

HETEROAROMATIC COMPOUNDS AS MUSCARINIC M4 RECEPTOR POSITIVE ALLOSTERIC MODULATORS (M4 PAMs)

FIELD OF INVENTION

5 The present invention relates to heteroaromatic compounds of formula (I), or their isotopic forms, stereoisomers, or pharmaceutically acceptable salts thereof as muscarinic M4 receptor positive allosteric modulators (M4 PAMs). The present invention also describes methods of making such compounds, pharmaceutical compositions comprising such compounds, and their use in the treatment of psychiatric and/or neurological disorders.

10 BACKGROUND OF THE INVENTION

 Currently, the available pharmacological treatments for psychiatric and/or neurological disorders such as schizophrenia, Alzheimer's disease, Parkinson's disease, Huntington's disease, depression have shown modest improvement with dose-limiting side effects leading to non-compliance and a partial response.

15 Targeting muscarinic acetylcholine receptors (mAChRs) is a promising approach for treating psychiatric and/or neurological disorders, as it provides new and improved pharmacological options. mAChRs, a G protein-coupled receptors (GPCRs), are widely expressed throughout the body. Five subtypes termed M1 through M5 that respond to the endogenous neurotransmitter acetylcholine (ACh) have been identified till date. They play
20 key role in regulating the activity of many important functions of the central and peripheral nervous system. The M1, M3, and M5 receptor subtypes usually couple to the G proteins Gq/G11, whereas the M2 and M4 receptor subtypes primarily couple to Gi/Go proteins (*Wess et al., 1996, Crit Rev Neurobiol.;10(1):69-99; Langmead et al, 2008, Pharmacol Ther.;117(2):232-243*).

25 The M4 mAChR subtype is of major therapeutic interest due to its expression in regions of the brain that are rich in dopamine and dopamine receptors, where it regulates dopaminergic neurons implicated in cognition, schizophrenia, psychosis, and addiction (*Kentaro et al., 2018, Chem. Pharm. Bull. 66(1), 37-44; Daniel et al., 2019, Drug Discov Today;24(12):2307-2314*).

30 Xanomeline, a M1/M4-preferring mAChR agonist, has shown to significantly reduce the behavioral symptoms in patients with Alzheimer's disease (*Bodick et al., 1997, Arch Neurol.;54(4):465-73*) although gastrointestinal side effects led to a high drop-out rate in

clinical trials. In a separate study, Xanomeline was shown to be efficacious against positive and negative symptoms of schizophrenia (*Shekhar et al., 2008, Am J Psychiatry;165(8):1033-9*). Xanomeline has shown antipsychotic-like activity in various preclinical behavioral models (*Mirza et al., 2003, CNS Drug Rev.;9(2):159-86*). Subsequent studies indicated that the antipsychotic-like effects of Xanomeline were absent in M4-KO mice (*Woolley et al., 2009 Eur J Pharmacol;603(1-3):147-9*). There is a high degree of conservation between muscarinic receptor subtypes at their orthosteric acetylcholine ligand binding sites which makes it difficult to identify a muscarinic subtype selective agonist. To circumvent this issue of selectivity and safety with the agonists, an alternative approach consists of developing selective muscarinic M4 receptor PAMs that act at the less conserved allosteric binding sites.

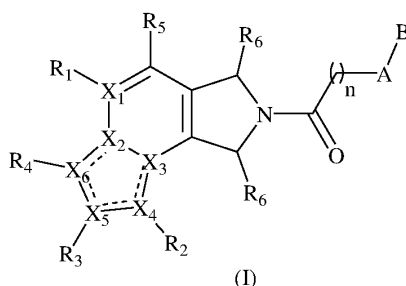
In this connection, a number of muscarinic M4 receptor PAMs have been described in the literature indicating cognitive enhancement and antipsychotic-like activity. For example, VU0467154 demonstrated antipsychotic-like activity, in rodent assays predictive of antipsychotic effects (*Gould et al., 2018, Neuropharmacology;128:492-502*). In addition, muscarinic M4 receptor PAMs have demonstrated procognitive benefits in rodent models of learning and memory (*Bubser et al., 2014 ACS Chem Neurosci.;5(10):920-42*).

Patent publications WO2018/002760, WO2018/234953, WO2021/099527, WO2023/064584, and US20180028501 disclose compounds that are muscarinic M4 receptor PAMs. While several muscarinic M4 receptor PAMs have been disclosed in the literature till date, no muscarinic M4 receptor PAM compound is launched in the market for the treatment of M4-mediated disease or disorders such as schizophrenia, Alzheimer's disease, psychosis, Parkinson's disease, pain, addiction and Huntington's disease. Therefore, there remains an unmet need for developing novel and more effective muscarinic M4 receptor PAMs for treatment of disorders that are affected by the muscarinic M4 receptors.

The present invention discloses novel compounds that are muscarinic M4 receptor PAMs with desirable profile. The compounds of this invention have potent affinity, selectivity, acceptable pharmacokinetic properties, good brain penetration and efficacy in animal models.

SUMMARY OF THE INVENTION

In first aspect, the present invention relates to a compound of formula (I),



or an isotopic form, or a stereoisomer, or a pharmaceutically acceptable salt thereof, wherein,

--- can be each independently a single bond or a double bond;

- 5 X_1 is N or C, provided that when X_1 is N then R_1 is absent;
 X_2 , X_3 , X_4 , X_5 and X_6 are independently selected from N or C, provided that at least one of X_2 , X_3 , X_4 , X_5 and X_6 is C; and provided that when X_4 , X_5 , or X_6 is N then R_2 , R_3 , or R_4 is absent;
 R_1 when present is selected from hydrogen, halogen, cyano, C_1 - C_4 alkyl, $-OC_1$ - C_4 alkyl, C_1 - C_4 haloalkyl, C_3 - C_7 cycloalkyl, or C_1 - C_4 alkoxyalkyl;
- 10 R_2 when present is selected from hydrogen, deuterium, halogen, C_1 - C_4 alkyl, $-OC_1$ - C_4 alkyl, C_1 - C_4 haloalkyl, C_3 - C_7 cycloalkyl, $-CH_2OH$, or C_1 - C_4 alkoxyalkyl;
 R_3 when present is selected from hydrogen, deuterium, halogen, C_1 - C_4 alkyl, $-OC_1$ - C_4 alkyl, C_1 - C_4 haloalkyl, C_3 - C_7 cycloalkyl, $-CH_2OH$, or C_1 - C_4 alkoxyalkyl;
- 15 R_4 when present is selected from hydrogen, deuterium, halogen, C_1 - C_4 alkyl, $-OC_1$ - C_4 alkyl, C_1 - C_4 haloalkyl, C_3 - C_7 cycloalkyl, $-CH_2OH$, or C_1 - C_4 alkoxyalkyl;
 R_5 is selected from hydrogen, halogen, $-NH_2$, $-NHCH_3$, C_1 - C_4 alkyl, C_1 - C_4 alkoxyalkyl, C_3 - C_7 cycloalkyl, or C_4 - C_{10} heterocycloalkyl;
 R_6 is independently selected from hydrogen or C_1 - C_4 alkyl;
- 20 A is selected from 3 to 7 membered cycloalkyl or 4 to 10 membered heterocycloalkyl, wherein cycloalkyl and heterocycloalkyl are optionally substituted with one to five substituents independently selected from the group consisting of hydrogen, halogen, deuterium, cyano, $-OC_1$ - C_4 alkyl, and C_1 - C_4 haloalkyl;
B is selected from 6 to 10 membered aryl or 5 to 10 membered heteroaryl, wherein aryl and
- 25 heteroaryl groups are optionally substituted with one to five substituents independently selected from the group consisting of hydrogen, deuterium, halogen, cyano, hydroxy, $-NH_2$, $NHCH_3$, C_1 - C_4 alkyl, C_1 - C_4 haloalkyl, $-OC_1$ - C_4 alkyl, $-OC_1$ - C_4 haloalkyl, and C_3 - C_7 cycloalkyl;
and

n is an integer from 0 to 3.

In another aspect, the present invention relates to a process for the preparation of the compound of formula (I), or an isotopic form, or a stereoisomer, or a pharmaceutically acceptable salt thereof.

5 In another aspect, the present invention relates to the compound of formula (I), or an isotopic form, or a stereoisomer, or a pharmaceutically acceptable salt thereof for use as muscarinic M4 receptor positive allosteric modulator.

In another aspect, the present invention relates to a method of treating muscarinic M4 receptor mediated diseases or disorders comprising administering to a patient in need
10 thereof a therapeutically effective amount of the compound of formula (I), or an isotopic form, or a stereoisomer, or a pharmaceutically acceptable salt thereof.

In another aspect, the present invention relates to a pharmaceutical composition comprising the compound of formula (I), or an isotopic form, or a stereoisomer, or a pharmaceutically acceptable salt thereof, and pharmaceutically acceptable excipients.

15 DETAILED DESCRIPTION OF THE INVENTION

Disclosed herein are muscarinic M4 receptor PAMs, methods of making such compounds, pharmaceutical compositions comprising such compounds, and method of treating muscarinic M4 receptor mediated disease or disorders such as psychiatric and/or neurological disorders.

20 Unless otherwise stated, the following terms used in the specification and claims have the meanings given below:

The term, "C₁-C₄alkyl" as used herein refers to branched or linear chain aliphatic hydrocarbon containing from one to four carbon atoms. Examples of C₁-C₄alkyl include, but are not limited to, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, and tert-
25 butyl.

The term, "C₁-C₄haloalkyl" as used herein refers to C₁-C₄alkyl as defined above wherein one or more hydrogen of the same or different carbon atoms is substituted with halogen atom. Examples of the C₁-C₄haloalkyl include, but are not limited to, fluoromethyl, 2-fluoroethyl, difluoromethyl and trifluoromethyl.

30 The term, "-OC₁-C₄alkyl" as used herein refers to C₁-C₄alkyl as defined above, attached to the parent molecular moiety through an oxygen atom. Examples of the -OC₁-C₄alkyl include, but are not limited to, methoxy, ethoxy, propoxy, isopropoxy and butyloxy.

The term “OC₁-C₄haloalkyl” as used herein refers to C₁-C₄haloalkyl as defined above that is bonded to the oxygen atom. Examples of the OC₁-C₄haloalkyl include, but are not limited to, -OCH₂F, -OCHF₂, and -OCF₃.

