fumaric, maleic, malic, mandelic, ascorbic, oxalic, succinic, tartaric, benzoic, acetic, methanesulphonic, ethanesulphonic, benzenesulphonic or p-toluencesulphonic acid. Pharmaceutically acceptable bases include alkali metal (e.g. sodium or potassium) and alkali earth metal (e.g. calcium or magnesium) hydroxides and organic bases, for example alkyl amines, aylalkyl amines and heterocyclic amines.

Other preferred salts according to the invention are quaternary ammonium compounds wherein an equivalent of an anion (X-) is associated with the positive charge of the N atom. X- may be an anion of various mineral acids such as, for example, chloride, bromide, iodide, sulphate, nitrate, phosphate, or an anion of an organic acid such as, for example, acetate, maleate, fumarate, citrate, oxalate, succinate, tartrate, malate, mandelate, trifluoroacetate, methanesulphonate and p-toluencesulphonate. X- is preferably an anion selected from chloride, bromide, iodide, sulphate, nitrate, acetate, maleate, oxalate, succinate or trifluoroacetate. More preferably X- is chloride, bromide, trifluoroacetate or methanesulphonate.

The present disclosure relates to compounds of formula (I), their stereoisomers, tautomers, prodrugs, pharmaceutically acceptable salts, polymorphs, solvates and formulations thereof,
wherein, ring A and ring B are independently selected from cycloalkyl, aryl, heterocyclyl or heteroaryl;

ring A and ring B is unsubstiuted or substituted with up to 4 substituents independently selected from alkyl, alkenyl, alkynyl, halogen, mono, di, tri or perhaloalkyl, nitrile, nitro, oxo, -NR\textsubscript{5}R\textsubscript{6}, -OR\textsubscript{5}, -S(0)\textsubscript{p}R\textsubscript{5}, -S(0)\textsubscript{p}NR\textsubscript{5}R\textsubscript{6}, -NR\textsubscript{5}S(0)\textsubscript{p}R\textsubscript{5}, -NR\textsubscript{5}C(0)R\textsubscript{5}, -OS(0)\textsubscript{p}R\textsubscript{5}, -NR\textsubscript{5}C(0)OR\textsubscript{5}, -NR\textsubscript{5}C(0)NR\textsubscript{5}R\textsubscript{6}, -NR\textsubscript{5}C(0)NR\textsubscript{5}R\textsubscript{6}, -NR\textsubscript{5}C(0)OR\textsubscript{5}, -CR\textsubscript{7}R\textsubscript{8},C(0)OR\textsubscript{5}, -CR\textsubscript{7}R\textsubscript{8},C(0)NR\textsubscript{5}R\textsubscript{6}, -CR\textsubscript{7}R\textsubscript{8},S(0)\textsubscript{p}NR\textsubscript{5}R\textsubscript{6}, -(CR\textsubscript{7}R\textsubscript{8}),N(0)R\textsubscript{5}C(0)R\textsubscript{5}, -(CR\textsubscript{7}R\textsubscript{8})\textsubscript{3}OR\textsubscript{5}, C(R\textsubscript{7}R\textsubscript{8})\textsubscript{3}NR\textsubscript{5}R\textsubscript{6} and C(R\textsubscript{7}R\textsubscript{8})\textsubscript{3}CO(R\textsubscript{5}); wherein each of R\textsubscript{3} and R\textsubscript{4} is unsubstituted or substituted with one or more substituents selected from halo, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, heterocycle, alkysulphonyl, oxo, nitro, cyano, -COOR\textsubscript{5}, -C(0)NR\textsubscript{5}R\textsubscript{6}, -OR\textsubscript{5}, -SR\textsubscript{5} or -NR\textsubscript{5}R\textsubscript{6}; wherein n = 0-4 and p = 0-2; or
R³ and R⁴ taken together form a monocyclic or a bicyclic ring system which is saturated or partially unsaturated and optionally have additional heteroatoms selected from O, N or S; said ring system is unsubstituted or substituted with 1 to 4 substituents independently selected from halo, alkyl, alkenyl, alkynyl, nito, cyano, -OR⁵, -SR⁵, -NR³R⁶, oxo, alkylsulfonyl, -COOR⁵, -C(0)NR⁵R⁶, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroaryalkyl;

R⁵ and R⁶ are independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl, heteroaryalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl and heterocyclylalkyl, or

R⁵ and R⁶ taken together form a monocyclic or a bicyclic ring system which is saturated or partially unsaturated and optionally have additional heteroatoms selected from O, N or S; said ring system is unsubstituted or substituted with 1 to 4 substituents independently selected from halo, alkyl, alkenyl, alkynyl, nito, cyano, -OR⁵, -SR⁵, -NR³R⁶, oxo, alkylsulfonyl, -COOR⁵, -C(0)NR³R⁶, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl or heteroaryalkyl;

R⁷ and R⁸ are independently selected from the group consisting of hydrogen, fluorine, OR⁵, alkyl, and perfluoroalkyl; or

R⁷ and R⁸ taken together form a monocyclic or a bicyclic ring system which is saturated or partially unsaturated and optionally have additional heteroatoms selected from O, N or S; said ring system is unsubstituted or substituted with 1 to 4 substituents independently selected from halo, alkyl, alkenyl, alkynyl, nitro, cyano, oxo, -OR⁵, -SR⁵, -NR³R⁶, alkylsulfonyl, -COOR⁵, -C(0)NR³R⁶, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl heteroaryl or heteroaryalkyl.

According to an embodiment, the present disclosure relates to compounds of formula (1) wherein:

ring A and ring B are independently selected from cycloalkyl, aryl, heterocyclyl or heteroaryl;

ring A and ring B are unsubstituted or substituted with up to 4 substituents independently selected from alkyl, alkenyl, alkynyl, halogen, mono, di, tri or perhaloalkyl, nitrile, nitro, oxo, -NR⁴R⁵, -OR⁴, -S(0)⁵R⁴, -S(0)⁵RN⁴R⁵, -NR⁴S(0)⁵R⁵, -NR⁴C(0)⁵R⁵, -OS(0)⁵R⁵, -NR⁴C(0)⁵OR⁵, -CR⁴R⁵CN(0)⁵OR⁴, -CR⁴R⁵CN(0)⁵NR⁴R⁵,
(CR\textsuperscript{6}R\textsuperscript{7})\textsubscript{m}C(0)R \textsuperscript{4}, cycloalkyi, cycloalkylalkyl, heterocyclyi, heterocycloalkyl, aryl, arylalkyl, heteroaryl or heteroaryalkyl; wherein \( n = 0-4 \) and \( p = 0-2 \);

ring C is a heterocyclyi or a heteroaryl each with at least one N-atom;

X is selected from \((\text{CHR} \textsuperscript{2})\textsubscript{N}, \text{N}R \textsuperscript{2}, \text{O} \text{ or } \text{S}(0) \text{R} \textsuperscript{2}\), wherein \( n = 1-2 \) and \( p = 0-2 \);

Y is \text{CR} or \text{N}; wherein \( R \) is selected from hydrogen, halogen, alkyl or fluoroalkyl;

R\textsuperscript{1} is selected from hydrogen, alkyl, halogen, haloalkyl or perhaloalkyl;

R\textsuperscript{2} is selected from hydrogen or alkyl; or

R\textsuperscript{1} and R\textsuperscript{2} taken together form a monocyclic or a bicyclic ring system which is saturated or partially unsaturated and optionally have additional heteroatoms selected from O, N or S;

R\textsuperscript{3} and R\textsuperscript{4} are independently selected from the group consisting of hydrogen, halogen, alkyl, alkenyl, alkynyl, cycloalkyi, cycloalkylalkyl, heterocyclyi, heterocycloalkyl, aryl, aryalkyl, heteroaryl, heteroaryalkyl, mono, di, tri or perhaloalkyl, nitrile, nitro, \text{-NR \textsuperscript{5}}, \text{-NR \textsuperscript{5}R \textsuperscript{6}}, \text{-OR \textsuperscript{5}}, S(0) \text{R} \textsuperscript{5}, \text{-NR \textsuperscript{3}S(0) \text{R} \textsuperscript{6}}, \text{-NR \textsuperscript{5}C(0)R \textsuperscript{6}}, \text{-OS(0) \text{R} \textsuperscript{6}}, \text{-NR \textsuperscript{5}C(0)OR \textsuperscript{6}}, \text{-CR \textsuperscript{2}R \textsuperscript{4} \text{C(0)OR \textsuperscript{5}}}, \text{-CR \textsuperscript{2}R \textsuperscript{4} \text{(CO)NR \textsuperscript{5}R \textsuperscript{6}}}, \text{-CR \textsuperscript{2}R \textsuperscript{4} \text{S(0) \text{R} \textsuperscript{6}}}, \text{-CR \textsuperscript{2}R \textsuperscript{4} \text{N(R \textsuperscript{3}C(0)R \textsuperscript{5}}}, \text{-CR \textsuperscript{2}R \textsuperscript{4} \text{N(R \textsuperscript{3}S(0) \text{R} \textsuperscript{6}}), \text{C(R \textsuperscript{2}R \textsuperscript{4}S(0) \text{R} \textsuperscript{6})}, \text{C(R \textsuperscript{2}R \textsuperscript{4}S(0) \text{R} \textsuperscript{6})}, \text{C(R \textsuperscript{2}R \textsuperscript{4}S(0) \text{R} \textsuperscript{6})}, \text{OR \textsuperscript{5}}, \text{OR \textsuperscript{5}}, \text{OR \textsuperscript{5}}, \text{SR \textsuperscript{5}} \text{or } \text{-NR \textsuperscript{3}R \textsuperscript{6}}; wherein each of \( R \text{\textsuperscript{3}} \) and \( R \text{\textsuperscript{4}} \) is unsubstituted or substituted with one or more substituents selected from halo, alkyl, alkenyl, alkynyl, cycloalkyi, aryl, heteroaryl, heterocycle, alkylsulphonyl, oxo, nitro, cyano, \text{-COOR \textsuperscript{5}}, \text{-C(0)NR \textsuperscript{5}R \textsuperscript{6}}, \text{-OR \textsuperscript{5}}, \text{-SR \textsuperscript{5}} \text{or } \text{-NR \textsuperscript{3}R \textsuperscript{6}}; wherein \( n = 0-4 \) and \( p = 0-2 \);

R\textsuperscript{5} and R\textsuperscript{6} are independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, aryl, aryalkyl, heteroaryl, heteroaryalkyl, cycloalkyi, cycloalkylalkyl, heterocyclyl and heterocycloalkyl;

R\textsuperscript{7} and R\textsuperscript{8} are independently selected from the group consisting of hydrogen, fluorine, \text{OR \textsuperscript{5}}, alkyl, and perfluoroalkyl.

According to another embodiment of the present invention, it provides compounds of formula (I) wherein:

ring A and ring B are independently selected from cycloalkyi, aryl, heterocyclyl or heteroaryl;

ring A and ring B are unsubstituted or substituted with up to 4 substituents independently selected from alkyl, halogen, mono, di, tri or perhaloalkyl, nitrile, \text{-NR \textsuperscript{4}R \textsuperscript{5}}, \text{-CR \textsuperscript{6}R \textsuperscript{7} \text{OR \textsuperscript{4}}}, \text{-CR \textsuperscript{6} \text{(CO)NR \textsuperscript{5}R \textsuperscript{6}}}, \text{-CR \textsuperscript{6} \text{C(0)OR \textsuperscript{4}}}, \text{-CR \textsuperscript{6} \text{C(0)NR \textsuperscript{5}R \textsuperscript{6}}}, \text{-CR \textsuperscript{6} \text{C(0)R \textsuperscript{4}}}, \text{-CR \textsuperscript{6} \text{C(0)R \textsuperscript{4}}}, \text{-cycoalkyi, heterocyclyl, aryl or heteroaryl; wherein } n = 0-4 \text{ and } p = 0-2 \text{;
Ring C is a heterocyclyl or a heteroaryl each with at least one N-atom; 
X is selected from (CHR)$^2$$_n$, NR$_2$, O or S(0)$_p$ wherein $n$ = 1-2 and $p$ = 0-2; 
Y is CR; wherein R is selected from hydrogen, halogen, alkyl or fluoroalkyl; 
R$^1$ is selected from hydrogen, alkyl, halogen, haloalkyl or perhaloalkyl; 
R$^2$ is selected from hydrogen or alkyl; or 
R$^1$ and R$^2$ taken together form a monocyclic or a bicyclic ring system which is saturated or partially unsaturated and optionally have additional heteroatoms selected from O, N or S; 
R$^3$ and R$^4$ are independently selected from the group consisting of hydrogen, halogen, alkyl, cycloalkyi, heterocyclyl, aryl, heteroaryl, mono, di, tri or perhaloalkyl, nitrile, -S(0)$_p$NR$^5$, -S(0)$_p$NR$^3$R$^5$, -S(0)$_p$NR$^3$S(0)$_p$NR$^3$R$^5$, -S(0)$_p$NR$^3$S(0)$_p$NR$^3$R$^5$, -S(0)$_p$NR$^3$S(0)$_p$NR$^3$R$^5$, -C(R$^7$R$^8$)$_n$OR$^5$, -C(R$^7$R$^8$)$_n$NR$^3$R$^6$ and C(R$^7$R$^8$)$_n$CO(R$^5$). wherein each of R$^3$ and R$^4$ is unsubstiuted or substituted with one or more substituents selected from halo, alkyl, cycloalkyi, aryl, heteroaryl, heterocycle, alkylsulphonyl, oxo, nitro, cyano, -COOR$^5$, -C(0)NR$^5$ -OR$^5$, -SR$^5$ or -NR$^3$R$^6$; wherein $n$ = 0-4 and $p$ = 0-2; 
R$^3$ and R$^6$ are independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyi and heterocyclyi; 
R$^5$ and R$^8$ are independently selected from the group consisting of hydrogen, fluorine, OR$^5$, alkyl, and perfluoroalkyl.

According to yet another embodiment of the present invention, it provides compounds of formula (1) wherein:

ring A and ring B are independently selected from cycloalkyi, aryl, heterocyclyl or heteroaryl; 
ring A and ring B are unsubstituted or substituted with up to 4 substituents independently selected from alkyl, halogen, mono, di, tri or perhaloalkyl, nitrile, -NR$^4$R$^5$, - (CR$^4$R$^7$)$_n$OR$^4$, -S(0)$_p$NR$^4$R$^5$, -(CR$^4$R$^7$)$_n$C(0)OR$^4$, -(CR$^4$R$^7$)$_n$C(0)NR$^4$R$^5$, -(CR$^4$R$^7$)$_n$C(0)R$^4$, cycloalkyi, heterocyclyi, aryl or heteroaryl; wherein $n$ = 0-4 and $p$ = 0-2; 
ring C is a heterocyclyl or a heteroaryl each with at least one N-atom; 
X is selected from (CHR)$^2$$_n$, NR$_2$, O or S(0)$_p$ wherein $n$ = 1-2 and $p$ = 0-2; 
Y is N; 
R$'$ is selected from hydrogen, alkyl, halogen, haloalkyl or perhaloalkyl; 
R$^2$ is selected from hydrogen or alkyl; or
R$^1$ and R$^2$ taken together form a monocyclic or a bicyclic ring system which is saturated or partially unsaturated and optionally have additional heteroatoms selected from O, N or S; R$^3$ and R$^4$ are independently selected from the group consisting of hydrogen, halogen, alkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, mono, di, tri or perhaloalkyl, nitrile, -S(0)$_p$R$^5$, -S(0)$_p$NR$^6$, -(CR$^8$)$_n$C(0)OR$^5$, -(CR$^8$)$_n$NR$^6$, -(CR$^8$)$_n$OR$^5$, C(R$^8$)$_n$NR$^6$ and C(R$^8$)$_n$CO(R$^5$), wherein each of R$^3$ and R$^4$ is unsubstituted or substituted with one or more substituents selected from halo, alkyl, cycloalkyl, aryl, heteroaryl, heterocycle, alkylsulphonyl, oxo, nitro, cyano, -COOR$^5$, -C(0)NR$^5$-OR$^5$, -SR$^5$ or -NR$^5$R$^6$; wherein n = 0-4 and p = 0-2; R$^5$ and R$^6$ are independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl and heterocyclyl; R$^7$ and R$^8$ are independently selected from the group consisting of hydrogen, fluorine, OR$^5$, alkyl, and perfluoroalkyl.

