Novel imidazo[1,2-a]pyridine cannabinoid receptor ligands and pharmaceutical compositions containing them

Title: NOVEL IMIDAZO[1,2-a]PYRIDINE CANNABINOID RECEPTOR LIGANDS AND PHARMACEUTICAL COMPOSITIONS CONTAINING THEM

Abstract: The present invention relates to novel imidazo[1,2-a]pyridine cannabinoid receptor ligands, in particular cannabinoid 1 (CB1) or cannabinoid 2 (CB2) receptor ligands, and uses thereof for treating diseases, conditions and/or disorders modulated by a cannabinoid receptors (such as pain, neurodegenerative disorders, eating disorders, weight loss or control, obesity and diabetes).

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NOVEL IMIDAZO[1,2-a]PYRIDINE CANNABINOID RECEPTOR LIGANDS AND PHARMACEUTICAL COMPOSITIONS CONTAINING THEM

Field of the Invention

The present invention relates to novel imidazo[1,2-a]pyridine cannabinoid receptor ligands, in particular cannabinoid 1 (CB1) or cannabinoid 2 (CB2) receptor ligands, and uses thereof for treating diseases, conditions and/or disorders modulated by a cannabinoid receptors (such as pain, neurodegenerative disorders, eating disorders, weight loss or control, obesity and diabetes).

Background of the Invention

The endogenous cannabinoid system comprises two main receptors, CB1 and CB2, and a number of ligands including anandamide and virodhamine which demonstrate the greatest activity at the cannabinoid receptor (Jonathan A W & Louis J A, *Obes Man.*, 5-19, 2005). Anandamide is the main fatty acid involved in the system, which is produced postsynaptically. It gains access to the extra cellular space and activates CB1 cannabinoid receptors located on presynaptic nerve terminals. This activation causes presynaptic inhibition of γ-aminobutyric acid or glutamate through inhibition of calcium channels, while simultaneously interfering with vesicle release and activating potassium channels. However, anandamide is prone to easy and rapid enzymatic hydrolysis. This represents a serious drawback in its use as a drug because, *inter alia*, substances which are susceptible to hydrolytic cleavage may undergo changes in the gastrointestinal tract.

CB1 receptors are predominantly located in the brain and other neurons, while CB2 receptors are predominantly located in immune cells. Stimulation of these receptors is known to affect the central and peripheral action on lipid and glucose metabolism in adipose tissue and most notably, helps to regulate food intake, energy balance and nicotine dependence as well as regulate fear and anxiety.

making food stimuli more salient and rapidly inducing eating even in satiated animals (Williams C M and Kirkham TC, Physiol. Behav., 76, 241-250, 2002).

Current data reveals that cannabinoids mediate suppression of inflammation in vitro and in vivo through stimulation of CB2 receptors (Ehrhart J, et.al J, Neuroinflammation, 2, 29, 2005). The inflammatory mediators such as nitric oxide, cytokines, and chemokines play an important role in microglial cell-associated neuron cell damage. Activated microglial cells have been implicated in a number of neurodegenerative disorders, including Alzheimer's disease, multiple sclerosis, HIV and dementia.

Compounds capable of modulating the Cannabinoid (CB) receptor activity can be used in the treatment of CB receptor mediated syndromes, diseases or disorders which include appetite, metabolism, diabetes, obesity, glaucoma associated intraocular pressure, mood, seizures, substance abuse, learning, cognition, memory, organ contraction, muscle spasm, respiratory, locomotor activity, movement, immune, inflammation, cell growth, eye-diseases, allergies and allergic reactions, pain, anxiety, psychotic afflictions, pathological states of brain, gastrointestinal disorders, nausea, vomiting, giddiness, urinary and fertility problems, cardiovascular diseases, neuroinflammatory pathologies, diseases of the central nervous system, neurodegenerative syndromes, diseases and disorders, sleep disorders, dermatological disorders, leukocyte activation-associated disorder, autoimmune diseases, nephrological pathologies, delayed or immediate hypersensitivity, infectious parasitic, and viral and bacterial diseases.

At present various CB modulators have been characterized as agonist, inverse agonists or antagonists to CBI and/or CB2 receptors. These modulators include, naphthalen-yl-(4-pentyloxy-naphthalen-l-yl) methanone (believed to be SAB-378), 4-(2,4-dichloro phenylamino)-N-(terahydro-pyran-4-ylmethyl)-2-trifluromethylbenzamide (GW-842166X), N-(I -piperidinyl)-5-(4-chlorophenyl)-l -(2,4-dichlorophenyl)-4-methyl pyrazole-3-carbox-amide (SR141716A) and 3-(4-chlorophenyl-N’-(4-chlorophenyl) sulfonyl-N-methyl-4-phenyl-4,5-dihydro-lH-pyrazole- 1-carboxamide (SLV-319).

These modulators have reached advanced stages of clinical trials for the treatment of pain, neurodegenerative disorders, psychotic disorders, neurological syndromes, diseases or disorders, eating disorders, Alzheimer's disease, alcohol dependency, diabetes, obesity and/or smoking cessation.
In addition to obesity, there also exists an unmet need for treatment of alcohol abuse. Health risks associated with alcoholism include impaired motor control and decision making, cancer, liver disease, birth defects, heart disease, drug/drug interactions, pancreatitis and interpersonal problems. Studies have suggested that endogenous cannabinoid tone plays a critical role in the control of ethanol intake. The endogenous CBR receptor antagonist SR-141716A has been shown to block voluntary ethanol intake in rats and mice. (See, Arnone, M., et al., "Selective Inhibition of Sucrose and Ethanol Intake by SR141716, an Antagonist of Central Cannabinoid (CBI) Receptors," Psychopharmacol, 132,104-106 (1997)). For a review, see, Hungund, B. L and B. S. Basavarajappa, "Are Anandamide and Cannabinoid Receptors involved in Ethanol Tolerance? A Review of the Evidence," Alcohol & Alcoholism. 35(2) 126-133, 2000.

Current treatments for alcohol abuse or dependence are generally impeded by non-compliance or potential hepatotoxicity. There is an unmet need for more effective treatments of alcohol abuse or dependence. PCT Publication No. WO 02/066477 discloses compounds which are antagonists of gonadotropin releasing hormone GnRH, which can be used for the treatment of a sex hormone dependent condition such as sex hormone dependent cancer, benign prostatic hypertrophy or myoma of the uterus. PCT Publication No. WO 2005/105798 Al, discloses substituted imidazo[1,2-a]pyridine compounds useful in the production of drugs.

Nevertheless, there still exists a need for safer and more effective therapeutic treatments for diseases, conditions and/or disorders modulated by cannabinoid receptors, including those modulated by CBI or CB2 receptors

Summary of the Invention

The present invention relates to CB receptor ligands of general formula (Ia) or (Ib)
pharmaceutically acceptable salts, pharmaceutically acceptable solvates, prodrugs, metabolites, polymorphs and N-oxides thereof,

wherein:

$R^1$ is hydrogen, halogen, nitro, cyano or substituted or unsubstituted alkyl;

$R^2_a$, $R^2_b$, $R^2_c$, $R^2_d$ and $R^2_e$ are independently hydrogen, halogen, nitro, cyano, OR$^0$ or substituted or unsubstituted alkyl;

$R^4$ and $R^5$ are independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted cycloalkenyl, substituted or unsubstituted cycloalkenylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroaryalkyl, substituted or unsubstituted heteroaryalkylalkyl, substituted or unsubstituted heterocyclic group, substituted or unsubstituted heterocyclicalkyl, $NR^dR^b$, $-NH-S(O)_mR^a$, $-C(O)O-R^a$, $-NH-CR^cR^b-C(0)-R^a$, $-C(0)NR^dR^b$, $-S(O)_mR^a$,

$-S(O)_mNR^dR^b$ or a protecting group or $R^4$ and $R^5$ may be joined together along with the nitrogen to which they are attached to form an optionally substituted 3 to 7 membered saturated or unsaturated cyclic ring, which may optionally include at least two heteroatoms selected from O, NR$^d$ or S($O)_m$;

each occurrence of $R^a$ and $R^b$ may be same or different and are independently hydrogen, nitro, halo, cyano, -OR$^0$, -SR$^c$ oxo, thio, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted cycloalkenyl, substituted or unsubstituted cycloalkenylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroaryalkyl, substituted or unsubstituted heterocyclic group, substituted or unsubstituted heterocyclicalkyl, $C(=B)-R^c$, $-C(O)O-R^d$, $-C(0)NR^dR^d$, $-S(O)_mR^c$, $-S(O)_mNR^dR^d$, $-NR^dR^d$, or a protecting group or $R^a$ and $R^b$ may be joined together with the atom to which they are both attached to form an optionally substituted 3 to 7 membered saturated or unsaturated cyclic ring, which may optionally include at least two heteroatoms selected from O, NR$^c$ or S;

each occurrence of B is independently O, S or NR$^c$;
R⁰ and Rᵈ are hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aryl, CN₅COORₑ, CORₑ or a protecting group;
Rₑ is hydrogen or substituted or unsubstituted C₁₋₆ alkyl; and

each occurrence of m is independently 0, 1 or 2.

Preferred is a compound of formula (Ia) or (Ib) wherein R⁴ is hydrogen, methyl, ethyl.

Further preferred is a compound of formula (Ia) or (Ib) where R⁵ is independently substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl or a substituted or unsubstituted heteroaryl group or a substituted or unsubstituted heterocyclic group.

Further preferred is a compound of formula (Ia) or (Ib) where R⁵ is methyl or ethyl, n-butyl, t-butyl, n-pentyl, n-hexyl, 2-hydroxy-ethyl, 3-hydroxy-propyl, 1,1-dimethylpropyl, 4-hydroxy-butyl, 5-hydroxy-pentyl, 2-hydroxy-l, 1-dimethyl-ethyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cyclohexymethyl, adamantyl, 3,4-difluorophenyl, phenyl-ethyl, 4-chlorobenzyl, 4-fluorobenzyl pyrrolidin-1-yl, piperidin-1-yl, morpholin-1-yl, or hexahydro-cyclopentatcipyrrrol-l-yl.

Further preferred is a compound of formula (Ia) or (Ib) where R⁴ and R⁵ may be joined together along with the nitrogen to which they are attached to form an optionally substituted 3 to 7 membered saturated or unsaturated cyclic ring, which may optionally include at least two heteroatoms selected from O, NRᵈ or S(O)ₖ.

Further preferred is a compound of formula (Ia) or (Ib) where R⁵ combines to form substituted or unsubstituted piperidin-l-yl, unsubstituted or unsubstituted piperazin-l-yl, substituted or unsubstituted pyrroldin-1-yl, substituted or unsubstituted azepanyl, substituted or unsubstituted diazapenayl, substituted or unsubstituted morpholinyl.

Further preferred is a compound of formula (Ia) or (Ib) where Rᵈ is SO₂CH₃, COORₑ, CORₑ, substituted or unsubstituted alkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aryl.

Further preferred is a compound of Formula (Ia) or (Ib) where Rᵈ is ethyl, propyl, methyl, pyridyl, phenyl, substituted or unsubstituted pyrroldin-1-yl, SO₂CH₃, COOCH₃ or COCH₃.
Further preferred is a compound of formula (Ia) or (Ib) where $R^1$, $R^2_a$ to $R^2_e$ or $R^3_a$ to $R^3_e$ are independently hydrogen, halogen, substituted or unsubstituted alkyl or -OR$^0$.

Further preferred is a compound of formula (Ia) or (Ib) where $R^1$ is chlorine.

Further preferred is a compound of formula (Ia) or (Ib) where $R^3_a$ is hydrogen, chlorine, bromine, iodine or methyl.

Further preferred is a compound of formula (Ia) or (Ib) where $R^3_c$ is hydrogen, chlorine, bromine, iodine, -CF$_3$ or tert-butyl.

Representative compounds of the present invention include those specified below pharmaceutically acceptable salts, pharmaceutically acceptable solvates, prodrugs, metabolites, polymorphs and N-oxides thereof. The present invention should not be construed to be limited to the following compounds:

1. 2-(4-Chlorophenyl)-3-phenyl imidazo[1,2a]pyridine-8-carboxylic acid piperidine-1-yl amide,

2. 2-(4-Chlorophenyl)-3-phenyl imidazo[1,2a]pyridine-8-carboxylic acid morpholine-1-yl amide,

3. 2-(4-Chlorophenyl)-3-phenyl imidazo[1,2a]pyridine-8-carboxylic acid adamantanane-1-yl amide,

4. 2-(4-Chlorophenyl)-3-phenylimidazo[1,2a]pyridine-8-carboxylic acid-(4-methanesulfonyl) piperazine-1-yl amide,

5. 2-(4-Chlorophenyl)-3-phenyl imidazo[1,2a]pyridine-8-carboxylic acid cyclohexyl amide,

6. 2-(4-Chlorophenyl)-3-phenyl imidazo[1,2a]pyridine-8-carboxylic acid-(4-chloro benzyl) amide,

7. 2,3-Bis-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid piperidine-1-yl amide,

8. 2,3-Bis-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid 1-butyl amide,

9. 2,3-Bis-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid cyclohexyl amide,
2-(4-Chlorophenyl)-3-(2,4-dichlorophenyl)imidazo[1,2a]pyridine-8-carboxylic acid piperidine-1-yl amide,

2-(4-Chlorophenyl)-3-(2,4-dichlorophenyl)imidazo[1,2a]pyridine-8-carboxylic acid morpholine-1-yl amide,

5-Chloro-2,3-Bis-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid piperidine-1-yl amide,

6-Chloro-2,3-Bis-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid azepane-1-yl amide,

6-Bromo-2,3-Bis-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid piperidine-1-yl amide,

3-(4-Chlorophenyl)-2-(2,4-dichlorophenyl)imidazo[1,2a]pyridine-8-carboxylic acid piperidine-1-yl amide,

3-(4-Chlorophenyl)-2-(2,4-dichlorophenyl)imidazo[1,2a]pyridine-8-carboxylic acid morpholine-1-yl amide,

6-Bromo-2,3-Bis-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid morpholine-1-yl amide,

2-(4-Bromophenyl)-6-chloro-3-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid piperidine-1-yl amide,

2-(4-Bromophenyl)-6-bromo-3-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid piperidine-1-yl amide,

6-Chloro-2,3-Bis-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid cyclohexyl amide,

3-(4-Bromophenyl)-6-chloro-2-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid piperidine-1-yl amide,

2,3-bis-(4-chlorophenyl)-6-iodoimidazo[1,2a]pyridine-8-carboxylic acid ethyl amide,

2,3-bis-(4-chlorophenyl)-6-iodoimidazo[1,2a]pyridine-8-carboxylic acid tert-butyl amide,

2,3-bis-(4-chlorophenyl)-6-iodoimidazo[1,2a]pyridine-8-carboxylic acid-2-(hydroxyl ethyl) amide,

2,3-bis-(4-chlorophenyl)-6-iodoimidazo[1,2a]pyridine-8-carboxylic acid-3-(hydroxyl propyl) amide,
26. 2,3-bis-(4-chlorophenyl)-6-iodo imidazo[1,2a]pyridine-8-carboxylic acid-4-(hydroxyl butyl) amide,
27. 2,3-Bis-(4-chlorophenyl)-6-iodo-imidazo[1,2-a]pyridine-8-carboxylic acid piperidin-1-ylamide,
28. 2,3-Bis (4-chlorophenyl)-6-iodo-imidazo[1,2-a]pyridine-8-carboxylic acid butylamide,
29. 2,3-Bis (4-chlorophenyl)-6-iodo-imidazo[1,2-a]pyridine-8-carboxylic acid ethylamide,
30. 2,3-Bis (4-chlorophenyl)-6-iodo-imidazo[1,2-a]pyridine-8-carboxylic acid (3-hydroxy-propyl)-amide hydrochloride,
31. 2-(4-Bromophenyl)-6-chloro-3-(4-Chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid-5-hydroxypentyl amide,
32. 2-(4-Bromophenyl)-6-chloro-3-(4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid (3-hydroxy-propyl)-amide,
33. 6-Chloro-3-(4-chlorophenyl)-2-(4-trifluoromethyl phenyl) imidazo[1,2a]pyridine-8-carboxylic acid cyclopentyl amide,
34. 6-Chloro-3-(4-chlorophenyl)-2-(4-trifluoromethyl phenyl) imidazo[1,2a]pyridine-8-carboxylic acid cyclohexyl amide,
35. 6-Chloro-3-(4-chlorophenyl)-2-(4-trifluoromethyl-phenyl)-imidazo [1,2-a]pyridine-8-carboxylic acid tert-butyl-amide,
36. 6-Chloro-2,3-Bis-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid -3,4-difluorophenyl amide,
37. 6-Chloro-2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid (4-hydroxy-butyl)-amide,
38. 6-Chloro-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid phenethylamide,
39. 6-Chloro-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid (3-hydroxy-propyl)-amide,
40. 6-Chloro-2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid tert-butylamide,
41. 6-Chloro-2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid benzylamide,
42. 2-(4-tert-Butylphenyl)-6-chloro-3-(4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid (3-hydroxy-propyl)-amide,
43. 6-Chloro-3-(4-chlorophenyl)-2-(4-iodophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid (3-hydroxy-propyl)-amide,

44. 2,3-bis-(4-chlorophenyl)-6-iodo imidazo[1,2a]pyridine-8-carboxylic acid pyrrolidine-1-yl amide,