The term, “C₁-C₄alkoxyalkyl” as used herein refers to C₁-C₄alkyl as defined above
5 wherein one or more hydrogen of the same or different carbon atoms is substituted with -OC₁-C₄alkyl group. Examples of C₁-C₄alkoxyalkyl group include, but are not limited to, methoxymethyl, ethoxymethyl, propoxymethyl and butoxymethyl.

The phrase, “3 to 7 membered cycloalkyl or C₃-C₇cycloalkyl” as used herein refers to a saturated monocyclic hydrocarbon ring containing from three to seven carbon atoms.
10 Examples of C₃-C₇cycloalkyl group include, but are not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and cycloheptyl.

The term, “halogen” as used herein refers to fluorine, chlorine, bromine or iodine. Preferably, halogen is fluorine, chlorine or bromine.

The phrase “4 to 10 membered heterocycloalkyl or C₄-C₁₀heterocycloalkyl” as used
15 herein refers to heterocycloalkyl substituent containing a total of 4 to 10 ring atoms, at least one of which is a heteroatom selected from nitrogen, oxygen or sulfur. Examples of 4 to 10 membered heterocycloalkyl include but are not limited to azetidiny, pyrrolidiny, tetrahydrofurany, tetrahydrothieny, tetrahydropyrany, tetrahydrothiopyrany, piperidiny, morpholinyl, thiomorpholinyl, piperazinyl, azepanyl and 1,4-oxaazepanyl.

20 The phrase, “6 to 10 membered aryl or C₆-C₁₀aryl” as used herein include but not limited to an all-carbon monocyclic or fused-ring polycyclic aromatic group having a conjugated pi-electron system containing from 6 to 10 carbon atoms. Examples of 6 to 10 membered aryl include but are not limited to phenyl or naphthyl.

The phrase, “5 to 10 membered heteroaryl or C₅-C₁₀heteroaryl” as used herein refers
25 to an aromatic heterocycle ring of 5, 6, 7, 8, 9, or 10 members, including both mono- and bicyclic ring systems, where at least one carbon atom of one or both of the rings is replaced with a heteroatom independently selected from oxygen, nitrogen, or sulfur, or at least two carbon atoms of one or both of the rings are replaced with a heteroatom independently selected from nitrogen, oxygen, and sulfur. Non-limiting examples of 5 to 10 membered
30 heteroaryl include 6-membered ring substituents such as pyridinyl, pyrazinyl, pyrimidinyl and pyridazinyl; 5-membered heteroaryls such as triazolyl, imidazolyl, furanyl, isoxazolyl, isothiazolyl, 1,2,3- oxadiazolyl, 1,2,4- oxadiazolyl, 1,2,5- oxadiazolyl, or 1,3,4-oxadiazolyl, oxazolyl, thiophene, thiazolyl, thiadiazolyl, isothiazolyl, and pyrazolyl; 6/5-membered fused

ring substituents such as indolyl, indazolyl, benzofuranyl, benzimidazolyl, benzothienyl, benzoxadiazolyl, benzothiazolyl, isobenzothiofuranyl, benzothiofuranyl, benzisoxazolyl, benzoxazolyl, benzodioxolyl, furanopyridinyl, purinyl, imidazopyridinyl, imidazopyrimidinyl, pyrrolopyridinyl, pyrazolopyridinyl, pyrazolopyrimidinyl, 5 thienopyridinyl, triazolopyrimidinyl, triazolopyridinyl (e.g., [1,2,4]triazolo[1,5-a]pyridin-2-yl), and anthranilyl; and 6/6-membered fused ring substituents such as quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, oxochromanyl, and 1,4-benzoxazinyl.

The phrase, "isotopic form" as used herein refers to the compound of formula (I) wherein one or more atoms of the compound of formula (I) are substituted by their 10 respective isotopes. Examples of isotopes that may be incorporated into the compounds disclosed herein include, but are not limited to, isotopes of hydrogen such as ^2H (deuterium) and ^3H (tritium or T), carbon such as ^{11}C , ^{13}C and ^{14}C , nitrogen such as ^{13}N and ^{15}N , oxygen such as ^{15}O , ^{17}O and ^{18}O , chlorine such as ^{36}Cl , fluorine such as ^{18}F and sulphur such as ^{35}S . Substitution with heavier isotopes, for example, replacing one or more key carbon-hydrogen 15 bonds with carbon-deuterium bond may show certain therapeutic advantages, resulting from longer metabolism cycles (e.g., increases in-vivo half life or reduced dosage requirements), improved safety or greater effectiveness and hence may be preferred in certain circumstances.

Representative examples of isotopic forms of the compounds of formula (I) can 20 include, without limitation, deuterated compounds of formula (I). The term "deuterated" as used herein, by itself or used to modify a compound or group, refers to replacement of one or more hydrogen atom(s), which is attached to carbon(s), with a deuterium atom. For example, the compounds of formula (I) can include in the definitions of one or more of its various variables, wherever applicable, deuterium, deuterated-alkyl, deuterated-alkoxy, 25 deuterated-cycloalkyl, deuterated-heterocyclyl, deuterated-aryl, deuterated-heteroaryl and the like. The term "deuterated-alkyl" refers to an $-(\text{C}_1\text{C}_4)\text{-alkyl}$ group as defined above, wherein at least one hydrogen atom bound to carbon is replaced by a deuterium. That is, in a deuterated alkyl group, at least one carbon atom is bound to a deuterium. In a deuterated alkyl group, it is possible for a carbon atom to be bound to more than one deuterium; it is 30 also possible that more than one carbon atom in the alkyl group is bound to a deuterium. Analogously, the term "deuterated" and the terms deuterated-heterocyclyl, deuterated-heteroaryl, deuterated-cycloalkyl, deuterated-aryl, deuterated-alkoxy each refer to the corresponding chemical moiety wherein at least one carbon is bound to a deuterium.

The term, "stereoisomer" as used herein refers to isomers of the compound of formula (I) that differ in the arrangement of their atoms in space. Compounds disclosed herein may exist as a single stereoisomer, racemates and/or mixtures of enantiomers and/or diastereomers. All such pure stereoisomers, racemates and mixtures thereof are intended to be within the scope of the present invention.

The phrase, "pharmaceutically acceptable salt" as used herein refers to a salt of the active compound i.e. the compound of formula (I), and is prepared by reaction with the appropriate acid or base, depending on the particular substituents found on the compounds described herein.

The phrase, "therapeutically effective amount" is defined as an amount of a compound of the present invention that (i) treats the particular disease, condition or disorder, (ii) eliminates one or more symptoms of the particular disease, condition or disorder, and/or (iii) delays the onset of one or more symptoms of the particular disease, condition or disorder described herein.

The phrase "M4 receptor positive allosteric modulators (PAMs)" as used herein refers to a ligand which interacts with an allosteric site of a receptor to augment the response produced by the endogenous ligand at the orthosteric binding site. The compounds of the invention are allosteric modulators of the M4 muscarinic acetylcholine receptor, including as positive allosteric modulators of the M4 muscarinic acetylcholine receptor and silent allosteric modulators of the M4 muscarinic acetylcholine receptor.

The phrase, "psychiatric disorders" as used herein refers to diseases or disorders such as anxiety, personality disorders, depression, post-traumatic stress disorder (PTSD), obsessive-compulsive disorder (OCD), bipolar disorder, attention-deficit/hyperactivity disorder (ADHD), schizophrenia, substance use disorders and other psychotic disorders.

The phrase, "neurological diseases or disorders" as used herein refers to diseases or disorders such as Alzheimer's disease, Rett syndrome, Huntington's disease, vascular dementia, Parkinson's disease, and amyotrophic lateral sclerosis (ALS).

The phrase, "cognitive disorders" as used herein refers to diseases or disorders such as amnesia, dementia, amnestic disorder, dementia due to Alzheimer's diseases, dementia due to human immunodeficiency virus (HIV) disease, dementia due to Huntington's disease, dementia due to Parkinson's disease, Lewy body dementia, vascular dementia, frontotemporal dementia, senile dementia, dementia associated with Down syndrome, dementia associated with Tourette's syndrome, dementia associated with post-menopause,

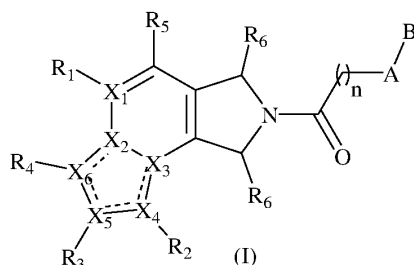
dementia in Creutzfeldt-Jakob disease, substance-induced persisting dementia, dementia in Pick's disease, dementia in Huntington's disease, traumatic brain injury, prion disease, HIV-associated neurocognitive disorders, and mild cognitive impairment.

The term, "patient" as used herein refers to an animal. Preferably the term "patient" refers to a mammal. The term mammal includes mice, rats, dogs, rabbits, pigs, monkeys, horses, guinea pigs and humans. More preferably the patient is human.

Embodiments

The present invention encompasses all the compounds described by the compound of formula (I) without any limitation, however, preferred aspects and elements of the invention are discussed herein below in the following embodiments.