Particular embodiments of the present invention are the compounds of formula (1) which is

2-[2-Cyclopentyloxy-(4-cyclopropanesulfonyl-phenyl)-methyl]-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers;
2-[2-Cyclohexyl-(4-cyclopropanesulfonyl-phenyl)-ethyl]-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers;
2-[2-Cyclohexyl-(4-methanesulfonyl-phenyl)-ethyl]-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers;
2-[2-Cyclohexyl-(4-Cyclopentanesulfonyl-phenyl)-ethyl]-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers;
2-[2-Cyclohexyl-(4-Cyclopropanesulfonyl-phenyl)-(tetrahydro-pyran-4-yl)-ethyl]-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers;
2-[2-Cyclohexyl-(4-Methanesulfonyl-phenyl)-ethyl]-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers;
2-[2-Cyclohexyl-(4-Cyclopentanesulfonyl-phenyl)-ethyl]-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers.
6-[2-Cyclohexyl-1-(4-cyclopropanesulfonfyl-phenyl)-ethyl]-5H-pyrrolo[2,3-b]pyrazine and its (+) and (-) enantiomers;
6-[1-(4-Methanesulfonfyl-phenyl)]-2-(tetrahydro-pyran-4-yl)-ethyl]-5H-pyrrolo[2,3-b]pyrazine and its (+) and (-) enantiomers;
6-[4-(Cyclopropanesulfonfyl-phenyl)-(tetrahydro-pyran-4-yloxy)-methyl]-5H-pyrrolo[2,3-b]pyrazine and its (+) and (-) enantiomers;
2-[1-(4-Methanesulfonfyl-phenyl)]-2-(tetrahydro-pyran-4-yl)-ethyl]-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers;
6-Chloro-2-[2-cyclopentyl-1-(4-methanesulfonfyl-phenyl)]-ethyl]-1 H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers;
2-[(4-Cyclopropanesulfonfyl-phenyl)-[(R)-(tetrahydro-furan-3-yloxy)-methyl]-1 H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers;
2-[(2,4-Difluoro-phenoxy)-(4-methanesulfonfyl-phenyl)-methyl]-1 H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers;
2-[(4-Chloro-phenoxy)-(4-methanesulfonfyl-phenyl)-methyl]-1 H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers;
2-[(2,4-Difluoro-phenoxy)-(4-methanesulfonfyl-phenyl)-methyl]-1 H-pyrrolu[2,3-b]pyridine and its (+) and (-) enantiomers;
2-[1-(4-Cyclopropanesulfonfyl-phenyl)]-2-(2,4-difluoro-phenyl)-ethyl]-1 H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers;
2-[1-(4-Cyclopropanesulfonfyl-phenyl)]-2-(3-fluoro-phenyl)-ethyl]-1 H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers;
2-[1-(4-Cyclopropanesulfonfyl-phenyl)]-2-thiophen-3-yl-ethyl]-1 H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers;
2-[1-(4-Cyclopropanesulfonfyl-phenyl)]-2-pyridin-3-yl-ethyl]-1 H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers;
2-[1-(4-Cyclopropanesulfonfyl-phenyl)]-2-pyridin-4-yl-ethyl]-1 H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers;
6-Cyclopentyloxy-(4-cyclopropanesulfonfyl-phenyl)-methyl]-5H-pyrrolo[2,3-b]pyrazine and its (+) and (-) enantiomers;
2-[2-Cyclohexyl-1-(4-cyclopropanesulfonfyl-phenyl)-ethyl]-6-methoxy-1 H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers;
2-[2-Cyclohexyl-1-(4-methanesulfonyl-phenyl)-ethyl]-1H-pyrrolo[2,3-b]pyridine-5-carboxylic acid and its (+) and (-) enantiomers;
6-Chloro-2-[1-(4-cyclopentanesulfonyl-phenyl)-2-cyclopentyl-ethyl]-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers;
5-Chloro-2-[1-(4-cyclopropanesulfonyl-phenyl)-2-(tetrahydro-pyran-4-yl)-ethyl]-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers;
6-[2-Cyclohexyl-1-(4-cyclopentanesulfonyl-phenyl)-ethyl]-7H-pyrrolo[2,3-d]pyrimidine and its (+) and (-) enantiomers;
6-[1-(4-Cyclopropanesulfonyl-phenyl)-(tetrahydro-pyran-4-yloxy)-methyl]-7H-pyrrolo[2,3-c]pyridazine and its (+) and (-) enantiomers;
3-Chloro-6-[2-cyclohexyl-1-(4-cyclopropanesulfonyl-phenyl)-ethyl]-5H-pyrrolo[2,3-b]pyrazine and its (+) and (-) enantiomers;
6-[1-(4-Methanesulfonyl-phenyl)-2-(tetrahydro-pyran-4-yl)-ethyl]-3-methoxy-5H-pyrrolo[2,3-b]pyrazine and its (+) and (-) enantiomers;
2-[Cyclopentyloxy-(4-cyclopropanesulfonyl-phenyl)-methyl]-1H-imidazo[4,5-b]pyrazine and its (+) and (-) enantiomers;
{2-[2-Cyclohexyl-1-(4-cyclopentanesulfonyl-phenyl)-ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yloxy]-acetic acid and its (+) and (-) enantiomers;
2-{2-Cyclohexyl-1-[4-(pyrrolidine-1-sulfonyl)-phenyl]-ethyl}-1H-pyrrolo[2,3-b]pyridine-5-carboxylic acid and its (+) and (-) enantiomers;
5-Chloro-2-[1-(4-cyclopentanesulfonyl-phenyl)-2-cyclopentyl-ethyl]-3H-imidazo[4,5-b]pyridine and its (+) and (-) enantiomers;
4-Chloro-2-[1-(4-cyclopropanesulfonyl-phenyl)-2-(tetrahydro-pyran-4-yl)-ethyl]-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers;
{6-[2-Cyclohexyl-1-(4-cyclopentanesulfonyl-phenyl)-ethyl]-7H-pyrrolo[2,3-d]pyrimidin-2-yloxy]-acetic acid and its (+) and (-) enantiomers;
6-[1-(4-Cyclopentanesulfonyl-phenyl)-(tetrahydro-pyran-4-yloxy)-methyl]-7H-pyrrolo[2,3-c]pyridazine and its (+) and (-) enantiomers;
3-Chloro-6-{[4-cyclopropanesulfonyl-phenyl]-2,4-difluoro-phenoxy]-methyl}-5H-pyrrolo[2,3-b]pyrazine and its (+) and (-) enantiomers;
6-{[4-Chloro-phenoxy]-(4-methanesulfonyl-phenyl)-methyl]-3-methoxy-5H-pyrrolo[2,3-b]pyrazine and its (+) and (-) enantiomers;
6-{Cyclopentyloxy-\[4-(piperidine-1-sulfonyl)-phenyl\]-methyl}-5H-pyrrolo[2,3-b]pyrazine and its (+) and (-) enantiomers;
4-{2-[2-Cyclohexyl-1-(4-cycloproanesulfonyl-phenyl)-ethyl]-1H-pyrrolo[2,3-b]pyridin-5-yloxy}benzoic acid and its (+) and (-) enantiomers;
2-[Cyclohexyloxy-(4-methanesulfonyl-phenyl)-methyl]-1H-pyrrolo[2,3-b]pyridine-5-carboxylic acid and its (+) and (-) enantiomers;
2-[(4-Chloro-phenyl)-cyclohexyloxy-methyl]-1H-pyrrolo[2,3-b]pyridine-5-carboxylic acid and its (+) and (-) enantiomers;
6-Chloro-2-[1-(4-cyclopentanesulfonyl-phenyl)-2-(4-methoxy-phenyl)-ethyl]-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers;
2-[(4-Cyclopropanesulfonyl-phenyl)-2-(tetrahydro-pyran-4-yl)-ethyl]-3H-imidazo[4,5-b]pyridine and its (+) and (-) enantiomers;
6-\{4-(Azetidine-1-sulfonyl)-phenyl\}-2-cyclohexyl-ethyl\}-7H-pyrrolo[2,3-d]pyrimidine and its (+) and (-) enantiomers;
4-Chloro-6-[4-(cyclopropanesulfonyl-phenyl)-p-tolyloxy-methyl]-7H-pyrrolo[2,3-c]pyridazine and its (+) and (-) enantiomers;
Azetidin-1-yl-{5-\[(3-chloro-5H-pyrrolo[2,3-b]pyrazin-6-yl)-(4-cycloproanesulfonyl-phenyl) methoxy\]-pyrazin-2-yl\}-methanone and its (+) and (-) enantiomers;
3-Isopropoxy-6-[1-(4-methanesulfonyl-phenyl)-2-(tetrahydro-pyran-4-yl)-ethyl]-5H-pyrrolo[2,3-b]pyrazine and its (+) and (-) enantiomers;
2-[(4-Cyclopropanesulfonyl-phenyl)-(tetrahydro-furan-3-yloxy)-methyl]-1H-imidazo[4,5-b]pyrazine and its (+) and (-) enantiomers;
2-[(4-Cyclopropanesulfonyl-phenyl)-(pyridin-3-yloxy)-methyl]-1H-pyrrolo[2,3-b]pyridine-5-carboxylic acid and its (+) and (-) enantiomers;
6-Chloro-2-{2-cyclopentyl-1-(4-tetrahydro-furan-3-sulfonyl)-phenyl}-ethyl\}-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers;
2-\{(6-[1-(4-Methanesulfonyl-phenyl)-2-(tetrahydro-pyran-4-yl)-ethyl]-7H-pyrrolo[2,3-d]pyrimidin-2-yl\}-acetic acid and its (+) and (-) enantiomers;
Compounds of formula I may be prepared as shown in the following reaction schemes and the description thereof, as well as relevant literature procedures that may be used by one skilled in the art. Exemplary reagents and procedures for these reactions appear hereinafter and in the working examples. Protection and deprotection in the schemes below may be carried out by procedures generally known in the art (see, for example, Greene, T. W. and Wuts, P.G.M., Protecting Groups in Organic Synthesis, 3rd Edition, 1999 [Wiley]).
According to an embodiment, the present disclosure relates to a process for the preparation of a compound of formula (I), its stereoisomer, tautomer, prodrug, pharmaceutically acceptable salt, polymorph, or solvates.

**General Synthesis**

**Scheme-1:**

Compounds of formula II wherein X is CHR² or O and all other symbols are defined herein above, which may be obtained following procedure as described in (WO2009047798, WO200208209, WO2006016178) may be reacted with compounds of formula II A wherein all symbols are defined herein above, using non nucleophilic base such as n-BuLi, sec-BuLi, t-BuLi, LDA, LiHMDS, NaHMDS and the like, in the presence of a suitable organic solvent such as tetrahydrofuran, diethylether and the like, at temperature ranging from -78 °C to room temperature. The resulting intermediates may be subjected for deprotection of N-boc group followed by cyclization in one pot using suitable reagents such as trifluoroacetic acid, HCl, and the like to provide compounds of formula I wherein X is CHR² or O, Y is CH and all other symbols are as defined herein above.

**Scheme-2:**

Compounds of formula III wherein X is CHR² or O, and all other symbols are defined herein above, may be reacted with compounds of formula III A wherein all symbols are defined herein above, in presence of a suitable non-nucleophilic base such as n-BuLi, sec-BuLi, t-BuLi, LDA, LiHMDS,
NaHMDS and the like at temperature ranging from -78°C to room temperature to provide compounds of formula I wherein X is CHR\(^2\) or O. Y is CH and all other symbols are as defined herein above.

**Scheme-3:**

Compounds of formula IV wherein all symbols are defined herein above may be reacted with an alcohol or phenol of formula IVA under Mitsunobu reaction conditions to provide compounds of formula I wherein X is O, and all other symbols are defined herein above.

**Scheme-4:**

Compounds of formula V wherein L\(^1\) is a leaving group such as halogen, OTs, OMs, OTf and the like and all other symbols are defined herein above may be reacted with an alcohol or phenol of formula IVA wherein X is O and B is defined herein above, under Nucleophilic substitution reaction conditions to provide compounds of formula I wherein X is O and all other symbols are as defined herein above.
Scheme-5:

Compounds of formula VI wherein all symbols are defined herein above may be reacted with compound of formula VIA wherein L is a leaving group such as halogen, OTs, OMs, OTf and B is defined herein above, under nucleophilic substitution reaction conditions to provide compounds of formula I wherein X is CHR and all other symbols are as defined herein above.

Scheme-6:

Compounds of formula VII wherein R and R form a cycloalkyl ring and all other symbols are defined herein above may be reacted with compounds of formula IIA under basic condition using a suitable non nucleophilic base such as n-BuLi, sec-BuLi, t-BuLi, LDA, LiHMDS, NaHMDS and the like in the presence of a suitable organic solvent such as tetrahydrofuran, diethylether and the like, at temperature ranging from -78 °C to room temperature. The resulting intermediate may be subjected for deprotection of N-boc group followed by cyclization in one pot using suitable reagents such as trifluoroacetic acid, HC1, and the like to provide compounds of formula I wherein X is CHR, R and R form a cycloalkyl ring and all other symbols are as defined herein above.
Scheme-7: Intermediate of formula III may be synthesized as outlined below in Scheme-7.

Compounds of formula VIII wherein X is CH₅ or O and all other symbols are defined herein above may be converted to compounds of formula IX under amide coupling methods and using ammonia as reported in literature. Compounds of formula IX may be dehydrated using suitable dehydrating agents such as trifluoroactic anhydride, acetic anhydride, oxalyl chloride, thionyl chloride and the like in presence or absence of any suitable organic solvents at temperature ranging from -10 °C to 100°C to provide compounds of formula III wherein X is CH₅ or O and all other symbols are as defined herein above.

Scheme-8: Intermediate of formula IV may be synthesized as outlined below in Scheme-8.

Compounds of formula (XX) may be reacted with a protected alkyne (XXA) anion at temperature ranging from -78 °C to room temperature to provide compounds of formula XI which may be deprotected to obtain compounds of formula XII. Compounds of formula XII may be protected to obtain compounds of formula XIII which may be reacted with compounds of formula XIIIIA, wherein LI is halogen or triflate and all other symbols are defined herein above, in presence of a palladium catalyst such as tris(dibenzylideneacetone)dipalladium, palladium(II)acetate,
transdichlorobis(triphenylphosphine) palladium (II) or tetrakis(triphenylphosphine)palladium and optionally an additive such as triphenylphosphine or tritertbutylphosphine and optionally a co-catalyst such as copper(I)iodide and optionally a base such as n-butyl amine, diethyl amine, triethyl amine, disopropyl amine or piperidine at temperatures ranging from 25 °C to 150 °C, to provide compounds of formula XIV. Compounds of formula XIV may be cyclized to compounds of formula XV under basic condition using a suitable base such as potassium tertiary butoxide, sodium hydride, potassium hydride and the like at temperature ranging from -78 °C to 100 °C. Compounds of formula XV may be deprotected to obtain intermediate of formula IV wherein Y is C, R¹ is H and all other symbols are defined herein above.

**Scheme-9:** Intermediates of formula V and VI may be synthesized as outlined below in Scheme-9.

Compounds of formula XVI may be reacted with compounds of formula IIA in the presence of a base such as n-BuLi, sec-BuLi, t-BuLi, LDA, LiHMDS, NaHMDS and the like, in a suitable organic solvent at temperature ranging from -78 °C to room temperature. The resulting intermediates may be cyclized following the procedure mentioned above in scheme-1 to obtain intermediate VI. Compounds of formula VI may be converted to compounds of formula V under halogenation conditions.

**Scheme-10:** Compounds of formula I can also be synthesized as outlined below in Scheme-11 when X is C, Y is N and ring C is aromatic.

Compounds of formula XVIII wherein all symbols are defined herein above, which may be obtained following procedure as described in (WO2008104994, WO2009047798, WO200208209, WO2006016178) may be converted to compounds of formula I using amide coupling conditions.
followed by cyclization under acidic condition. Acid mediated cyclization can be carried at temperature ranging from -5 °C to 80 °C, using acid such as Trifluoroacetic acid, hydrochloric acid etc.

**Amide Coupling Conditions: Condition-I:** The amide coupling of carboxylic acid with amine or ammonia (amidation) may be carried out using any suitable amide coupling regents such as oxalyl chloride, thionyl chloride, BOP-Cl, DCC, HOBT, HOAt, HATU, EDCI, alkylchloroformate and the like in the presence of organic non-nucleophilic bases such as triethyl amine, diisopropylethyl amine, pyridine, N-methyl pyrroldine, N,N-dimethylaminopyridine, DBU, DABCO, other hindered amines and pyridines. The amide coupling reaction may be carried out in the presence of solvents such as dichloromethane, dichloroethane, DMF, dimethylacetamide, THF, acetonitrile or mixture of them may be used at a temperature ranging from -5 to 150 °C. The reaction may be carried out optionally in presence of catalytic amount of DMF. **Condition-II:** Amide coupling on carboxylic acid ester may be carried out by heating the ester and amine either in the absence of solvent or in presence of high boiling solvent like toluene, xylene, DMSO. Amide coupling may be carried out in presence of trialkyl aluminium (Chem. Commun., 2008, 1100-1 102).

**Halogenation Conditions:** Halogenation reaction may be carried out using reagents such as N-halosuccinimide, dihalogens and the like, in presence of radical generating reagents like peroxides such as benzoylperoxide. Solvents used for this reaction include, but are not limited to, carbon tetra chloride and ethers or mixtures thereof. The reaction may be carried out at a temperature ranging from -5 to 80 °C.