45. 6-Bromo-3-(4-Chlorophenyl)-2-(2-chlorophenyl)imidazo[1,2a]pyridine-8-carboxylic acid piperidine-1-yl amide,

46. 6-Bromo-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid (4-hydroxy-butyl)-amide,

47. 6-Bromo-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid tert-butyl-amide,

48. 6-Bromo-2,3-Bis (4-chlorophenyl)-imidazo[1,2-a]pyridin-8-carboxylic acid (3-hydroxy propyl)-amide,

49. [3-(4-Bromophenyl)-6-chloro-2-(4-chlorophenyl) imidazo[1,2a] pyridin-8-yl] piperidine-1yl methanone,

50. 2-(4-Bromophenyl)-6-chloro-3-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid (hexahydro cyclopenta-[c]-pyrrol-2-yl)-amide,

51. 8-Bromo-2,3-bis-(4-chloro phenyl) imidazo[1,2a]pyridine-6-carboxylic acid tert-butyl amide,

52. 8-Bromo-2,3-bis-(4-Chloro phenyl) imidazo[1,2a]pyridine-6-carboxylic acid -(2-hydroxy-1,1-dimethyl-ethyl) amide,

53. 8-Bromo-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid cyclopropylamide,

54. [8-Bromo-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-6-yl]-pyrrolidin-1-yl-methanone,

55. 8-Bromo-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid isopropylamide,

56. 8-Bromo-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid ethyl methyl-amide,

57. 8-Bromo-2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid (4-hydroxy -butyl)-amide,

58. 8-Bromo-2,3-bis-(4-chlorophenyl)-imidazo [1,2-a]pyridine-6-carboxylic acid ethylamide,
59. 8-Bromo-2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid tert-butylamide hydrochloride,
60. [8-Bromo-2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-yl]-[4-methylpiperazin-1-yl]-methanone,
61. 8-Bromo-2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid dimethylamide,
62. 8-Bromo-3-(4-chlorophenyl)-2-(2-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid tert-butylamide,
63. 8-Bromo-3-(2-chlorophenyl)-2-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid tert-butylamide,
64. [8-Chloro-2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-[4-methylpiperazin-1-yl]-methanone,
65. 8-Chloro-2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid morpholin-4-ylamide,
66. 8-Chloro-2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid butylamide,
67. 8-Chloro-2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid cyclobutylamide,
68. 8-Chloro-2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid tert-butylamide,
69. [8-Chloro-2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-morpholin-4yl-methanone,
70. 8-Chloro-2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid pentylamide,
71. 8-Chloro-2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid diethylamide,
72. [8-Chloro-2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-perhydroazepin-1-yl-methanone,
73. 8-Chloro-2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid hexylamide,
74. [8-Chloro-2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-pyrrolidin-1-yl-methanone,
75. [8-Chloro-2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-[4-methyl-1,4]diazepan-1-yl-methanone,
76. 8-Chloro-3-(4-chlorophenyl)-2-(2-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid pentylamide,
77. 8-Chloro-3-(2-chlorophenyl)-2-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid pentylamide,
78. [8-Chloro-3-(4-chlorophenyl)-2-(2-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-morpholin-4-yl-methanone,
79. [8-Chloro-3-(2,4-dichlorophenyl)-2-phenyl-imidazo[1,2-a]pyridine-6-yl]-morpholin-4-yl-methanone,
80. 2,3-Bis-(4-chlorophenyl)-8-iodo-imidazo[1,2-a]pyridin-6-carboxylic acid dimethylamide,
81. 8-Chloro-2-(4-fluoro-phenyl)-3-(4-methoxy-phenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid pentylamide,
82. [2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-yl]-(4-methanesulfonyl-piperazin-1-yl)-methanone,
83. [2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-yl]-pyrrolidin-1-yl)-methanone,
84. [2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-piperidin-1-yl-methanone,
85. [2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-(4-pyridin-2-yl-piperazin-1-yl)-methanone,
86. [2,3-Bis (4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-perhydro-azepin-1-yl-methanone,
87. 2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid adamantan-1-yl amide,
88. 2,3-Bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid pentylamide,
89. 2,3-Bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid cyclohexylmethyl-amide,
90. 2,3-Bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid piperidin-1-ylamide,
91. 2,3-Bis (4-chlorophenyl)-imidazo[1,2-a]pyridin-6-carboxylic acid tert-butyl amide,
92. 3-(4-Bromophenyl)-2-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid fe/Y-butylamide,
93. 2-(4-Bromophenyl)-3-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid fert-butylamidine,
94. [2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-(4-propyl-piperazin-1-yl)-methanone,
95. [2,3-Bis (4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-(4-phenyl-piperazin-1-yl)-methanone,
96. [2,3-Bis (4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-niorpholin-4-yl-methanone,
97. [2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-(4-methyl-piperazin-1-yl)-methanone,
98. [2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone,
99. 2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid methyl-pyridin-4-yl-amide,
100. 4-[2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carbonyl]-piperazine-l-carboxylic acid methyl ester,
101. 1-[4-[2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carbonyl]-piperazine-1-yl]-ethanone,
102. [2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-(4-methyl-perhydro-1,4-diazepin-1-yl)-methanone,
103. [2-(4-chlorophenyl)-3-(4-methoxyphenyl)-imidazo[1,2-a]pyridin-6-yl]-perhydro-azezin-1-yl-niethanone,
104. [2,3-Bis-(4-chloro-phenyl)-imidazo[1,2-a]pyridin-8-yl]-pyrrolidin-1-yl-methanone,
105. 2-(4-Bromophenyl)-3-(4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid cyclohexylamide,
106. 2-(4-Bromophenyl)-3-(4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid pentylamide,
107. 2-(4-Bromophenyl)-3-(4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid tert-butylamidate,
108. [2,3-Bis (4-chlorophenyl)-imidazo[1,2-a]pyridin-8-yl]-(4-pyrind-2-yl-piperazin-1-yl)-methanone,
109. 2,3-Bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid cyclohexylmethyl-amide,

110. 2,3-Bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid 4-chloro benzylamide,

111. 2,3-Bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid 4-fluoro benzylamide,

112. 2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid (1,1-dimethyl propyl)-amide,

113. 2-(4-Chlorophenyl)-3-(2,4-dichlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid tert-butylamide,

114. 8-Chloro-3-(4-etilyl-phenyl)-2-(4-fluoro-phenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid dimethylamide,

115. [8-Chloro-2-(4-chloro-phenyl)-3-p-tolyl-imidazo[1,2-a]pyridin-6-yl]-(4-methyl-iperazin-1-yl)-methanone, and

pharmaceutically acceptable salts, pharmaceutically acceptable solvates, prodrugs, metabolites, polymorphs and N-oxides thereof.

The present invention also provides a pharmaceutical composition comprising at least one compound of the present invention and a pharmaceutically acceptable excipient (such as a pharmaceutically acceptable carrier or diluent). Preferably, the pharmaceutical composition comprises a therapeutically effective amount of the compound(s) of the present invention.

The compounds and pharmaceutical compositions of the present invention are useful in the treatment, amelioration, and/or prevention of diseases, conditions and/or disorders modulated by a cannabinoid receptor (CB), especially those modulated by the CBl or CB2 receptor.

The present invention further provides a method of treating a disease, condition and/or disorder modulated by a cannabinoid receptor (CB), and in particular the CBl or CB2 receptor, in a subject in need thereof by administering to the subject a therapeutically effective amount of a compound or a pharmaceutical composition of the present invention.

Detailed Description of the Invention

Definitions
The term "alkyl" refers to a straight or branched hydrocarbon chain radical consisting solely of carbon and hydrogen atoms, containing no unsaturation, having from one to eight carbon atoms, and which is attached to the rest of the molecule by a single bond, e.g., methyl, ethyl, n-propyl, 1-methylethyl (isopropyl), n-butyl, n-pentyl, and 1,1-dimethylethyl (t-butyl).

The term "alkenyl" refers to an aliphatic hydrocarbon group containing a carbon-carbon double bond and which may be a straight or branched chain having 2 to about 10 carbon atoms, e.g., ethenyl, 1-propenyl, 2-propenyl (allyl), iso-propenyl, 2-methyl-1-propenyl, 1-buteny1, and 2-butenyl.

The term "alkynyl" refers to a straight or branched chain hydrocarbyl radical having at least one carbon-carbon triple bond, and having 2 to about 12 carbon atoms (with radicals having 2 to about 10 carbon atoms being preferred), e.g., ethynyl, propynyl, and butynyl.

The term "alkoxy" denotes an alkyl group attached via an oxygen linkage to the rest of the molecule. Representative examples of such groups are -OCH₃ and -OC₂H₅.

The term "cycloalkyl" denotes a non-aromatic mono or multicyclic ring system of 3 to about 12 carbon atoms, such as cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl. Examples of multicyclic cycloalkyl groups include, but are not limited to, perhydronapththyl, adamantyl and norbornyl groups, bridged cyclic groups and spirrobicyclic groups, e.g., sprio (4,4) non-2-yl.

The term "cycloalkylalkyl" refers to a cyclic ring-containing radical having 3 to about 8 carbon atoms directly attached to an alkyl group. The cycloalkylalkyl group may be attached to the main structure at any carbon atom in the alkyl group that results in the creation of a stable structure. Non-limiting examples of such groups include cyclopropylmethyl, cyclobutylethyl, and cyclopentylethyl.

The term "cycloalkenyl" refers to a cyclic ring-containing radical having 3 to about 8 carbon atoms with at least one carbon-carbon double bond, such as cyclopropenyl, cyclobuteny1, and cyclopenteny1.

The term "aryl" refers to an aromatic radical having 6 to 14 carbon atoms such as phenyl, naphthyl, tetrahydronapthyl, indanyl, and biphenyl.

The term "arylalkyl” refers to an aryl group as defined above directly bonded to an alkyl group as defined above, e.g., -CH₂C₆H₅ and -C₂H₅C₆H₅.
The term "heterocyclic ring" refers to a stable 3- to 15-membered ring radical which consists of carbon atoms and from one to five heteroatoms selected from nitrogen, phosphorus, oxygen and sulfur. For purposes of this invention, the heterocyclic ring radical may be a monocyclic, bicyclic or tricyclic ring system, which may include fused, bridged or spiro ring systems, and the nitrogen, phosphorus, carbon, oxygen or sulfur atoms in the heterocyclic ring radical may be optionally oxidized to various oxidation states. In addition, the nitrogen atom may be optionally quaternized; and the ring radical may be partially or fully saturated (i.e., heterocyclic or heteroaryl). Examples of such heterocyclic ring radicals include, but are not limited to, azetidinyl, acridinyl, benzodioxolyl, benzodioxanyl, benzofurnyl, carbazolyl, cinnolinyl, dioxolanyl, indolizinyln, naphthyridinyl, perhydroazepinyl, phenazinyl, phenothiazinyl, phenoxazinyl, phthalazinyl, pyridyl, pteridinyl, purinyl, quinazolinyl, quinoxalinyln, quinolinyl, isoquinolinyl, tetrazoal, imidazolyl, tetrahydroisouinolyl, piperidinyl, piperazinyln, 2-oxopiperazinyl, 2-oxopiperidinyl, 2-oxopyrroldinyl, 2-oxoazepinyl, azepinyln, pyrrolyln, 4-piperidonyln, pyrrolidinyl, pyrazinyl, pyrimidinyl, pyridinyl, oxazolyl, oxazolinyl, oxasolidinyl, triazolyl, indanyl, isoxazolyl, isoxasolidinyl, morpholinyl, thiazolyl, thiazolinyl, thiazolidinyl, isothiazolyl, quinuclidinyl, isothiazolidinyl, indolyln, isoindolinyln, indolinyln, isoindolinyl, octahydroindolinyln, octahydroisoindolinyln, quinolyl, isoquinolyl, decahydroisoquinolyl, benzimidazolyl, thiazolazolyl, benzopyranlyln, benzothiazolyl, benzooxazolyl, furyl, tetrahydrofurfuryln, tetrahydroprpyranlyln, thielyn, benzothienyl, thiamorpholinyl, thiamorpholinyl sulfoxide, thiamorpholinyl sulfone, dioxaphospholanyln, oxadiazolyl, chromanyln, and isochromanyln. The heterocyclic ring radical may be attached to the main structure at any heteroatom or carbon atom that results in the creation of a stable structure.

The term "heterocyclyl" refers to a heterocyclic ring radical as defined above. The heterocyclyl ring radical may be attached to the main structure at any heteroatom or carbon atom that results in the creation of a stable structure.

The term "heterocyclyalkyl" refers to a heterocyclic ring radical directly bonded to an alkyl group. The heterocyclylalkyl radical may be attached to the main structure at any carbon atom in the alkyl group that results in the creation of a stable structure.
The term "heteroaryl" refers to an aromatic heterocyclic ring radical. The heteroaryl ring radical may be attached to the main structure at any heteroatom or carbon atom that results in the creation of a stable structure.

The term "heteroarylalkyl" refers to a heteroaryl ring radical directly bonded to an alkyl group. The heteroarylalkyl radical may be attached to the main structure at any carbon atom in the alkyl group that results in the creation of a stable structure.

Unless otherwise specified, the term "substituted" as used herein refers to substitution with any one or any combination of the following substituents: hydroxy, halogen, carboxyl, cyano, nitro, oxo (=O), thio (=S), substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted aryalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkyalkyl, substituted or unsubstituted cycloalkyalkyl, substituted or unsubstituted cycloalkenyl, substituted or unsubstituted alkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heterocyclylalkyl ring, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted heterocyclic ring, substituted or unsubstituted guanidine, -COOR, -C(O)R, -C(S)R, -C(O)NR, -C(O)ONR, -NRCONR, -N(R)=N-N(R), -NR2CONR, -N(R)SOR, -N(R)SO2R, -(=N-N(R)R), -NR=C(O)OR, -NR2, -NR=C(O)R, -NR=C(S)R, -NR2C(S)R, -NR2C(S)NR, -NR2SO2R, -NR2SO2R, -NR2C2R, -OR2C(O)OR, -OC(O)R, -OC(O)NR, -R2NR2C(O)R, -R2OR, -R2C(O)OR, -R2C(O)NR, -R2C(O)R, -R2OC(O)R, -SR, -SOR, -SO2R, and -ONO2, wherein Rx, Ry and Rz are independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted aryalkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkyalkyl, substituted or unsubstituted cycloalkenyl, substituted or unsubstituted cycloalkenylalkyl, substituted or unsubstituted heterocyclic ring, substituted or unsubstituted heterocyclylalkyl, or substituted or unsubstituted amino.

According to one embodiment, the substituents in the aforementioned "substituted" groups cannot be further substituted. For example, when the substituent on "substituted alkyl" is "substituted aryl", the substituent on "substituted aryl" cannot be "substituted alkenyl".
The term "protecting group" or "PG" refers to a substituent that is employed to block or protect a particular functionality while other functional groups on the compound may remain reactive. For example, an "amino-protecting group" is a substituent attached to an amino group that blocks or protects the amino functionality in the compound. Suitable amino-protecting groups include, but are not limited to, acetyl, trifluoroacetyl, t-butoxycarbonyl (BOC), benzylxycarbonyl (CBz) and 9-fluorenymethylenoxycarbonyl (Fmoc). Similarly, a "hydroxy-protecting group" refers to a substituent of a hydroxy group that blocks or protects the hydroxy functionality. Suitable hydroxy-protecting groups include, but are not limited to, acetyl, benzyl, tetrahydropyranyl and silyl. A "carboxy-protecting group" refers to a substituent of the carboxy group that blocks or protects the carboxy functionality. Suitable carboxy-protecting groups include, but are not limited to, -CH$_2$CH$_2$SO$_2$Ph, cyanoethyl, 2-(trimethylsilyl)ethyl, 2-(trimethylsilyl)ethoxymethyl, 2-(p-toluenesulfonyl)ethyl, 2-(p-nitrophenylsulfenyl)ethyl, 2-(diphenylphosphino)-ethyl, and nitroethyl. For a general description of protecting groups and their use, see, T. W. Greene, Protective Groups in Organic Synthesis, John Wiley & Sons, New York, 1991.

The term "cannabinoid receptor" refers to any one of the known or heretofore unknown subtypes of the class of cannabinoid receptors that may be bound by a cannabinoid modulator compound of the present invention; in particular, a cannabinoid receptor selected from the group consisting of a CB1 receptor and a CB2 receptor.

The term "modulator" further refers to the use of a compound of the invention as a CB receptor agonist, partial agonist, antagonist or inverse-agonist.

The term "prodrug" refers to a compound that is transformed in vivo to yield a compound of Formula (I) or a pharmaceutically acceptable salt, hydrate or solvate thereof. The transformation may occur by various mechanisms, such as through hydrolysis in blood. A discussion of the use of prodrugs is provided by T. Higuchi and W. Stella, "Pro-drugs as Novel Delivery Systems," Vol. 14 of the A.C.S. Symposium Series, and in Bioreversible Carriers in Drug Design, ed. Edward B. Roche, American Pharmaceutical Association and Pergamon Press, 1987.

The term "treating" or "treatment" of a state, disorder or condition includes:

(1) preventing or delaying the appearance of clinical symptoms of the state, disorder or condition developing in a subject that may be afflicted with or
predisposed to the state, disorder or condition but does not yet experience or display clinical or subclinical symptoms of the state, disorder or condition;

(2) inhibiting the state, disorder or condition, i.e., arresting or reducing the development of the disease or at least one clinical or subclinical symptom thereof;

(3) relieving the disease, i.e., causing regression of the state, disorder or condition or at least one of its clinical or subclinical symptoms.