In one embodiment, the present invention relates to the compound of formula (I),



or an isotopic form, or a stereoisomer, or a pharmaceutically acceptable salt thereof, wherein,

--- can be each independently a single bond or a double bond;

X₁ is N or C, provided that when X₁ is N then R₁ is absent;

X₂, X₃, X₄, X₅ and X₆ are independently selected from N or C, provided that at least one of X₂, X₃, X₄, X₅ and X₆ is C; and provided that when X₄, X₅, or X₆ is N then R₂, R₃, or R₄ is absent;

R₁ when present is selected from hydrogen, halogen, cyano, C₁-C₄alkyl, -OC₁-C₄alkyl, C₁-C₄haloalkyl, C₃-C₇cycloalkyl, or C₁-C₄alkoxyalkyl;

R₂ when present is selected from hydrogen, deuterium, halogen, C₁-C₄alkyl, -OC₁-C₄alkyl, C₁-C₄haloalkyl, C₃-C₇cycloalkyl, -CH₂OH, or C₁-C₄alkoxyalkyl;

R₃ when present is selected from hydrogen, deuterium, halogen, C₁-C₄alkyl, -OC₁-C₄alkyl, C₁-C₄haloalkyl, C₃-C₇cycloalkyl, -CH₂OH, or C₁-C₄alkoxyalkyl;

R₄ when present is selected from hydrogen, deuterium, halogen, C₁-C₄alkyl, -OC₁-C₄alkyl, C₁-C₄haloalkyl, C₃-C₇cycloalkyl, -CH₂OH, or C₁-C₄alkoxyalkyl;

R₅ is selected from hydrogen, halogen, -NH₂, -NHCH₃, C₁-C₄alkyl, C₁-C₄alkoxyalkyl, C₃-C₇cycloalkyl, or C₄-C₁₀heterocycloalkyl;

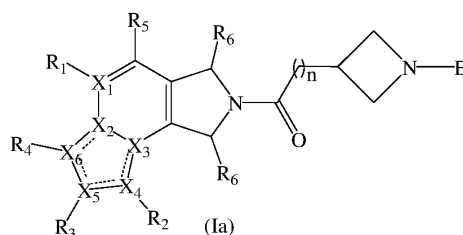
R₆ is independently selected from hydrogen or C₁-C₄alkyl;

A is selected from 3 to 7 membered cycloalkyl or 4 to 10 membered heterocycloalkyl,
 5 wherein cycloalkyl and heterocycloalkyl are optionally substituted with one to five substituents independently selected from the group consisting of hydrogen, halogen, deuterium, cyano, -OC₁-C₄alkyl, and C₁-C₄haloalkyl;

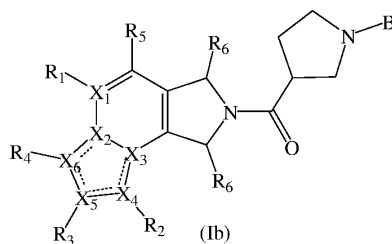
B is selected from 6 to 10 membered aryl or 5 to 10 membered heteroaryl, wherein aryl and heteroaryl groups are optionally substituted with one to five substituents independently
 10 selected from the group consisting of hydrogen, deuterium, halogen, cyano, hydroxy, -NH₂, NHCH₃, C₁-C₄alkyl, C₁-C₄haloalkyl, -OC₁-C₄alkyl, -OC₁-C₄haloalkyl, and C₃-C₇cycloalkyl;
 and

n is an integer from 0 to 3.

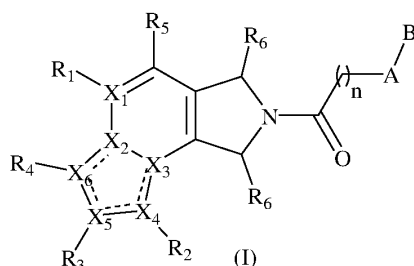
In certain embodiment, the compound of formula (I) is further defined by formula
 15 (Ia) or an isotopic form, or a stereoisomer, or a pharmaceutically acceptable salt thereof,
 wherein all indicated variables are as defined above in the formula (I),



In certain embodiment, the compound of formula (I) is further defined by formula
 (Ib) or an isotopic form, or a stereoisomer, or a pharmaceutically acceptable salt thereof,
 20 wherein all indicated variables are as defined above in the formula (I),



In another embodiment, the present invention relates to method of treating or preventing diseases or disorders mediated by muscarinic M₄ receptors, comprising administering to a patient a therapeutically effective amount of a compound having the
 25 structure of formula (I),



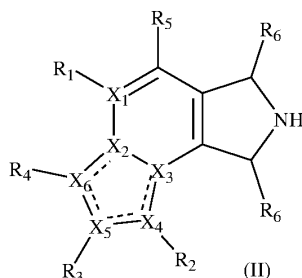
or an isotopic form, or a stereoisomer, or a pharmaceutically acceptable salt thereof,
wherein,

--- can be each independently a single bond or a double bond;

- 5 X_1 is N or C, provided that when X_1 is N then R_1 is absent;
 X_2 , X_3 , X_4 , X_5 and X_6 are independently selected from N or C, provided that at least one of X_2 , X_3 , X_4 , X_5 and X_6 is C; and provided that when X_4 , X_5 , or X_6 is N then R_2 , R_3 , or R_4 is absent;
- R_1 when present is selected from hydrogen, halogen, cyano, C_1 - C_4 alkyl, $-OC_1$ - C_4 alkyl, C_1 - C_4 haloalkyl, C_3 - C_7 cycloalkyl, or C_1 - C_4 alkoxyalkyl;
- 10 R_2 when present is selected from hydrogen, deuterium, halogen, C_1 - C_4 alkyl, $-OC_1$ - C_4 alkyl, C_1 - C_4 haloalkyl, C_3 - C_7 cycloalkyl, $-CH_2OH$, or C_1 - C_4 alkoxyalkyl;
- R_3 when present is selected from hydrogen, deuterium, halogen, C_1 - C_4 alkyl, $-OC_1$ - C_4 alkyl, C_1 - C_4 haloalkyl, C_3 - C_7 cycloalkyl, $-CH_2OH$, or C_1 - C_4 alkoxyalkyl;
- 15 R_4 when present is selected from hydrogen, deuterium, halogen, C_1 - C_4 alkyl, $-OC_1$ - C_4 alkyl, C_1 - C_4 haloalkyl, C_3 - C_7 cycloalkyl, $-CH_2OH$, or C_1 - C_4 alkoxyalkyl;
- R_5 is selected from hydrogen, halogen, $-NH_2$, $-NHCH_3$, C_1 - C_4 alkyl, C_1 - C_4 alkoxyalkyl, C_3 - C_7 cycloalkyl, or C_4 - C_{10} heterocycloalkyl;
- R_6 is independently selected from hydrogen or C_1 - C_4 alkyl;
- 20 A is selected from 3 to 7 membered cycloalkyl or 4 to 10 membered heterocycloalkyl, wherein cycloalkyl and heterocycloalkyl are optionally substituted with one to five substituents independently selected from the group consisting of hydrogen, halogen, deuterium, cyano, $-OC_1$ - C_4 alkyl, and C_1 - C_4 haloalkyl;
- B is selected from 6 to 10 membered aryl or 5 to 10 membered heteroaryl, wherein aryl and
- 25 heteroaryl groups are optionally substituted with one to five substituents independently selected from the group consisting of hydrogen, deuterium, halogen, cyano, hydroxy, $-NH_2$, $NHCH_3$, C_1 - C_4 alkyl, C_1 - C_4 haloalkyl, $-OC_1$ - C_4 alkyl, $-OC_1$ - C_4 haloalkyl, and C_3 - C_7 cycloalkyl;
- and

n is a integer from 0 to 3.

In another embodiment, the present invention relates to a compound of Formula (II) or a pharmaceutically acceptable salt thereof:



5 wherein,

--- can be each independently a single bond or a double bond;

X₁ is selected from C or N;

X₂ is selected from C or N;

X₃ is selected from C or N;

10 X₄ is selected from C or N;

X₅ is selected from C or N;

X₆ is selected from C or N;

Provided that at least one of X₁, X₂, X₃, X₄, X₅ and X₆ is C; provided that when X₁, X₂, X₃, X₄, X₅ or X₆ is N then R₁, R₂, R₃, or R₄ is absent;

15 R₁ when present is selected from hydrogen, halogen, C₁-C₄alkyl, -OC₁-C₄alkyl, C₁-C₄haloalkyl, C₃-C₇cycloalkyl, or C₄-C₁₀heterocycloalkyl;

R₂ when present is selected from hydrogen, halogen, C₁-C₄alkyl, -OC₁-C₄alkyl, C₁-C₄haloalkyl, C₃-C₇cycloalkyl, or C₄-C₁₀heterocycloalkyl;

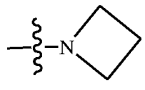
20 R₃ when present is selected from hydrogen, halogen, C₁-C₄alkyl, -OC₁-C₄alkyl, C₁-C₄haloalkyl, C₃-C₄cycloalkyl, or C₄-C₁₀heterocycloalkyl;

R₄ when present is selected from hydrogen, halogen, C₁-C₄alkyl, -OC₁-C₄alkyl, C₁-C₄haloalkyl, C₃-C₇cycloalkyl, or C₄-C₁₀heterocycloalkyl;

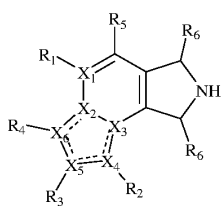
R₅ is selected from hydrogen, halogen, C₁-C₄alkyl, -OC₁-C₄alkyl, C₁-C₄haloalkyl, C₃-C₇cycloalkyl, or C₄-C₁₀heterocycloalkyl; and

25 R₆ is selected from hydrogen or C₁-C₄alkyl.

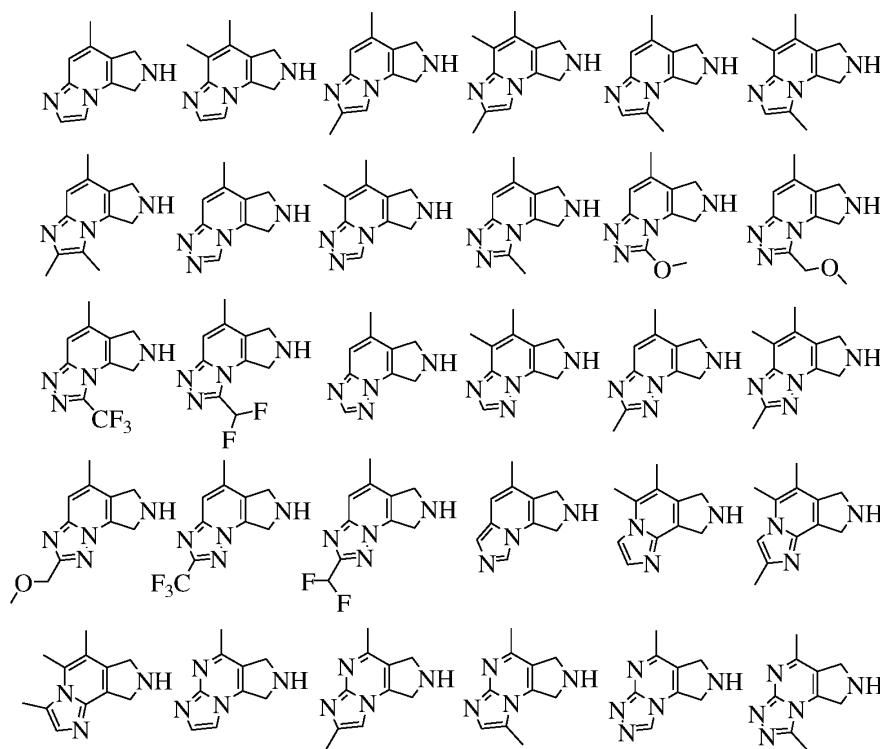
In another embodiment, the present invention relates to a compound of Formula (II) or a pharmaceutically acceptable salt thereof, wherein R₁ is selected from hydrogen, chloro,

fluoro, methyl, ethyl, methoxy, ethoxy, CHF₂, or CF₃; wherein R₂ is selected from hydrogen, chloro, fluoro, methyl, ethyl, methoxy, ethoxy, CHF₂, or CF₃; wherein R₃ is selected from hydrogen, chloro, fluoro, methyl, ethyl, methoxy, ethoxy, CHF₂, or CF₃; wherein R₄ is selected from hydrogen, chloro, fluoro, methyl, ethyl, methoxy, ethoxy, CHF₂, or CF₃; wherein R₅ is selected from hydrogen, chloro, fluoro, methyl, ethyl, methoxy, ethoxy, CHF₂, CF₃ or ; wherein R₆ is selected from hydrogen, methyl or ethyl.