**Conditions for Nucleophilic Substitution: Condition-1:** For heteroatom based nucleophile: Nucleophilic substitution reaction may be carried out using any suitable organic or inorganic bases. Organic bases may be selected from a group consisting of mono, di or trialkyl amines particularly methyamine. ethylamine, dimethylamine, diethylamine or triethylamine. Inorganic bases may be selected from a group consisting of alkali and alkaline earth metal hydrides, hyroxides, carbonates and bicarbonates or mixtures thereof. Solvents used for this reaction may be selected from a group consisting of lower alcohols, acetone, acetonitrile, DMSO, DMF, dimethylacetamide, THF and toluene, or mixtures thereof. The reaction may be carried out at a temperature in the range of 0 to 150 °C. **Condition 2:** For Carbon centered nucleophile. The reactions can be carried out using strong non nucleophilic bases like, BuLi, LDA, LiHMDS, KOtBu, NaHMDS to generate carbon centered nucleophile. Reactions can be done in anhydrous condition and using aprotic solvents like THF, diethylether, dioxane, benzene etc.
**Conditions for Mitsunobu reaction:** The Mitsunobu reaction between alcohol and phenol, to obtain the corresponding ether, may be carried out in THF using triphenylphosphine (TPP) and diethyl azodicarboxylate (DEAD) or diisopropyl azodicarboxylate (DIAD) as reagents.

Above mentioned conditions, for the respective functional group transformations, are only to illustrated the type of synthesis. More specific conditions for above transformations are well documented and referred in the literature (R. C. Larock in Comprehensive Organic Transformations, Wiley-VCH Publication; B. M. Trost and I. Fleming Ed. Comprehensive Organic Synthesis, Elsevier Publication).

Wherever desired or necessary, in any of the above mentioned processes, any of the compounds of formula (I) may be converted into a pharmaceutically acceptable salt or vice versa or converting one salt form into another pharmaceutically acceptable salt form.

According to an embodiment, the present disclosure relates to compounds of formula (I) their stereoisomers, tautomers, prodrugs, pharmaceutically acceptable salts, polymorphs, solvates and formulations thereof, which are glucokinase activators, and are beneficial for the prophylaxis, management, treatment, control of progression, or adjunct treatment of diseases and/or medical conditions where the activation of glucokinase would be beneficial, such as diabetes, dyslipidemia, metabolic syndrome, and/or diabetes-related complications including retinopathy, nephropathy, neuropathy, ischemic heart disease, arteriosclerosis, β-cell dysfunction, and as therapeutic and/or prophylactic agents for obesity.

According to yet another embodiment, the present disclosure relates to compounds of formula (I) their stereoisomers, tautomers, prodrugs, pharmaceutically acceptable salts, polymorphs, solvates and formulations thereof, which are liver selective Glucokinase activators, useful for the treatment of hyperglycemia, diabetes, obesity, dyslipidemia, metabolic syndrome and like, in mammals and have minimum hypoglycemic potential.

A further embodiment of the disclosure includes a method of treatment of glucokinase activator mediated disease by administering a therapeutically effective amount of a compound of formula (I) to a mammal in need of such treatment.

By "pharmaceutically acceptable salts" as used herein, it covers salts of compounds of formula (I) prepared from pharmaceutically acceptable non-toxic bases or acids including inorganic or organic bases and inorganic or organic acids. Inorganic bases salts include aluminum, ammonium, calcium, copper, ferric, ferrous, lithium, magnesium, manganic salts, manganous,
potassium, sodium, zinc, and the like. Salts derived from pharmaceutically acceptable organic non-toxic bases include salts of primary, secondary, and tertiary amines, substituted amines including naturally occurring substituted amines, cyclic amines, and basic ion exchange resins, such as arginine, betaine, caffeine, choline, N,N’-dibenzylethylene-diamine, diethylamine, 2-diethylaminoethanol, 2-dimethylaminoethanol, ethanolamine, ethylenediamine, N-ethyl-morpholine, N-ethylpiperidine, glucamine, glucosamine, histidine, hydrabamine, isopropylamine, lysine, methylglucamine, morfoline, piperazine, piperidine, polyamine resins, procaine, purines, theobromine, triethylamine, trimethylamine, tripropylamine, tromethamine, and the like. Salts in the solid form may exist in more than one crystal structure, and may also be in the form of hydrates.

When the compound of the present disclosure is basic, salts may be prepared from pharmaceutically acceptable non-toxic acids, including inorganic and organic acids, such as acetic, benzenesulfonic, benzoic, camphorsulfonic, citric, ethanesulfonic, fumaric, gluconic, glutamic, hydrobromic, hydrochloric, isethionic, lactic, maleic, malic, mandelic, methanesulfonic, mucic, nitric, pamoic, pantothenic, phosphoric, succinic, sulfuric, tartaric, p-toluenesulfonic acid, and the like. Particularly preferred are hydrochloric, maleic, phosphoric, citric, hydrobromic, sulfuric, fumaric, and tartaric acids.

By “therapeutically effective amount” in this disclosure, it means an amount of compound of formula (I), its polymorphs, stereoisomers, pharmaceutically acceptable salt, solvate or pro-drug thereof, that is sufficient for effective treatment of obesity and/or type II diabetes. The therapeutically effective amount or dosage of a compound according to this disclosure can vary within wide limits. The dosage will depend on individual requirements in each particular case including the specific compound(s) being administered, the manner of administration, the severity of condition being treated, as well as the patient being treated, which is readily determinable by a person skilled in the art.

In using a compound of formula (I), its polymorphs, stereoisomers, pharmaceutically acceptable salt, solvate or pro-drug thereof, for therapeutic or prophylactic purposes it will generally be administered so that a daily dose in the range, for example, about 0.01 mg to 100 mg per kg body weight is received, given if required in divided doses. In general lower doses will be administered when a parenteral route is employed. Thus, for example, for intravenous administration, a dose in the range, for example, about 0.01 mg to 30 mg per kg body weight will generally be used. Similarly, for administration by inhalation, a dose in the range, for example, about 0.01 mg to 30 mg per kg body weight will be used.
The disclosure also relates to compound of formula (I), or its polymorph, stereoisomer, prodrug, solvate or a pharmaceutically acceptable salt thereof, for treating a disease through Glucokinase activation.

The disclosure also relates to compounds of formula (I), or its polymorph, stereoisomer, prodrug, solvate or a pharmaceutically acceptable salt thereof, for treating a disease through Glucokinase modulation or regulation.

The disclosure also relates to compounds of formula (I), or its polymorph, stereoisomer, prodrug, solvate or a pharmaceutically acceptable salt thereof, for treating a disease through Glucokinase deinhibition.

The disclosure also relates to compounds of formula (I), or its polymorph, stereoisomer, prodrug, solvate or a pharmaceutically acceptable salt thereof, for prophylactic or therapeutic treatment of hyperglycemia or diabetes, particularly type II diabetes.

The disclosure also relates to compounds of formula (I), or its polymorph, stereoisomer, prodrug, solvate or a pharmaceutically acceptable salt thereof, for preventing diabetes, particularly type II diabetes, in a human demonstrating pre-diabetic hyperglycemia or impaired glucose tolerance.

The disclosure also relates to compounds of formula (I), or its polymorph, stereoisomer, prodrug, solvate or a pharmaceutically acceptable salt thereof, for combined treatment or preventing diabetes and obesity.

The disclosure also relates to compounds of formula (I), or its polymorph, stereoisomer, prodrug, solvate or a pharmaceutically acceptable salt thereof, for treating or preventing obesity.

The disclosure also relates to compounds of formula (I), or its polymorph, stereoisomer, prodrug, solvate or a pharmaceutically acceptable salt thereof, for enhancing the secretion of enteroinsretins, like GLP-1 and GIP, thereby managing diseases or disorders associated with modulation of secretions of enteroinsretins, such as hyperglycemia, insulin resistance, impaired glucose tolerance, obesity, gastric emptying, gastroparesis, satiety, leptin resistance, dyslipidemia, wound healing, diabetic complications, such as nephropathy, retinopathy, neuropathy and cataracts.

The disclosure also relates to the use of compounds of formula (I), or its polymorphs, stereoisomers, pharmaceutically acceptable salt, solvate or pro-drug thereof, in the prophylactic or therapeutic treatment of dyslipidemia.
The disclosure also relates to compound of formula (I), or its stereoisomers, tautomers, prodrugs, pharmaceutically acceptable salts, polymorphs, solvates and formulations thereof, for treating hyperglycemia, IGT, Syndrome X, type 2 diabetes, type 1 diabetes, dyslipidemia or hyperlipidemia, hypertension, for the treatment or prophylaxis of obesity, for lowering of food intake, for appetite regulation, for regulating feeding behaviour.

The disclosure further relates to compounds of formula (I), its polymorphs, stereoisomers, pharmaceutically acceptable salt, solvate or pro-drug thereof, for use in the manufacture of medicament for the treatment of diabetes, obesity, metabolic syndrome X, insulin resistance, impaired glucose tolerance and dyslipidemia.

The disclosure also relates to the use of a compounds of formula (I), its polymorphs, stereoisomers, pharmaceutically acceptable salt, solvate or pro-drug thereof, in the manufacture of a medicament for the activation of Glucokinase. The disclosure also relates to the use of a compounds of formula (I), its polymorphs, stereoisomers, pharmaceutically acceptable salt, solvate or pro-drug thereof, in the manufacture of a medicament for the prevention of diabetes, particularly type II diabetes, in a human demonstrating pre-diabetic hyperglycemia or impaired glucose tolerance.

The disclosure also relates to a method of prophylactic or therapeutic treatment of hyperglycemia or diabetes, particularly type II diabetes, comprising a step of administering an effective amount of a compound of formula (I), its polymorphs, stereoisomers, pharmaceutically acceptable salt, solvate or pro-drug thereof.

The disclosure also relates to a method for the prevention of diabetes, particularly type II diabetes, in a human demonstrating pre-diabetic hyperglycemia or impaired glucose tolerance comprising a step of administering an effective prophylactic amount of a compound of formula (I), its polymorphs, stereoisomers, pharmaceutically acceptable salt, solvate or pro-drug thereof.

The disclosure also relates to a method of combined treatment of diabetes and obesity by administering an effective amount of a compound of formula (I), its polymorph, stereoisomer, prodrug, solvate or a pharmaceutically acceptable salt thereof, to a mammal in need of such treatment.

The disclosure also relates to the use of a compound of formula (I), its polymorphs, stereoisomers, pharmaceutically acceptable salt, solvate or pro-drug thereof, for the prevention of diabetes, particularly type II diabetes, in a human demonstrating pre-diabetic hyperglycemia or impaired glucose tolerance.
The disclosure also relates to the use of a compound of formula (I), its polymorphs, stereoisomers, pharmaceutically acceptable salt, solvate or pro-drug thereof, for use as medicament, for the prophylactic or therapeutic treatment of hyperglycemia or diabetes, particularly type II diabetes.

The disclosure also relates to the use of a compound of formula (I), its polymorphs, stereoisomers, pharmaceutically acceptable salt, solvate or pro-drug thereof, in the manufacture of a medicament for the prophylactic or therapeutic treatment of hyperglycemia or diabetes, particularly type II diabetes.

The disclosure also relates to the use of a compound of formula (I), their stereoisomers, tautomers, prodrugs, pharmaceutically acceptable salts, polymorphs, and solvates, in the manufacture of a medicament for use in combined treatment or prevention of diabetes and obesity.

The disclosure also relates to the use of a compound of formula (I), their stereoisomers, tautomers, prodrugs, pharmaceutically acceptable salts, polymorphs, solvates and formulations thereof for prophylactic or therapeutic treatment of a disease selected from a group consisting of a disease needing Glucokinase activation, a disease needing Glucokinase deinhibition, hyperglycemia, 1GT, Syndrome X, type 2 diabetes, type 1 diabetes, dyslipidemia, hyperlipidemia, hypertension, insulin resistance, impaired glucose tolerance, obesity, gastric emptying, gastroparesis, satiety, leptin resistance, dyslipidemia, wound healing, nephropathy, retinopathy, neuropathy and cataracts.

The disclosure also relates to the use of a compound of formula (I), their stereoisomers, tautomers, prodrugs, pharmaceutically acceptable salts, polymorphs, solvates and formulations thereof for lowering of food intake, for appetite regulation, for regulating feeding behaviour, for enhancing the secretion of enteroincretins like GLP-1 and GIP.

The disclosure also relates to the use of a compound of formula (I), their stereoisomers, tautomers, prodrugs, pharmaceutically acceptable salts, polymorphs, solvates and formulations thereof for preventing diabetes, particularly type II diabetes, in a human demonstrating pre-diabetic hyperglycemia or impaired glucose tolerance, preventing obesity and preventing dyslipidemia.

The disclosure also relates to the use of a compound of formula (I), their stereoisomers, tautomers, prodrugs, pharmaceutically acceptable salts, polymorphs, solvates and formulations thereof for combined treatment or prevention of diabetes and obesity.

The disclosure also relates to pharmaceutical composition comprising, as an active ingredient, at least one compound of formula (I), or its stereoisomers, tautomers, prodrugs,
pharmaceutically acceptable salts, polymorphs, and solvates thereof, together with one or more pharmaceutically acceptable carriers or excipients.

The compounds and compositions of the present disclosure may be optionally employed in combination with one or more, from current or future therapy, other anti-diabetic agents or anti-hyperglycemic agents, which include, for example, (a) insulin secretagogues such as sulfonylureas (e.g. Amaryl, glyburide, glimepiride, glipizide, etc.); (b) Insulinotropic sulfonyl urea receptor ligands such as meglitinides (e.g. nateglinide, rapaglinide); (c) biguanides (e.g. metformin etc.); (d) glucagon antagonists (e.g. a peptide or non-peptide glucagon antagonist); (e) glucosidase inhibitors (e.g. acarbose, miglitol, etc.); (f) glucose sensitive insulinotropic agents (e.g. GLP-1, GLP-1 mimetics e.g Exendin-4; GLP-1, GPR-119, GPR-40, GPR 120 and like other receptor modulators chosen from small molecule or from peptides); (g) insulin sensitizers (e.g. rosiglitazone, pioglitazone, balaglitazone etc.); (h) Dipeptidyl peptidase-IV inhibitors (e.g. sitagliptin, vildagliptin, saxagliptin etc.); (i) insulin and insulin analogs; (j) SGLT-1 and SGLT-2 inhibitors (e.g. dapagliflozin, canagliflozin); (k) H1 beta-HSD1 inhibitors (e.g. INCB-13739, AMG 221) and the like. The said additional therapeutic agent is added in a dose range of about 0.01 mg to 100 mg per kg body weight.

The compounds and compositions of the present disclosure may also be optionally employed in combination with one or more, from current or future therapy, anti-obesity agents (e.g. sibutramine, orlistat, rimonabant etc.) and the like.

The compounds and compositions of the present disclosure may also be optionally employed in combination with one or more, from current or future therapy, dyslipidemic agents which include, for example: (a) fibrates (e.g. gemfibrozil, fenofibrate); (b) Niacin; (c) Statins (e.g. rosvuavatatin, atorvastatin, simvastatin); (d) cholesterol absorption inhibitors (e.g. Ezetimibe); (e) bile acid sequestrants (e.g. cholestyramine) and the likes.

The compounds and compositions of the present disclosure may also be optionally employed in combination with one or more, from current or future therapy, antihypertensive agents such as: (a) diuretics (e.g hydrocholorothiazides, mannitol, indapamide, furosemide); (b) angiotensin converting enzyme (ACE) inhibitors (e.g. captopril, enalapril); (c) Angiotensin-II receptor type-1 blockers (ARB) (e.g. losartan, irbesartan); (d) rennin inhibitors (e.g aliskerin); (e) β-adrenergic receptor blockers (e.g. atenolol, metoprolol); (f) calcium channel blockers (e.g. amlodipine, nifedipine); (g) aldosterone receptor antagonist (e.g. spironolactone); (h) aldosterone synthase
inhibitors (e.g. FAD286). The said additional therapeutic agent is added in a dose range of about 0.01 mg to 100 mg per kg body weight.

The compounds and compositions of the present disclosure and the other therapeutic agents such as described above may be administered simultaneously, sequentially or separately.

The pharmaceutical compositions of the present disclosure comprise a compound of formula (I), polymorphs, stereoisomers, pharmaceutically acceptable salt, solvate or pro-drug thereof, as an active ingredient, a pharmaceutically acceptable carrier and optionally other therapeutic active agent in any suitable ratios.

The disclosure also relates to pharmaceutical composition comprising, as an active ingredient, at least one compound of formula (I), or its stereoisomers, tautomers, prodrugs, pharmaceutically acceptable salts, polymorphs, and solvates thereof, wherein the pharmaceutically acceptable therapeutically active agent is selected from anti-diabetic agents, anti-hyperglycemic agents, anti-obesity agents, anti-hypertensive agents or anti-dyslipidemic agents.