The benefit to a subject to be treated is either statistically significant or at least perceptible to the subject or to the physician.

The term "subject" includes mammals (especially humans) and other animals, such as domestic animals (e.g., household pets including cats and dogs) and non-domestic animals (such as wildlife).

A "therapeutically effective amount" means the amount of a compound that, when administered to a subject for treating a state, disorder or condition, is sufficient to effect such treatment. The "therapeutically effective amount" will vary depending on the compound, the disease and its severity and the age, weight, physical condition and responsiveness of the subject to be treated.

Pharmaceutically acceptable salts forming part of this invention include salts derived from inorganic bases (such as Li, Na, K, Ca, Mg, Fe, Cu, Zn, and Mn), salts of organic bases (such as N,N'-diacetylenediamine, glucamine, triethylamine, choline, hydroxide, dicyclohexylamine, metformin, benzylamine, trialkylamine, and thiamine), salts of chiral bases (such as alkylphenylamine, glycine, and phenyl glycinol), salts of natural amino acids (such as glycine, alanine, valine, leucine, isoleucine, norleucine, tyrosine, cystine, cysteine, methionine, proline, hydroxy proline, histidine, ornithine, lysine, arginine, and serine), salts of non-natural amino acids (such as D-isomers or substituted amino acids), salts of guanidine, salts of substituted guanidine (wherein the substituents are selected from nitro, amino, alkyl, alkenyl, or alkylnyl), ammonium salts, substituted ammonium salts, and aluminum salts. Other pharmaceutically acceptable salts include acid addition salts (where appropriate) such as sulphates, nitrates, phosphates, perchlorates, borates, hydrohalides, acetates (such as trifluoroacetate), tartrates, maleates, citrates, furnarates, succinates, palmoates, methanesulphonates, benzoates, salicylates, benzenesulfonates, ascorbates, glycerophosphates, and ketoglutarates. Yet other pharmaceutically acceptable salts include, but are not limited to, quaternary ammonium salts of the
compounds of invention with alkyl halides or alkyl sulphates (such as MeI or (Me)\(_2\)SO\(_4\)).

Pharmaceutically acceptable solvates includes hydrates and other solvents of crystallization (such as alcohols). The compounds of the present invention may form solvates with low molecular weight solvents by methods known in the art.

**Pharmaceutical Compositions**

The pharmaceutical composition of the present invention comprises at least one compound of the present invention and a pharmaceutically acceptable excipient (such as a pharmaceutically acceptable carrier or diluent). Preferably, the pharmaceutical composition comprises a therapeutically effective amount of the compound(s) of the present invention. The compound of the present invention may be associated with a pharmaceutically acceptable excipient (such as a carrier or a diluent) or be diluted by a carrier, or enclosed within a carrier which can be in the form of a capsule, sachet, paper or other container.

Examples of suitable carriers include, but are not limited to, water, salt solutions, alcohols, polyethylene glycols, polyhydroxyethoxylated castor oil, peanut oil, olive oil, gelatin, lactose, terra alba, sucrose, dextrin, magnesium carbonate, sugar, cyclodextrin, amylose, magnesium stearate, talc, gelatin, agar, pectin, acacia, stearic acid or lower alkyl ethers of cellulose, silicic acid, fatty acids, fatty acid amines, fatty acid monoglycerides and diglycerides, pentaerythritol fatty acid esters, polyoxyethylene, hydroxymethylcellulose and polyvinylpyrrolidone.

The carrier or diluent may include a sustained release material, such as glycercyl monostearate or glycercyl distearate, alone or mixed with a wax.

The pharmaceutical composition may also include one or more pharmaceutically acceptable auxiliary agents, wetting agents, emulsifying agents, suspending agents, preserving agents, salts for influencing osmotic pressure, buffers, sweetening agents, flavoring agents, colorants, or any combination of the foregoing. The pharmaceutical composition of the invention may be formulated so as to provide quick, sustained, or delayed release of the active ingredient after administration to the subject by employing methods known in the art.

The pharmaceutical compositions of the present invention may be prepared by conventional techniques, e.g., as described in *Remington: The Science and Practice of Pharmacy*, 20\(^{th}\) Ed., 2003 (Lippincott Williams & Wilkins). For example, the active compound can be mixed with a carrier, or diluted by a carrier, or enclosed within a
carrier, which may be in the form of an ampoule, capsule, sachet, paper, or other container. When the carrier serves as a diluent, it may be a solid, semi-solid, or liquid material that acts as a vehicle, excipient, or medium for the active compound. The active compound can be adsorbed on a granular solid container, for example, in a sachet.

The pharmaceutical compositions may be in conventional forms, for example, capsules, tablets, aerosols, solutions, suspensions or products for topical application.

The route of administration may be any route which effectively transports the active compound of the invention to the appropriate or desired site of action. Suitable routes of administration include, but are not limited to, oral, nasal, pulmonary, buccal, subdermal, intradermal, transdermal, parenteral, rectal, depot, subcutaneous, intravenous, intraurethral, intramuscular, intranasal, ophthalmic (such as with an ophthalmic solution) or topical (such as with a topical ointment). The oral route is preferred.

Solid oral formulations include, but are not limited to, tablets, capsules (soft or hard gelatin), dragees (containing the active ingredient in powder or pellet form), troches and lozenges. Tablets, dragees, or capsules having talc and/or a carbohydrate carrier or binder or the like are particularly suitable for oral application. Preferable carriers for tablets, dragees, or capsules include lactose, cornstarch, and/or potato starch. A syrup or elixir can be used in cases where a sweetened vehicle can be employed.

A typical tablet that may be prepared by conventional tableting techniques may contain: (1) Core: Active compound (as free compound or salt thereof), 250 mg colloidal silicon dioxide (Aerosil®), 1.5 mg microcrystalline cellulose (Avicel®), 70 mg modified cellulose gum (Ac-Di-Sol®), and 7.5 mg magnesium stearate; (2) Coating: HPMC, approx. 9 mg Mywacett 9-40 T and approx. 0.9 mg acylated monoglyceride.

Liquid formulations include, but are not limited to, syrups, emulsions, soft gelatin and sterile injectable liquids, such as aqueous or non-aqueous liquid suspensions or solutions.

For parenteral application, particularly suitable are injectable solutions or suspensions, preferably aqueous solutions with the active compound dissolved in polyhydroxylated castor oil.

**Methods of Treatment and Combination Therapy**
The present invention provides compounds and pharmaceutical formulations thereof that are useful in the treatment, amelioration, and/or prevention of diseases, conditions and/or disorders modulated by a cannabinoid receptor (CB), especially those modulated by the CB1 or CB2 receptor.

The present invention further provides a method of treating a disease, condition and/or disorder modulated by a cannabinoid receptor (CB), and in particular the CB1 or CB2 receptor, in a subject in need thereof by administering to the subject a therapeutically effective amount of a compound or a pharmaceutical composition of the present invention.

Diseases, conditions, and/or disorders that are modulated by a CB receptor, include, but are not limited to, appetite disorders, metabolism disorders, catabolism disorders, diabetes, obesity, glaucoma-associated intraocular pressure, social related disorders, mood disorders, seizures, substance abuse, learning disorders, cognition disorders, memory disorders, organ contraction, muscle spasm, respiratory disorders, locomotor activity disorders, movement disorders, immune disorders (such as autoimmune disorders), inflammation, cell growth, pain and neurodegenerative related syndromes, disorders and diseases.

Appetite related syndromes, disorders or diseases include, but are not limited to, obesity, overweight conditions, anorexia, bulimia, cachexia, dysregulated appetite and the like. Obesity related syndromes, disorders or diseases include, but are not limited to, obesity as a result of genetics, diet, food intake volume, metabolic syndrome, disorder or disease, hypothalamic disorder or disease, age, abnormal adipose mass distribution, abnormal adipose compartment distribution, compulsive eating disorders, motivational disorders which include the desire to consume sugars, carbohydrates, alcohols or drugs or any ingredient with hedonic value and the like.

Symptoms associated with obesity related syndromes, disorders, and diseases include, but are not limited to, reduced activity.

Metabolism related syndromes, disorders or diseases include, but are not limited to, metabolic syndrome, dyslipidemia, elevated blood pressure, diabetes, insulin sensitivity or resistance, hyperinsulinemia, hypercholesterolemia, hyperlipidemias, hypertriglyceridemias, arteriosclerosis, atherosclerosis, other cardiovascular diseases, osteoarthritis, dermatological diseases, sleep disorders, cholelithiasis, hepatomegaly, steatosis, abnormal alanine aminotransferase levels, polycystic ovarian disease, inflammation, and the like.
Diabetes related syndromes, disorders or diseases include, but are not limited to, glucose dysregulation, insulin resistance, glucose intolerance, hyperinsulinemia, dyslipidemia, hypertension, obesity, hyperglycemia and the like.

Catabolism related syndromes, disorders or diseases include, but are not limited to, catabolism in connection with pulmonary dysfunction and ventilator dependency; cardiac dysfunction, e.g., associated with valvular disease, myocardial infarction, cardiac hypertrophy or congestive heart failure.

Social or mood related syndromes, disorders or diseases include, but are not limited to, depression, anxiety, psychosis, social affective disorders, cognitive disorders and the like.

Substance abuse related syndromes, disorders or diseases include, but are not limited to, drug abuse and drug withdrawal. Abused substances include, but are not limited to, alcohol, amphetamines (or amphetamine like substances), caffeine, cannabis, cocaine, hallucinogens, inhalants, opioids, heroin abuse, phencyclidine (or phencyclidine-like compounds), sedative-hypnotics or benzodiazepines, combinations of any of the foregoing. The compounds and pharmaceutical compositions can also be used to treat withdrawal symptoms and substance-induced anxiety or mood disorder.

Learning, cognition or memory related syndromes, disorders or diseases include, but are not limited to, memory loss or impairment as a result of age, disease, side effects of medications (adverse events) or the like. Memory impairment is a primary symptom of dementia and can also be a symptom associated with such diseases as Alzheimer's disease, schizophrenia, Parkinson's disease, Huntington's disease, Pick's disease, Creutzfeld-Jakob disease, HIV, cardiovascular disease, and head trauma as well as age-related cognitive decline. Generally, dementias are diseases that include memory loss and additional intellectual impairment separate from memory. The compounds and pharmaceutical compositions of the present invention are also useful in treating cognitive impairments related to attentional deficits, such as attention deficit disorder.

Muscle spasm syndromes, disorders or diseases include, but are not limited to, multiple sclerosis, cerebral palsy and the like.

Locomotor activity and movement syndromes, disorders or diseases include, but are not limited to, stroke, Parkinson's disease, multiple sclerosis, epilepsy and the like.
Respiratory related syndromes, disorders or diseases include, but are not limited to, diseases of the respiratory tract, chronic pulmonary obstructive disorder, emphysema, asthma, bronchitis and the like.

Autoimmune or inflammation related syndromes, disorders or diseases include, but are not limited to, psoriasis, lupus erythematosus, diseases of the connective tissue, Sjogren's syndrome, ankylosing spondylarthritis, rheumatoid arthritis, reactional arthritis, undifferentiated spondylarthritis, Behcet's disease, autoimmune hemolytic anaemias, multiple sclerosis, amyotrophic lateral sclerosis, amyloses, graft rejection or diseases affecting the plasma cell line; allergic diseases: delayed or immediate hypersensitivity, allergic rhinitis, contact dermatitis or allergic conjunctivitis infectious parasitic, viral or bacterial diseases (such as AIDS and meningitis), inflammatory diseases (such as diseases of the joints including, but not limited to, arthritis, rheumatoid arthritis, osteoarthritis, spondylitis, gout, vasculitis; Crohn's disease, inflammatory bowel disease (IBD) and irritable bowel syndrome (IBS)), osteoporosis, pain, chronic pain of the inflammatory type, allergies, rheumatoid arthritis, dermatitis, immunodeficiency, chronic neuropathic pain and the like.

Cell growth related syndromes, disorders or diseases include, but are not limited to, dysregulated mammalian cell proliferation, breast cancer cell proliferation, prostrate cancer cell proliferation and the like.

Pain related syndromes, disorders or diseases include, but are not limited to, central and peripheral pathway mediated pain, bone and joint pain, migraine headache associated pain, cancer pain, menstrual cramps, labor pain and the like.

Neurodegenerative related syndromes, disorders or diseases include, but are not limited to, Parkinson's disease, multiple sclerosis, epilepsy, ischemia or secondary biochemical injury collateral to traumatic head or brain injury, brain inflammation, eye injury or stroke and the like.

The compounds of this invention may also be used in conjunction with other pharmaceutical agents for the treatment of the diseases, conditions and/or disorders described herein. Therefore, methods of treatment that include administering compounds of the present invention in combination with other pharmaceutical agents are also provided. Suitable pharmaceutical agents that may be used in combination with the compounds of the present invention include, but are not limited to, anti-obesity agents such as apolipoprotein-B secretion/microsomal triglyceride transfer
protein (apo-B/MTP) inhibitors, $11\beta$-hydroxy steroid dehydrogenase-1 (ll $\beta$-HSD type 1) inhibitors, peptide YY$_{3-36}$ or analogs thereof, MCR-4 agonists, cholecystokinin-A (CCK-A) agonists, monoamine reuptake inhibitors (such as sibutramine), sympathomimetic agents, $\beta_3$ adrenergic receptor agonists, dopamine receptor agonists (such as bromocriptine), melanocyte-stimulating hormone receptor analogs, 5HT$_2c$ receptor agonists, melanin concentrating hormone antagonists, leptin (the OB protein), leptin analogs, leptin receptor antagonists, galanin antagonists, lipase inhibitors (such as tetrahydrolipstatin, i.e. orlistat), anorectic agents (such as a bombesin agonist), neuropeptide-Y receptor antagonists, thyromimetic agents, dehydroepiandrosterone or an analog thereof, glucocorticoid receptor agonists or antagonists, orexin receptor antagonists, glucagon-like peptide-1 (GLP-I) receptor agonists, Protein Tyrosine Phosphatase (PTP-IB) inhibitors, dipeptidyl peptidase IV (DPP-IV) inhibitors, ciliary neurotrophic factors (such as Axokine™ available from Regeneron Pharmaceuticals, Inc., Tarrytown, N.Y. and Procter & Gamble Company, Cincinnati, Ohio), human agouti-related protein (AGRP) inhibitors, ghrelin receptor antagonists, histamine 3 receptor antagonists or inverse agonists, and neuromedin U receptor agonists. Other anti-obesity agents, including the preferred agents set forth herein below, are well known, or will be readily apparent in light of the instant disclosure, to one of ordinary skill in the art.

Especially preferred are anti-obesity agents such as orlistat, sibutramine, bromocriptine, ephedrine, leptin, peptide YY$_{3-36}$ or an analog thereof (including the complete peptide YY), and pseudoephedrine. Preferably, compounds of the present invention and combination therapies are administered in conjunction with exercise and a sensible diet.

Anti-obesity agents for use in the combinations, pharmaceutical compositions, and methods of the invention can be prepared using methods known to one of ordinary skill in the art, for example, sibutramine can be prepared as described in U.S. Pat. No. 4,929,629; bromocriptine can be prepared as described in U.S. Pat. Nos. 3,752,814 and 3,752,888; orlistat can be prepared as described in U.S. Pat. Nos. 5,274,143, 5,420,305, 5,540,917, and 5,643,874; and PYY$_{3-36}$ (including analogs) can be prepared as described in U.S. Patent Publication No. 2002/0141985 and International Publication No. WO 03/027637. All of the above recited references are incorporated herein by reference.
Other suitable pharmaceutical agents that may be administered in combination with the compounds of the present invention include agents designed to treat tobacco abuse (e.g., nicotine receptor partial agonists, bupropion hydrochloride (also known under the tradename Zyban™) and nicotine replacement therapies), agents to treat erectile dysfunction (e.g., dopaminergic agents, such as apomorphine), ADD/ADHD agents (e.g., Ritalin™ (methylphenidate hydrochloride), Strattera™ (atomoxetine hydrochloride), Concerta™ (methylphenidate hydrochloride) and Adderall™ (amphetamine aspartate; amphetamine sulfate; dextroamphetamine saccharate; and dextroamphetamine sulfate)), and agents to treat alcoholism, such as opioid antagonists (e.g., naltrexone (also known under the tradename ReVia™) and nalmefene), disulfiram (also known under the tradename Antabuse™), and acamprosate (also known under the tradename Campral™)). In addition, agents for reducing alcohol withdrawal symptoms may also be co-administered, such as benzodiazepines, beta-blockers, clonidine, carbamazepine, pregabalin, and gabapentin (Neurontin™). Treatment for alcoholism is preferably administered in combination with behavioral therapy including such components as motivational enhancement therapy, cognitive behavioral therapy, and referral to self-help groups, including Alcohol Anonymous (AA).