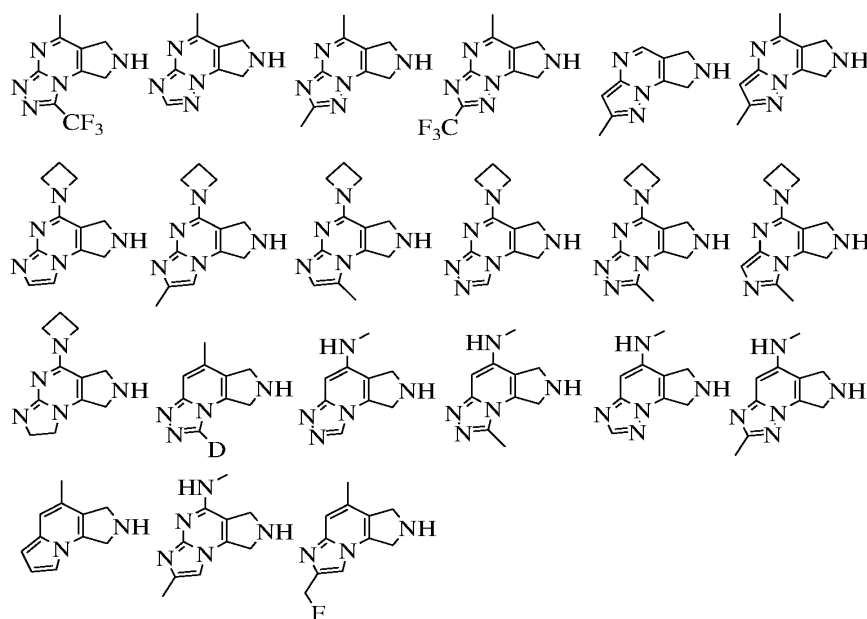
In another embodiment, the ring



is selected from,



10



In another embodiment, the present invention relates to the compound of formula (I) or an isotopic form, a stereoisomer, or a pharmaceutically acceptable salt thereof is selected from:

- 5 1-(2,5-Dimethyl-6,8-dihydro-1,3,7,8b-tetraaza-as-indacen-7-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 1-(2,5-Dimethyl-6,8-dihydro-1,3,7,8b-tetraaza-as-indacen-7-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone;
- 1-(2,5-Dimethyl-6,8-dihydro-1,3,7,8b-tetraaza-as-indacen-7-yl)-2-(1-pyridin-3-yl)-azetidin-
- 10 3-yl)-ethanone;
- 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(2,5-dimethyl-6,8-dihydro-1,3,7,8b-tetraaza-as-indacen-7-yl)-ethanone;
- 1-(2,5-Dimethyl-6,8-dihydro-1,3,7,8b-tetraaza-as-indacen-7-yl)-2-(1-pyridin-4-yl)-azetidin-
- 3-yl)-ethanone;
- 15 2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(2,5-dimethyl-6,8-dihydro-1,3,7,8b-tetraaza-as-indacen-7-yl)-ethanone;
- (2,5-Dimethyl-6,8-dihydro-1,3,7,8b-tetraaza-as-indacen-7-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone;
- (2,5-Dimethyl-6,8-dihydro-1,3,7,8b-tetraaza-as-indacen-7-yl)-(1-pyridin-3-yl)-pyrrolidin-
- 20 3(R)-yl)-methanone;

- 1-(4,7-Dimethyl-1,3-dihydro-2,6,8a-triaza-as-indacen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 1-(4,7-Dimethyl-1,3-dihydro-2,6,8a-triaza-as-indacen-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone;
- 5 1-(4,7-Dimethyl-1,3-dihydro-2,6,8a-triaza-as-indacen-2-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone;
- 1-(4,7-Dimethyl-1,3-dihydro-2,6,8a-triaza-as-indacen-2-yl)-2-(1-pyridin-4-yl-azetidin-3-yl)-ethanone;
- 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(4,7-dimethyl-1,3-dihydro-2,6,8a-
- 10 triaza-as-indacen-2-yl)-ethanone;
- 1-(4,7-Dimethyl-1,3-dihydro-2,6,8a-triaza-as-indacen-2-yl)-2-[1-(3-trifluoromethyl-phenyl)-azetidin-3-yl]-ethanone;
- (4,7-Dimethyl-1,3-dihydro-2,6,8a-triaza-as-indacen-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone;
- 15 1-(4-Methyl-1,3-dihydro-2,6,8a-triaza-as-indacen-2-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone;
- 1-(4-Methyl-1,3-dihydro-2,6,8a-triaza-as-indacen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 1-(4-Methyl-1,3-dihydro-2,7,8a-triaza-as-indacen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-
- 20 yl)-azetidin-3-yl]-ethanone;
- 1-(4,5-Dimethyl-6,8-dihydro-2,3a,7-triaza-as-indacen-7-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 1-(4,5-Dimethyl-6,8-dihydro-2,3a,7-triaza-as-indacen-7-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone;
- 25 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(4,5-dimethyl-6,8-dihydro-2,3a,7-triaza-as-indacen-7-yl)-ethanone;
- 1-(4,5-Dimethyl-6,8-dihydro-1,2,3a,7-tetraaza-as-indacen-7-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 1-(4,5-Dimethyl-6,8-dihydro-1,2,3a,7-tetraaza-as-indacen-7-yl)-2-[1-(6-trifluoromethyl-
- 30 pyridin-3-yl)-azetidin-3-yl]-ethanone;
- 1-(4,5-Dimethyl-6,8-dihydro-1,2,3a,7-tetraaza-as-indacen-7-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone;

- 2-[1-(2-Trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(3,4,5-trimethyl-6,8-dihydro-1,2,3a,7-tetraaza-as-indacen-7-yl)-ethanone;
- 1-(5,6-Dimethyl-7,9-dihydro-pyrrolo[3,4-c][1,2,4]triazolo[1,5-a]pyridin-8-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 5 1-(5,6-Dimethyl-7,9-dihydro-pyrrolo[3,4-c][1,2,4]triazolo[1,5-a]pyridin-8-yl)-2-(1-pyridin-3-yl)-azetidin-3-yl)-ethanone;
- 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(5,6-dimethyl-7,9-dihydro-pyrrolo[3,4-c][1,2,4]triazolo[1,5-a]pyridin-8-yl)-ethanone;
- 2-[1-(2-Trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(2,5,6-trimethyl-7,9-dihydro-pyrrolo[3,4-c][1,2,4]triazolo[1,5-a]pyridin-8-yl)-ethanone;
- 10 2-(1-Pyridin-3-yl)-azetidin-3-yl)-1-(2,5,6-trimethyl-7,9-dihydro-pyrrolo[3,4-c][1,2,4]triazolo[1,5-a]pyridin-8-yl)-ethanone;
- 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(2,5,6-trimethyl-7,9-dihydro-pyrrolo[3,4-c][1,2,4]triazolo[1,5-a]pyridin-8-yl)-ethanone;
- 15 1-(4,5-Dimethyl-6,8-dihydro-1,3a,7-triaza-as-indacen-7-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 1-(4,5-Dimethyl-6,8-dihydro-1,3a,7-triaza-as-indacen-7-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone;
- 1-(4,5-Dimethyl-6,8-dihydro-1,3a,7-triaza-as-indacen-7-yl)-2-(1-pyridin-3-yl)-azetidin-3-yl)-ethanone;
- 20 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(4,5-dimethyl-6,8-dihydro-1,3a,7-triaza-as-indacen-7-yl)-ethanone;
- (4,5-Dimethyl-6,8-dihydro-1,3a,7-triaza-as-indacen-7-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone;
- 25 1-(5-Methyl-6,8-dihydro-2,3,4,7,8b-pentaaza-as-indacen-7-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 1-(5-Azetidin-1-yl-6,8-dihydro-2,3,4,7,8b-pentaaza-as-indacen-7-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone;
- 1-(5-Azetidin-1-yl-6,8-dihydro-2,3,4,7,8b-pentaaza-as-indacen-7-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 30 1-(5-Azetidin-1-yl-6,8-dihydro-2,3,4,7,8b-pentaaza-as-indacen-7-yl)-2-[1-(2-difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;

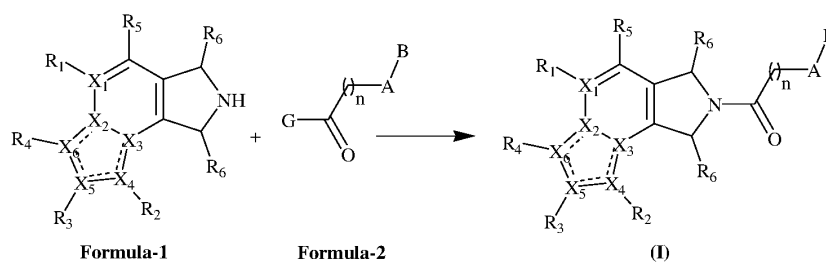
- 1-(2-Methyl-6,8-dihydro-1,4,7,8b-tetraaza-as-indacen-7-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 1-(2-Methyl-6,8-dihydro-1,4,7,8b-tetraaza-as-indacen-7-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone;
- 5 1-(2,5-Dimethyl-6,8-dihydro-1,4,7,8b-tetraaza-as-indacen-7-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone;
- 1-(2,5-Dimethyl-6,8-dihydro-1,4,7,8b-tetraaza-as-indacen-7-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 1-(4-Methyl-1,3-dihydro-2,5,6,8a-tetraaza-as-indacen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 10 1-(4-Methyl-1,3-dihydro-2,5,6,8a-tetraaza-as-indacen-2-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone;
- 1-(1,5-Dimethyl-6,8-dihydro-2,3,4,7,8b-pentaaza-as-indacen-7-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone; or
- 15 1-(1,5-Dimethyl-6,8-dihydro-2,3,4,7,8b-pentaaza-as-indacen-7-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone.