The pharmaceutical compositions of the present disclosure comprising compounds of formula (I), polymorphs, stereoisomers, pharmaceutically acceptable salt, solvate or prodrugs thereof, may be manufactured in a manner that is known in the art, e.g. by means of conventional mixing, encapsulating, dissolving, granulating, emulsifying, entrapping, dragee making, or lyophilizing processes. These pharmaceutical preparations can be formulated with therapeutically inert, inorganic or organic carriers such as lactose, corn starch or derivatives thereof, talc, steric acid or its salts as carriers for tablets, coated tablets, dragees and hard gelatin capsules. For soft gelatin capsules suitable carriers include vegetable oils, waxes and fats. Suitable carriers for the manufacture of solutions and syrups are water, polyols, saccharose, invert sugar and glucose. Suitable carriers for injection are water, alcohols, polyols, glycerine, vegetable oils, phospholipids and surfactants. Suitable carriers for suppositories are natural or hardened oils, waxes, fats and semi-liquid polyols.

The pharmaceutical preparations can also contain preserving agents, solubilizing agents, stabilizing agents, wetting agents, emulsifying agents, sweetening agents, coloring agents, flavoring agents, salts for varying the osmotic pressure, buffers, coating agents or antioxidants. They can also contain other therapeutically valuable substances, including additional active ingredients other than those of formula (I), its polymorphs, stereoisomers, pharmaceutically acceptable salt, solvate or prodrugs thereof.
The pharmaceutical compositions containing the active ingredient of compound of formula (1), its polymorphs, stereoisomers, pharmaceutically acceptable salt, solvate or prodrugs thereof, maybe in a form suitable for oral use, for example, as tablets, troches, lozenges, aqueous or oily suspensions, dispersible powders or granules, emulsions, hard or soft capsules, or syrups or elixirs; sterile injectable aqueous or oleaginous suspension; suppositories; topical use, for example creams, ointments, jellies, solutions or suspension etc including mouth washes and gargles. These compositions can be manufactured by any method known in the art with the active ingredient combined with non-toxic pharmaceutically acceptable excipients.

While the disclosure has been described and illustrated with reference to certain preferred embodiments thereof, those skilled in the art will appreciate that various changes, modifications and substitutions can be made therein without departing from the spirit and scope of the present disclosure. For example, the specific pharmacological responses observed may vary according to and depending on the particular active compound selected or whether there are present pharmaceutical carriers, as well as the type of formulation and mode of administration employed, and such expected variations or differences in the results are contemplated in accordance with the objects and practices of the present disclosure.

Examples

The disclosure is further illustrated by the following examples which in no way should be construed as being further limiting. One skilled in the art will readily appreciate that the specific methods and results described are merely illustrative. All stereoisomers of the compounds of the instant disclosure are contemplated, either in admixture or in pure or substantially pure form. The compounds of the present disclosure can have asymmetric centers at any of the carbon atoms, consequently, compounds of formula (I) can exist in enantiomeric, or diastereomeric forms, or in mixtures thereof. The processes for preparation can utilize racemates, enantiomers, or diastereomers as starting materials. When diastereomeric or enantiomeric products are obtained as mixtures, they can be separated by conventional methods for example, chromatographic separation or fractional crystallization or through diastereomeric salt formation. When intended, a desired enantiomer or diastereomer can also be obtained by following appropriate enantioselective or diastereoselective reactions.

Structures of the intermediates as well as the final compounds were confirmed by nuclear magnetic resonance spectra for proton (1H NMR) and LCMS.
Example-Al: 2-(2-Cyclopentyl-l-(4-cyclopropanesulfonyl-phenyl)-ethyI]-lH-pyrrolo|2,3-bjpyridine

Step: 1 Synthesis of 2-(2-Cyclopentyl-l-(4-cyclopropanesulfonyl-phenyl)-ethyl]-lH-pyrrolo[2,3-b]pyridine:

Anhydrous THF (8.0 mL) was added to (3-methyl-pyridin-2-yl)-carbamic acid tert-butyl ester (0.3 gm, 1.44 mmol) the solution was cooled to -10 °C and n-BuLi (1.6 M in hexanes, 2.7 mL, 4.32 mmol) was added to the solution and the mixture was stirred at the same temperature for 30 min. 3-Cyclopentyl-2-(4-cyclopropanesulfonyl-phenyl)-propionic acid methylester (0.43 gm, 1.29 mmol) (WO 2006/016178 Al, US 06/320050 Bl) was dissolved in anhydrous THF (5 mL) under inert atmosphere, solution was added slowly to the reaction mixture at -10 °C and was allowed to stir at same temperature for 30 min. and the reaction mixture was stirred for 1 hr at 25 °C. Reaction was quenched by addition of satd. aq. NH₄Cl (25 mL), aq mixture was then extracted with ethyl acetate (3X25 mL), combined organic layer was washed with brine followed by water, dried over anhydrous sodium sulfate, sodium sulfate was filtered and washed with ethyl acetate and solvent was removed under reduced pressure to provide the crude intermediate. Anhydrous dichloromethane (3 mL) was added to the crude intermediate obtained as mentioned above under inert atmosphere and followed by trifluoroacetic acid (10 mL) and reaction mixture was stirred at 25 °C for 6 hr. The reaction mixture was concentrated under vacuum, residue was neutralized with satd. aq. NaHCO₃, mixture was then extracted with ethyl acetate (3X25 mL), organic layer was washed with brine followed by water, dried over anhydrous sodium sulfate, sodium sulfate was filtered and washed with ethyl acetate and solvent was removed under reduced pressure to provide the crude product. The crude product obtained was purified by preparative HPLC to give 0.055 gm of the pure product.

1H NMR (400 MHz, CDC13): δ 0.99-1.03 (m, 2H), 1.14-1.24 (m, 3H), 1.25-1.34 (m, 2H), 1.41-1.53 (m, 3H), 1.57-1.81 (m, 3H), 2.07-2.15 (m, 1H), 2.22-2.27 (m, 1H), 2.40-2.44 (m, 1H), 4.25 (t, J = 8.0 Hz, 1H), 6.38 (s, 1H), 7.05 (dd, J = 7.6 Hz, J = 4.8 Hz, 1H), 7.47 (d, J = 8.4 Hz, 2H), 7.82 (d, 6.8 Hz,
2H), 7.87 (dd, J = 8.0 Hz, J = 1.6 Hz, 1H), 8.15 (dd, J = 4.8 Hz, 1.6 Hz, 1H), 10.04 (bs, 1H). MS (EI) m/z: 395.1 (M+1).

**Example-A2:2-[(4-Cyclopropanesulfonyl-phenyl)-(tetrahydro-pyran-4-yloxy)-inethyl]-IH-pyrrolo[2,3-b]pyridine**

**Step I:** p-ToIuene sulfonyl hydrazone (4-cyclopropyl sulfonyl) phenyl acetic acid ethyl ester:
A mixture of (4-cyclopropanesulfonyl-phenyl) oxo acetic acid ethyl ester (0.5 gm, 1.77 mmole) (WO 2009/047798) and p-toluene sulfonyl hydrazide (0.48 gm, 2.3 mmol) in toluene (15 ml) was refluxed for 16 hr using a Dean-Stark apparatus. Reaction mixture was concentrated to give the crude product which was purified by column chromatography over silica gel to provide p-toluene sulfonyl hydrazone (4-cyclopropyl sulfonyl) phenyl acetic acid ethyl ester (0.5 gm).
MS (EI) m/z: 451.0 (M+1).

**Step II:** (4-Cyclopropanesulfonyl-phenyl) diazo acetic acid ethyl ester:
To a solution of p-toluene sulfonyl hydrazone (4-cyclopropyl sulfonyl) phenyl acetic acid ethyl ester (0.5 gm, 1.23 mmole) in methylene chloride (6 ml), was added ethylamine (0.17 mL, 1.35 mmol) and stirred at 25 °C for 1 hr. Reaction mixture was concentrated to provide (4-cyclopropanesulfonyl-phenyl) diazo acetic acid ethyl ester (0.5 gm) which was used for next reaction.
MS (EI) m/z: 295.1 (M+1).

**Step III:** (4-Cyclopropanesulfonyl-phenyl)-[(tetrahydro-pyran-4-yloxy)]-acetic acid ethyl ester:
(4-Cyclopropanesulfonyl-phenyl) diazo acetic acid ethyl ester (2.5 gm, 8.43 mmol) was dissolved in DCM (50 mL) under argon atmosphere. To this solution, 3-hydroxy tetrahydropryan (2.00 mL, 21.09 mmol) was added followed by rhodium(I)acetate dimer (156mg, 0.35 mmol). Mixture was stirred at 25 °C for overnight. Reaction mixture was diluted with DCM (50 mL), organic layer was
washed with water followed by brine solution, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure to give a crude product which was purified by column chromatography to provide (4-cyclopropanesulfonyl-phenyl)-[(tetrahydro-pyran-4-yloxy)]-acetic acid ethyl ester (2.50 gm).

\[ ^1H \text{ NMR (400 MHz, CDCl}_3\] \: \delta \ 1.00-1.05 \text{ (m, 2H), 1.20-1.26 \text{ (m, 3H), 1.31-1.36 \text{ (m, 2H), 1.64-1.70 \text{ (m, 1H), 1.71-1.80 \text{ (m, 1H), 1.86-1.90 \text{ (m, 1H), 1.95-2.01 \text{ (m, 1H), 2.43-2.46 \text{ (m, 1H), 3.38-3.47 \text{ (m, 2H), 3.60-3.67 \text{ (m, 1H), 3.89-4.01 \text{ (m, 2H), 4.14-4.22 \text{ (m, 2H) 5.10 \text{ (s, 1H), 7.67 \text{ (d, J=8.4 Hz, 2H), 7.88 \text{ (d, J=8.0 Hz, 2H). MS (EI) } m/z: 369.10 \text{ (M+1).}}}

\text{Step IV: \ 2-[(4-Cyclopropanesulfon}}y\text{-phenyl)-(tetrahydro-pyran-4-yloxy)-methyl]-IH-pyrrolo[2,3-b]pyridine:}

Starting from the product of step-III and following procedure used for \textbf{Example-A1}, the desired \textbf{Example A2} was obtained.

\[ ^1H \text{ NMR (400 MHz, CDCl}_3\] \: \delta \ 1.01-1.05 \text{ (m, 2H), 1.32-1.36 \text{ (m, 2H), 1.68-1.67 \text{ (m, 2H), 1.88-1.98 \text{ (m, 2H), 2.40-2.46 \text{ (m, 1H), 3.36-3.44 \text{ (m, 2H), 3.66-3.74 \text{ (m, 1H), 3.92-3.99 \text{ (m, 2H), 5.84 \text{ (s, 1H), 6.95 \text{ (s, 1H), 7.08 \text{ (dd, J = 7.9, 4.9 Hz, 1H), 7.64 \text{ (d, J = 8.3 Hz, 2H), 7.82-7.86 \text{ (aromatics, 3H), 8.26 \text{ (dd, J = 4.9, 1.5 Hz, 1H). MS (EI) } m/z: 413.2 \text{ (M+1).}}}

\textbf{Table:1 Examples A3 to A15 were prepared following procedures used for Examples A1 & A2 from appropriate starting materials.}

<table>
<thead>
<tr>
<th>Sl.No.</th>
<th>Structure</th>
<th>MS (EI) m/z</th>
<th>IUPAC Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>A3</td>
<td><img src="image1" alt="Structure" /></td>
<td>397 (M+1)</td>
<td>2-[[Cyclopropyloxy-(4-cyclopropanesulfonyl-phenyl)-methyl]-1H-pyrrolo[2,3-b]pyridine</td>
</tr>
<tr>
<td>A4</td>
<td><img src="image2" alt="Structure" /></td>
<td>409.1 (M+1)</td>
<td>2-[2-Cyclohexyl-(4-cyclopropanesulfonyl-phenyl)-ethyl]-1H-pyrrolo[2,3-b]pyridine</td>
</tr>
<tr>
<td>A5</td>
<td><img src="image1" alt="Chemical Structure" /></td>
<td>369.1 (M+1)</td>
<td>2-[2-Cyclohexyl-1-(4-methanesulfonyl-phenyl)-ethyl]-1H-pyrrolo[2,3-b]pyridine</td>
</tr>
<tr>
<td>-----</td>
<td>-------------------------------</td>
<td>------------</td>
<td>---------------------------------------------------------------------</td>
</tr>
<tr>
<td>A6</td>
<td><img src="image2" alt="Chemical Structure" /></td>
<td>423 (M+1)</td>
<td>2-[1-(4-Cyclopentanesulfonyl-phenyl)-2-cyclopentyl-ethyl]-1H-pyrrolo[2,3-b]pyridine</td>
</tr>
<tr>
<td>A7</td>
<td><img src="image3" alt="Chemical Structure" /></td>
<td>411 (M+1)</td>
<td>2-[1-(4-Cyclopropanesulfonyl-phenyl)-2-(tetrahydro-pyran-4-yl)-ethyl]-1H-pyrrolo[2,3-b]pyridine</td>
</tr>
</tbody>
</table>
| A8  | ![Chemical Structure](image4) | 437.1 (M+1) | 2-[2-Cyclohexyl-1-(4-cyclopentanesulfonyl-phenyl)-ethyl]-1H-pyrrolo[2,3-b]pyridine  
MS (EI) m/z: |
<p>| A9  | <img src="image5" alt="Chemical Structure" /> | 383 (M+1)  | 2-[2-Cyclohexyl-1-(4-methanesulfonyl-phenyl)-ethyl]-1H-pyrrolo[2,3-b]pyridine |</p>
<table>
<thead>
<tr>
<th>A10</th>
<th><img src="image" alt="Chemical Structure" /></th>
<th>410.2 (M+1)</th>
<th>6-[2-Cyclohexyl-1-(4-cyclopropanesulfonyl-phenyl)-ethyl]-5H-pyrrolo[2,3-b]pyrazine</th>
</tr>
</thead>
<tbody>
<tr>
<td>A11</td>
<td><img src="image" alt="Chemical Structure" /></td>
<td>386.1 (M+1)</td>
<td>6-[1-(4-Methanesulfonyl-phenyl)-2-(tetrahydro-pyran-4-yl)-ethyl]-5H-pyrrolo[2,3-b]pyrazine</td>
</tr>
<tr>
<td>A12</td>
<td><img src="image" alt="Chemical Structure" /></td>
<td>414.1 (M+1)</td>
<td>6-[4-Cyclopropanesulfonylethyl]-(tetrahydro-pyran-4-yl)oxy]-methyl]-5H-pyrrolo[2,3-b]pyrazine</td>
</tr>
<tr>
<td>A13</td>
<td><img src="image" alt="Chemical Structure" /></td>
<td>385.3 (M+1)</td>
<td>2-[1-(4-Methanesulfonyl-phenyl)-2-(tetrahydro-pyran-4-yl)-ethyl]-1H-pyrrolo[2,3-b]pyridine</td>
</tr>
<tr>
<td>A14</td>
<td><img src="image" alt="Chemical Structure" /></td>
<td>403.2 M([^{35}Cl+1]) base peak, 405.2 M([^{35}Cl+1])</td>
<td>6-Chloro-2-[2-cyclopentyl-1-(4-methanesulfonyl-phenyl)-ethyl]-1H-pyrrolo[2,3-b]pyridine</td>
</tr>
</tbody>
</table>
Example-B1: 2-[(2,4-Difluoro-phenoxy)-(4-methanesulfonyl-phenyl)-methyl]-lH-pyrrolo[2,3-b]pyridine

Step I: Synthesis of l-(4-Methylsulfanyl-phenyl)-3-trimethylsilanyl-prop-2-yn-l-ol:
n-BuLi (54.88 mL, 87.82 mmol, 1.6M in hexanes) was added to the solution of trimethylsilyl acetylene (7.9 gm, 80.5 mmol) in anhydrous THF (100 mL) at -78 °C under inert atmosphere. The reaction mixture was stirred at -78 °C for 1 hr and 4-methylthio benzaldehyde (10 mL, 73.18 mmol) was slowly added to the reaction mixture at -78 °C. The reaction mixture was then stirred at 25 °C for 2 hr, reaction mixture was diluted with satd. aq. NH₄Cl (100 mL), mixture was then extracted with ethyl acetate (3X100 mL), combined organic layer was washed with water followed by brine, dried over anhydrous sodium sulfate, sodium sulfate was filtered and washed with ethylacetate and solvent was removed under reduced pressure to provide the product (19.6 gm).

^1H NMR- (400 MHz, CDC13), δ 0.2 (s, 9H), 1.19 (d, J=6 Hz, 1H), 2.48 (s, 3H), 5.4 1 (d, J=6.4Hz, H), 7.26 (d, J=8.4 Hz, 2H), 7.46 (d, J=8.4 Hz, 2H). MS (EI) m/z: 232.9 (M - OH).
Step II: Synthesis of 1-(4-Methylsulfanyl-phenyl)-prop-2-yn-1-ol.