Other pharmaceutical agents that may be useful include antihypertensive agents; antidepressants (e.g., fluoxetine hydrochloride (Prozac™)); cognitive improvement agents (e.g., donepezil hydrochloride (Aircept™) and other acetylcholinesterase inhibitors); neuroprotective agents (e.g., memantine); antipsychotic medications (e.g., ziprasidone (Geodon™), risperidone (Risperdal™), and olanzapine (Zyprexa™)); insulin and insulin analogs (e.g., LysPro insulin); GLP-1 (7-37) (insulinotropin) and GLP-I (7-36)-NH₂; sulfonylureas and analogs thereof: chlorpropamide, glibenclamide, tolbutamide, tolazamide, acetohexamide, Glypizide®, glimepiride, repaglinide, meglitinide; biguanides: metformin, phenformin, buformin; α2-agonists and imidazolines: midaglizole, isaglidole, deriglidole, idazoxan, efaroxan, fluparoxan; other insulin secretagogues: linogliride, A-4166; glitazones: ciglitazone, Actos® (pioglitazone), englitazone, troglitazone, darglitazone, Avandia® (BRL49653); fatty acid oxidation inhibitors: clomoxir, etomoxir; α-glucosidase inhibitors: acarbose, miglitol, emiglitate, voglibose, MDL-25,637, camiglibose, MDL-73,945; β-agonists: BRL 35135, BRL 37344, RO 16-8714, ICI D7114, CL 316,243; phosphodiesterase inhibitors: L-386,398; lipid-lowering agents: benfmorex:
fenfluramine; vanadate and vanadium complexes (e.g., Naglivan®) and peroxovanadium complexes; amylin antagonists; glucagon antagonists; gluconeogenesis inhibitors; somatostatin analogs; antilipolytic agents: nicotinic acid, acipimox, WAG 994, pramlintide (Symlin™), AC 2993, nateglinide, aldose reductase inhibitors (e.g., zopolrestat), glycogen phosphorylase inhibitors, sorbitol dehydrogenase inhibitors, sodium-hydrogen exchanger type 1 (NHE-I) inhibitors and/or cholesterol biosynthesis inhibitors or cholesterol absorption inhibitors, especially a HMG-CoA reductase inhibitor, or a HMG-CoA synthase inhibitor, or a HMG-CoA reductase or synthase gene expression inhibitor, a CETP inhibitor, a bile acid sequesterant, a fibrate, an ACAT inhibitor, a squalene synthetase inhibitor, an anti-oxidant or niacin. The compounds of the present invention may also be administered in combination with a naturally occurring compound that acts to lower plasma cholesterol levels. Such naturally occurring compounds are commonly called nutraceuticals and include, for example, garlic extract, Hoodia plant extracts, and niacin.

The compounds of the present invention (including the pharmaceutical compositions and processes used therein) may be used alone or in combination with other pharmaceutical agents in the manufacture of a medicament for the therapeutic applications described herein.

Methods of Preparation

The compounds according to the present invention may be prepared by the following processes. For example, the compound of formula (Ia) and (Ib) where R₁, R₂, R₃, R⁴ & R⁵ are as defined above in the general description, can be synthesized as shown in scheme I-V;

Scheme - 1

Step I:

Step 2:
The intermediate of formula (2a) (wherein Z is substituted or unsubstituted alkyl or substituted or unsubstituted arylalkyl) can be prepared by treating 2-amino nicotinic acid (Ia) with an acid chloride, such as (thionyl chloride or oxalyl chloride, preferably thionyl chloride) in a suitable solvent (such as methanol, ethanol, or isopropanol preferably ethanol) either at room temperature or at elevated temperature, preferably at reflux temperature of the suitable solvent used. The intermediate of formula (2a) (with or without purification) can be reacted further with a suitable halo-succinimide (such as N-chlorosuccinimide, N-bromosuccinimide or N-iodosuccinimide) in a suitable solvent (such as tetrahydrofuran or carbon tetrachloride or acetonitrile, preferably tetrahydrofuran) to give the intermediate of formula (3a) (wherein R¹ is halogen).

In the second step, the intermediate of formula (3a) can be reacted with the intermediate of formula (4a) (wherein X is a halogen) in a suitable solvent (such as dimethoxyethane or dimethyl formamide or ethanol or acetonitrile or combination thereof) in the optional presence of a organic or inorganic base (such as sodium bicarbonate or sodium carbonate or potassium carbonate or triethylamine), preferably at an elevated temperature (80 °C or above), to yield an intermediate of formula (5a). The intermediate of formula (5a) can then be hydrolysed by a suitable base such as lithium hydroxide or sodium hydroxide or potassium hydroxide or potassium carbonate or the like in a suitable solvent such as tetrahydrofuran or 1,4-dioxane or
methanol or ethanol or water or a mixture thereof to give an intermediate of formula (6a).

The intermediate of formula (6a) can then be converted to a corresponding acid chloride, for example, by treatment with thionyl chloride or oxalyl chloride in a suitable solvent (such as benzene, toluene, dichloromethane, or chloroform). The acid chloride thus obtained (with or without purification) can be dissolved in a suitable solvent (such as dichloromethane or chloroform, or dichloroethane) followed by the addition of an amine of formula $NHR^4R^5$, optionally, in the presence of an organic base (such as triethylamine or pyridine) to give a compound of formula (Ia).

Alternately, the compound of formula (6a) can be treated with an activating reagent such as (benzotriazol-1-yl-oxy)tris(dimethylamino)phosphonium hexafluoro phosphate (BOP), optionally, in the presence of a suitable solvent (such as dimethyl formamide) and an organic base (such as triethylamine or pyridine, preferably triethylamine), followed by the addition of an amine of formula $NHR^4R^5$ to obtain a compound of formula (Ia).

Scheme II
The compounds of the formula (Ia) can be prepared according to the Scheme II. The intermediate of formula (3a) can be reacted with the intermediate of formula (7a) (wherein Li is hydrogen or halogen and X is halogen) in one or more suitable solvent, for example, dimethoxyethane, dimethyl formamide, ethanol, acetonitrile or mixtures thereof) optionally in the presence of one or more organic or inorganic base, for example, sodium bicarbonate, sodium carbonate, potassium carbonate, triethylamine, preferably at higher temperature (e.g., 80°C or above) to yield an intermediate of formula 8a. The compound of formula 8a (wherein L₁ = H) can be reacted further with a suitable halo-succinimide, for example, N-chlorosuccinimide, N-bromosuccinimide or N-iodosuccinimide, in one or more suitable solvent, for example, tetrahydrofuran, carbon tetrachloride, acetonitrile to give the intermediate of formula 9a. Then the compounds of formula 8a (wherein L₁ = halogen) or 9a can be treated with a compound of formula A in the presence of a coupling agent, such as bis(triphenylphosphine)palladium(II) chloride, tetrakis(triphenylphosphine)palladium(0), bis(triphenylphosphine)palladium(II) chloride,
acetate or mixtures thereof, in one or more suitable solvent, for example, aprotic polar (e.g., tetrahydrofuran, diethylether, 1,4-dioxane) polar protic (e.g., methanol, ethanol, isopropanol, tert-butanol), toluene or mixtures thereof in the presence of a base such as cesium fluoride or the like to form a compound formula 10. The intermediate of formula 10 thus obtained can be converted to the compound of formula (Ia) following the steps as described for the synthesis of (Ia) from (5a) in Scheme-I above.

Scheme - III

Step 1:

The intermediate of formula (2b) (wherein Z is substituted or unsubstituted alkyl or substituted or unsubstituted arylalkyl) can be prepared by treating 6-amino nicotinic acid (1) with an acid chloride, such as (thionyl chloride or oxalyl chloride, preferably thionyl chloride) in a suitable solvent (such as methanol, ethanol, isopropanol or tertiary butanol, preferably ethanol) either at room temperature or at elevated temperature, preferably at reflux temperature of the suitable solvent used.

The intermediate of formula (2b) (with or without purification) can be reacted further with a suitable halo-succinimide (such as N-chlorosuccinimide, N-bromosuccinimide or N-iodosuccinimide) in a suitable solvent (such as tetrahydrofuran or carbon
tetrachloride or acetonitrile) to give the intermediate of formula (3b) (wherein R^1 is halogen).

In the second step, the intermediate of formula (3b) can be reacted with the intermediate of formula (4b) (wherein X is a halogen) in a suitable solvent (such as dimethoxyethane or dimethyl formamide or ethanol) in the optional presence of a organic or inorganic base (such as sodium bicarbonate or sodium carbonate or potassium carbonate or triethylamine), preferably at an elevated temperature (80 °C or above), to yield an intermediate of formula (5b). The intermediate of formula (5b) can then be hydrolysed to give an intermediate of formula (6b) following the steps as described for the preopration of 6a from 5a in schem 1.

The intermediate of formula (6b) can then be converted to a corresponding acid chloride, for example, by treatment with thionyl chloride or oxalyl chloride in a suitable solvent (such as benzene, toluene, dichloromethane, or chloroform). The acid chloride thus obtained (with or without purification) can be dissolved in a suitable solvent (such as dichloromethane or chloroform, or dichloroethane) followed by the addition of an amine of formula NHR^4R^5, optionally, in the presence of an organic base (such as triethylamine or pyridine) to give a compound of formula (Ib).

Alternately, the compound of formula (6b) can be treated with an activating reagent such as (benzotriazol-1-yl-oxy)tris(dimethylamino)phosphonium hexafluorophosphate (BOP), optionally, in the presence of a suitable solvent (such as dimethyl formamide) and an organic base (such as triethylamine or pyridine, preferably triethylamine), followed by the addition of an amine of formula NHR^4R^5 to obtain a compound of formula (Ib).
The compound of formula (3b) (wherein Z is substituted or unsubstituted alkyl or substituted or unsubstituted arylalkyl, R¹ is hydrogen or halogen) is treated with compound of formula 7b (wherein X is halogen) to form a compound of formula 8b in one or more suitable solvent, for example, aprotic polar (e.g., dimethylformamide, dimethoxymethane, acetonitrile, dimethylacetamide, tetrahydrofuran) protic polar (e.g., methanol, ethanol, isopropanol, tert-butanol) or mixtures thereof in presence of one or more organic or inorganic base, for example, triethylamine, pyridine, sodium bicarbonate, sodium carbonate, potassium carbonate, lithium carbonate, sodium hydroxide, potassium hydroxide, lithium hydroxide, triethylamine, methylamine or phenylamine, preferably in the absence of a base to form a compound of formula 8b at elevated temperature (80 °C or above).
The compound of formula 8b is treated with halo-succinimide, for example, N-chlorosuccinimide, N-bromosuccinimide or N-iodosuccinimide in one or more suitable solvent, for example, tetrahydrofuran, carbon tetrachloride, acetonitrile, dimethoxyethane or mixture thereof to give a compound of formula 9b.

The compound of formula 9b is further hydrolyzed in presence of one or more base, for example, sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium methoxide, sodium ethoxide, potassium methoxide, potassium ethoxide, sodium carbonate, potassium carbonate in one or more suitable solvent, for example, polar protic (e.g., methanol, ethanol, isopropanol, tert-butanol, water, aprotic polar (e.g., tetrahydrofuran, diethylether, 1,4-dioxane or mixtures thereof to form a compound of formula 12.

The compound of formula 12 can be converted to compound of formula Ib₂ by i) Path A or ii) Path B

Path A: The compound of formula 12 can be treated with a compound of formula A in the presence of a coupling agent, such as bis(triphenylphosphine)palladium(II) chloride, tetrakis(triphenylphosphine)palladium(0), bis(triphenylphosphine)palladium(π-acetate or mixtures thereof, in one or more suitable solvent, for example, aprotic polar (e.g., tetrahydrofuran, diethylether, 1,4-dioxane) polar protic (e.g., methanol, ethanol, isopropanol, tert-butanol) or mixtures thereof in the presence of a suitable base such aqueous sodium carbonate, potassium carbonate or cesium fluoride, preferably aqueous sodium carbonate to form a compound formula 11b.

The compound of formula lib can be reacted with thionyl chloride, oxalyl chloride, phosphorous trichloride or phosphorus pentachloride in one or more suitable solvent, for example, hydrocarbon solvents (e.g., benzene, toluene, xylene) halogenated solvents (e.g., dichloromethane, dichloroethane, chloroform, carbontetrachloride) to form an acid chloride which is further treated with an amine of formula -NHR₄R₅ to form a compound of formula 1b.

Alternatively, the compound of formula lib can be treated with one or more activating agents, for example, benzotriazol- 1-yl-oxy)tris(dimethylamino)phosphonium hexafluoro phosphate, Lawesson's reagent, diethylchlorophosphite, isobutyl chloroformate in presence of a base, for example, triethylamine, trimethylamine, pyridine, or mixtures thereof in suitable solvent, for example, aprotic polar (e.g., dimethylformamide, dimethylacetamide, acetonitrile,
dimethylsulfoxide or mixtures thereof) followed by treatment with an amine of formula \( \text{NHR}^4\text{R}^5 \) to form a compound of formula Ib.

Path B: The compound of formula 12 can be reacted with thionyl chloride, oxalyl chloride, phosphorous trichloride or phosphorus pentachloride in one or more suitable solvent, for example, hydrocarbon solvents (e.g., benzene, toluene, xylene) halogenated solvents (e.g., dichloromethane, dichloroethane, chloroform, carbontetrachloride) to form an acid chloride which is further treated with an amine of formula \(-\text{NHR}^4\text{R}^5\) optionally in presence of one or more base, for example, triethylamine, trimethylamine, pyridine in one or more solvent, for example, (e.g., dichloromethane, dichloroethane, chloroform, carbontetrachloride) to form a compound of formula 13.

Alternately, the compound of formula 12 can be reacted with one or more activating agents, for example, benzotriazol-1-yl-oxy)tris(dimethylamo)phosphonium hexafluoro phosphate, Lawesson's reagent, diethylchlorophosphite, isobutyl chloroformate in presence of a base, for example, triethylamine, trimethylamine, pyridine, or mixtures thereof in suitable solvent, for example, aprotic polar (e.g., dimethylformamide, dimethylacetamide, acetonitrile, dimethylsulfoxide or mixtures thereof) followed by treatment with an amine of formula \( \text{NHR}^4\text{R}^5 \) to form a compound of formula 13.

The compound of formula 13 can be treated with a compound of formula A in the presence of a coupling agent, such as bis(triphenylphosphine)palladium(II) chloride, tetrakis(triphenylphosphine)palladium(0), bis(triphenylphosphine)palladium(II) acetate or mixtures thereof, in one or more suitable solvent, for example, aprotic polar (e.g., tetrahydrofuran, diethylether, 1,4-dioxane) polar protic (e.g., water, methanol, ethanol, isopropanol, tert-\( \text{b-Xanol} \)) or mixtures thereof optionally in presence of one or more base, for example, sodium carbonate, potassium carbonate, sodium hydroxide, potassium hydroxide to form a compound formula Ib.
The compound of formula (3b) can be reacted with the compound of formula (4b) (wherein X is a halogen) optionally in one or more suitable solvent, for example, aprotic polar (e.g., dimethoxyethane, dimethylformamide, acetonitrile, dimethylsulfoxide or mixtures thereof), polar protic (e.g., ethanol, methanol, water or mixtures thereof) optionally in presence of one or more organic or inorganic base, for example, sodium bicarbonate, sodium carbonate, potassium carbonate, triethylamine or pyridine, preferably at higher temperature (80 °C or above) to form a compound of formula (5b). The compound of formula (5b) can then be hydrolysed in presence of one or more base, for example, sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium carbonate, potassium carbonate in one or more solvent, for example aprotic polar (e.g., tetrahydrofuran, diethylether, 1,4-dioxane) polar protic (e.g., methanol, ethanol, isopropanol, tert/-butanol, water) or mixtures thereof to form a compound of formula (6b).

The compound of formula (6b) can be treated with thionyl chloride, oxalyl chloride, phosphorous trichloride or phosphorus pentachloride in one or more suitable
solvent, for example, hydrocarbon solvents (e.g., benzene, toluene, xylene) halogenated solvents (e.g., dichloromethane, dichloroethane, chloroform, carbontetrachloride) to form an acid chloride which is further treated with an amine of formula amine of formula \( \text{HN} \text{N} \cdot \text{P} \) in the presence of an organic base such as triethylamine or pyridine to obtain a compound of formula 14 (wherein \( P_1 \) is protecting group).

Alternately, the compound of formula 6b can be reacted with one or more activating agents, for example, benzotriazol-l-yl-oxy)tris(dimethylamino)phosphonium hexafluoro phosphate, Lawesson's reagent, diethylchlorophosphite, oxalyl chloride, isobutyl chloroformate in presence of a base, for example, triethylamine, trimethylamine, pyridine, or mixtures thereof in suitable solvent, for example, aprotic polar (e.g., dimethylformamide, dimethylacetamide, acetonitrile, dimethylsulfoxide or mixtures thereof) followed by treatment in presence of one or more organic or inorganic base, for example, triethylamine, trimethylamine, pyridine or mixtures thereof followed by the addition of an amine of formula \( \text{HN} \text{N} \cdot \text{P} \) to obtain a compound of formula 14 (wherein \( P_1 \) is protecting group).

The compound of formula 14 can be deprotected to form a compound of formula 14 in presence of acid, for example, hydrochloric acid or trifluoroacetic acid in one or more suitable solvent, for example diethyl ether, ethyl acetate, tetrahydrofuran, dimethoxyethane or mixtures thereof.