Experimental procedure

The below scheme depicts a general process for the preparation of the compound of formula (I), wherein X_1 , X_2 , X_3 , X_4 , X_5 , X_6 , R_1 , R_2 , R_3 , R_4 , R_5 , R_6 , n , A and B are as defined herein above. Further, G is a leaving group selected from OH or halogen.

20

Scheme:



Preparation of the compound of formula (I)

A compound of formula-1 is reacted with a compound of formula-2 in a solvent selected from DMF, THF or DCM in presence of coupling agent selected from HATU, TBTU, pyBop or triethylamine at room temperature for 4 to 16 h. The obtained reaction mixture was extracted with suitable organic solvent, washed with brine, dried over Na_2SO_4 ,

25

filtered and concentrated in vacuo to get a residual mass that was purified by column chromatography to obtain the compound of formula (I).

Preparation of pharmaceutically acceptable salts of the compound of formula (I)

5 The compound of formula (I) can optionally be converted into its pharmaceutically acceptable salt by reaction with the appropriate acid or base. Suitable pharmaceutically acceptable salts will be apparent to those skilled in the art. The salts are formed with inorganic acids e.g., hydrochloric, hydrobromic, sulfuric, nitric or phosphoric acid, or organic acids e.g., oxalic, succinic, maleic, acetic, citric, malic, tartaric, benzoic, p-toluic, p-toluenesulfonic, benzenesulfonic acid, methanesulfonic or naphthalene sulfonic acid.

10 Preparation of stereoisomer's of the compound of formula (I)

The stereoisomer's of the compounds of formula (I) may be prepared by one or more conventional ways presented below:

- a. One or more of the reagents may be used in their optically active form.
- b. Optically pure catalyst or chiral ligands along with metal catalyst may be employed
15 in the reduction process. The metal catalyst may be rhodium, ruthenium, indium and the like. The chiral ligands may preferably be chiral phosphines.
- c. The mixture of stereoisomers may be resolved by conventional methods such as forming diastereomeric salts with chiral acids, chiral amines, chiral amino alcohols or chiral amino acids. The resulting mixture of diastereomers may then be separated
20 by methods such as fractional crystallization, chromatography and the like, which is followed by an additional step of isolating the optically active product from the resolved material salt.
- d. The mixture of stereoisomers may be resolved by conventional methods such as microbial resolution, resolving the diastereomeric salts formed with chiral acids or
25 chiral bases. Chiral acids that can be employed may be tartaric acid, mandelic acid, lactic acid, camphorsulfonic acid, amino acids and the like. Chiral bases that can be employed may be cinchona alkaloids, brucine or a basic amino acid such as lysine, arginine and the like.

In another embodiment, the suitable pharmaceutically acceptable salt includes
30 acetate, hydrochloride, hydrobromide, oxalate, fumarate, tartrate, maleate, benzoate, mesylate and succinate.

In another embodiment of the present invention, the compound of formula (I) or an isotopic form, a stereoisomer or a pharmaceutically acceptable salt thereof, for use as muscarinic M4 receptor positive allosteric modulators (PAMs).

5 In another embodiment of the present invention, the compound of formula (I) or an isotopic form, a stereoisomer or a pharmaceutically acceptable salt thereof, for use in the manufacture of medicament for treating or preventing diseases or disorders mediated by muscarinic M4 receptors.

10 In another embodiment, the present invention relates to a method of treating or preventing diseases or disorders mediated by muscarinic M4 receptors in a patient, comprising administering to the patient in need thereof a therapeutically effective amount of the compound of formula (I) or an isotopic form, a stereoisomer or a pharmaceutically acceptable salt thereof.

15 In another embodiment, the present invention relates to a method of treating or preventing diseases or disorders mediated by muscarinic M4 receptors are selected from psychiatric disorders, neurological disorders, pain disorders, sleep disorders, or cognitive disorders.

20 In another embodiment, the present invention relates to a compound of formula (I), or an isotopic form, or a stereoisomer or a pharmaceutically acceptable salt thereof, for use in the treatment of diseases or disorders selected from psychiatric disorders, neurological disorders, pain disorders, sleep disorders, or cognitive disorders.

25 In another embodiment, the present invention relates to a use of the compound of formula (I), or an isotopic form, or a stereoisomer or a pharmaceutically acceptable salt thereof, for the treatment of diseases or disorders selected from psychiatric disorders, neurological disorders, pain disorders, sleep disorders, or cognitive disorders.

30 In another embodiment, the present invention relates to a use of the compound of formula (I), or an isotopic form, or a stereoisomer or a pharmaceutically acceptable salt thereof, in the manufacture of medicament for treatment of diseases or disorders selected from psychiatric disorders, neurological disorders, pain disorders, sleep disorders, or cognitive disorders.

In some embodiments, the psychiatric disorder are selected from anxiety, personality disorders, depression, post-traumatic stress disorder (PTSD), obsessive-compulsive disorder (OCD), bipolar disorder, attention-deficit/hyperactivity disorder (ADHD), schizophrenia, substance use disorders and other psychotic disorders.

In some embodiments, other psychotic disorders include psychosis associated with Alzheimer's disease, psychosis associated with Parkinson's disease, psychotic depression, psychosis associated with stroke, psychosis associated with epilepsy, psychosis associated with multiple sclerosis, psychosis associated with traumatic brain injury, substance-induced
5 persisting delirium, or any other diseases with psychotic features.

In some embodiments, the neurological diseases or disorders are selected from the group consisting of Alzheimer's disease, Rett syndrome, Huntington's disease, vascular dementia, Parkinson's disease, and amyotrophic lateral sclerosis (ALS).

In some embodiments, the cognitive disorders are selected from the group consisting
10 of amnesia, dementia, amnesic disorder, dementia due to Alzheimer's diseases, dementia due to HIV disease, dementia due to Huntington's disease, dementia due to Parkinson's disease, Lewy body dementia, vascular dementia, frontotemporal dementia (FTD), senile dementia, dementia associated with Down syndrome, dementia associated with Tourette's syndrome, dementia associated with post-menopause, dementia in Creutzfeldt-Jakob
15 disease, substance-induced persisting dementia, dementia in Pick's disease, dementia in Huntington's disease, traumatic brain injury, prion disease, HIV-associated neurocognitive disorders, mild cognitive impairment or any other diseases with cognitive symptoms.

In some embodiments, the present invention relates to a method of treating or preventing diseases or disorders mediated by muscarinic M4 receptors are selected from
20 schizophrenia.

In some embodiments, the treatment of schizophrenia includes treatment of cognitive impairment in schizophrenia, positive symptoms of schizophrenia and/or negative symptoms of schizophrenia.

In some embodiments, cognitive impairment in schizophrenia include but are not
25 limited to attention and vigilance, concentration, executive functions, processing speed, verbal learning, working memory, problem solving and/or social cognition.

In some embodiments, positive symptoms of schizophrenia include but are not limited to hallucinations, delusions, conceptual disorganization, excitement, grandiosity, suspiciousness/persecution and hostility.

30 In some embodiments, negative symptoms of schizophrenia include but are not limited to blunted affect, emotional withdrawal, poor rapport, passive/apathetic social withdrawal, difficulty in abstract thinking, lack of spontaneity & flow of conversation and stereotyped thinking.

In another embodiment, the present invention comprises pharmaceutical compositions. Such pharmaceutical compositions comprise the compound of formula (I), or an isotopic form or a stereoisomer or a pharmaceutically acceptable salt thereof, of the invention presented with a pharmaceutically acceptable carrier. The carrier can be a solid, a liquid, or both, and may be formulated with the compound as a unit-dose composition, for example, pills, tablets, coated tablets, capsules, powder, granules, pellets, patches, implants, films, liquids, semi-solids, gels, aerosols, emulsions, elixirs and the like.

The compounds of the present invention may be administered by any suitable route, preferably in the form of a pharmaceutical composition adapted to such a route, and in a dose effective for the treatment intended. The active compounds and compositions, for example, may be administered orally, rectally, parenterally, or topically.

The dose of the active compounds can vary depending on factors such as age and weight of patient, nature and severity of the disease to be treated and other factors. Therefore, any reference regarding therapeutically effective amounts of the compounds of general formula (I), stereoisomers and pharmaceutically acceptable salts thereof refer to the aforementioned factors.

The following abbreviations are used herein

AcOH	:	Acetic acid
AMP	:	Adenosine monophosphate
20 BINAP	:	2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
BOC	:	Tert-butyloxycarbonyl
CDCl ₃	:	Deuterated chloroform
Cs ₂ CO ₃	:	Cesium carbonate
DCM	:	Dichloromethane
25 DIBAL-H	:	Diisobutylaluminium hydride
DMA.DMA	:	<i>N, N</i> -Dimethylacetamide dimethyl acetal
DMAP	:	4-(Dimethylamino)pyridine
DMF	:	<i>N, N</i> -Dimethyl formamide
DMSO	:	Dimethylsulfoxide
30 EC ₅₀	:	Half maximal effective concentration
g	:	Gram

	HATU	:	2-(7-Aza-1 <i>H</i> -benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate
	h	:	Hour(s)
	hM4 PAM	:	human muscarinic M4 Positive Allosteric Modulator
5	IPA	:	Isopropyl alcohol
	MeOH	:	Methanol
	mL	:	Millilitre
	mol	:	Mole
	Na ₂ CO ₃	:	Sodium carbonate
10	NaOtBu	:	Sodium tert-butoxide
	Na ₂ SO ₄	:	Sodium sulphate
	ppm	:	parts per million
	psi	:	Pound per square inch
	Pd(dppf)Cl ₂	:	1,1'-Bis(diphenylphosphino)ferrocene)palladium(II) dichloride
15	Pd ₂ dba ₃	:	Tris(dibenzylideneacetone)dipalladium
	POCl ₃	:	Phosphoryl chloride
	pyBop	:	(Benzotriazol-1-yloxy)tripyrrolidinophosphonium hexafluorophosphate
20	RT	:	Room Temperature
	SM	:	Starting material
	THF	:	Tetrahydrofuran
	TBTU	:	2-(1 <i>H</i> -Benzotriazole-1-yl)-1,1,3,3-tetramethylaminium tetrafluoroborate
25	T3P	:	Propylphosphonic anhydride

EXAMPLES

The compounds of the present invention were prepared according to the following experimental procedures, using appropriate materials and conditions. The following examples are provided by way of illustration only but not to limit the scope of the present invention.