1-(4-Methylsulfanyl-phenyl)-3-trimethylsilanyl-prop-2-yn-1-ol (19.6 gm, 78.4 mmol) was taken in methanol (150 mL) along with potassium carbonate (5.4 gm, 39.2 mmol) and the reaction mixture was stirred at 25 °C for 2 hr. The reaction mixture was concentrated and diluted with water (100 mL). Extracted with ethyl acetate (3X100 mL). The combined organic layer was washed with water followed by brine, dried over anhydrous sodium sulfate, sodium sulfate was filtered and washed with ethyl acetate and solvent was removed under reduced pressure to provide the product (14.8 gm).

H NMR- (CDC13), δ 2.23 (d, J=6.4 Hz, 1H), 2.48 (s, 3H), 2.67 (d, J=2.0 Hz, 1H), 5.42-5.43 (dd, J=5.6, 1.6Hz, 1H), 7.26 (d, J=8.4 Hz, 2H), 7.46 (d, J=8.4 Hz, 2H). MS (EI) mlz: 160.9 (M - OH).

Step III: Synthesis of 1-(4-Methanesulfonyl-phenyl)-prop-2-yn-1-ol.

The stirring solution of 1-(4-Methylsulfanyl-phenyl)-prop-2-yn-1-ol (14.8 gm, 83 mmol) in dichloromethane (150 ml) was cooled to 0 °C and to it mCPBA (35.8 gm, 207 mmol) was added in portions. After complete addition the reaction mixture was stirred for 2 hr. The reaction mixture was filtered and the residue was washed with dichloromethane (3X100 mL), the combined filtrate and washings was washed with sat. aq. Sodium thiosulphate (200 mL), followed by sat. aq. Sodium bicarbonate (200 mL) and brine. The organic layer was dried over anhydrous sodium sulfate, sodium sulfate was filtered and washed with dichloromethane and solvent was removed under reduced pressure to provide the crude product. The crude compound was purified by column chromatography (silica gel 60-120 mesh, 5%-30% ethyl acetate in hexanes as eluent) to give the pure product (13.9 gm).

H NMR- (400 MHz, CDC13), δ 2.48 (d, J=6 Hz, 1H), 2.73 (d, J=2.4 Hz, 1H), 3.05 (s, 3H), 5.56 (d, J=3.6 Hz, 1H), 7.77 (d, J=8 Hz, 2H), 7.96 (d, J=8.4 Hz, 2H). MS (EI) mlz: 210.8 (M + 1).

Step IV: Synthesis of tert-Butyl-[l-(4-methanesulfonyl-phenyl)-prop-2-ynoxy]-dimethylsilane.

1-(4-Methanesulfonyl-phenyl)-prop-2-yn-1-ol (17.4 gm 83 mmol) was taken in anhydrous DMF (80 mL). To the solution TBDMSCl (15 gm, 99.63 mmol) and imidazole (6.7 gm, 99.6 mmol) were added and the reaction mixture was stirred at 60 °C for 16 hr in inert atmosphere. The reaction mixture was diluted with water (500 mL) then extracted with ethyl acetate (3X200 mL). The combined organic layer was washed with water followed by brine, dried over anhydrous sodium sulfate, sodium sulfate was filtered and washed with ethylacetate and solvent was removed under reduced pressure to provide the crude product. The crude product was purified by column chromatography (silica gel 60-120 mesh, 20% ethylacetate in hexanes as eluent) to give the pure product (15.5 gm).
\( ^1H \) NMR- (CDCl3), \( \delta 0.17 \) (s, 3H), 0.2 (s, 3H), 0.94 (s, 9H), 2.60 (d, J=2.4 Hz, 1H), 3.05 (s, 3H), 5.54 (d, J=2 Hz, 1H), 7.7 (d, J=8 Hz, 2H), 7.94 (d, J=8.8 Hz, 2H). MS (EI) \( m/z \): 325 (M +1).

**Step V:** Synthesis of 3-[3-((tert-Butyl-dimethyl-silanyloxy)-3-(4-methanesulfonyl-phenyl)-prop-1-ynyl]-pyridin-2-ylamine.

To the suspension of 2-amino-3-iodopyridine (0.26 gm, 1.1 mmol), Cul (0.024 gm, 0.1 mmol) and \( \text{PdCl}_2(\text{PPh}_3)_2 \) in dry and degassed THF (10 mL), tert-Butyl-[1-(4-methanesulfonyl-phenyl)-prop-2-ynloxyj-dimethyl-silane (0.5 gm, 1.5 mmol) and triethylamine (0.36 gm, 3.5 mmol) were added under inert atmosphere and the reaction mixture was stirred at 25 °C for 2 hr. The reaction mixture was diluted with diethylether (20 mL) and filtered to remove solids, residue was washed with diethylether (3 X 10 mL), organic solvent was removed under reduced pressure to provide the crude product. The crude compound was purified by preparative TLC to give the pure product (0.26 gm).

\( ^1H \) NMR- (CDCl3), \( \delta 0.21 \) (s, 3H), 0.25 (s,3H), 0.98 (s, 9H), 3.08 (s, 3H), 4.95 (s,1H), 6.61-6.64 (m, 1H), 7.50-7.52 (m, 1H)7.76 (d, J=8 Hz, 2H), 7.98 (d, J=8.4 Hz, 2H), 8.04 (m, 1H). MS (EI) \( m/z \): 417 (M +1).

**Step VI:** Synthesis of 2-[(tert-Butyl-dimethyl-silanyloxy)-(4-methanesulfonI-phenyl)-methyl]-1H-pyrrolo[2,3-b]pyridine.

To a stirring suspension of 3-[3-(tert-Butyl-dimethyl-silanyloxy)-3-(4-methanesulfonl-phenyl)-prop-1-ynyl]-pyridin-2-ylamine (1.56 gm, 3.7 mmol), potassium tert.butoxide (1.09 gm, 9.73 mmol) in toluene (10 ml), was added 18-Crown-6 (0.98 gm, 3.7 mmol) and the reaction mixture was stirred at 25 °C for 30 min. The reaction mixture was concentrated and diluted with ethylacetate (25 mL), washed with water (25 mL) followed by brine, dried over anhydrous sodium sulfate, sodium sulfate was filtered and washed with ethylacetate and the solvent was removed under reduced pressure to provide the crude product. The crude compound was purified by column chromatography (silica gel 60-120 mesh, 10-40% ethylacetate in hexanes as eluent) to give the pure product (0.6 gm).

\( ^1H \) NMR (400 MHz, CDCl3), \( \delta 0.21 \) (s, 3H), 0.25 (s,3H), 0.93 (s, 9H), 3.03 (s, 3H), 6.038 (s,1H), 6.315 (s, 1H), 7.04-7.07 (m, 1H), 7.65 (d, J=8 Hz, 2H),7.84-7.86 (m, 1H), 7.91 (d, J=8 Hz, 2H), 8.23 (d, J=4 Hz, 1H). MS (EI) \( m/z \): 417 (M +1).

**Step VII:** Synthesis of 4-(Methanesulfonyl-phenyl)-(1H-pyrrolo[2,3-b]pyridin-2-yl)-methanol.

Anhydrous THF (20 mL) was added to 2-[{(tert-Butyl-dimethyl-silanyloxy)-(4-methanesulfonl-phenyl)-methyl]-1H-pyrrolo[2,3 -b]pyridine (0.6 gm, 1.4 mmol) under inert atmosphere. To this solution TBAF (1 M in THF, 0.75 gm, 2.9 mmol) was added. The reaction mixture was stirred at 25 °C for 16 hr. The reaction mixture was diluted with water (20 mL), mixture was then extracted with ethyl acetate (3X25 mL), combined organic layer was washed with water followed by brine, dried
over anhydrous sodium sulfate. Sodium sulfate was filtered and washed with ethyl acetate and solvent was removed under reduced pressure to provide the product (0.2 gm).

\[ \text{H NMR (400 MHz, CDCl3): } \delta 3.16 \text{ (s, 3H), 5.95 (d, } J=4.4 \text{ Hz, 1H), 6.22 (d, } J=1.6 \text{ Hz, 1H), 6.33 (d, } J=4.4 \text{ Hz, 1H), 6.96-6.99 (m, 1H), 7.07 (dd, } J=8.4 \text{ Hz, 2H), 7.82 (d, } J=8 \text{ Hz, 1H), 7.88 (d, } J=8.4 \text{ Hz, 2H), 8.11 (d, } J=4.8 \text{ Hz, 1H). MS (EI) m/z: 303.2 (M+1).}\]

**Step VIII: Synthesis 2-[(2,4-Difluoro-phenoxy)-(4-methanesulfonyl-phenyl)-methyl]-1H-pyrrolo[2,3-b] pyridine.**

The mixture of (4-Methanesulfonyl-phenyl)-(1H-pyrrolo[2,3-b]pyridin-2-yl)-methanol (0.2 gm, 0.66 mmol), 2,4-difluorophenol (0.085 gm, 0.66 mmol) and triphenylphosphine (0.34 gm, 1.32 mmol) was taken in anhydrous THF (4 mL) under inert atmosphere and cooled to 0 °C. To it ditert.butyl azodicarboxylate (0.3 gm, 1.32 mmol) was added and the reaction mixture was stirred at 25 °C for 7 hr. The reaction mixture was diluted with water (10 mL), mixture was then extracted with ethyl acetate (3x15 mL), combined organic layer was washed with water followed by brine, dried over anhydrous sodium sulfate, sodium sulfate was filtered and washed with ethyl acetate and solvent was removed under reduced pressure to provide the crude product. The crude compound was purified by column chromatography (silica gel 60-120 mesh) followed by preparative HPLC to give the pure product (0.03 gm).

\[ \text{H NMR (400 MHz, 400 MHz, CDCl3): } \delta 3.10 \text{ (s, 3H), 6.37 (s, 1H), 6.41 (s, 1H), 6.60-6.70 (m, 1H), 6.85-6.95 (m, 2H), 7.07 (dd, } J=7.8, 4.9 \text{ Hz, 1H), 7.77 (d, } J=8.8 \text{ Hz, 2H), 7.89 (dd, } J=7.8, 1.5 \text{ Hz, 1H), 7.96 (d, } J=8.3 \text{ Hz, 2H), 8.25 (dd, } J=8.0 \text{ Hz, 1.5 Hz, 1H), 11.15 (bs, 1H). MS (EI) m/z 415.2 (M+1).}\]

**Table:2 Example B2** was prepared following procedure used for Example-B1 from appropriate starting materials.

<table>
<thead>
<tr>
<th>Sl.No.</th>
<th>Structure</th>
<th>MS (EI) m/z</th>
<th>IUPAC Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>B2</td>
<td><img src="image" alt="Structure" /></td>
<td>413 [M(35Cl) +1], 415 [M(37Cl) +1]</td>
<td>2-[(4-Chloro-phenoxy)-(4-methanesulfonyl-phenyl)-methyl]-1H-pyrrolo[2,3-b]pyridine</td>
</tr>
</tbody>
</table>
Example CI: 2-[(2,4-Difluoro-phenoxy)-(4-methanesulfonyl-phenyl)-methyl]-lH-pyrrolo[2,3-b]pyridine

![Diagram](image)

Step 1 Synthesis of 2-[(2,4-Difluoro-phenoxy)-(4-methanesulfonyl-phenyl)-methyl]-lH-pyrrolo[2,3-b]pyridine

(2,4-Difluoro-phenoxy)-(4-methanesulfonyl-phenyl)-acetic acid (0.85 g, 2.48 mmol) was dissolved in 20 ml dry DCM under argon atmosphere. To this solution, HATU (1.20 g, 2.98 mmol) was added followed by DIPEA (0.82 ml, 4.97 mmol). Mixture was stirred at 25 °C for 15 min. Pyridine-2,3-diamine (0.27 g, 2.48 mmol) was added and further stirred for overnight. Reaction mixture was quenched by addition of 20 ml water, extracted with DCM (3 X 30 ml), combined organic layer was washed with brine solution, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure to obtain crude intermediate. The crude was dissolved in 2 ml dry DCM, to this solution 10 ml TFA was added slowly and stirred overnight at 25 °C. Reaction mixture was concentrated under reduced pressure, neutralized by aq. sat. solution of NaHCO₃, extracted with ethyl acetate (3 X 20 ml). The combined organic layer was washed with brine solution, dried over anhydrous sodium sulfate, and concentrated under reduced pressure to obtain the crude product which was then purified by column chromatography to provide 2-[(2,4-Difluoro-phenoxy)-(4-methanesulfonyl-phenyl)-methyl]-lH-pyrrolo[2,3-b]pyridine (30 mg).

'H NMR (400 MHz, CDCl₃): δ 2.94 (s, 3H), 6.51 (s, 1H), 6.61-6.67 (m, 1H), 6.80-6.86 (m, 1H), 6.92-6.98 (m, 1H), 7.24 (dd, J = 4.9 & 8.1 Hz, 1H), 7.80 (d, J = 8.3 Hz, 2H), 7.88 (d, J = 8.3 Hz, 2H), 8.05 (dd, J = 8.1, 1.2 Hz, 1H), 8.39 (dd, J = 4.9, 1.2 Hz, 1H). MS (EI) m/z: 416.1 (M+1).

Example DI: 2-[(4-Cyclopropanesulfonyl-phenyl)-2-(2,4-difluoro-phenyl)-ethyl]-lH-pyrrolo[2,3-b]pyridine:

![Diagram](image)
Step I: Synthesis of 2-(4-Cyclopropanesulfonyl-phenyl)-3-(2,4-difluoro-phenyl)-propionic acid ethyl ester:

(4-Cyclopropanesulfonyl-phenyl)-acetic acid ethyl ester 1.0 g (3.73 mMol; synthesized as per ref: WO200947798) was taken in 10 ml of anhydrous THF under an inert atmosphere and kept stirring at 0 oC. To it was added LiHMDS 0.635 g (3.8 mMol, 3.8 ml 1M solution in THF) in dropwise fashion and continued to stir for half an hour. To above reaction mixture 2,4-difluorobenzyl bromide 0.771 g (3.726 mMol) was charged in dropwise fashion. The reaction was allowed to come to room temperature. Completion of reaction was confirmed by TLC. Reaction mixture was quenched with saturated ammonium chloride and diluted with ethyl acetate. The organic layer was separated and washed with brine and dried over anhydrous sodium sulphate. The solvent was removed under reduced pressure and the residue was purified by column chromatography to get an oily product (1.177 gm).

1H NMR- (400 MHz, CDC13), δ 1.01 - 1.06 (m, 2H), 1.15 (t, J = 7.0 Hz, 3H), 1.33-1.37 (m, 2H), 2.43-2.47 (m, 1H), 3.06 (dd, J = 13.6, 7.0 Hz, 1H), 3.37 (dd, J = 13.6, 8.6 Hz, 1H), 3.96 (app.t, J = 8.4, 7.2 Hz, 1H), 4.10 (q, J = 7.0 Hz, 2H), 6.71-6.79 (m, 2H), 7.02 (dd, J = 15.2, 8.4 Hz, 1H), 7.48 (d, J = 8.4 Hz, 2H), 7.4 (d, J = 8.8 Hz, 2H).

Mass = 412.2(M+1)

Step II: 2-[l-(4-Cyclopropanesulfonyl-phenyl)-2-(2,4-difluoro-phenyl)-ethyl]-lH-pyrrolo[2,3-b]pyridine:

(3-Methyl-pyridin-2-yl)-carbamic acid tert-butyl ester 0.3 g (1.44 mMol) was taken in 5 ml of dry THF and stirred in an inert atmosphere at -10 oC. To it was added n-BuLi 0.276 g (4.321 mMol, ~3 ml 1.6 M solution in hexane) in dropwise fashion and continued to stir at same temperature for 1 hr. To above reaction mixture the solution of 2-(4-cyclopropanesulfonyl-phenyl)-3-(2,4-difluoro-phenyl)-propionic acid ethyl ester 0.511 g (1.295 mMol), dissolved in 5 ml of dry THF was added slowly at 0 oC and then allowed the reaction mixture to come to room temperature and continued to stir for overnight. Reaction was quenched by saturated ammonium chloride solution and extracted two times with ethyl acetate. The combined organic layer was washed with brine and dried over anhydrous sodium sulphate. Solvent was removed under reduced pressure and the residue was dissolved in 5 ml of trifluoroacetic acid and stirred at room temperature for 8 hours. Trifluoroacetic acid was evaporated and the residue was neutralized with saturated bicarbonate. The aqueous layer was extracted two times with ethyl acetate. The combined organic layer was washed with brine and
dried over anhydrous sodium sulphate. Solvent was removed reduced pressure and the residue was purified by LCMS to get the pure product.

1H NMR- (400 MHz, DMSO-d6), 8 0.98-1.02 (m, 2H), 1.05-1.07 (m, 2H), 2.76-2.80 (m, 1H), 3.39 (dd, J = 13.8, 8.5 Hz, 1H), 3.59 (dd, J = 13.8, 8.5 Hz, 1H), 4.60 (t, J = 8 Hz, 1H), 6.45 (s, 1H), 6.93(dt, J = 8.8, 2.4 Hz, 1H), 6.99 (dd, J = 7.9, 4.8 Hz, 1H), 7.12 (dt, J = 8.8, 2.4 Hz, 1H), 7.30 (dd, J = 15.6, 8.4 Hz, 1H), 7.60 (d, J = 8.4 Hz, 2H), 7.80 (d, J = 8.2 Hz, 2H), 7.84 (d, J = 7.9 Hz, 1H), 8.11 (dd, J = 4.6, 1.3 Hz, 1H), 11.7 (s, 1H).