The compound of formula 15 can be reacted with \( R^d-X \) in presence of one or more base, for example, potassium carbonate, cesium carbonate, sodium hydroxide, potassium hydroxide or mixtures thereof in one or more suitable solvent, for example, dimethoxyethane, dimethyl formamide, acetonitrile, dimethylsulfoxide, dichloromethane, dichloroethane, chloroform or mixtures thereof to form a compound of formula 16.
Intermediate 1: 2-Amino nicotinic acid ethyl ester

To a suspension of 2-amino nicotinic acid (2.0 gm, 14.48 mmol) in ethanol (25 mL) was added thionyl chloride (5.7 gm, 43.37 mmol) drop wise at 60 °C under stirring. The resultant reaction mixture was then refluxed for 15 hrs. The volatile matters were removed under reduced pressure and the residue was diluted with ethyl acetate and the organic layer was washed with aqueous saturated sodium bicarbonate solution, water and brine followed by drying over sodium sulfate and concentrated to give the corresponding ester (1.90 gm, 79%) which was used without further purification. \(^1\)H NMR(CDCl\(_3\), 300 MHz, ppm): 5.82-8.16 (m, 2H), 6.67-6.23 (m, 2H), 4.39-4.32 (q, J=7.2 Hz, 2H), 1.41-1.37 (t, J=7.2 Hz, 3H).

Intermediate 2: 6-Amino nicotinic acid ethyl ester

To a suspension of 6-amino nicotinic acid (1.0 gm, 7.23 mmol) in ethanol (20 mL) was added thionyl chloride (1.6 mL, 21.68 mmol) drop wise at 60 °C under inert atmosphere and constant stirring. The resultant reaction mixture was then refluxed for 18 hrs. The volatile matters were then removed under reduced pressure and the residue was diluted with ethyl acetate and the organic layer was washed with aqueous saturated sodium bicarbonate solution, water and brine consecutively followed by drying over sodium sulfate and finally concentrated to give the corresponding ester (1.15 gm, 95.8%) in spectroscopically pure form which was used without further purification in the next step. \(^1\)H NMR(DMSO-d\(_6\), 300 MHz, ppm): δ 8.49 (d, J=1.8 Hz, IH), 7.83-7.79 (dd, J=8.7 & 2.7 Hz, IH), 6.83 (bs, 2H), 6.44 (d, J=8.7 Hz, IH), 4.26-4.18 (q, J=6.9 Hz, 2H), 1.29-1.25 (t, J=6.9 Hz, 3H).

Intermediate 3: 2-Amino-5-chloro nicotinic acid ethyl ester

N-Chlorosuccinimide (502 mg, 3.75 mmol) was charged in portion to the solution of 2-amino nicotinic acid ethyl ester (500 mg, 3.01 mmol) in dry tetrahydrofuran (15 mL) at room temperature under nitrogen atmosphere and stirred for 15 hrs. After removing the volatile matters the residue was subjected to silica gel column chromatography and the product was isolated using ethyl acetate and petroleum ether mixture as eluent in 71.2% yield (430 mg). \(^1\)H NMR (DMSO-d\(_6\), 300 MHz, ppm): δ 8.25 (d, J=2.7 Hz, IH), 8.03 (d, J=2.7 Hz, IH), 7.34 (bs, 2H), 4.32-4.25 (q, J=7.2 Hz, 2H), 1.34-1.29 (t, J=7.2 Hz, 3H).
Intermediate 4: 2-Amino-5-bromo nicotinic acid ethyl ester

This derivative was prepared according to the procedure as described above for 2-amino-5-chloro nicotinic acid ethyl ester using N-bromosuccinimide instead of N-chlorosuccinimide in 76.2% yield. $^1$H NMR (DMSO-$d_6$, 300 MHz, ppm): $\delta$ 8.30-8.29 (d, J=2.7 Hz, IH), 8.13-8.12 (d, J=2.7 Hz, IH), 7.35 (s, 2H), 4.32-4.25 (q, J=7.2 Hz, 2H), 1.34-1.29 (t, J=7.2 Hz, 3H).

Intermediate 5: 2-Amino-5-iodo nicotinic acid ethyl ester

This derivative was prepared according to the procedure as described above for 2-amino-5-chloro nicotinic acid ethyl ester using N-iodosuccinimide instead of N-chlorosuccinimide in 16% yield. $^1$H NMR (DMSO-$d_6$, 300 MHz, ppm): $\delta$ 8.36 (d, J=2.1 Hz, IH), 8.23 (d, J=2.4 Hz, IH), 7.31 (s, 2H), 4.31-4.24 (q, J=7.2 Hz, 2H), 1.33-1.28 (t, J=6.9 Hz, 3H).

Intermediate 6: 6-Amino-5-bromo nicotinic acid ethyl ester

N-Bromo succinimide (932 mg, 5.23 mmol) was charged in portion to the solution of 6-amino nicotinic acid ethyl ester (580 mg, 3.49 mmol) in dry tetrahydrofuran (25 mL) at room temperature under nitrogen atmosphere and stirred for 15 hrs. After removing the volatile matters under vacuum, the residue was subjected to silica gel column chromatography and the product was isolated using ethyl acetate and petroleum ether mixture as eluent in 58.5% yield (500 mg). $^1$H NMR (DMSO-$d_6$, 300 MHz, ppm): $\delta$ 8.50 (d, J=2.1 Hz, IH), 8.08 (d, J=1.8 Hz, IH), 7.17 (bs, 2H), 4.28-4.21 (q, J=6.9 Hz, 2H), 1.31-1.26 (t, J=6.9 Hz, 3H).

The intermediates 7 to 10 were prepared according to the process as described above

6-Amino-5-iodo-nicotinic acid ethyl ester; 6-Amino-5-bromo-nicotinic acid ethyl ester; 6-Amino-nicotinic acid ethyl ester and 6-Amino-5-chloro-nicotinic acid ethyl ester.

Intermediate 11: 2-Bromo-l-(4-chlorophenyl)-2-phenyl ethanone

To a solution of l-(4-Chlorophenyl)-2-phenyl ethanone, prepared following literature (J. Med. Chem., 2004, 47, P627), (500 mg, 2.17 mmol) in benzene (15 mL), was added bromine (347 mg, 2.17 mmol) slowly at room temperature and the resultant solution was continued to stir for 2 hrs. at the same temperature. After removing the volatile matters on rotary evaporator the residue was dissolved in dichloromethane and washed with saturated sodium bicarbonate solution. The organic phase was dried over sodium sulfate and concentrated. The residue was then subjected
to silica gel column chromatography and the pure compound (450 mg, 67%) was isolated using ethyl acetate and petroleum ether as mixture.

$^1$H NMR (CDCl$_3$, 300 MHz, ppm): £ 7.94-7.91 (dd, J= 6.9 Hz and 1.8 Hz, 2H); 7.52-7.49 (dd, J= 7.5Hz and 1.2 Hz, 2H); 7.44-7.33 (m, 5H); 6.31 (s, 1H).

The intermediates 12 to 31 were prepared according to the process as described above:

Bromo-2-(4-chlorophenyl)- 1-(4-trifluoromethylphenyl) ethanone; 2-Bromo-1,2-bis-(4-chlorophenyl)ethanone; 2-Bromo-2-(4-bromophenyl)- 1-(4-chloro-phenyl)-ethanone; 2-Bromo-1-(4-bromophenyl)-2-(4-chlorophenyl)-ethanone; 2-Bromo-2-(4-chlorophenyl)-1 -(2-chloro phenyl) ethanone; 2-Bromo- 1-(4-chlorophenyl)-2-(2,4-dichloro-phenyl)-ethanone; 2-Bromo-2-(4-chlorophenyl)- 1-(2,4-dichloro-phenyl)-ethanone; 2-Bromo-2-(4-chlorophenyl)-1 -(4-iodophenyl)-ethanone; 2-(4-chlorophenyl)-I-(4-iodophenyl)-ethanone:2-Bromo-1-(4-bromophenyl)-ethanone; 2-Bromo-2-(4-chlorophenyl)-1 -phenyl-ethanone- 2-Bromo-2-(4-chlorophenyl)-l -phenyl-ethanone; 2-(2,4-Dichlorophenyl)-l -phenyl-ethanone; 2-Bromo-2-(2,4-dichlorophenyl)-l -phenyl-ethanone; 2,2-Dibromo-1-(4-tert-butyl phenyl)-ethanone; 2-(2-Chlorophenyl)-1-(4-chlorophenyl)-ethanone; 2-Bromo-2-(2-chlorophenyl)- 1-(4-chlorophenyl)-ethanone; 2-(4-Bromophenyl)-1-(4-chlorophenyl)-ethanone; 2-Bromo-2-(4-bromophenyl)- 1-(4-chlorophenyl)-ethanone and 2-Bromo- 1-(4-trifluoromethyl phenyl)-ethanone.

Intermediate 32: 2-f4-ChlorophenvD-3-phenyl imidazo[1.2alPyridine-8-carboxylic acid ethyl ester

A mixture of 2-Amino nicotinic acid ethyl ester (1.0 gm, 6.02 mmol) and 2-Bromo-1-(4-chlorophenyl)-2-phenyl ethanone (1.86 gm, 6.02 mmol) in dimethyl formamide (10 mL) was heated at 80 °C for 3 hrs. Then the reaction mixture was diluted with ethyl acetate and the organic portion was washed with water (3x40 mL) followed by drying over sodium sulfate, concentrated and the product was purified by column chromatography using a mixture of ethyl acetate and petroleum ether followed by methanol and chloroform in 50.7% yield (1.15 gm). $^1$H NMR (DMSO-d$_6$, 300 MHz, ppm): £ 8.21 (d, J=7.2 Hz, IH), 7.91 (d, J=7.2 Hz, IH), 7.63-7.60 (m, 5H), 7.53-7.51 (m, 2H), 7.40 (d, J=8.7 Hz, 2H), 7.02-6.98 (t, J=6.9 Hz, IH), 4.46-4.38 (q, J=6.9 Hz, 2H), 1.42-1.37 (J=6.9 Hz, 3H).
The intermediates 33 to 72 were prepared according to the above procedure as described for intermediate 32 (J Med. Chem., 2005, 48, P1823).

6-Chloro-2,3-bis-(4-chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid ethyl ester; 6-Bromo-2,3-bis-(4-chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid ethyl ester; 3-(4-bromophenyl)-6-Chloro-2-(4-chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid ethyl ester; 2-(4-Bromophenyl)-6-Chloro-3-(4-chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid ethyl ester; 6-Bromo-2-(4-Bromophenyl)-3-(4-chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid ethyl ester; 6-Chloro-3-(4-chlorophenyl)-2-(4-trifluoromethylphenyl)imidazo[1,2a]pyridine-8-carboxylic acid ethyl ester; 2,3-bis-(4-chlorophenyl)-6-iodo imidazo[1,2a]pyridine-8-carboxylic acid ethyl ester; 6-Bromo-3-(4-Chlorophenyl)-2-(2-chlorophenyl)imidazo[1,2a]pyridine-8-carboxylic acid ethyl ester; 8-Bromo-2,3-bis-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid ethyl ester; Bis-2,3-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid ethyl ester; 2-(4-Chlorophenyl)-3-(2,4-dichlorophenyl)imidazo[1,2a]pyridine-8-carboxylic acid ethyl ester; 2-(4-Chlorophenyl)-6-Chloro-3-(4-chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid ethyl ester; 3-(4-Chlorophenyl)-6-chloro-2-(4-chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid ethyl ester; 3-(4-Chlorophenyl)-6-chloro-2-(4-chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid ethyl ester; 6-Chloro-2,3-bis-(4-chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid ethyl ester; 8-Bromo-2,3-bis-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid ethyl ester; 8-Chloro-2,3-bis-(4-chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid ethyl ester; 8-Chloro-2,3-bis-(4-chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid ethyl ester; 8-Chloro-2,3-bis-(4-chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid ethyl ester; 8-Chloro-2,3-bis-(4-chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid ethyl ester; 8-Chloro-
3-(2-chlorophenyl)-2-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid ethyl ester; 8-Chloro-3-(4-chlorophenyl)-2-(2-chlorophenyl)-imidazo[1,2-a]pyridin-6-carboxylic acid ethyl ester; 8-chloro-3-(2,4-dichlorophenyl)-2-phenyl-imidazo[1,2-a]pyridine-6-carboxylic acid ethyl ester; 2,3-Bis-(4-chlorophenyl)-8-iodo-imidazo[1,2-a]pyridine-6-carboxylic acid ethyl ester; 3-(4-Bromophenyl)-2-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid ethyl ester; 2-(4-Bromophenyl)-3-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid ethyl ester; 8-Chloro-2-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid ethyl ester; 3-Bromo-8-chloro-2-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid ethyl ester; 3-Bromo-8-chloro-2-(4-fluorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid dimethylamide; 2-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid ethyl ester and 3-Bromo-2-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid ethyl ester.

**Intermediate 73:** 2-(4-Chlorophenyl)-3-phenyl imidazo[1,2-a]pyridine-8-carboxylic acid ethyl ester.

The ester (1.2 gm, 3.18 mmol) as prepared above was hydrolyzed by 10% sodium hydroxide in water at room temperature over 3 hrs. The volatile matters were removed under reduced pressure and the residue was acidified to pH 5.0 with acetic acid at 0°C and the precipitated acid (950 mg, 85.5%) was filtered off, washed with water and dried thoroughly. 1H NMR (DMSOd_6, 300 MHz, ppm): δ 8.22 (d, J=6.6 Hz, IH), 7.94 (d, J=6.9 Hz, IH), 7.64-7.59 (m, 5H), 7.56-7.53 (m, 2H), 7.42 (d, J=9.0 Hz, 2H), 7.08-7.04 (t, J=6.9 Hz, IH).

The following intermediates 74 to 106 were prepared according to the process as described above:
- 2,3-bis-(4-chlorophenyl)-6-iodo imidazo[1,2a]pyridine-8-carboxylic acid; 6-Chloro-3-(4-chlorophenyl)-2-(4-trifluoromethylphenyl)imidazo[1,2a]pyridine-8-carboxylic acid; 6-Bromo-3-(4-Chlorophenyl)-2-(2-chlorophenyl)imidazo[1,2a]pyridine-8-carboxylic acid; 6-Chloro-2,3-bis-(4-chlorophenyl)imidazo[1,2a]pyridine-8-carboxylic acid; 6-Bromo-2,3-bis-(4-chlorophenyl)imidazo[1,2a]pyridine-8-carboxylic acid; 6-Bromo-2-(4-Bromophenyl)-3-(4-chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid; 3-(4-bromophenyl)-6-(2-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid.
Chloro-2-(4-chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid; 2-(4-Bromophenyl)-6-Chloro-3-(4-chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid; 8-Bromo-2,3-bis-(4-Chloro phenyl) imidazo[1,2a]pyridine-6-carboxylic acid; 3-Bromo-2-(4-chlorophenyl)-imidazo[1,2a]pyridine-6-carboxylic acid; 2-(4-Chlorophenyl)-3-(2,4-dichlorophenyl) imidazo[1,2a]pyridine-8-carboxylic acid; 2-(4-Bromophenyl)-6-Chloro-3-(4-chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid; 3-(4-Bromophenyl)-6-chloro-2-(4-chlorophenyl) imidazo[1,2a]pyridine-8-carboxylic acid; 2-(4-Bromophenyl)-6-chloro-3-(4-chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid; 6-Chloro-3-(4-chlorophenyl)-2-(4-trifluoromethyl-phenyl)imidazo[1,2a]pyridine-8-carboxylic acid; 2-(4-Bromophenyl)-6-chloro-3-(4-chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid; 3-(4-Bromophenyl)-2-(4-chlorophenyl)-imidazo[1,2a]pyridine-6-carboxylic acid; 8-Bromo-3-(2-chlorophenyl)-2-(4-chlorophenyl)-imidazo[1,2a]pyridine-6-carboxylic acid; 8-Chloro-2,3-bis-(4-chlorophenyl)-imidazo[1,2a]pyridine-6-carboxylic acid; 8-Chloro-3-(2-chlorophenyl)-2-(4-chlorophenyl)-imidazo[1,2a]pyridine-6-carboxylic acid; 8-Chloro-3-(2,4-dichlorophenyl)-2-phenyl-imidazo[1,2a]pyridine-6-carboxylic acid; 8-Chloro-3-(4-chloro-phenyl)-imidazo[1,2a]pyridine-6-carboxylic acid; 8-Chloro-3-(2,4-dichlorophenyl)-2-phenyl-imidazo[1,2a]pyridine-6-carboxylic acid; 2,3-Bis-(4-chlorophenyl)-8-iodo-imidazo[1,2a]pyridine-6-carboxylic acid; 3-(4-Bromophenyl)-2-(4-chlorophenyl)-imidazo[1,2a]pyridine-6-carboxylic acid; 2-(4-Bromophenyl)-3-(4-chloro-phenyl)-imidazo[1,2a]pyridine-8-carboxylic acid; 2,3-Bis-(4-chlorophenyl)-3-(4-chloro-phenyl)-imidazo[1,2a]pyridine-6-carboxylic acid; 3-Bromo-8-chloro-2-(4-chloro-phenyl)-imidazo[1,2a]pyridine-6-carboxylic acid and [3-Bromo-8-chloro-2-(4-chloro-phenyl)-imidazo[1,2a]pyridin-6-yl]-[(4-methyl-piperazin-1-yl)-methanone. **Examples**

**Example 1**: 2-(4-Chlorophenyl)\_V3-phenyl imidazo[1,2a]pyridine-8-carboxylic acid piperidine-1-yl amide

**Step 1**: 2-(4-Chlorophenyl)-3-phenyl imidazo[1,2a]pyridine-8-carboxylate chloride
To a suspension of 2-(4-Chlorophenyl)-3-phenylimidazo[1,2-a]pyridine-8-carboxylic acid (450 mg, 1.3 mmol) in dry benzene (25 mL) was added oxalyl chloride (492 mg, 0.34 mL, 3.87 mmol) at room temperature followed catalytic amount of dimethyl formamide (DMF) and the resultant reaction mixture was stirred for 4 hrs. at the same temperature. The workup followed by removal of the volatile matters under high vacuum to give the acid chloride that was used in the next step without further purification.