Preparation of Intermediates:

Intermediate-1: 2,5-Dimethyl-7,8-dihydro-6H-1,3,7,8b-tetraaza-as-indacene hydrochloride**Step-1: 6-Amino-2-chloro-4-methyl-nicotinonitrile**

A stirred mixture of methanolic ammonia (150 mL, 12% w/v solution) and 2,6-dichloro-4-methyl-nicotinonitrile (30 g, 0.160 mol) in methanol (60 mL) were heated in a sealed tube at 110 - 120 °C for 24 h. The reaction mixture was cooled to RT and concentrated to get a residual mass that was purified by column chromatography using 5 - 10 % ethyl acetate in DCM to obtain the title compound. Yield: 5.3 g (2nd eluting - 20 %); ¹H - NMR (CDCl₃, 400 MHz) δ ppm: 2.41 (s, 3H), 4.98 (bs, 2H), 6.27 (s, 1H); Mass (m/z): 167.9, 169.7 (M+H)⁺.

Step-2: N-(6-Chloro-5-cyano-4-methyl-pyridin-2-yl)-N'-hydroxy-acetamidine

N,N-Dimethylacetamide dimethyl acetal (12.4 mL, 0.074 mol) was added to a stirred solution of 6-amino-2-chloro-4-methyl-nicotinonitrile (5 g, 0.029 mol) in isopropanol (50 mL) at RT and then the reaction mixture was refluxed at 80 - 90 °C for 3 h. The reaction mixture cooled to 55 - 60 °C and added hydroxylamine hydrochloride (5.1 g, 0.074 mol) and stirred for 16 h at same temperature during which solids precipitated. These solids were filtered and dried in vacuo to obtain the title compound. Yield: 4.1 g (68 %); ¹H - NMR (DMSO-*d*₆, 400 MHz) δ ppm: 2.22 (s, 3H), 2.40 (s, 3H), 7.73 (s, 1H), 8.48 (bs, 2H); Mass (m/z): 225.0, 226.9 (M+H)⁺.

Step-3: 5-Chloro-2,7-dimethyl-[1,2,4]triazolo[1,5-a]pyridine-6-carbonitrile

T3P solution (13 mL, 0.020 mol, 50% in ethyl acetate) was added to a stirred solution of N-(6-chloro-5-cyano-4-methyl-pyridin-2-yl)-N'-hydroxy-acetamidine (3 g, 0.013 mol) in THF (30 mL) at RT and the reaction mixture was refluxed for 24 h. The reaction mixture was concentrated to get a residual mass which was diluted with water (100 mL), basified with saturated Na₂CO₃ solution during which solids precipitated. These solids were concentrated from DCM to obtain the title compound. Yield: 2.2 g (80 %); ¹H - NMR (CDCl₃, 400 MHz) δ ppm: 2.65 (s, 6H), 7.48 (s, 1H); Mass (m/z): 207.0, 209.0 (M+H)⁺.

Step-4: 6-Cyano-2,7-dimethyl-[1,2,4]triazolo[1,5-a]pyridine-5-carboxylic acid methyl ester

Pd(dppf)Cl₂·DCM (1.33 g, 0.0016 mol) followed by triethylamine (7.82 mL, 0.054 mol) were added to a stirred solution of 5-chloro-2,7-dimethyl-[1,2,4]triazolo[1,5-a]pyridine-6-carbonitrile (2.8 g, 0.013 mol) in methanol (150 mL) and the contents were

heated at 70 °C under 50 psi pressure of carbon monoxide in an autoclave for 5 h. The reaction mixture was cooled to RT, filtered and concentrated to get a residual mass that was purified by column chromatography using 25 – 40 % ethyl acetate in DCM to obtain the title compound. Yield: 0.7 g (25 %); ¹H – NMR (DMSO-*d*₆, 400 MHz) δ ppm: 2.50 (s, 3H), 2.58 (s, 3H), 4.09 (s, 3H), 7.99 (s, 1H); Mass (m/z): 231.0 (M+H)⁺.

Step-5: 2,5-Dimethyl-6,7-dihydro-1,3,7,8b-tetraaza-as-indacen-8-one

Raney nickel (2.8 g) was added to a solution of 6-cyano-2,7-dimethyl-[1,2,4]triazolo[1,5-a]pyridine-5-carboxylic acid methyl ester (0.7 g, 0.003 mol) in methanol (50 ml) and the reaction mixture was stirred under H₂ (gas) balloon pressure for 48 h. The reaction mixture then filtered and concentrated to get a residual mass that was purified by column chromatography using 8 - 10 % MeOH in DCM to obtain the title compound. Yield: 0.35 g (55 %); ¹H – NMR (DMSO-*d*₆, 400 MHz) δ ppm: 2.42 (s, 3H), 2.50 (s, 3H), 4.43 (s, 2H), 7.73 (s, 1H), 9.04 (s, 1H); Mass (m/z): 202.9 (M+H)⁺.

Step-6: 2,5-Dimethyl-8-oxo-6,8-dihydro-1,3,7,8b-tetraaza-as-indacene-7-carboxylic acid tert-butyl ester

Boc anhydride (0.91 g, 0.004 mol) followed by DMAP (30 mg, 0.0002 mol) was added to a stirred solution of 2,5-dimethyl-6,7-dihydro-1,3,7,8b-tetraaza-as-indacen-8-one (0.34 g, 0.0016 mol) in DCM (10 mL) at RT and maintained for overnight. The reaction mixture was concentrated in vacuo to get a residual mass that was purified by column chromatography using 2 - 4 % MeOH in DCM to obtain the title compound. Yield: 0.38 g (65 %); ¹H – NMR (CDCl₃, 400 MHz) δ ppm: 1.62 (s, 9H), 2.49 (s, 3H), 2.68 (s, 3H), 4.74 (s, 2H), 7.67 (s, 1H); Mass (m/z): 303.2 (M+H)⁺.

Step-7: 8-Hydroxy-2,5-dimethyl-6,8-dihydro-1,3,7,8b-tetraaza-as-indacene-7-carboxylic acid tert-butyl ester

DIBAL-H (0.28 g, 0.0019 mol) was added to a stirred solution of 2,5-dimethyl-8-oxo-6,8-dihydro-1,3,7,8b-tetraaza-as-indacene-7-carboxylic acid tert-butyl ester (0.2 g, 0.0006 mol) in THF (10 mL) at 0 - 10 °C. The reaction mixture further stirred at RT for 3 h. Sodium sulphate decahydrate (1 g) and ethyl acetate (25 mL) was added to the reaction mixture, stirred for 1 h, then filtered through hyflow. The filtrate was concentrated in vacuo to obtain the title compound that was used as such for next step without further purification. Yield: 0.2 g; Mass (m/z): 305.1 (M+H)⁺.

Step-8: 2,5-Dimethyl-6,8-dihydro-1,3,7,8b-tetraaza-as-indacene-7-carboxylic acid tert-butyl ester

Sodium cyanoborohydride (0.10 g, 0.0016 mol) was added to a stirred solution of 8-hydroxy-2,5-dimethyl-6,8-dihydro-1,3,7,8b-tetraaza-as-indacene-7-carboxylic acid tert-butyl ester (0.2 g, 0.0006 mol) in acetic acid (10 mL) at RT and stirred for 16 h. The reaction mixture was concentrated in vacuo to get a residual mass that was purified by column chromatography using 2 - 4 % MeOH in DCM to obtain the title compound. Yield: 0.1 g (55 %); ¹H – NMR (DMSO-*d*₆, 400 MHz) δ ppm: 1.48 (s, 9H), 2.36 (s, 3H), 2.50 (s, 3H), 4.65 – 4.66 (bs, 2H), 4.87 – 4.91 (bs, 2H), 7.48 (s, 1H); Mass (m/z): 288.9 (M+H)⁺.

Step-9: 2,5-Dimethyl-7,8-dihydro-6H-1,3,7,8b-tetraaza-as-indacene hydrochloride

IPA.HCl (2 mL, 10 vol., 12% w/v solution) was added to a stirred solution of 2,5-dimethyl-6,8-dihydro-1,3,7,8b-tetraaza-as-indacene-7-carboxylic acid tert-butyl ester (0.1 g, 0.0003 mol) in methanol (10 mL) and the reaction mixture was maintained at 50 - 55 °C for 5 h and then the reaction mixture was concentrated in vacuo to obtain the title compound (intermediate-1). Yield: 0.6 g (77 %); ¹H – NMR (DMSO-*d*₆, 400 MHz) δ ppm: 2.41 (s, 3H), 2.50 (s, 3H), 4.65 (bs, 2H), 4.87 (bs, 2H), 7.60 (s, 1H), 10.53 (bs, 1H); Mass (m/z): 188.8 (M+H)⁺.

Intermediate-2: 4,7-Dimethyl-2,3-dihydro-1H-2,6,8a-triaza-as-indacene hydrochloride

Step-1: 5-Chloro-2,7-dimethyl-imidazo[1,2-a]pyridine-6-carbonitrile

Chloroacetone (41 g, 0.447 mol) was added to a stirred solution of 6-amino-2-chloro-4-methyl-nicotinonitrile (5 g, 0.0298 mol, step-1 of intermediate-1) in water (50 mL) at RT. The reaction mixture was refluxed at 100 – 110 °C for 48 h. After cooling to RT, the reaction mixture was concentrated in vacuo to get a residual mass, which was then diluted with water (10 mL). The mixture was basified with a saturated Na₂CO₃ solution to a pH of 9 to 10 during which solids precipitated. These solids were filtered and dried in vacuo to obtain the title compound. Yield: 0.5 g (8.1 %); ¹H – NMR (CDCl₃, 400 MHz) δ ppm: 2.48 (s, 3H), 2.57 (s, 3H), 7.36 (s, 1H), 7.53 (s, 1H); Mass (m/z): 205.9, 207.8 (M+H)⁺.