MS (EI) m/z: (M + 1) = 439.1

Table 2: Example D2 to D5 were prepared following procedure used for Example-D1 from appropriate starting materials.

<table>
<thead>
<tr>
<th>Sl.No.</th>
<th>Structure</th>
<th>MS (EI) m/z</th>
<th>IUPAC Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>D2</td>
<td><img src="image" alt="Structure D2" /></td>
<td>421.2 (M + 1)</td>
<td>2-[1-(4-Cyclopropanesulfonyl-phenyl)-2-(3-fluorophenyl)-ethyl]-1H-pyrrolo[2,3-b]pyridine</td>
</tr>
<tr>
<td>D3</td>
<td><img src="image" alt="Structure D3" /></td>
<td>409.1(M + 1)</td>
<td>2-[1-(4-Cyclopropanesulfonyl-phenyl)-2-thiophen-3-yl-ethyl]-1H-pyrrolo[2,3-b]pyridine</td>
</tr>
<tr>
<td>D4</td>
<td><img src="image" alt="Structure D4" /></td>
<td>404.1(M + 1)</td>
<td>2-[1-(4-Cyclopropanesulfonyl-phenyl)-2-pyridin-3-yl-ethyl]-1H-pyrrolo[2,3-b]pyridine</td>
</tr>
<tr>
<td>D5</td>
<td><img src="image" alt="Structure D5" /></td>
<td>404.2(M + 1)</td>
<td>2-[1-(4-Cyclopropanesulfonyl-phenyl)-2-pyridin-4-yl-ethyl]-1H-pyrrolo[2,3-b]pyridine</td>
</tr>
</tbody>
</table>
Example E1 and E2 are Chirally Pure Compounds

Analytical methods used for chiral separation of A2:
Column-OJ-RH (150X4.6)mm, 5µm, Flow:1ml min⁻¹, M. Phase: Methanol, Column Temp. 40°C; RT: 3.73/4.89min; Detection wavelength: 224 nm.

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Structure</th>
<th>MS (EI) m/z</th>
<th>IUPAC Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>E1</td>
<td><img src="structure1.png" alt="Structure" /></td>
<td>413.1 (M + 1)</td>
<td>2-[(4-Cyclopropanesulfonyl-phenyl)-(tetrahydro-pyran-4-yloxy)-methyl]-1H-pyrrolo[2,3-b]pyridine.</td>
</tr>
<tr>
<td>E2</td>
<td><img src="structure2.png" alt="Structure" /></td>
<td>413.1 (M + 1)</td>
<td>2-[(4-Cyclopropanesulfonyl-phenyl)-(tetrahydro-pyran-4-yloxy)-methyl]-1H-pyrrolo[2,3-b]pyridine.</td>
</tr>
</tbody>
</table>

The below list of examples, but not to be limited to these, can also be synthesized following the general synthesis described above:

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>IUPAC Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>6-[Cyclopentyloxy-(4-cyclopropanesulfonyl-phenyl)-methyl]-5H-pyrrolo[2,3-b]pyrazine</td>
</tr>
<tr>
<td>2.</td>
<td>2-[2-Cyclohexyl-1-(4-cyclopropanesulfonyl-phenyl)-ethyl]-6-methoxy-1H-pyrrolo[2,3-b]pyridine</td>
</tr>
<tr>
<td>3.</td>
<td>2-[2-Cyclohexyl-1-(4-methanesulfonyl-phenyl)-ethyl]-1H-pyrrolo[2,3-b]pyridine-5-carboxylic acid</td>
</tr>
<tr>
<td>4.</td>
<td>6-Chloro-2-[1-(4-cyclopentanesulfonyl-phenyl)-2-cyclopentyl-ethyl]-1H-pyrrolo[2,3-b]pyridine</td>
</tr>
<tr>
<td>5.</td>
<td>5-Chloro-2-[1-(4-cyclopropanesulfonyl-phenyl)-2-(tetrahydro-pyran-4-yl)-ethyl]-1H-pyrrolo[2,3-b]pyridine</td>
</tr>
<tr>
<td>6.</td>
<td>6-[2-Cyclohexyl-1-(4-cyclopentanesulfonyl-phenyl)-ethyl]-7H-pyrrolo[2,3-d]pyrimidine</td>
</tr>
<tr>
<td>7.</td>
<td>6-[4-(Cyclopropanesulfonyl-phenyl)-(tetrahydro-pyran-4-yloxy)-methyl]-7H-pyrrolo[2,3-b]pyridine</td>
</tr>
<tr>
<td></td>
<td>Chemical Structure</td>
</tr>
<tr>
<td>---</td>
<td>----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>8</td>
<td>3-Chloro-6-[2-cyclohexyl-1-(4-cyclopropanesulfonyl-phenyl)-ethyl]-5H-pyrrolo[2,3-b]pyrazine</td>
</tr>
<tr>
<td>9</td>
<td>6-[1-(4-Methanesulfonfonyl-phenyl)-2-(tetrahydro-pyran-4-yl)-ethyl]-3-methoxy-5H-pyrrolo[2,3-b]pyrazine</td>
</tr>
<tr>
<td>10</td>
<td>2-[Cyclopentyl-oxy-(4-cyclopropanesulfonyl-phenyl)-methyl]-1H-imidazo[4,5-b]pyrazine</td>
</tr>
<tr>
<td>11</td>
<td>2-[2-Cyclohexyl-1-(4-cyclopropanesulfonyl-phenyl)-ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yloxy]-acetic acid</td>
</tr>
<tr>
<td>12</td>
<td>2-[2-Cyclohexyl-1-(4-(pyrrolidine-1-sulfonyl)-phenyl)-ethyl]-1H-pyrrolo[2,3-b]pyridine-5-carboxylic acid</td>
</tr>
<tr>
<td>13</td>
<td>5-Chloro-2-[1-(4-cyclopentanesulfonyl-phenyl)-2-cyclopentyl-ethyl]-3H-imidazo[4,5-b]pyridine</td>
</tr>
<tr>
<td>14</td>
<td>4-Chloro-2-[1-(4-cyclopropanesulfonyl-phenyl)-2-(tetrahydro-pyran-4-yl)-ethyl]-1H-pyrrolo[2,3-b]pyridine</td>
</tr>
<tr>
<td>15</td>
<td>6-[2-Cyclohexyl-1-(4-cyclopentanesulfonyl-phenyl)-ethyl]-7H-pyrrolo[2,3-d]pyrimidin-2-yloxy]-acetic acid</td>
</tr>
<tr>
<td>16</td>
<td>6-[4-(4-Cyclopropanesulfonyl-phenyl)-(tetrahydro-pyran-4-yl-oxy)-methyl]-7H-pyrrolo[2,3-c]pyridazine</td>
</tr>
<tr>
<td>17</td>
<td>3-Chloro-6-[2-(2,4-difluoro-phenoxy)-methyl]-5H-pyrrolo[2,3-b]pyrazine</td>
</tr>
<tr>
<td>18</td>
<td>6-[4-(4-Chloro-phenoxy)-(4-methanesulfonfonyl-phenyl)-methyl]-3-methoxy-5H-pyrrolo[2,3-b]pyrazine</td>
</tr>
<tr>
<td>19</td>
<td>6-{Cyclopentyl-oxy-[4-(piperidine-1-sulfonyl)-phenyl]-methyl]-5H-pyrrolo[2,3-b]pyrazine</td>
</tr>
<tr>
<td>20</td>
<td>4-{2-[2-Cyclohexyl-1-(4-cyclopropanesulfonyl-phenyl)-ethyl]-1H-pyrrolo[2,3-b]pyridin-5-yloxy]-benzoic acid</td>
</tr>
<tr>
<td>21</td>
<td>2-[Cyclopentyl-oxy-(4-methanesulfonfonyl-phenyl)-methyl]-1H-pyrrolo[2,3-b]pyridine-5-carboxylic acid</td>
</tr>
<tr>
<td>22</td>
<td>2-[4-Chloro-phenyl-cyclohexyl-oxy-methyl]-1H-pyrrolo[2,3-b]pyridine-5-carboxylic acid</td>
</tr>
<tr>
<td>23</td>
<td>6-Chloro-2-[1-(4-cyclopentanesulfonyl-phenyl)-2-(4-methoxy-phenyl)-ethyl]-1H-pyrrolo[2,3-b]pyridine</td>
</tr>
<tr>
<td>24</td>
<td>2-[1-(4-Cyclopropanesulfonyl-phenyl)-2-(tetrahydro-pyran-4-yl)-ethyl]-3H-imidazo[4,5-b]pyridine</td>
</tr>
<tr>
<td>25.</td>
<td>6-[[4-(Azetidine-1-sulfonyl)-phenyl]-2-cyclohexyl-ethyl]-7H-pyrrolo[2,3-d]pyrimidine</td>
</tr>
<tr>
<td>26.</td>
<td>4-Chloro-6-[(4-cyclopropanesulfonyl-phenyl)-p-tolyloxy-methyl]-7H-pyrrolo[2,3-c]pyridazine</td>
</tr>
<tr>
<td>27.</td>
<td>Azetidin-1-yl-[[5-[(3-chloro-5H-pyrrolo[2,3-b]pyrazin-6-yl)-(4-cyclopropanesulfonyl-phenyl)-methoxy]pyrazin-2-yl]-methanone</td>
</tr>
<tr>
<td>28.</td>
<td>3-Isopropoxy-6-[(4-methanesulfonyl-phenyl)-2-(tetrahydro-pyran-4-yl)-ethyl]-5H-pyrrolo[2,3-b]pyrazine</td>
</tr>
<tr>
<td>29.</td>
<td>2-[(4-Cyclopropanesulfonyl-phenyl)-(tetrahydro-furan-3-yloxy)-methyl]-1H-imidazo[4,5-b]pyrazine</td>
</tr>
<tr>
<td>30.</td>
<td>2-[[4-(Cyclopropanesulfonyl-phenyl)-(pyridin-3-yloxy)-methyl]-acetic acid</td>
</tr>
<tr>
<td>31.</td>
<td>2-[[2-Piperidin-4-yl1][4-(pyrrolidine-1-sulfonyl)-phenyl]-ethyl]-1H-pyrrolo[2,3-b]pyridine-5-carboxylic acid</td>
</tr>
<tr>
<td>32.</td>
<td>6-Chloro-2-[[2-cyclopentyl-1-[4-(tetrahydro-furan-3-sulfonyl)-phenyl]-ethyl]-1H-pyrrolo[2,3-b]pyridine</td>
</tr>
<tr>
<td>33.</td>
<td>2-[1-(4-Cyclopropanesulfonyl-phenyl)-2-(tetrahydro-pyran-4-y-b-ethyl]-4-ethoxy-1H-pyrrolo[2,3-b]pyridine</td>
</tr>
<tr>
<td>34.</td>
<td>6-[1-(4-Methanesulfonyl-phenyl)-2-(tetrahydro-pyran-4-y)-ethyl]-7H-pyrrolo[2,3-d]pyrimidin-2-yl]-acetic acid</td>
</tr>
<tr>
<td>35.</td>
<td>2-[[4-(Piperidine-4-sulfonyl)-phenyl)-(tetrahydro-pyran-4-yloxy)-methyl]-1H-pyrrolo[2,3-b]pyridine</td>
</tr>
<tr>
<td>36.</td>
<td>3-Chloro-6-[(5-chloro-pyridin-3-yloxy)-(4-cyclopropanesulfonyl-phenyl)-methyl]-5H-pyrrolo[2,3-b]pyrazine</td>
</tr>
<tr>
<td>37.</td>
<td>6-[6-Chloro-pyridin-3-yloxy)-(4-methanesulfonyl-phenyl)-methyl]-3-nethoxy-5H-pyrrolo[2,3-b]pyrazine</td>
</tr>
<tr>
<td>38.</td>
<td>2-[1-(4-Cyclopropanesulfonyl-phenyl)-2-(tetrahydro-pyran-4-y)-cyclopropyl]-1H-pyrrolo[2,3-b]pyridine</td>
</tr>
<tr>
<td>39.</td>
<td>Azetidin-1-yl-[[4-1-(6-chloro-1H-pyrrolo[2,3-b]pyridin-2-yl)-2-cyclopentyl-ethyl]-phenyl]-methanone</td>
</tr>
<tr>
<td>40.</td>
<td>2-[(4-PhenoxyrnethyI-phenyl)-(tetrahydro-pyran-4-yloxy)-methyl]-1H-pyrrolo[2,3-b]pyridine</td>
</tr>
</tbody>
</table>
| 41. | 2-[[1-(4-Isoproxy-phenyl)-2-piperidin-4-yl-ethyl]-1H-pyrrolo[2,3-b]pyridine-5-
Glucokinase Activity Assay:

The glucokinase (GK) assay is a coupled enzymatic assay. GK catalyzes the first step of glycolysis, the conversion of glucose to glucose-6-phosphate (G6P) in the presence of ATP. G6P in turn is converted by glucose-6-phosphate dehydrogenase (G6PD) to 6-phosphogluconate, a process that requires NAD, resulting in NADH formation. Since the GK-catalyzed step is the rate-limiting step of this coupled enzymatic process, the rate of accumulation of 6-phosphogluconate and NADH is directly proportional to the rate of glucose phosphorylation by GK. The rate of the GK-catalyzed reaction can therefore be measured by monitoring the increase in NADH absorbance at 340 nm.

The assay is carried out according to the protocol outlined in Hariharan et al (1997), Diabetes 46: 11-16. Briefly, the test compounds are incubated in a reaction mix containing 25 mM HEPES (pH 7.2), 10 mM MgCl₂, 100 mM KCl, 5 mM ATP, 2 mM DTT, 0.5 mM NAD, 1 U/ml Leuconostoc mesenteroides G6PD, 0.3 U/ml of purified human recombinant GK, and different concentrations of glucose. Enzymatic activity is calculated from the initial reaction velocity, measured from the change in NADH absorbance as a function of time.

Compounds described in formula (I), in concentration ranges from 1.0 nM to 500 µM, are tested in the purified human recombinant glucokinase assay described above. A compound is considered to be a glucokinase activator if it, in its testable range of concentrations, yields a higher
rate of glucose phosphorylation than in its absence at a particular glucose concentration, for example at 5 mM glucose.

**Characterization of glucokinase activators from the in vitro glucokinase assay:**

Compounds of general formula (I) are tested in the in vitro GK enzymatic assay to monitor dose-dependent effect on glucokinase activation (in kinetic mode), as described above, at various glucose concentrations. The $S_{0.5}$ of glucokinase for glucose at different concentration of each compound of interest is calculated from the following modified version of the Michaelis-Menten equation. $V = V_{max} \ [S] \left( \frac{S_{0.5}^n + [S]^n}{S_{0.5}^n + [S]^n} \right)$, where $[S]$ is the glucose concentration and $n$ is the Hill coefficient (taken as 1.7 to account for the sigmoidal kinetics of glucokinase with respect to glucose). The $S_{0.5}$ is plotted against the log of the compound concentration. The change in the $S_{0.5}$ of glucokinase ($\Delta S_{0.5}$) for glucose is calculated by subtracting the $S_{0.5}$ at each concentration of the compound from the $S_{0.5}$ in the vehicle control. The $\Delta S_{0.5}$ is then normalized to a percent scale, where the $S_{0.5}$ in the vehicle control is set to 0% and 0 mM glucose is set to 100%. The % $\Delta S_{0.5}$ is then plotted against the log of the compound concentration. The EC$_{50}$ and E$_{max}$ of % change in $S_{0.5}$ is obtained from the sigmoidal fit of the data. Detailed protocol has been described in our copending application no. 409/CHE/2007 which is incorporated herein by reference. Characterization data of some representative glucokinase activators of the present disclosure, which are illustrative but not limiting, are given in table I below.

The glucokinase activation data of some representative compounds of the present disclosure, which are illustrative but not to be construed as limiting the scope or spirit of the disclosure, are given in the table I.