Step 2: To the solution of 2-(4-Chlorophenyl)-3-phenylimidazo[1,2-a]pyridine-8-carbonyl chloride, prepared as defined above (160 mg, 0.433 mmol) in dichloromethane (15 mL) was added 1-amino piperidine (43.4 mg, 0.433 mmol) under inert atmosphere and at room temperature followed by the addition of triethylamine (87.5 mg, 0.867 mmol) and then the mixture was continued to stir at ambient temperature for 15 hrs. The mixture was diluted with chloroform and washed with water (2x40 mL) and the organic layer was then dried over sodium sulfate and concentrated. The product was purified over silica gel column chromatography using methanol and chloroform mixture as eluent as off white solid (45 mg, 24.1%). M.P: 206-208 0C. IR (neat): cm⁻¹ 3436, 1672. ₁H NMR (CDCl₃, 300 MHz, ppm): δ 11.39 (s, IH), 8.29 (d, J=6.9 Hz, IH), 7.99 (d, J=6.9 Hz, IH), 7.62-7.56 (m, 5H), 7.45-7.43 (m, 2H), 7.30 (d, J=8.4 Hz, 2H), 6.93-6.88 (t, J=6.9 Hz, IH), 3.06 (bs, 4H), 1.86-1.82 (m, 4H) 1.57 (bs, 2H). MS (m/z): 431 (M⁺+H-I). Purity (HPLC): 93.3%.

The compounds in examples 2 to 80 were prepared according to the process as described for example 1 using the appropriate intermediate:

Example 2: 2-(4-Chlorophenyl)-3-phenylimidazo[1,2-a]pyridine-8-carboxylic acid morpholine-1-yl amide, MS (m/z): 433 (M⁺+I); m. pt: 210-211 0C.

Example 3: 2-(4-Chlorophenyl)-3-phenylimidazo[1,2-a]pyridine-8-carboxylic acid adamantan-1-yl amide, MS (m/z): 482.1.

Example 4: 2-(4-Chlorophenyl)-3-phenylimidazo[1,2-a]pyridine-8-carboxylic acid-(4-methanesulfonyl) piperazine-1-yl amide, MS (m/z): 495.8, 497.3; m. pt: 134-136 0C.

Example 5: 2-(4-Chlorophenyl)-3-phenylimidazo[1,2-a]pyridine-8-carboxylic acid cyclohexyl amide, MS (m/z): 430 (M⁺+I); m. pt.: 197-199 0C.

Example 6: 2-(4-Chlorophenyl)-3-phenylimidazo[1,2-a]pyridine-8-carboxylic acid-(4-chloro benzyl) amide, m. pt.: 177-180 0C.
Example 7: 2,3-Bis-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid piperidine-1-yl amide, MS (m/z): 465.1, 467.1; m. pt: 224-227 0C.

Example 8: 2,3-Bis-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid 1-butyl amide, m. pt.: 165-167 0C.

Example 9: 2,3-Bis-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid cyclohexyl amide, m. pt.: 216-218 0C.

Example 10: 2-(4-Chlorophenyl)-3-(2,4-dichlorophenyl)imidazo[1,2a]pyridine-8-carboxylic acid piperidine-1-yl amide, m. pt.: 237-240 0C.

Example 11: 2-(4-Chlorophenyl)-3-(2,4-dichlorophenyl)imidazo[1,2a]pyridine-8-carboxylic acid morpholine-1-yl amide, MS (m/z): 501.1 (M+), 503.1 (M+2).

Example 12: 5-Chloro-2,3-Bis-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid piperidine-1-yl amide, m. pt: 275-276 0C.

Example 13: 6-Chloro-2,3-Bis-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid azepan-1-ylamide, m. pt.: 248-249 0C.

Example 14: 6-Bromo-2,3-Bis-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid piperidine-1-yl amide, MS (m/z): 543 (M+), 545 (M+2); m. pt.: 290 0C.

Example 15: 3-(4-Chlorophenyl)-2-(2,4-dichlorophenyl)imidazo[1,2a]pyridine-8-carboxylic acid piperidine-1-yl amide, m. pt.: 247-249 0C.

Example 16: 3-(4-Chlorophenyl)-2-(2,4-dichlorophenyl)imidazo[1,2a]pyridine-8-carboxylic acid morpholine-1-ylamide, m. pt.: 250-253 0C.

Example 17: 6-Bromo-2,3-Bis-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid morpholine-1-ylamide, m. pt.: >300 0C (Decomp).

Example 18: 2-(4-Bromophenyl)-6-chloro-3-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid piperidine-1-yl amide, MS (m/z): 543.1 (M+), 545.1 (M+2); m. pt.: >260 0C.

Example 19: 2-(4-Bromophenyl)-6-bromo-3-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid piperidine-1-yl amide, MS (m/z): 589.1 (M+1), 591.1; m. pt.: >260 0C.

Example 20: 6-Chloro-2,3-Bis-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid cyclohexyl amide, m. pt.: 252-255 0C.

Example 21: 3-(4-Bromophenyl)-6-chloro-2-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid piperidine-1-yl amide, m. pt.: 275-279 0C.
Example 22: 2,3-bis-(4-chlorophenyl)-6-iodoimidazo[1,2a]pyridine-8-carboxylic acid ethyl amide, m.pt. >270 °C.

Example 23: 2,3-bis-(4-chlorophenyl)-6-iodo imidazo[1,2a]pyridine-8-carboxylic acid tert-butyl amide, MS [m/z]: 564, 566; m.pt. >270 °C.

Example 24: 2,3-bis-(4-chlorophenyl)-6-iodo imidazo[1,2a]pyridine-8-carboxylic acid-2-(hydroxyl ethyl) amide, m.pt. 269-270 °C.

Example 25: 2,3-bis-(4-chlorophenyl)-6-iodoimidazo[1,2a]pyridine-8-carboxylic acid-2-(hydroxyethyl) amide, m.pt.: 269-270 °C.

Example 26: 2,3-bis-(4-chlorophenyl)-6-iodo imidazo[1,2a]pyridine-8-carboxylic acid-3-(hydroxyl propyl) amide, m.pt.: >270 °C.

Example 27: 2,3-Bis-(4-chlorophenyl)-6-iodo-imidazo[1,2-a]pyridine-8-carboxylic acid piperidin-1-ylamide, MS [m/z]: 591.32 [M+]; m.pt. >270 °C.

Example 28: 2,3-Bis (4-chlorophenyl)-6-iodo-imidazo[1,2-a]pyridine-8-carboxylic acid butylamide, m.pt.: 235-237 °C.

Example 29: 2,3-Bis (4-chlorophenyl)-6-iodo-imidazo[1,2-a]pyridine-8-carboxylic acid ethylamide, m.pt.: >270 °C.

Example 30: 2,3-Bis (4-chlorophenyl)-6-iodo-imidazo[1,2-a]pyridine-8-carboxylic acid (3-hydroxy-propyl)-amide hydrochloride, m.pt.: 235-236 °C.

Example 31: 2-(4-Bromophenyl)-6-chloro-3-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid-5-hydroxypropyl amide, m.pt.: 201-205 °C.

Example 32: 2-(4-Bromophenyl)-6-chloro-3-(4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid (3-hydroxy-propyl)-amide, m.pt.: 209-211 °C.

Example 33: 6-Chloro-3-(4-chlorophenyl)-2-(4-trifluoromethyl phenyl) imidazo[1,2a]pyridine-8-carboxylic acid cyclopropyl amide, m.pt.: 214-216 °C.

Example 34: 6-Chloro-3-(4-chlorophenyl)-2-(4-Trifluoromethyl phenyl) imidazo[1,2a]pyridine-8-carboxylic acid cyclohexyl amide, MS [m/z]: 532.2, 534.1; m.pt: 232-233 °C.

Example 35: 6-Chloro-3-(4-chlorophenyl)-2-(4-trifluoromethyl-phenyl)imidazo[1,2-a]pyridine-8-carboxylic acid tert-butyl-amide, m.pt: 260-260.5 °C.

Example 36: 6-Chloro-2,3-Bis-(4-Chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid -3,4-difluorophenyl amide, m.pt.: >270 °C.

Example 37: 6-Chloro-2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid (4-hydroxy-butyl)-amide, MS [m/z]: 488.38 [M+H]+; m.pt.: 223-226 °C.
Example 38: 6-Chloro-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid phenethylamide, MS [m/z]: 520.24 [M+]; m.pt.: 213-216 °C.

Example 39: 6-Chloro-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid (3-hydroxy-propyl)-amide, MS [m/z]: 474.21 [M+H]+; m.pt.: 219-221 °C.

Example 40: 6-Chloro-2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid tert-butylamide, MS [m/z]: 472.25 [M+H]+; m.pt.: 267-269 °C.

Example 41: 6-Chloro-2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid benzylamide, MS [m/z]: 506.17 [M+H].

Example 42: 2-(4-tert-Butylphenyl)-6-chloro-3-(4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid (3-hydroxy-propyl)-amide, m.pt.: 193-194 °C.

Example 43: 6-Chloro-3-(4-chlorophenyl)-2-(4-iodophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid (3-hydroxy-propyl)-amide, m.pt.: 239-240 °C; MS [m/z]: 566.05 [M+H]+.

Example 44: 2,3-bis-(4-chlorophenyl)-6-iodo imidazo[1,2a]pyridine-8-carboxylic acid pyrrolidine-1-yl amide, m.pt.: >270 °C.

Example 45: 6-Bromo-3-(4-Chlorophenyl)-2-(2-chlorophenyl)imidazo[1,2-a]pyridine-8-carboxylic acid piperidine-1-yl amide, m.pt.: 198-201 °C.

Example 46: 6-Bromo-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid (4-hydroxy-butyl)-amide, m.pt.: 235-236.6 °C; MS [m/z]: 534.28 [M+H]+.

Example 47: 6-Bromo-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid tert-butyl-amide, m.pt.: >260 °C.

Example 48: 6-Bromo-2,3-Bis (4-chlorophenyl)-imidazo[1,2-a]pyridin-8-carboxylic acid (3-hydroxy propyl)-amide, m.pt.: 224-225.6 °C; MS [m/z]: 520.07 [M+H]+.

Example 49: [3-(4-Bromophenyl)-6-chloro-2-(4-chlorophenyl) imidazo[1,2a]pyridin-8-y1] piperidine-1-yl methanone, m.pt.: 233-234 °C.

Example 50: 2-(4-Bromophenyl)-6-chloro-3-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid (hexahydro cyclopenta-[c]-pyrrol-2-yl)-amide, m.pt.: 236-237 °C.

Example 51: 8-Bromo-2,3-bis-(4-chloro phenyl) imidazo[1,2a]pyridine-6-carboxylic acid tert-butyl amide, m.pt.: 209-211 °C.

Example 52: 8-Bromo-2,3-bis-(4-Chloro phenyl) imidazo[1,2a]pyridine-6-carboxylic acid -(2-hydroxy- 1,1-dimethyl-ethyl) amide, m.pt.: 240-242 °C.

Example 53: 8-Bromo-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid cyclopropylamide, MS [m/z]: 502.14 [M+H]+; m.pt.: 257-260 °C.
Example 54: [8-Bromo-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-6-yl]-pyrrolidin-1-yl-methanone, MS [m/z]: 516.33 [M+H]+; m. pt.: 228-230 °C.

Example 55: 8-Bromo-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid isopropylamide, MS [m/z]: 504.29 [M+H]+; m. pt.: 206-207 °C.

Example 56: 8-Bromo-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid ethyl methyl-amide, MS [m/z]: 504.28 [M+H]+; m. pt.: 185-186 °C.

Example 57: 8-Bromo-2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid (4-hydroxy-butyl)-amide, m.pt.: 138-142 °C.

Example 58: 8-Bromo-2,3-bis-(4-chlorophenyl)-imidazo [1,2-a]pyridine-6-carboxylic acid ethylamide, m.pt.: 149-152 °C.

Example 59: 8-Bromo-2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid tert-butylamide hydrochloride, m.pt.: 258-259 °C.

Example 60: [8-Bromo-2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-yl]-(4-methylpiperazin-l-yl)-methanone, MS [m/z]: 545.35 [M+H]+; m. pt.: >250 °C.

Example 61: 8-Bromo-2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid dimethylamide, m.pt.: 202-205 °C.

Example 62: 8-Bromo-3-(4-chlorophenyl)-2-(2-chlorophenyl)-imidazo[l,2-a]pyridine-6-carboxylic acid tert-butylamide, MS [m/z]: 518.25 [M+H]+; m. pt.: 158.5 °C.

Example 63: 8-Bromo-3-(2-chlorophenyl)-2-(4-chlorophenyl)-imidazo[l,2-a]pyridine-6-carboxylic acid tert-butylamide, MS [m/z]: 518.19 [M+H]+; m.pt.: >260 0°C.

Example 64: [8-Chloro-2,3-bis-(4-chlorophenyl)-imidazo[l,2-a]pyridine-6-yl]-(4-methylpiperazin-l-yl)-methanone, MS [m/z]: 499.42 [M+H]+; m.pt.: 188-191 °C.

Example 65: 8-Chloro-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid morpholm-4-ylamide, m.pt.: >250 C; MS [m/z]: 499.32 [M+H]+.

Example 66: 8-Chloro-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid butylamide, MS [m/z]: 472.27 [M+H]+; m.pt.: 186-192 °C.

Example 67: 8-Chloro-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid cyclobutylamide, MS [m/z]: 472.24 [M+H]+; m.pt.: 204-205 °C.

Example 68: 8-Chloro-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid tert-butylamide, MS [m/z]: 472.18 [M+H]+; m.pt.: 248-252 °C.

Example 69: [8-Chloro-2,3-bis(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-yl]-moφ holin-4yl-methanone, MS [m/z]: 486.28 [M+H]+; m.pt.: 174-178 °C (decomp.).
Example 70: 8-Chloro-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid pentylamide, MS [m/z]: 486.25 [M+H]^+; m.pt: 84.2 °C.

Example 71: 8-Chloro-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid diethylamide, MS [m/z]: 472.37 [M+H]^+; m.pt.: 187-188 °C.

Example 72: [8-Chloro-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-perhydro-azepin-1-yl-methanone, MS [m/z]: 498.46 [M+H]^+; m.pt.: 183-185 °C.

Example 73: 8-Chloro-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid hexylamide, MS [m/z]: 500.47 [M+H]^+; m.pt.: 120-124 °C.

Example 74: [8-Chloro-2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-pyrrolidin-1-yl-methanone, MS [m/z]: 472.50 [M+H]^+; m.pt.: 216-220 °C.

Example 75: 8-Chloro-3-(4-chlorophenyl)-2-(2-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid pentylamide, MS [m/z]: 486.35 [M+H]^+; m.pt.: 185-190 °C.

Example 71: 8-Chloro-3-(4-chlorophenyl)-2-(2-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid ethyl ester

Step 1: 8-Chloro-2-(4-fluoro-phenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid ethyl ester

Step 2: 3-Bromo-8-chloro-2-(4-fluoro-phenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid ethyl ester

Step 3: 3-Bromo-8-chloro-2-(4-fluoro-phenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid

Step 4: 3-Bromo-8-chloro-2-(4-fluoro-phenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid pentylamide
Step 5: 8-Chloro-2-(4-fluoro-phenyl)-3-(4-methoxy-phenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid pentylamide

Example 82: [2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-yl]-(4-methanesulfonyl-piperazin-1-yl)-methanone

Step 1: [2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid ethyl

Step 2: [2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid

Step 3: 4-[2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carbonyl]-piperazin-1-carboxylic acid tert-butyl ester

Step 4: [2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-yl]-piperazin-1-yl-methanone

Deprotection of the tert-butyloxy carbonyl group was carried out by treating 4-[2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carbonyl]-piperazin-1-carboxylic acid tert-butyl ester (730 mg, 1.32 mmol) in the presence of ethyl acetate saturated with HCl (20 mL) overnight at room temperature. The reaction mixture was then diluted with ethyl acetate (100 mL) followed by neutralization of the organic layer with saturated solution of NaHCO₃ (60 mL). Layers were then separated and the organic components were extracted from the aqueous layer with chloroform (100 mL). Both ethyl acetate and chloroform layers were then combined, dried over Na₂SO₄ and concentrated to give 490 mg of the title compound as pale yellow solid (82%). ¹H NMR (DMSO-d₆, 300 MHz): 58.07 (s, 1H); 7.73 (d, J=9.0 Hz, 1H); 7.68 (d, J=8.7 Hz, 2H); 7.60-7.56 (dd, J=2.7 Hz and 8.7 Hz, 4H); 7.43 (d, J=8.4 Hz, 2H); 7.36 (d, J=8.7 Hz, 1H); 3.42 (b s, 4H); 2.66 (b s, 4H).