5-Chloro-2,7-dimethyl-imidazo[1,2-a]pyridine-6-carbonitrile was converted to intermediate-2 by following the procedure given in step-4 to step-9 of intermediate-1 with some non-critical variations. ¹H – NMR (DMSO-*d*₆, 400 MHz) δ ppm: 2.50 (s, 6H), 4.70 (s, 2H), 4.93 (s, 2H), 7.60 (s, 1H), 8.09 (s, 1H), 10.87 (s, 2H); Mass (m/z): 188.0 (M+H)⁺.

Intermediate-3: 4-Methyl-2,3-dihydro-1H-2,6,8a-triaza-as-indacene hydrochloride

Step-1: 5-Chloro-7-methyl-imidazo[1,2-a]pyridine-6-carbonitrile

Chloroacetaldehyde (1.16 g, 0.0149 mol, 50% aq. solution) was added to a stirred solution of 6-amino-2-chloro-4-methyl-nicotinonitrile (0.5 g, 0.00298 mol, step-1 of intermediate-1) in ethanol (10 mL) at RT. The reaction mixture was refluxed at 75 – 85 °C for 16 h. After cooling to RT, the reaction mixture was concentrated in vacuo to get a residual mass which was then diluted with water (10 mL) and basified with saturated Na₂CO₃ solution to a pH of 9 to 10 during which solids precipitated. These solids were filtered and dried in vacuo to obtain the title compound. Yield: 0.46 g (80 %); ¹H – NMR (CDCl₃, 400 MHz) δ ppm: 2.59 – 2.60 (d, 3H), 7.49 (s, 1H), 7.76 – 7.76 (d, *J* = 1.2 Hz, 1H), 7.78 (s, 1H); Mass (m/z): 191.8, 193.5 (M+H)⁺.

5-Chloro-7-methyl-imidazo[1,2-a]pyridine-6-carbonitrile was converted to intermediate-3 by following the procedure given in step-4 to step-9 of intermediate-1 with some non-critical variations. Mass (m/z): 174.1 (M+H)⁺.

Intermediate-4: 4,5-Dimethyl-7,8-dihydro-6H-2,3a,7-triaza-as-indacene hydrochloride

Step-1: 4-Methanesulfonyloxymethyl-6,7-dimethyl-1,3-dihydro-pyrrolo[3,4-c]pyridine-2-carboxylic acid tert-butyl ester

Methanesulfonyl chloride (1.8 mL, 0.023mol) was added to a stirred solution of 4-hydroxymethyl-6,7-dimethyl-1,3,3a,4-tetrahydro-pyrrolo[3,4-c]pyridine-2-carboxylic acid tert-butyl ester (2.2 g, 0.0079 mol, prepared as per the procedure disclosed in step-2 of Preparation P6 on page 77 of WO2018234953) and Et₃N (3.4 mL, 0.023 mol) in DCM at 0 - 5 °C and maintained for 4 h. The reaction mixture was then poured on to water and product was extracted using DCM (50 mL x 3). The organic extracts were combined, washed with brine (50 mL), dried over Na₂SO₄, filtered and concentrated in vacuo to obtain the title compound that was used as such for next step without further purification. Yield: 3.3 g; Mass (m/z): 357.0 (M+H)⁺.

Step-2: 4-Aminomethyl-6,7-dimethyl-1,3-dihydro-pyrrolo[3,4-c]pyridine-2-carboxylic acid tert-butyl ester

Methanolic ammonia (30 mL, 12% w/v solution) was added to a stirred solution of 4-methanesulfonyloxymethyl-6,7-dimethyl-1,3,3a,4-tetrahydro-pyrrolo[3,4-c]pyridine-2-carboxylic acid tert-butyl ester (3.3 g, 0.009 mol) in methanol (30 mL) at RT and maintained for 16 h. The reaction mixture was concentrated in vacuo to obtain the title compound that was used as such for next step without further purification. Yield: 3.2 g; Mass (m/z): 277.8 (M+H)⁺.

Step-3: 4-Formylaminomethyl-6,7-dimethyl-1,3-dihydro-pyrrolo[3,4-c]pyridine-2-carboxylic acid tert-butyl ester

Ethyl formate (64 mL, 20 vol) was added to a stirred solution of 4-aminomethyl-6,7-dimethyl-1,3,3a,4-tetrahydro-pyrrolo[3,4-c]pyridine-2-carboxylic acid tert-butyl ester (3.2 g, 0.011 mol) and Et₃N (5 mL, 0.034 mol) in ethanol (10 mL) at RT. The reaction mixture was refluxed for 7 h, cooled to RT, poured on to water and product was extracted using DCM (50 mL x 3). The organic extracts were combined, washed with brine (50 mL), dried over Na₂SO₄, filtered and concentrated in vacuo to obtain the title compound that was used as such for next step without further purification. Yield: 2.0 g; Mass (m/z): 306.2 (M+H)⁺.

Step-4: 4,5-Dimethyl-6,8-dihydro-2,3a,7-triaza-as-indacene-7-carboxylic acid tert-butyl ester

POCl₃ (1.58 mL, 0.016 mol) was added to a stirred solution of 4-formylaminomethyl-6,7-dimethyl-1,3,3a,4-tetrahydro-pyrrolo[3,4-c]pyridine-2-carboxylic acid tert-butyl ester (2 g, 0.006 mol) and Et₃N (6.0 mL, 0.041 mol) in DCM (25 mL) at 0 - 5 °C and then stirred at RT for 30 min. The reaction mixture was poured on to water, basified with saturated Na₂CO₃ solution to a pH of 9 to 10, and product was extracted using DCM (50 mL x 3). The organic extracts were combined, washed with brine (50 mL), dried over Na₂SO₄, filtered and concentrated in vacuo to obtain a residual mass that was purified by column chromatography using 1.5 - 2.0% MeOH in DCM to obtain the title compound. Yield: 0.4 g (22%); ¹H – NMR (CDCl₃, 400 MHz) δ ppm: 1.52 (s, 9H), 2.21 (s, 3H), 2.54 (s, 3H), 4.57 – 4.58 (m, 2H), 4.77 – 4.81 (m, 2H), 7.33 – 7.34 (d, J = 4.40 Hz, 1H), 8.05 (s, 1H), Mass (m/z): 288.4 (M+H)⁺.

Step-5: 4,5-Dimethyl-7,8-dihydro-6H-2,3a,7-triaza-as-indacene hydrochloride

IPA.HCl (1 mL, 18 % w/v solution) was added to a stirred solution of 4,5-dimethyl-6,8-dihydro-2,3a,7-triaza-as-indacene-7-carboxylic acid tert-butyl ester (0.13 g, 0.0004 mol) in methanol (10 mL) and the reaction mixture was maintained at RT for 5 h and then the reaction mixture was concentrated in vacuo to obtain the title compound. Yield: Quantitative; ¹H – NMR (CD₃OD, 400 MHz) δ ppm: 2.41 (s, 3H), 2.75 (s, 3H), 4.79 – 4.93 (m, 4H), 8.15 – 8.16 (s, 1H), 9.64 – 9.65 (s, 1H), Mass (m/z): 188.0 (M+H)⁺.

Intermediate-5: 4-Methyl-2,3-dihydro-1H-2,7,8a-triaza-as-indacene hydrochloride

4-Methyl-2,3-dihydro-1H-2,7,8a-triaza-as-indacene hydrochloride was prepared from 2-hydroxymethyl-4-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridine-6-carboxylic acid tert-butyl ester (prepared as per the procedure disclosed in steps 1-4 of Preparation P5 on pages 82 & 83 of WO2018002760) by following the procedure as described in step-1 to step-5 of intermediate-4 with some non-critical variations. Yield: 0.086 (70 %); ¹H – NMR (CD₃OD, 400 MHz) δ ppm: 2.32 (s, 3H), 4.71 – 4.72 (m, 2H), 4.76 – 4.93 (m, 2H), 7.62 (s, 1H), 7.97 (s, 1H), 9.49 (s, 1H), Mass (m/z): 174.1 (M+H)⁺.

Intermediate-6: 4,5-Dimethyl-7,8-dihydro-6H-1,2,3a,7-tetraaza-as-indacene hydrochloride

10 Step-1: 4-Chloro-6,7-dimethyl-2,3-dihydro-1H-pyrrolo[3,4-c]pyridine hydrochloride

POCl₃ (15 mL, 5 vol. to SM) was added to 6,7-dimethyl-4-oxo-1,3,4,5-tetrahydro-pyrrolo[3,4-c]pyridine-2-carboxylic acid tert-butyl ester (3 g, 0.0113 mol, prepared as per the procedure disclosed in step-1 of Preparation P1 on page 70 of WO2018234953) at 0 - 10 °C and then reaction mixture was maintained at 90 - 100 °C for 16 h. The reaction mixture was concentrated in vacuo to obtain the title compound. Yield: 2.0 g; Mass (m/z): 182.2, 183.3 (M+H)⁺.

Step-2: 4-Chloro-6,7-dimethyl-1,3-dihydro-pyrrolo[3,4-c]pyridine-2-carboxylic acid tert-butyl ester

Boc anhydride (4.97 g, 0.0228 mol) was added to a stirred solution of 4-Chloro-6,7-dimethyl-2,3-dihydro-1H-pyrrolo[3,4-c]pyridine hydrochloride (2.0 g, 0.0091 mol) and Et₃N (4.61 g, 0.0456 mol) in DCM (40 mL) at RT and maintained for 4 h. The reaction mixture was poured on to water and product was extracted using DCM (50 mL x 3). The organic extracts were combined, washed with brine (50 mL), dried over Na₂SO₄, filtered and concentrated in vacuo to obtain a residual mass that was purified by column chromatography using 1 - 2 % MeOH in DCM to obtain the title compound. Yield: 1.1 g (42 %); ¹H – NMR (CDCl₃, 400 MHz) δ ppm: 1.52 (s, 9H), 2.16 (s, 3H), 2.49 (s, 3H), 4.62 (s, 2H), 4.67 (s, 2H); Mass (m/z): 282.4, 284.7 (M+H)⁺.