**Table I: EC$_{50}$ of GK activators**

<table>
<thead>
<tr>
<th>Ex-No.</th>
<th>EC$_{50}$ (µM) at 5 mM Glucose</th>
<th>EC$<em>{50}$ (µM) for % $\Delta S</em>{0.5}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1</td>
<td>0.055</td>
<td>0.047</td>
</tr>
<tr>
<td>A2</td>
<td>0.22</td>
<td>0.16</td>
</tr>
<tr>
<td>A5</td>
<td>0.35</td>
<td>0.15</td>
</tr>
<tr>
<td>A7</td>
<td>0.18</td>
<td>0.1</td>
</tr>
<tr>
<td>A2</td>
<td>0.22</td>
<td>0.16</td>
</tr>
<tr>
<td>B1</td>
<td>0.32</td>
<td>0.28</td>
</tr>
<tr>
<td>E1</td>
<td>0.08</td>
<td>0.033</td>
</tr>
<tr>
<td>E2</td>
<td>0.436</td>
<td>0.270</td>
</tr>
</tbody>
</table>
We claim:

1. A compound of formula (I)

or its stereoisomers, tautomers, prodrugs, pharmaceutically acceptable salts, polymorphs, solvates and formulations wherein,

ring A and ring B are independently selected from cycloalkyl, aryl, heterocyclyl or heteroaryl;

ring A and ring B is unsubstituted or substituted with up to 4 substituents independently selected from alkyl, alkenyl, alkynyl, halogen, mono, di, tri or perhaloalkyl, nitrile, nitro, oxo, -NR'R', -OR', -S(0)R', -S(0)pNR'R', -NR'S(0)R', -NR'C(0)R', -OS(0)pR', -NR'C(0)OR', -(CR'R')C(0)OR, -(CR'R')CO(0)R', wherein n = 0-4 and p = 0-2;

ring C is a heterocyclyl or a heteroaryl each with at least one N-atom;

X is selected from (CHR')nNR', O or S(0)p wherein n = 1-2 and p = 0-2;

Y is CR or N; wherein R is selected from hydrogen, halogen, alkyl, fluoroalkyl, OR' or aryl;

R1 is selected from hydrogen, alkyl, halogen, haloalkyl or perhaloalkyl;

R2 is selected from hydrogen or alkyl; or

R1 and R2 taken together form a monocyclic or a bicyclic ring system which is saturated or partially unsaturated and optionally have additional heteroatoms selected from O, N or S;

R3 and R4 are independently selected from a group consisting of hydrogen, halogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, arylalkyl. heteroaryl, heteroarylalkyl, mono, di, tri or perhaloalkyl, nitrile, nitro, -NR'R', -OR', -S(0)pR', -S(0)pNR'R', -NR'S(0)pR', -NR'C(0)R', -OS(0)pR', -NR'C(0)OR', -(CR'R')C(0)OR', -(CR'R')CO(0)R', -(CR'R')S(0)pNR'R', -(CR'R')N(S(0)pNR')R', -(CR'R')S(0)pNR'R', C(R'R')N(R')R' and C(R'R')CO(R'), wherein
each of $R^3$ and $R^4$ is unsubstituted or substituted with one or more substituents selected from halo, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, heterocycle, alkylsulphonyl, oxo, nitro, cyano, -COOR, -C(0)NR $^5$R$^6$, -OR, -SR or -NR $^5$R$^6$; wherein $n = 0$-$4$ and $p = 0$-$2$; or

$R^3$ and $R^4$ taken together form a monocyclic or a bicyclic ring system which is saturated or partially unsaturated and optionally have additional heteroatoms selected from O, N or S; said ring system is unsubstituted or substituted with 1 to 4 substituents independently selected from halo, alkyl, alkenyl, alkynyl, nito, cyano, -OR, -SR, -NR$^5$R$^6$, oxo, alkylsulfonyl, -COOR, -C(0)NR $^5$R$^6$, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

$R^5$ and $R^6$ are independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl and heterocyclylalkyl, or

$R^5$ and $R^6$ taken together form a monocyclic or a bicyclic ring system which is saturated or partially unsaturated and optionally have additional heteroatoms selected from O, N or S; said ring system is unsubstituted or substituted with 1 to 4 substituents independently selected from halo, alkyl, alkenyl, alkynyl, nito, cyano, -OR, -SR, -NR$^5$R$^6$, oxo, alkylsulfonyl, -COOR, -C(0)NR $^5$R$^6$, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl or heteroarylalkyl;

$R^7$ and $R^8$ are independently selected from the group consisting of hydrogen, fluorine, OR$^5$, alkyl, and perfluoroalkyl; or

$R^7$ and $R^8$ taken together form a monocyclic or a bicyclic ring system which is saturated or partially unsaturated and optionally have additional heteroatoms selected from O, N or S; said ring system is unsubstituted or substituted with 1 to 4 substituents independently selected from halo, alkyl, alkenyl, alkynyl, nito, cyano, oxo, -OR, -SR, -NR$^5$R$^6$, alkylsulfonyl, -COOR, -C(0)NR $^5$R$^6$, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl or heteroarylalkyl.
2. The compound as claimed in claim 1, or its stereoisomers, tautomers, prodrugs, pharmaceutically acceptable salts, polymorphs, solvates and formulations thereof, wherein ring A and ring B are independently selected from C₃-C₁₀ cycloalkyl, aryl, heterocyclyl or heteroaryl;

ring A and ring B are unsubstituted or substituted with up to 4 substituents independently selected from alkyl, alkenyl, alkylnyl, halogen, mono, di, tri or perhaloalkyl, nitrile, nitro, oxo, -NR₄R⁵, -OR⁴, -S(0)ₚR⁴, -S(0)ₚNR₄R⁵, -NR₄S(0)ₚR⁵, -NR₄C(0)R⁵, -OS(0)ₚR⁵, -NR₄C(0)OR₅, -(CR₄R⁷)ₙC(0)OR₄, - (CR₄R⁷)ₙC(0)NR₄R⁵, -(CR₄R⁷)ₙC(0)R⁴, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl or heteroarylalkyl;

wherein n = 0-4 and p = 0-2;

ring C is a heterocyclyl or a heteroaryl each with at least one N-atom;

X is selected from (CHR₃)ₙ, NR₂, O or S(0)ₚ wherein n = 1-2 and p = 0-2;

Y is CR or N; wherein R is selected from hydrogen, halogen, alkyl or fluoroalkyl;

R¹ is selected from hydrogen, alkyl, halogen, haloalkyl or perhaloalkyl;

R² is selected from hydrogen or alkyl; or

R¹ and R² taken together form a monocyclic or a bicyclic ring system which is saturated or partially unsaturated and optionally have additional heteroatoms selected from O, N or S;

R³ and R⁴ are independently selected from the group consisting of hydrogen, halogen, alkyl, alkenyl, alkylnyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, mono, di, tri or perhaloalkyl, nitrile, nitro, -NR₅, -NR₅R⁶, -OR₅, -S(0)ₚR⁵, -S(0)ₚNR₅R⁶, -NR₅S(0)ₚR⁶, -NR₅C(0)R⁶, -OS(0)ₚR⁶, -NR₅C(0)OR₅, -(CR₅R⁷)ₙC(0)OR₅, -(CR₅R⁷)ₙC(0)NR₅R⁶, -(CR₅R⁷)ₙC(0)R⁶, -(CR₅R⁷)ₙN(R₅)C(0)R⁵, -(CR₅R⁷)ₙOR₅, C(R₅R⁷)ₙNR₅R⁶ and C(R₅R⁷)ₙCO(R₅), wherein each of R³ and R⁴ is unsubstituted or substituted with one or more substituents selected from halo, alkyl, alkenyl, alkylnyl, cycloalkyl, aryl, heteroaryl, heterocycle, alkylsulphonyl, oxo, nitro, cyano, -COOR₅, -(CO)(0)NR₅R⁶, -OR₅, -SR₅ or -NR₅R⁶; wherein n = 0-4 and p = 0-2;

R⁵ and R⁶ are independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkylnyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl and heterocycloalkyl;

R⁷ and R⁸ are independently selected from the group consisting of hydrogen, fluorine, OR⁵, alkyl, and perfluoroalkyl.
3. The compound as claimed in claim 1, or its stereoisomers, tautomers, prodrugs, pharmaceutically acceptable salts, polymorphs, solvates and formulations wherein,
ring A and ring B are independently selected from C<sub>3</sub>-C<sub>10</sub> cycloalkyl, aryl, heterocyclyl or heteroaryl;
ring A and ring B are unsubstituted or substituted with up to 4 substituents independently selected from alkyl, halogen, mono, di, tri or perhaloalkyl, nitrile, -NR<sub>2</sub>, -(CR<sub>2</sub>)<sub>2</sub>OR<sub>4</sub>,
-S(0)<sub>n</sub>R<sub>5</sub>, -(CR<sub>2</sub>)<sub>n</sub>OR<sub>4</sub>, -(CR<sub>2</sub>)<sub>n</sub>C(0)OR<sub>4</sub>, -(CR<sub>2</sub>)<sub>n</sub>C(0)NR<sub>4</sub>, -C(0)R<sub>4</sub>,
cycloalkyl, heterocyclyl, aryl or heteroaryl; wherein n = 0-4 and p = 0-2;
ring C is a heterocyclyl or a heteroaryl each with at least one N-atom;
X is selected from (CHR<sub>3</sub>)<sub>n</sub>, NR<sub>2</sub>, O or S(0)<sub>n</sub> where n = 1-2 and p = 0-2;
Y is CR; R is selected from hydrogen, halogen, alkyl or fluoroalkyl;
R<sup>1</sup> is selected from hydrogen, alkyl, halogen, haloalkyl or perhaloalkyl;
R<sup>2</sup> is selected from hydrogen or alkyl; or
R<sup>1</sup> and R<sup>2</sup> taken together form a monocyclic or a bicyclic ring system which is saturated or partially unsaturated and optionally have additional heteroatoms selected from O, N or S;
R<sup>3</sup> and R<sup>4</sup> are independently selected from a group consisting of hydrogen, halogen, alkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, mono, di, tri or perhaloalkyl, nitrile, -S(0)<sub>n</sub>R<sub>5</sub>, -(CR<sup>r</sup>)<sub>n</sub>R<sub>6</sub>, -(CR<sup>r</sup>)<sub>n</sub>C(0)OR<sub>4</sub>, -(CR<sup>r</sup>)<sub>n</sub>NR<sub>4</sub>R<sub>6</sub>, -(CR<sup>r</sup>)<sub>n</sub>OR<sub>4</sub>, C(R<sup>r</sup>)<sub>n</sub>NR<sub>4</sub>R<sub>6</sub> and C(R<sup>r</sup>)<sub>n</sub>CO(R<sup>r</sup>), wherein each of R<sup>3</sup> and R<sup>4</sup> is unsubstituted or substituted with one or more substituents selected from halo, alkyl, cycloalkyl, aryl, heteroaryl, heterocycle, alkylsulphonyl, oxo, nitro, cyano, -COOR<sub>n</sub>, -C(0)NR<sub>r</sub>-OR<sub>r</sub>, -SR<sub>r</sub> or -NR<sub>r</sub>-R<sub>r</sub>; wherein n = 0-4 and p = 0-2;
R<sup>5</sup> and R<sup>6</sup> are independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl or heterocyclyl;
R<sup>7</sup> and R<sup>8</sup> are independently selected from the group consisting of hydrogen, fluorine, OR<sub>r</sub>, alkyl, and perfluoroalkyl.

4. The compound as claimed in claim 1, or its stereoisomers, tautomers, prodrugs, pharmaceutically acceptable salts, polymorphs, solvates and formulations thereof wherein,
ring A and ring B are independently selected from C<sub>3</sub>-C<sub>10</sub> cycloalkyl, aryl, heterocyclyl or heteroaryl;
ring A and ring B are unsubstituted or substituted with up to 4 substituents independently selected from alkyl, halogen, mono, di, tri or perhaloalkyl. nitrile, -NR<sub>2</sub>, -(CR<sub>2</sub>)<sub>n</sub>OR<sub>4</sub>, -
S(0) R 4 , -S(0) R 4 R 5 , -(CR R 7 ) n C(0) OR 4 , -(CR R 7 ) n C(0) NR 5 , -(CR R 7 ) n C(0) R 4 ,
cycloalkyl, heterocyclyl, aryl or heteroaryl; wherein n = 0-4 and p = 0-2;
ring C is a heterocyclyl or a heteroaryl each with at least one N-atom;
X is selected from (CHR) n NR 2 , O or S(0) R wherein n = 1-2 and p = 0-2;
Y is NR. R is selected from hydrogen, halogen, alkyl or fluoroalkyl;
R 1 is selected from hydrogen, alkyl, halogen, haloalkyl or perhaloalkyl:
R 2 is selected from hydrogen or alkyl; or
R 1 and R 2 taken together form a monocyclic or a bicyclic ring system which is saturated or
partially unsaturated and optionally have additional heteroatoms selected from O, N or S;
R 3 and R 4 are independently selected from the group consisting of hydrogen, halogen, alkyl,
cycloalkyl, heterocyclyl, aryl, heteroaryl, mono, di, tri or perhaloalkyl, nitrile, -S(0) R 4 , -
S(0) R 4 R 5 , -(CR R 7 ) n C(0) OR 4 , -(CR R 7 ) n C(0) NR 5 , -(CR R 7 ) n C(0) R 4 ,
-C(R R 7 ) n C(0) OR 4 , -(CR R 7 ) n C(0) NR 5 , -(CR R 7 ) n C(0) R 4 , -(CR R 7 ) n C(0) OR 4 ,
-(CR R 7 ) n C(0) NR 5 , -(CR R 7 ) n C(0) R 4 , -(CR R 7 ) n C(0) OR 4 , -(CR R 7 ) n C(0) NR 5 , -(CR R 7 ) n C(0) R 4 ,
wherein each of R 3 and R 4 is unsubstituted or substituted with one or more substituents selected from halo, alkyl,
cycloalkyl, aryl, heteroaryl, heterocycle, alkylsulphonyl, oxo, nitro, cyano, -COOR 5 , -
C(0)OR 5 , -OR 5 , -SR 5 or -NR 5 R 6 ; wherein n = 0-4 and p = 0-2;
R 3 and R 5 are independently selected from the group consisting of hydrogen, alkyl,
alkenyl, alkenyl, aryl, heteroaryl, cycloalkyl and heterocyclyl;
R 7 and R 8 are independently selected from the group consisting of hydrogen,
fluorine, OR 5 , alkyl, and perfluoroalkyl.