Step 5: [2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-yl]-(4-methanesulfonyl-piperazin-1-yl)-methanone

To a cold [-5°C] stirred solution of [2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-yl]-piperazin-1-yl-methanone (100 mg, 0.22 mmol) in dichloromethane (10 mL) was added triethylamine (62 µL, 0.44 mmol) followed by methanesulphonyl chloride (19 µL, 0.24 mmol) and stirring was continued for 2 hrs. at the same temperature. The reaction mixture was then diluted with chloroform (50 mL) and the organic layer was washed with saturated solution of aqueous sodium bicarbonate (30 mL) followed by water (2 X 30 mL), dried over sodium sulfate and concentrated. The crude was subjected to column chromatography over silica gel using a mixture of
petroleum ether and ethyl acetate to obtain 70 mg [60%] of the title compound as an off white solid. $^1$H NMR (DMSO-d$_6$, 300 MHz): 58.16 (s, 1H); 7.76 (d, J=9.3 Hz, 5H); 7.69 (d, J=8.4 Hz, 2H); 7.59 (d, J=7.5 Hz, 4H); 7.43 (d, J=8.7 Hz, 2H); 7.39 (d, J=9.6 Hz, 1H); 3.62 (b, 4H); 3.16 (b, 4H); 2.89 (s, 3H). MS [m/z]: 529.45 [M$^+$]. m.pt: >270 °C.

The following compound were synthesized following the procedure as described above:

Example 83: [2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-yl]-pyrrolidin-1-yl-methanone, MS [m/z]: 436.41 [M$^+$]; m.pt: 216-218 °C.

Example 84: [2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-piperidin-1-yl-methanone, MS [m/z]: 450.49 [M+H]$^+$; m.pt: 220-225 °C.

Example 85: [2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-(4-pyridin-2-yl-piperazin-1-yl)-methanone, MS [m/z]: 528.38 [M+H]$^+$; m.pt: 183-186 °C.

Example 86: [2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-perhydro-azepin-1-yl-methanone, MS [m/z]: 464.48 [M+H]$^+$; m.pt: 140-142 °C.

Example 87: 2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid adamantan-1-yl amide, MS [m/z]: 516.53 [M+H]$^+$; m.pt: >260 °C.

Example 88: 2,3-Bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid pentylamide, m.pt: 140-142 °C.

Example 89: 2,3-Bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid cyclohexylmethyl-amide, MS [m/z]: 478.43 [M+H]$^+$; m.pt: 220-221 °C.

Example 90: 2,3-Bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid piperidin-1-ylamide, MS [m/z]: 465.30 [M$^+$]; m.pt: 230-231 °C.

Example 91: 2,3-Bis (4-chlorophenyl)-imidazo[1,2-a]pyridin-6-carboxylic acid tert-butyl amide, m.pt: >260 °C.

Example 92: 3-(4-Bromophenyl)-2-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid tert-butylamide, m.pt: >250 °C.

Example 93: 2-(4-Bromophenyl)-3-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid tert-butylamide, MS [m/z]: 484.23 [M+H]$^+$; m.pt: >260 °C.

Example 94: [2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-(4-propyl-piperazin-1-yl)-methanone

To a suspension of [2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-yl]-piperazin-1-yl-methanone (130 mg, 0.29 mmol) in dimethyl formamide (10 mL) and
potassium carbonate (91.4 mg, 0.66 mmol) was added 1-bromopropane (78 mg, 0.63 mmol) and the reaction mixture was stirred for 3 days at the ambient temperature. The reaction mixture was then diluted with water (50 mL) and was extracted with dichloromethane (4x50 mL). The combined organic layer was then washed with brine (30 mL), dried over sodium sulfate and concentrated. The product was then purified by silica gel column chromatography (25 mg, Yield: 18%). \(^1\)H NMR (DMSO\(_d6\), 300 MHz): 58.07 (s, IH); 7.73 (d, J=93 Hz, IH); 7.68 (d, J=8.4 Hz, 2H); 7.58 (d, J=5.7 Hz, 4H); 7.43 (d, J=8.4 Hz, 2H); 7.36 (d, J=93 Hz, IH); 3.50 (b, s, 4H); 2.34 (b, s, 4H); 2.27–2.22 (t, J=7.5 Hz, 2H); 1.50-1.36 (m, 2H); 0.87-0.82 (t, J=7.5 Hz, 3H). m.pt: 190-193 °C. MS [m/z]: 493.45 [M+H]⁺.

Example 95: [2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-(4-phenylpiperazin-1-yl)-methanone, MS [m/z]: 527.49 [M+H]⁺; m.pt: 192.5-193.8 °C.

Example 96: [2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-morpholin-4-yl-methanone, MS [m/z]: 452.41 [M+H]⁺; m.pt.: 209.1-209.8 °C.

Example 97: [2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-(4-methylpiperazin-1-yl)-methanone, m.pt.: 200-201 °C.  

Example 98: [2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone, MS [m/z]: 519.43 [M+H]⁺; m.pt.: 171-174 °C.

Example 99: 2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid methyl-pyridin-4-yl-amide, MS [m/z]: 473.50 [M+H]⁺; m.pt.: 182-184 °C.

Example 100: 4-[2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-yl]-piperazin-1-yl-methanone, MS [m/z]: 527.49 [M+H]⁺; m.pt.: 192.5-193.8 °C.

Example 101: 2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-piperazin-1-yl-methanone, MS [m/z]: 519.43 [M+H]⁺; m.pt.: 171-174 °C.  

Example 102: 4-[2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-piperazin-1-yl-methanone, MS [m/z]: 527.49 [M+H]⁺; m.pt.: 192.5-193.8 °C.

Example 103: 2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-carboxylic acid methyl ester

To a cold [0 °C] solution of [2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-yl]-piperazin-1-yl-methanone [100 mg, 0.221 mmol] in CH\(_2\)Cl\(_2\) [10 mL] was added triethylamine [62 µL, 0.443 mmol] followed by methyl chloroformate [19 µL, 0.244 mmol]. The reaction mixture was stirred allowing it to warm to 15 °C and the stirring was continued at the same temperature for another 4 hr. The reaction mixture was then diluted with chloroform [50 mL] and was washed with saturated solution of NaHCO\(_3\) [30 mL]. The organic layer was then washed with water [2 X 30 mL], dried over Na\(_2\)SO\(_4\) and concentrated. The crude was then loaded on silica gel column chromatography to obtain 65 mg [Yield: 58%] of the title compound as a pale yellow solid.
\(^1\)HNMR (DMSO-d\(_6\), 300 MHz): 88.14 (s, 1H); 7.74 (d, J=9.3 Hz, 1H); 7.68 (d, J=8.4 Hz, 2H); 7.58 (d, J=6.9 Hz, 4H); 7.43 (d, J=8.4 Hz, 2H); 7.38 (d, J=9.0 Hz, 1H); 3.62 (b s, 3H); 3.51 (b s, 4H); 3.41 (b s, 4H). m. p.: 209-210 °C. MS [m/z]: 509.50 [M\(^+\)].

Example 101: 1-(4-[2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carbonyl]-piperazine-1-yl)-ethanone, MS [m/z]: 493.54 [M+H\(^+\)]; m.p.: >105 °C (decomp.).

This compound was prepared according to the procedure as described for the synthesis of 4-[2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carbonyl]-piperazine-1-carboxylic acid methyl ester.

Example 102: [2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-(4-methylperhydro-1,4-diazepin-1-yl)-methanone, MS [m/z]: 479.41 [M\(^+\)]; m.p.: 142-146 °C.

Example 103: [2-(4-chlorophenyl)-3-(4-methoxyphenyl)-imidazo[1,2-a]pyridin-6-yl]-perhydro-azepin-1-yl-methanone

Step 1: 2-(4-chlorophenyl)-3-(4-methoxyphenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid. \(^1\)H NMR (DMSO-d\(_6\), 300 MHz): 58.43 (s, 1H); 7.70 (s, 2H); 7.64 (d, J=8.4 Hz, 2H); 7.49 (d, J=7.8 Hz, 2H); 7.41 (d, J=8.1 Hz, 2H); 7.20 (d, J=8.1 Hz, 2H); 3.88 (s, 3H).

Step 2: [2-(4-chlorophenyl)-3-(4-methoxyphenyl)-imidazo[1,2-a]pyridin-6-yl]-perhydro-azepin-1-yl-methanone, m.p.: 165-167 °C. MS [m/z]: 479.41 [M\(^+\)].

Example 104: [2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-8-yl]-pyrrolidin-1-yl-methanone, MS [m/z]: 436.31; m.p.: 264-266 °C.

Example 105: 2-(4-Bromophenyl)-3-(4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid cyclohexylamide, MS [m/z]: 510.26; m.p.: 234-236 °C.

Example 106: 2-(4-Bromophenyl)-3-(4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid pentylamide, MS [m/z]: 498.22 [M+H\(^+\)]; m.p.: 182-183 °C.

Example 107: 2-(4-Bromophenyl)-3-(4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid tert-butylamide, MS [m/z]: 484.17 [M+H\(^+\)]; m.p.: 228-230 °C.

Example 108: [2,3-Bis (4-chlorophenyl)-imidazo[1,2-a]pyridin-8-yl]-(4-pyridin-2-yl-piperazin-1-yl)-methanone, MS [m/z]: 528.37 [M+H\(^+\)]; m.p.: 199.5-201 °C.

Example 109: 2,3-Bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid cyclohexylmethylamide, m.p.: 192-194 °C. MS [m/z]: 478.35 [M+H\(^+\)].

Example 110: 2,3-Bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid 4-chloro benzylamide, MS [m/z]: 506.35 [M+H\(^+\)]; m.p.: 178-179 °C.

Example 111: 2,3-Bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid 4-fluoro benzylamide, MS [m/z]: 490.31 [M+H\(^+\)]; m.p.: 172.9-173.5 °C.
Example 112: 2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid (1,1-dimethyl propyl)-ariiide, m.pt: 186.7-1 88° C.

Example 113: 2-(4-Chlorophenyl)-3-(2, 4-dichlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid tert-butylamide, MS [m/z]: 472.16 [M+H]+; m.pt.: 266-268° C.

Example 114: 8-Chloro-3-(4-ethyl-phenyl)-2-(4-fluoro-phenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid dimethylamide, MS [m/z]: 422.5.

Example 115: [8-Chloro-2-(4-chloro-phenyl)-3-p-tolyl-imidazo [1,2-a]pyridin-6-yl]-(4-methyl-iperazin-1-yl)-methanone, MS [m/z]: 479.6; m.pt.: 209-212 0°C.

Example 116: Protocol for in-vitro assay using hCBl-CHO membranes

In this assay, [3H]-CP-55, 940 was used as the radioligand to bind human CBl receptor expressed on the membranes from CHO cells (hCBl-CHO cell line was generated in-house which can be displaced by unlabeled ligands having affinity to the CBl receptor.

The assay was performed according to the modified method of Ross et al., 1999 (Br. J. Pharmacol. 128, 735-743). The reaction was set up in a total volume of 200 µl in PEI (Poly(ethyleneimine)) (0.2 %) precoated Millipore GFB (Glass Fibre-B) filter plates. ImM stocks of test compounds were prepared in DMSO and tested at a final concentration of 300 nM. The non-specific binding was determined by 0.5 µM CP-55, 940. The total reaction mixture contained Tris-BSA buffer (50mM Tris, 5 mM MgCl₂, 1 mM EDTA₃pH 7.4 with 0.1 % BSA), unlabelled CP-55, 940 (0.5 µM) or test samples, [3H]-CP-55, 940 (0.75 nM ) and 50 µg of human CBl receptor preparation. The assay mixture (with or without the test compound) was incubated at 37 °C for 1 hour. The reaction was stopped by rapid filtration under vacuum and the radioactivity on the filters was measured by liquid scintillation counting.

Example 117: Protocol for in-vitro assay using hCB2-CHO membranes

In this assay, [3H]-CP-55, 940 was used as the radioligand to bind human CB2 receptor expressed on the membranes from CHO cells (hCB2-CHO cell line was procured form Euroscreen) which can be displaced by unlabeled ligands having affinity to the CB2 receptor.

The assay was performed according to the modified method of Ross et al., 1999 (Br. Jrnl. Pharmacol. 128, 735-743). The reaction was set up in a total volume of 200 µl in PEI (Poly(ethyleneimine)) (0.2 %) precoated Millipore GFB (Glass Fibre-B) filter plates. ImM stocks of test compounds were prepared in DMSO and tested at a final concentration of 300 nM. The non-specific binding was determined by 0.5 µM CP-55, 940. The total reaction mixture contained Tris-BSA buffer (50mM Tris, 5 mM MgCl₂, 1 mM EDTA₃pH 7.4 with 0.1 % BSA), unlabelled CP-55, 940 (0.5 µM) or test samples, [3H]-CP-55, 940 (0.75 nM ) and 50 µg of human CB2 receptor preparation. The assay mixture (with or without the test compound) was incubated at 37 °C for 1 hour. The reaction was stopped by rapid filtration under vacuum and the radioactivity on the filters was measured by liquid scintillation counting.
volume of 200 µl in PEI (0.2 %) precoated Millipore GFB filter plates. ImM stocks of test compounds were prepared in DMSO and tested at a final concentration of 300 nM. The non-specific binding was determined by 0.5 µM CP-55, 940. The total reaction mixture contained Tris-BSA buffer (50 mM Tris, 5 mM MgCl₂, 1 mM EDTA, pH 7.4 with 0.1 % BSA), unlabelled CP-55, 940 (0.5 µM) or test samples, [³H]-CP-55, 940 (0.75 nM) and 0.5 µg of human CB2 receptor preparation. The assay mixture (with or without the test compound) was incubated at 30 °C for 1 hour. The reaction was stopped by rapid filtration under vacuum and the radioactivity on the filters was measured by liquid scintillation counting.

The percent (%) displacement by a test ligand was calculated by comparing the specific bound values. The results of the assay are shown in the Table 1 below.

Table 1

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Although the invention herein has been described with reference to particular embodiments, it is to be understood that these embodiments are merely illustrative of the principles and applications of the present invention. It is therefore to be understood that numerous modifications may be made to the illustrative embodiments and that other arrangements may be devised without departing from the spirit and scope of the present invention as described above.

AU publications and patent applications cited in this application are herein incorporated by reference to the same extent as if each individual publication or patent application was specifically and individually indicated to be incorporated herein by reference.
WE CLAIM:

1. A compound having the structure of formula (Ia) or (Ib)

```
(Ia)  (Ib)
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2. pharmaceutically acceptable salts, pharmaceutically acceptable solvates, 
prodrugs, metabolites, polymorphs and N-oxides thereof,

wherein:

R^1 is hydrogen, halogen, nitro, cyano or substituted or unsubstituted alkyl;

R^2, R^b, R^c, R^d and R^2, R^b, R^c, R^d, and R^e are independently hydrogen, halogen, nitro, cyano, OR^0 or substituted or unsubstituted alkyl;

R^4 and R^5 are independently hydrogen, substituted or unsubstituted alkyl, 
substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, 
substituted or unsubstituted cycloalkyl, substituted or unsubstituted 
cycloalkylalkyl, substituted or unsubstituted cycloalkenyl, substituted or 
unsubstituted cycloalkenylalkyl, substituted or unsubstituted 
cycloalkenylalkyl, substituted or unsubstituted heteroaryl, substituted or 
unsubstituted heteroaryalkyl, substituted or unsubstituted heterocyclic 
group, substituted or unsubstituted heterocyclylalkyl, -NR^aR^b, -NH-S(O)^m-R^a 
- C(O)O-R^a, -NH-CR^aR^b-C(O)-R \ -C(O)NR^aR^b, -S(O)^m-R^a, -S(O)^m-NR^aR^b 
or a protecting group or R^4 and R^5 may be joined together along with the 
nitrogen to which they are attached to form an optionally substituted 3 to 7 
membered saturated or unsaturated cyclic ring, which may optionally include 
at least two heteroatoms selected from O, NR^d or S(O)_n;

each occurrence of R^a and R^b may be same or different and are independently 
hydrogen, nitro, halo, cyano, -OR^c, -SR^0, oxo, thio, substituted or 
unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or 
unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or 
unsubstituted cycloalkylalkyl, substituted or unsubstituted cycloalkenyl, 
substituted or unsubstituted cycloalkenylalkyl, substituted or unsubstituted
aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted heterocyclic group, substituted or unsubstituted heterocyclylalkyl, -C(=B)-R°, -C(O)O-R°, -C(O)NR°R°, -S(O)°-R°, -S(O)°-NR°R°, -NR°R°, or a protecting group or R° and R° may be joined together with the atom to which they are both attached to form an optionally substituted 3 to 7 membered saturated or unsaturated cyclic ring, which may optionally include at least two heteroatoms selected from O, S, or NR°; each occurrence of B is independently O, S or NR°;

R° and R° are hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aryl, CN, COOR°, C0R° or a protecting group; R° is hydrogen or substituted or unsubstituted Ci° alkyl; and each occurrence of m is independently 0, 1 or 2.

The compound according to claim 1, wherein R° is hydrogen, substituted or unsubstituted alkyl; R° is independently substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl or a substituted or unsubstituted heterocyclic group; R° is SO2CH3, COOR°, C0R°, substituted or unsubstituted alkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aryl; R° to R° or R° to R° are independently hydrogen, halogen, substituted or unsubstituted alkyl or -OR°.

The compound according to claim 1, wherein R° is hydrogen, methyl, ethyl; R° is ethyl, n-butyl, t-butyl, n-pentyl, n-hexyl, 2-hydroxy-ethyl, 3-hydroxy-propyl, 1,1-dimethylpropyl, 4-hydroxy-butyl, 5-hydroxy-pentyl, 2-hydroxy-l, 1-dimethyl-ethyl, cyclobutyl, cyclopentyl, cyclohexyl, cyclohexymethyl, adamantyl, 3,4-difluorophenyl, phenyl-ethyl, 4-chlorobenzyl, 4-fluorobenzyl pyrrolidin-1-yl, piperidin-1-yl, morpholinyl, or hexahydro-cyclopenta[c]pyrrol-2-yl, R° is ethyl, methyl, pyridyl, phenyl, substituted or unsubstituted pyrrolidin-1-yl, COOCH3, COCH3; R° is chlorine, bromine, iodine or methyl, R° is chlorine; R° is chlorine, bromine or methoxy; R° is hydrogen or chlorine; R° is hydrogen, chlorine, bromine, iodine, -CF3 or tert-butyl; R° and R° combines to form substituted or unsubstituted piperazin-1-yl, substituted or unsubstituted piperazin-1-yl,
substituted or unsubstituted pyrrolidin-1-yl, substituted or unsubstituted azepanyl, substituted or unsubstituted diazapenayl, substituted or unsubstituted morpholinyl.

4. A compound, which is:

5. 2-(4-Chlorophenyl)-3-phenyl imidazo[1,2a]pyridine-8-carboxylic acid piperdine-1-yl amide,

2-(4-Chlorophenyl)-3-phenyl imidazo[1,2a]pyridine-8-carboxylic acid morpholine-1-yl amide,

10. 2-(4-Chlorophenyl)-3-phenyl imidazo[1,2a]pyridine-8-carboxylic acid adamnatane-1-yl amide,

15. 2-(4-Chlorophenyl)-3-phenylimidazo[1,2a]pyridine-8-carboxylic acid-(4-methanesulfonyl) piperazine-1-yl amide,

2-(4-Chlorophenyl)-3-phenyl imidazo[1,2a]pyridine-8-carboxylic acid cyclohexyl amide,

20. 2-(4-Chlorophenyl)-3-phenyl imidazo[1,2a]pyridine-8-carboxylic acid-(4-chloro benzyl) amide,

2,3-Bis-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid piperidine-1-yl amide,

25. 2,3-Bis-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid 1-butyl amide,

2,3-Bis-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid cyclohexyl amide,

30. 2-(4-Chlorophenyl)-3-(2,4-dichlorophenyl)imidazo[1,2a]pyridine-8-carboxylic acid piperidine-1-yl amide,

35. 2-(4-Chlorophenyl)-3-(2,4-dichlorophenyl)imidazo[1,2a]pyridine-8-carboxylic acid morpholine-1-yl amide,

5-Chloro-2,3-Bis-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid piperidine-1-ylamide,

40. 6-Chloro-2,3-Bis-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid azapen-1-ylamide,

6-Bromo-2,3-Bis-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid piperidine-1-ylamide,

45. 3-(4-Chlorophenyl)-2-(2,4-dichlorophenyl)imidazo[1,2a]pyridine-8-carboxylic acid piperidine-1-ylamide,
3-(4-Chlorophenyl)-2-(2,4-dichlorophenyl)imidazo[1,2a]pyridine-8-carboxylic acid morpholine-1-ylamide,

6-Bromo-2,3-Bis-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid morpholine-1-ylamide,

2-(4-Bromophenyl)-6-chloro-3-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid piperidine-1-ylamide,

2-(4-Bromophenyl)-6-bromo-3-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid piperidine-1-ylamide,

6-Chloro-2,3-Bis-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid cyclohexylamide,

3-(4-Bromophenyl)-6-chloro-2-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid piperidine-1-ylamide,

2,3-bis-(4-chlorophenyl)-6-iodoimidazo[1,2a]pyridine-8-carboxylic acid ethylamide,

2,3-bis-(4-chlorophenyl)-6-iodoimidazo[1,2a]pyridine-8-carboxylic acid tert-butylamide,

2,3-bis-(4-chlorophenyl)-6-iodoimidazo[1,2a]pyridine-8-carboxylic acid 2-(hydroxyl ethyl)amide,

2,3-bis-(4-chlorophenyl)-6-iodoimidazo[1,2a]pyridine-8-carboxylic acid 3-(hydroxyl propyl)amide,

2,3-bis-(4-chlorophenyl)-6-iodoimidazo[1,2a]pyridine-8-carboxylic acid 4-(hydroxyl butyl)amide,

2,3-Bis-(4-chlorophenyl)-6-iodo-imidazo[1,2a]pyridine-8-carboxylic acid piperidin-1-ylamide,

2,3-Bis-(4-chlorophenyl)-6-iodo-imidazo[1,2a]pyridine-8-carboxylic acid butylamide,

2,3-Bis-(4-chlorophenyl)-6-iodo-imidazo[1,2a]pyridine-8-carboxylic acid ethylamide,

2,3-Bis-(4-chlorophenyl)-6-iodo-imidazo[1,2a]pyridine-8-carboxylic acid (3-hydroxy-propyl)-amide hydrochloride,

2-(4-Bromophenyl)-6-chloro-3-(4-Chlorophenyl)-imidazo[1,2a]pyridine-8-carboxylic acid-5-hydroxypropyl amide,
2-(4-Bromophenyl)-6-chloro-3-(4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid (3-hydroxy-propyl)-amide,

6-Chloro-3-(4-chlorophenyl)-2-(4-trifluoromethyl phenyl) imidazo[1,2a]pyridine-8-carboxylic acid cyclopentyl amide,

6-Chloro-3-(4-chlorophenyl)-2-(4-trifluoromethyl phenyl) imidazo[1,2a]pyridine-8-carboxylic acid cyclohexyl amide,

6-Chloro-3-(4-chlorophenyl)-2-(4-trifluoromethyl-phenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid tert-butyl-amide,

6-Chloro-2,3-Bis-(4-Chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid -3,4-difluorophenyl amide,

6-Chloro-2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid (4-hydroxy-butyl)-amide,

6-Chloro-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid phenethylamide,

6-Chloro-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid (3-hydroxy-propyl)-amide,

6-Chloro-2,3-bis-(4-chlorophenyl)-imidazo[l,2-a]pyridine-8-carboxylic acid tert-butylamide,

6-Chloro-2,3-bis-(4-chlorophenyl)-imidazo[l,2-a]pyridine-8-carboxylic acid benzylamide,

2-(4-tert-Butylphenyl)-6-chloro-3-(4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid (3-hydroxy-propyl)-amide,

6-Chloro-3-(4-chlorophenyl)-2-(4-iodophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid (3-hydroxy-propyl)-amide,

2,3-bis-(4-chlorophenyl)-6-iodo imidazo[1,2-a]pyridine-8-carboxylic acid pyrrolidine-1-yl amide,

6-Bromo-3-(4-Chlorophenyl)-2-(2-chlorophenyl)imidazo[1,2a]pyridine-8-carboxylic acid piperidine-1-yl amide,

6-Bromo-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid (4-hydroxy-butyl)-amide,

6-Bromo-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid tert-butyl-amide,

6-Bromo-2,3-Bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid (3-hydroxy propyl)-amide,
[3-(4-Bromophenyl)-6-chloro-2-(4-chlorophenyl) imidazo[1,2a]pyridin-8-yl] piperidine-yl methanone,

2-(4-Bromophenyl)-6-chloro-3-(4-Chlorophenyl)- imidazo[1,2a]pyridine-8-carboxylic acid (hexahydro cyclopenta-[c]-pyrrol-2-yl)-amide,

8-Bromo-2,3-bis-(4-chloro phenyl) imidazo[1,2a]pyridine-6-carboxylic acid tert-butyl amide,

8-Bromo-2,3-bis-(4-Chloro phenyl) imidazo[1,2a]pyridine-6-carboxylic acid - (2-hydroxy-1,1-dimethyl-ethyl) amide,

8-Bromo-2,3-bis (4-chlorophenyl)-imidazo[1,2a]pyridine-6-carboxylic acid cyclopropylamide,

[8-Bromo-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-6-yl] -pyrrolidin-1-yl-methanone,

8-Bromo-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid isopropylamide,

8-Bromo-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid ethyl methyl-amide,

8-Bromo-2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid (4-hydroxy-butyl)-amide,

8-Bromo-2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid ethylamide,

8-Bromo-2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid tert-butylamide hydrochloride,

[8-Bromo-2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-yl]- (4-methylpiperazin-1-yl)-methanone,

8-Bromo-2,3-bis-(4-chlorophenyl)-imidazo [1,2-a]pyridine-6-carboxylic acid dimethylamide,

8-Bromo-3-(4-chlorophenyl)-2-(2-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid tert-butylamide,

8-Bromo-3-(2-chlorophenyl)-2-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-carboxylic acid tert-butylamide,

[8-Chloro-2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]- (4-methyl piperazin-1-yl)-methanone,
8-Chloro-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid morpholin-4-ylamide,

8-Chloro-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid butylamide,

8-Chloro-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid cyclobutylamide,

8-Chloro-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid tert-butylamide,

[8-Chloro-2,3-bis(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-yl] -morpholin-4-yl-methanone,

8-Chloro-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid pentylamide,

8-Chloro-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid diethylamide,

[8-Chloro-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-perhydroazepin-1-yl-methanone,

8-Chloro-2,3-bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid hexylamide,

[8-Chloro-2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-pyrrolidin-1-yl-methanone,

[8-Chloro-2,3-bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]- (4-methyl-1,4)diazepan-1-yl) -methanone,

8-Chloro-3-(4-chlorophenyl)-2-(2-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid pentyamide,

8-Chloro-3-(2-chlorophenyl)-2-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid pentyamide,

[8-Chloro-3-(4-chlorophenyl)-2-(2-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-morpholin-4-yl-methanone,

[8-Chloro-3-(2,4-dichlorophenyl)-2-phenyl-imidazo[1,2-a]pyridine-6-yl]-morpholin-4-yl-methanone,

2,3-Bis-(4-chlorophenyl)-8-iodo-imidazo[1,2-a]pyridin-6-carboxylic acid dimethylamide,

8-Chloro-2-(4-fluoro-phenyl)-3-(4-methoxy-phenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid pentyamide,
[2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-yl]-(4-methanesulfonyl-piperazin-1-yl)-methanone,

[2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-yl]-pyrrolidin-1-yl-methanone,

[2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-piperidin-1-yl-methanone,

[2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-(4-pyridin-2-yl-piperazin-1-yl)-methanone,

[2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-perhydro-azepin-1-yl-methanone,

2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid adamantanyl-1-yl amide,

2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid pentylamide,

2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid cyclohexylmethyl-amide,

2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid piperidin-1-ylamide,

2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-carboxylic acid tert-butyl amide,

3-(4-Bromophenyl)-2-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid tert-butylamide,

2-(4-Bromophenyl)-3-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid tert-butylamide,

[2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-(4-propyl-piperazin-1-yl)-methanone,

[2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-(4-phenyl-piperazin-1-yl)-methanone,

[2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-morpholin-4-yl-methanone,

[2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-(4-methyl-piperazin-1-yl)-methanone,
[2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl]-(4-pyrrolidin-1-yl-piperidin-1-yl)-methanone,

2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid methyl-pyridin-4-yl-amide,

4-[2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carbonyl]-piperazine-1-carboxylic acid methyl ester,

1-[4-[2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-6-carbonyl]-piperazin-1-yl]-ethanone,

[2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridin-6-yl)-(4-methyl-perhydro-1,4-diazepin-1-yl)-methanone,

[2-(4-chlorophenyl)-3-(4-methoxyphenyl)-imidazo[1,2-a]pyridin-6-yl]-perhydro-azepin-1-yl-methanone,

[2,3-Bis-(4-chloro-phenyl)-imidazo[1,2-a]pyridin-8-yl]-pyrrolidin-1-yl-methanone,

2-(4-Bromophenyl)-3-(4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid cyclohexylamide,

2-(4-Bromophenyl)-3-(4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid pentylamide,

2-(4-Bromophenyl)-3-(4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid tert-butylamide,

[2,3-Bis (4-chlorophenyl)-imidazo[1,2-a]pyridin-8-yl]-(4-pyridin-2-yl-piperazin-1-yl)-methanone,

2,3-Bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid cyclohexylmethyl-amide,

2,3-Bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid 4-chloro benzylamide,

2,3-Bis (4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid 4-fluoro benzylamide,

2,3-Bis-(4-chlorophenyl)-imidazo[1,2-a]pyridine-8-carboxylic acid (1,1-dimethyl propyl)-amide,

2-(4-Chlorophenyl)-3-(2,4-dichlorophenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid tert-butylamide,

8-Chloro-3-(4-ethyl-phenyl)-2-(4-fluoro-phenyl)-imidazo[1,2-a]pyridine-6-carboxylic acid dimethylamide,
[8-Chloro-2-(4-chloro-phenyl)-3-p-tolyl-imidazo[1,2-a]pyridin-6-yl]-(4-methyl-iperazin-1-yl)-methanone, and pharmaceutically acceptable salts, pharmaceutically acceptable solvates, prodrugs, metabolites, polymorphs and N-oxides thereof.

5. A pharmaceutical composition comprising one or more compounds of claim 1, and optionally together with one or more pharmaceutically acceptable excipients, carriers, diluents or a mixture thereof.

6. A method for preventing, ameliorating or treating a cannabinoid receptor mediated diseases, disorders or syndromes comprising administering to the subject in need thereof therapeutically effective amounts of one or more compounds of claim 1 or a pharmaceutical composition of claim 5.

7. The method according to claim 6, wherein disease, disorder or syndrome is selected from appetite disorders, metabolism disorders, catabolism disorders, diabetes, obesity, ophthalmic diseases, social related disorders, mood disorders, seizures, substance abuse, learning disorders, cognition disorders, memory disorders, organ contraction, muscle spasm, respiratory disorders, disorders and diseases, locomotor activity disorders, movement disorders, immune disorders, inflammation, cell growth, pain or neurodegenerative related syndromes.

8. A process for preparing compounds of formula (Ia),

![Diagram](Ia)

wherein $R^1, R^2, R^3, R^4, R^5$ and $R^a$ are same as defined in claim 1, which process comprises the steps of:

a) reacting the compound of formula 1a with acid chloride

![Diagram](1a)

to form a compound of formula 2a (wherein $Z$ is as defined earlier)
b) reacting the compound of formula 2a with halogenating agent to form a compound of formula 3a (wherein, \( R^1 \) is halogen)

c) reacting the compound of formula 3a with compound of formula 4a to form a compound of formula 5a

d) hydrolyzing the compound of formula 5a to form a compound of formula 6a

e) reacting the compound of formula 6a with an amine of formula \( \text{NHR}^4\text{R}^5 \) to form a compound of formula (Ia).

A process for preparing compounds of formula (Ia),
wherein $R_1$, $R_2^-R_2^{e}$, $R_3^-R_3^{e}$, $R^4$ and $R^5$ are same as defined in claim I 5
which process comprises the steps of:

a) reacting the compound of formula 3a with compound of formula 7a

\[
\begin{align*}
\text{3a} & \quad \text{7a}
\end{align*}
\]

to form a compound of formula 8a

b) halogenating the compound of formula 8a to form compound of formula 9a

\[
\begin{align*}
\text{8a} & \quad \text{9a}
\end{align*}
\]
c) reacting the compound of formula 8a or 9a with compound of formula A

\[
\begin{align*}
\text{8a} & \quad \text{9a}
\end{align*}
\]
to form a compound of formula 1(F1)

d) hydrolyzing the compound of formula 10 to form a compound of formula 11a

\[
\begin{align*}
\text{10} & \quad \text{11a}
\end{align*}
\]
c) reacting the compound of formula 11a with an amine of formula $NHR^4R^5$ to form a compound of formula (Ia).
10. A process for preparing compounds of formula (Ib),

a) reacting the compound of formula 1b with acid chloride

b) reacting the compound of formula 2b with halogenating agent to form a compound of formula 3b (wherein, R₁ is halogen)

c) reacting the compound of formula 3b with compound of formula 4b

to form compound of formula 5b
d) hydrolyzing the compound of formula 5b to form compound of formula 6b

c) reacting the compound of formula 6a with an amine of formula NHR^4R^5 to form a compound of formula (lb).

A process for preparing compounds of formula (lb),

a) reacting the compound of formula 3b with compound of formula 7 to form compound of formula 8b

b) reacting the compound of formula 8b with halo-succinimide to form compound of formula 9b

c) hydrolyzing the compound of formula 9b to form compound of formula 12
d) reacting the compound of formula 12 with compound of formula A

to form a compound of formula lib

Alternatively,

f) reacting the compound of formula 12 with acid chloride followed by treating it with amine of formula \( \text{NHR}^4\text{R}^5 \) to form a compound of formula 13

g) reacting the compound of formula lib with amine of formula \( \text{NHR}^4\text{R}^5 \) or reacting the compound of formula 13 with compound of formula A to form a compound of formula (lb).

12. A process for preparing compounds of formula 16,

a) reacting the compound of formula 3b with compound of formula 4b
to form a compound of formula 5b

b) hydrolyzing the compound of formula 5b to form compound of formula 6b

c) reacting the compound of formula 6b with amine of formula

(wherin P₁ is protecting group) to form a compound of formula 14

d) deprotecting the compound of formula 14 to form compound of formula 15

e) reacting the compound of formula 15 with Rᵈ-X to form compound of formulal 6.