5. A compound as claimed in claim 1 which is
2-[2-Cyclopentyl-(4-cyclopropanesulfonyl-phenyl)-ethyl]-1H-pyrrolo[2,3-b]pyridine and its
(+)- and (-)- enantiomers,
2-[4-(4-Cyclopropanesulfonyl-phenyl)-(tetrahydro-pyran-4-yloxy)-methyl]-1H-pyrrolo[2,3-
b]pyridine and its (+)- and (-)- enantiomers,
2-[Cyclopentylloxy-(4-cyclopropanesulfonyl-phenyl)-methyl]-1 H-pyrrolo[2,3-b]pyridine and its
(+)- and (-)- enantiomers,
2-[2-Cyclohexyl-(4-cyclopropanesulfonyl-phenyl)-ethyl]-1H-pyrrolo[2,3-b]pyridine and its (+)
and (-)- enantiomers,
2-[2-Cyclohexyl-(4-methanesulfonyl-phenyl)-ethyl]-1H-pyrrolo[2,3-b]pyridine and its (+)
and (-)- enantiomers,
2-[1-(4-Cyclopentanesulfonyl-phenyl)-2-cyclopentyl-ethyl]-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers,
2-[1-(4-Cyclopropanesulfonyl-phenyl)-2-(tetrahydro-pyran-4-yl)-ethyl]-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers,
2-[2-Cyclohexyl-1-(4-cyclopentanesulfonyl-phenyl)-ethyl]-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers,
2-[2-Cyclohexyl-1-(4-methanesulfonyl-phenyl)-ethyl]-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers,
6-[2-Cyclohexyl-1-(4-cyclopentanesulfonyl-phenyl)-ethyl]-5H-pyrrolo[2,3-b]pyrazine and its (+) and (-) enantiomers,
6-[1-(4-Methanesulfonyl-phenyl)-2-(tetrahydro-pyran-4-yl)-ethyl]-5H-pyrrolo[2,3-b]pyrazine and its (+) and (-) enantiomers,
6-[4-Cyclopropanesulfonyl-phenyl)-(tetrahydro-pyran-4-yloxy)-methyl]-5H-pyrrolo[2,3-b]pyrazine and its (+) and (-) enantiomers,
2-[1-(4-Methanesulfonyl-phenyl)-2-(tetrahydro-pyran-4-yl)-ethyl]-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers,
6-Chloro-2-[2-cyclopentyl-1-(4-methanesulfonyl-phenyl)-ethyl]-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers,
2-[(4-Cyclopropanesulfonyl-phenyl)-[(R)-(tetrahydro-furan-3-yl)oxy]-methyl]-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers,
2-[(2,4-Difluoro-phenoxy)-(4-methanesulfonyl-phenyl)-methyl]-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers,
2-[(4-Chloro-phenoxy)-(4-methanesulfonyl-phenyl)-methyl]-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers,
2-[(2,4-Difluoro-phenoxy)-(4-methanesulfonyl-phenyl)-methyl]-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers,
2-[1-(4-Cyclopropanesulfonyl-phenyl)-2-(2,4-difluoro-phenyl)-ethyl]-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers,
2-[1-(4-Cyclopropanesulfonyl-phenyl)-2-pyridin-3-yl-ethyl]-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers,
2-[1-(4-Cyclopropanesulfonyl-phenyl)-2-pyridin-4-yl-ethyl]-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers,
6-[Cyclopentyloxy-(4-cyclopropanesulfonyl-phenyl)-methyl]-5H-pyrrolo[2,3-b]pyrazine and its (+) and (-) enantiomers,
2-[2-Cyclohexyl-1-(4-cyclopropanesulfonyl-phenyl)-ethyl]-6-methoxy-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers,
6-Chloro-2-[1-(4-cyclopentanesulfonyl-phenyl)-2-cyclopentyl-ethyl]-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers,
5-Chloro-2-[1-(4-cyclopropanesulfonyl-phenyl)-2-(tetrahydro-pyran-4-yl)-ethyl]-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers,
6-[2-Cyclohexyl-1-(4-cyclopentanesulfonyl-phenyl)-ethyl]-7H-pyrrolo[2,3-d]pyrimidine and its (+) and (-) enantiomers,
6-[4-Cyclopropanesulfonyl-phenyl)-(tetrahydro-pyran-4-yloxy)-methyl]-7H-pyrrolo[2,3-c]pyridazine and its (+) and (-) enantiomers,
3-Chloro-6-[2-cyclohexyl-1-(4-cyclopropanesulfonyl-phenyl)-ethyl]-5H-pyrrolo[2,3-b]pyrazine and its (+) and (-) enantiomers,
6-[1-(4-Methanesulfonyl-phenyl)-2-(tetrahydro-pyran-4-yl)-ethyl]-3-methoxy-5H-pyrrolo[2,3-b]pyrazine and its (+) and (-) enantiomers,
2-[Cyclopentyloxy-(4-cyclopropanesulfonyl-phenyl)-methyl]-1H-imidazo[4,5-b]pyrazine and its (+) and (-) enantiomers,
[2-2-Cyclohexyl-1-(4-cyclopropanesulfonyl-phenyl)-ethyl]-1H-pyrrolo[2,3-b]pyridin-6-yloxy]-acetic acid and its (+) and (-) enantiomers,
2-[2-Cyclohexyl-1-[4-(pyrrolidine-1-sulfonyl)-phenyl]-ethyl]-1H-pyrrolo[2,3-b]pyridine-5-carboxylic acid and its (+) and (-) enantiomers,
5-Chloro-2-[1-(4-cyclopentanesulfonyl-phenyl)-2-cyclopentyl-ethyl]-3H-imidazo[4,5-b]pyrazine and its (+) and (-) enantiomers,
4-Chloro-2-[1-(4-cyclopropanesulfonyl-phenyl)-2-(tetrahydro-pyran-4-yl)-ethyl]-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers,
{6-[2-Cyclohexyl-1-(4-cyclopentanesulfonyl-phenyl)-ethyl]-7H-pyrrolo[2,3-d]pyrimidin-2-yl]-acetic acid and its (+) and (-) enantiomers,
6-[(4-Cyclopentanesulfonyl-phenyl)-(tetrahydro-pyran-4-yloxy)-methyl]-7H-pyrrolo[2,3-c]pyridazine and its (+) and (-) enantiomers,
3-Chloro-6-[(4-cyclopropanesulfonyl-phenyl)-(2,4-difluoro-phenoxy)-methyl]-5H-pyrrolo[2,3-b]pyrazine and its (+) and (-) enantiomers,
6-[(4-Chloro-phenoxy)-(4-methanesulfonyl-phenyl)-methyl]-3-methoxy-5H-pyrrolo[2,3-bjpyrazine and its (+) and (-) enantiomers,
6-[(Cycloptentloxy-[4-(piperidine-1-sulfonyl)-phenyl]-methyl]-5H-pyrrolo[2,3-bjpyrazine and its (+) and (-) enantiomers,
4- {[2-[2-Cyclohexyl-1-(4-cyclopropanesulfonyl-phenyl)-ethyl]-1 H-pyrrolo[2,3-b]pyridin-5-yloxyj-benzoic acid and its (+) and (-) enantiomers,
2-[Cyclohexyloxy-(4-methanesulfonyl-phenyl)-methyl]- 1H-pyrrolo[2,3-b]pyridine-5-carboxylic acid and its (+) and (-) enantiomers,
2-[(4-Chloro-phenyl)cyclohexyloxy-methyl]-1 H-pyrrolo[2,3-b]pyridine-5-carboxylic acid and its (+) and (-) enantiomers,
6-Chloro-2-[1-(4-cyclopentanesulfonyl-phenyl)-2-(4-methoxy-phenyl)-ethyl]- 1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers,
2-[1-(4-Cyclopropanesulfonil-phenyl)-2-(tetrahydro-pyran-4-yl)-ethyl]-3H-imidazo[4,5-b]pyridine and its (+) and (-) enantiomers,
6- [1-[4-(Azetidine-l-sulfonyl)-phenyl]-2-cyclohexyl-ethyl]-7H-pyrrolo[2,3-d]pyrimidine and its (+) and (-) enantiomers,
4-Chloro-6-[(4-cyclopropanesulfonil-phenyl)-p-tolyloxy-methyl]-7H-pyrrolo[2,3-c]pyridazine and its (+) and (-) enantiomers,
Azetidin-1-yl-[5-[(3-chloro-5H-pyrrolo[2,3-b]pyrazin-6-yl)-(4-cyclopropanesulfonyl-phenyl]-methoxy]-pyrazin-2-yl ]-methanone and its (+) and (-) enantiomers,
3-Isopropoxy-6-[1-[4-methanesulfonil-phenyl]-2-(tetrahydro-pyran-4-yl)-ethyl]-5H-pyrrolo[2,3-b]pyrazine and its (+) and (-) enantiomers,
2-[(4-Cyclopropanesulfonil-phenyl)-(tetrahydro-furan-3-yloxy)-methyl]- 1H-imidazo[4,5-b]pyrazine and its (+) and (-) enantiomers,
2-[(4-Cyclopropanesulfonil-phenyl)-(pyridin-3-yloxy)-methyl]- 1H-pyrrolo[2,3-b]pyridin-6-yloxyj-acetic acid and its (+) and (-) enantiomers,
2-{2-Piperidin-4-yl-1-[4-(pyrrolidine-1-sulfonyl)-phenyl]-ethyl}-1H-pyrrolo[2,3-b]pyridine-5-carboxylic acid and its (+) and (-) enantiomers,

6-Chloro-2-[2-cyclopentyl-1-[4-(tetrahydro-furan-3-sulfonyl)-phenyl]-ethyl]-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers.

2-[1-(4-Cyclopropanesulfonyl-phenyl)-2-(tetrahydro-pyran-4-yl)-ethyl]-4-ethoxy-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers,

6-[1-(4-Methanesulfonyl-phenyl)-2-(tetrahydro-pyran-4-yl)-ethyl]-7H-pyrrolo[2,3-d]pyrimidin-2-yl]-acetic acid and its (+) and (-) enantiomers,

2-[4-(Piperidine-4-sulfonyl)-phenyl)-(tetrahydro-pyran-4-yloxy)-methyl]-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers,

3-Chloro-6-[5-chloro-pyridin-3-yloxy)-(4-cyclopropanesulfonyl-phenyl)-methyl]-5H-pyrrolo[2,3-b]pyrazine and its (+) and (-) enantiomers,

6-[(6-Chloro-pyridin-3-yloxy)-(4-methanesulfonyl-phenyl)-methyl]-3-methoxy-5H-pyrrolo[2,3-b]pyrazine and its (+) and (-) enantiomers,

2-[1-(4-Cyclopropanesulfonyl-phenyl)-2-(tetrahydro-pyran-4-yl)-cyclopropyl]-1H-pyrrolo[2,3-b]pyridine,

Azetidin-1-yl-[4-[1-(6-chloro-1H-pyrrolo[2,3-b]pyridin-2-yl)-2-cyclopentyl-ethyl]-phenyl]-methanone and its (+) and (-) enantiomers,

2-[4-Phenoxy-methyl-phenyl)-(tetrahydro-pyran-4-yloxy)-methyl]-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers,

2-[4-Isoproxy-phenyl)-2-piperidin-4-yl-ethyl]-1H-pyrrolo[2,3-b]pyridine-5-carboxylic acid and its (+) and (-) enantiomers,

2-[4-Cyclopropanesulfonyl-phenyl)-(tetrahydro-pyran-4-yloxy)-methyl]-5-phenyl-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers,

2-[4-Cyclopropanesulfonyl-phenyl)-(tetrahydro-pyran-4-yloxy)-methyl]-5-pyrazol-1-yl-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers,

2-[4-Cyclopropanesulfonyl-phenylHtetrahydro-pyran-4-yloxy)-methyl]-5-morpholin-4-yl-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers,

4-[2-[4-Cyclopropanesulfonyl-phenyl)-(tetrahydro-pyran-4-yloxy)-methyl]-1H-pyrrolo[2,3-b]pyridin-5-yloxy]-benzoic acid and its (+) and (-) enantiomers,

2-[4-Cyclopropanesulfonyl-phenyl)-(tetrahydro-pyran-4-yloxy)-methyl]-3-trifluoromethyl-1H-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers and
2-[l-(4-cyclopropylsulfonylphenyl)-l-tetrahydropyran-4-yloxy-ethyl]-lH-pyrrolo[2,3-b]pyridine and its (+) and (-) enantiomers.

6. A compound of formula (I), as claimed in any one of the claims 1 to 5, or its stereoisomers, tautomers, prodrugs, pharmaceutically acceptable salts, polymorphs, solvates and formulations thereof, for treating a disease through Glucokinase activation.

7. A compound of formula (I), as claimed in any one of the claims 1 to 5, or its stereoisomers, tautomers, prodrugs, pharmaceutically acceptable salts, polymorphs, solvates and formulations thereof, for treating a disease through Glucokinase deinhibition.

8. A compound of formula (I), as claimed in any one of the claims 1 to 5, or its stereoisomers, tautomers, prodrugs, pharmaceutically acceptable salts, polymorphs, solvates and formulations thereof, for prophylactic or therapeutic treatment of hyperglycemia or diabetes, particularly type II diabetes.

9. A compound of formula (I), as claimed in any one of the claims 1 to 5, or its stereoisomers, tautomers, prodrugs, pharmaceutically acceptable salts, polymorphs, solvates and formulations thereof, for preventing diabetes, particularly type II diabetes, in a human demonstrating pre-diabetic hyperglycemia or impaired glucose tolerance.

10. A compound of formula (I), as claimed in any one of the claims 1 to 5, or its stereoisomers, tautomers, prodrugs, pharmaceutically acceptable salts, polymorphs, solvates and formulations thereof, for combined treatment or prevention of diabetes and obesity.

11. A compound of formula (I), as claimed in any one of the claims 1 to 5, or its stereoisomers, tautomers, prodrugs, pharmaceutically acceptable salts, polymorphs, solvates and formulations thereof, for treating or preventing obesity.

12. A compound of formula (I), as claimed in any one of the claims 1 to 5, or its stereoisomers, tautomers, prodrugs, pharmaceutically acceptable salts, polymorphs, solvates and formulations thereof, for treatment or prevention of dyslipidemia.
13. A compound of formula (I), as claimed in any one of the claims 1 to 5, or its stereoisomers, tautomers, prodrugs, pharmaceutically acceptable salts, polymorphs, solvates and formulations thereof, for combined treatment or prevention of diabetes, obesity and dyslipidemia.

14. A compound of formula (I), as claimed in any one of the claims 1 to 5, or its stereoisomers, tautomers, prodrugs, pharmaceutically acceptable salts, polymorphs, solvates and formulations thereof, for treating hyperglycemia, IGT, Syndrome X, type 2 diabetes, type 1 diabetes, dyslipidemia or hyperlipidemia, hypertension, for the treatment or prophylaxis of obesity, for lowering of food intake, for appetite regulation, for regulating feeding behaviour.

15. A compound of formula (I), as claimed in any one of the claims 1 to 5, or its stereoisomers, tautomers, prodrugs, pharmaceutically acceptable salts, polymorphs, solvates and formulations thereof, for enhancing the secretion of enteroincretins, like GLP-1 and GIP, thereby managing diseases or disorders associated with modulation of secretions of enteroincretins, like hyperglycemia, insulin resistance, impaired glucose tolerance, obesity, gastric emptying, gastroparesis, satiety, leptin resistance, dyslipidemia, wound healing, diabetic complications, such as nephropathy, retinopathy, neuropathy and cataracts.

16. A pharmaceutical composition comprising, as an active ingredient, at least one compound of formula (I), as claimed in any one of the claims 1 to 5, or its stereoisomers, tautomers, prodrugs, pharmaceutically acceptable salts, polymorphs, and solvates thereof, together with one or more pharmaceutically acceptable carriers or excipients.

17. A pharmaceutical composition comprising, as an active ingredient, at least one compound of formula (I), as claimed in any one of the claims 1 to 5, or its stereoisomers, tautomers, prodrugs, pharmaceutically acceptable salts, polymorphs, and solvates thereof, in combination with one or more pharmaceutically acceptable therapeutically active agents.

18. The pharmaceutical composition as claimed in claim 17 wherein, the pharmaceutically acceptable therapeutically active agent is selected from antidiabetic agents, anti-hyperglycemic agents, anti-obesity agents, anti-hypertensive agents or anti-dyslipidemic agents.
19. The pharmaceutical composition as claimed in claim 17 or 18 wherein the pharmaceutically acceptable therapeutically active agent is selected from insulin secretagogues like sulfonylureas selected from amaryl, glyburide, glimepiride, glipryide, glipizide; insulinotropic sulfonyl urea receptor ligands like meglitinides selected from nateglinide, rapaglinide; biguanides like metformin, phenformin, buformin; glucagon antagonists like a peptide or non-peptide glucagon antagonist; glucosidase inhibitors like acarbose, miglitol; glucose sensitive insulinotropic agents like GLP-1, GLP-1 mimetics like exendin-4; insulin sensitizers like troglitazone, rosiglitazone, pioglitazone; dipeptidyl peptidase-IV inhibitors like sitagliptin, vildagliptin; sibutramine, orlistat, rimonabant; fibrates like gemfibrozil, fenofibrate; niacin; statins like rosuvatatin, atorvastatin, simvastatin; cholesterol absorption inhibitors like ezetimibe; bile acid sequestrants like cholestyramine; diuretics like hydrochlorothiazides, mannitol, indapamide, furosemide; angiotensin converting enzyme (ACE) inhibitors like captopri, enalapril; angiotensin-I1 receptor type-I blockers (ARB) like losartan, irbesartan; rennin inhibitors like aliskerin; β-adrenergic receptor blockers like atenolol, metoprolol; calcium channel blockers like amlodipine, nifedipine; aldosterone receptor antagonist like spironolactone, aldosterone synthase inhibitors like FAD286.

20. A use of compound of formula (I) as claimed in any of the claims 1-5, its polymorphs, stereoisomers, pharmaceutically acceptable salt, solvate or pro-drug thereof, in the manufacture of a medicament for the activation of Glucokinase.

21. A method of treatment of glucokinase activator mediated disease by administering a therapeutically effective amount of a compound of formula (I) as claimed in any of the claims 1-5, its polymorphs, stereoisomers, pharmaceutically acceptable salt, solvate or pro-drug thereof to a mammal in need of such treatment.

22. A method of combined treatment or prevention of diabetes, obesity and dislipidemia by administering an effective amount of a compound of formula (I) as claimed in any of the claims 1-5, its polymorph, stereoisomer, prodrug, solvate or a pharmaceutically acceptable salt thereof, to a mammal in need of such treatment.

23. A method of combined treatment of diabetes and obesity by administering an effective amount of a compound of formula (I) as claimed in any of the claims 1-5, its polymorph, stereoisomer, prodrug, solvate or a pharmaceutically acceptable salt thereof, to a mammal in need of such treatment.
INTERNATIONAL SEARCH REPORT

International application No
PCT/IN201Q/009844

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D471/04 C07D487/04 A61K31/437 A61K31/4985 A61K31/519
ADD. A61K31/5025 A61P3/10 A61P9/12 A61P3/06

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)
C07D

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

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal , BEI LSTEIN Data, CHEM ABS Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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<td>EP 1 460 067 A1 (TAKEO CHEMICAL INDUSTRIES LTD [JP]; TAKEDA PHARMACEUTICAL [JP]) 22 September 2004 (2004-09-22) page 123; table 11; compound Ref 105</td>
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<td>Wo 2005/049019 A1 (NOVO NORDISK AS [DK]; LAU JESPER F [DK]; VEDS0E PER [DK]; KOEPE JANOS) 2 June 2005 (2005-06-02) claims 1, 7 page 5, line 21 - page 6, line 17</td>
<td>1-4, 6-23</td>
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<td>Wo 2009/047798 A2 (ADVINUS THERAPEUTICS PRIVATE L [IN]; BHUNIYA DEBANATH [IN]; SANDEEP BH) 16 April 2009 (2009-04-16) cited in the application on claims 1, 18-21, 23-26</td>
<td>1-4, 6-23</td>
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Further documents are listed in the continuation of Box C. See patent family annex.

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Date of mailing of the international search report
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Brandstetter, T
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