Step-3: 4-Hydrazino-6,7-dimethyl-1,3-dihydro-pyrrolo[3,4-c]pyridine-2-carboxylic acid tert-butyl ester

30 Hydrazine hydrate (5 mL, 5 vol. to SM) was added to a stirred solution of 4-chloro-6,7-dimethyl-1,3-dihydro-pyrrolo[3,4-c]pyridine-2-carboxylic acid tert-butyl ester (1 g, 0.0035 mol) in ethanol (10 mL) and the reaction mixture was refluxed for 48 h. The reaction

mixture was concentrated in vacuo to obtain a residual mass that was purified by column chromatography using 1 - 5 % MeOH in DCM to obtain the title compound. Yield: 150 mg (15 %); Mass (m/z): 279.2 (M+H)⁺.

Step-4: 4,5-Dimethyl-6,8-dihydro-1,2,3a,7-tetraaza-as-indacene-7-carboxylic acid tert-butyl ester

A mixture of triethyl orthoformate (3 mL, 20 vol. to SM) and 4-hydrazino-6,7-dimethyl-1,3-dihydro-pyrrolo[3,4-c]pyridine-2-carboxylic acid tert-butyl ester (0.15 g, 0.00053 mol) was stirred at 150 - 160 °C for 6 h in a sealed tube. The reaction mixture was cooled to RT and concentrated in vacuo to obtain a residual mass that was purified by column chromatography using 1 - 5 % MeOH in DCM to obtain the title compound. Yield: 0.11g (72 %); ¹H – NMR (CDCl₃, 400 MHz) δ ppm: 1.53 (s, 9H), 2.26 (s, 3H), 2.63 (s, 3H), 4.71 – 4.73 (t, *J* = 3.2 Hz, 2H), 5.03 – 5.06 (m, 2H), 8.75 (s, 1H); Mass (m/z): 288.7 (M+H)⁺.

Step-5: 4,5-Dimethyl-7,8-dihydro-6H-1,2,3a,7-tetraaza-as-indacene hydrochloride

IPA.HCl (0.25 mL, 0.0017 mol, 18 % w/v solution) was added to a stirred solution of 4,5-dimethyl-6,8-dihydro-1,2,3a,7-tetraaza-as-indacene-7-carboxylic acid tert-butyl ester (0.1 g, 0.0003 mol) in methanol (10 mL) and stirred at 50 - 55 °C for 5 h. The reaction mixture was concentrated in vacuo to obtain the title compound. Yield: 60 mg (77 %); ¹H – NMR (DMSO-*d*₆, 400 MHz) δ ppm: 2.27 (s, 3H), 2.69 (s, 3H), 4.67 (s, 2H), 4.82 (s, 2H), 9.52 (s, 1H), 10.41 (bs, 2H); Mass (m/z): 188.8 (M+H)⁺.

Intermediate-7: 3,4,5-Trimethyl-7,8-dihydro-6H-1,2,3a,7-tetraaza-as-indacene hydrochloride

Intermediate-7 was obtained by following the procedure given in step-1 to step-5 of intermediate-6 with some non-critical variations, wherein, in step-4 triethyl orthoacetate was used in the reaction instead of triethyl orthoformate. Mass (m/z): 203.0 (M+H)⁺.

Intermediate-8: 2,5,6-trimethyl-8,9-dihydro-7H-pyrrolo[3,4-c][1,2,4]triazolo[1,5-a]pyridine hydrochloride:

Step-1: 4-[(N-Hydroxy-acetimidoyl)-amino]-6,7-dimethyl-1,3-dihydro-pyrrolo[3,4-c]pyridine-2-carboxylic acid tert-butyl ester

4-[(N-Hydroxy-acetimidoyl)-amino]-6,7-dimethyl-1,3-dihydro-pyrrolo[3,4-c]pyridine-2-carboxylic acid tert-butyl ester was prepared from 4-amino-6,7-dimethyl-1,3-dihydro-pyrrolo[3,4-c]pyridine-2-carboxylic acid tert-butyl ester (2.3 g, 0.00871, prepared as per the procedure disclosed in step-1 of Preparation P3 on page 73 of WO2018234953)

by following the procedure as described in step-2 of intermediate-1 with some non-critical variations. Yield: 1.5 g (53 %); Mass (m/z): 320.1 (M+H)⁺.

Step-2: 2,5,6-Trimethyl-7,9-dihydro-pyrrolo[3,4-c][1,2,4]triazolo[1,5-a]pyridine-8-carboxylic acid tert-butyl ester

5 2,5,6-Trimethyl-7,9-dihydro-pyrrolo[3,4-c][1,2,4]triazolo[1,5-a]pyridine-8-carboxylic acid tert-butyl ester was prepared by using the procedure as described in step-3 of intermediate-1 with some non-critical variations. Yield: 0.5 g (45 %); ¹H – NMR (DMSO-*d*₆, 400 MHz) δ ppm: 1.48 (s, 9H), 2.24 – 2.25 (d, 3H), 2.32 – 2.33 (d, 3H), 2.67 (s, 3H), 4.69 (s, 2H), 4.77 – 4.80 (m, 2H); Mass (m/z): 303.2 (M+H)⁺.

10 **Step-3: 2,5,6-Trimethyl-8,9-dihydro-7H-pyrrolo[3,4-c][1,2,4]triazolo[1,5-a]pyridine hydrochloride**

 2,5,6-Trimethyl-8,9-dihydro-7H-pyrrolo[3,4-c][1,2,4]triazolo[1,5-a]pyridine hydrochloride was prepared by using the procedure as described in step-9 of intermediate-1 with some non-critical variations. Yield: 60 mg (77 %); ¹H – NMR (DMSO-*d*₆, 400 MHz) δ ppm: 2.49 (d, 3H), 2.87 (d, 3H), 3.34 (d, 3H), 4.66 (s, 2H), 4.76 (s, 2H), 9.79 (bs, 2H); Mass (m/z): 203.0 (M+H)⁺.

Intermediate-9: 5,6-Dimethyl-8,9-dihydro-7H-pyrrolo[3,4-c][1,2,4]triazolo[1,5-a]pyridine hydrochloride

 Intermediate-9 was obtained by following the procedure given in step-1 to step-3 of intermediate-8 with some non-critical variations. In step-1 of intermediate-9, dimethylformamide dimethyl acetal was used in the reaction instead of dimethylacetamide dimethyl acetal. Yield: 60 mg (80 %); ¹H – NMR (DMSO-*d*₆, 400 MHz) δ ppm: 2.32 (s, 3H), 2.75 (s, 3H), 4.69 (s, 2H), 4.81 (s, 2H), 8.53 (s, 1H), 10.04 (bs, 2H); Mass (m/z): 188.9 (M+H)⁺.

25 **Intermediate-10: 4,5-Dimethyl-7,8-dihydro-6H-1,3a,7-triaza-as-indacene hydrochloride**

Step-1: 4-Chloro-6,7-dimethyl-1,3-dihydro-pyrrolo[3,4-c]pyridine-2-carboxylic acid ethyl ester

 Ethyl chloroformate (0.8 mL, 0.0082 mol) was added to a stirred solution of 4-chloro-6,7-dimethyl-2,3-dihydro-1H-pyrrolo[3,4-c]pyridine hydrochloride (1.5 g, 0.0068 mol) and triethylamine (2.9 mL, 0.02 mol) in dichloromethane (50 mL) at 0 – 10 °C and then stirred at RT for 3 h. The reaction mixture then poured on to water (50 mL) and product

extracted with dichloromethane (50 mL x 2). Combined organic extracts, washed with brine (50), dried over Na₂SO₄, filtered and concentrated in vacuo to obtain a residual mass that was purified by column chromatography using 25 - 30% ethyl acetate in hexanes to obtain title compound. Yield: 1.07 g (61%); ¹H – NMR (DMSO-*d*₆, 400 MHz) δ ppm: 1.21 – 1.24 (t, *J* = 6.8 Hz, 3H), 2.10 – 2.11 (d, *J* = 4.4 Hz, 3H), 2.63 (s, 3H), 4.09 – 4.14 (q, *J* = 6.8 Hz, 2H), 4.55 – 4.654 (m, 4H); Mass (m/z): 255.0, 257.0 (M+H)⁺.

Step-2: 4-(2,2-Dimethoxy-ethylamino)-6,7-dimethyl-1,3-dihydro-pyrrolo[3,4-c]pyridine-2-carboxylic acid ethyl ester

Pd₂dba₃ (0.19 g, 0.00021 mol), BINAP (0.26 g, 0.00042 mol) and NaO^tBu (0.81 g, 0.0084 mol) were added sequentially to a stirred solution of 4-chloro-6,7-dimethyl-1,3-dihydro-pyrrolo[3,4-c]pyridine-2-carboxylic acid ethyl ester (1.07 g, 0.0042 mol) and aminoacetaldehyde dimethyl acetal (0.53 g, 0.0050 mol) in toluene (50 mL) and the reaction mixture was refluxed under N₂ atmosphere for 6 h. The reaction mixture was then poured on to water and product was extracted using DCM (50 mL x 3). The organic extracts were combined, washed with brine, dried over Na₂SO₄, filtered and concentrated in vacuo to obtain a residual mass that was purified by column chromatography using 1 - 2 % MeOH in DCM to obtain title compound. Yield: 0.85 g (63 %); ¹H – NMR (DMSO-*d*₆, 400 MHz) δ ppm: 1.21 – 1.25 (t, *J* = 6.8 Hz, 3H), 1.97 – 1.99 (d, *J* = 5.2 Hz, 3H), 2.25 (s, 3H), 3.27 (s, 6H), 3.38 – 3.39 (m, 2H), 4.08 – 4.13 (q, *J* = 6.8 Hz, 2H), 4.38 – 4.53 (m, 5H), 6.03 (m, 1H);, Mass (m/z): 324.1 (M+H)⁺.

Step-3: 4,5-Dimethyl-6,8-dihydro-1,3a,7-triaza-as-indacene-7-carboxylic acid ethyl ester

A mixture of 4-(2,2-dimethoxy-ethylamino)-6,7-dimethyl-1,3-dihydro-pyrrolo[3,4-c]pyridine-2-carboxylic acid ethyl ester (0.85 g, 0.0026 mol) and trifluoroacetic acid (25 mL) was refluxed for 48 h. The reaction mixture was then concentrated to obtain a crude mass. This crude mass was diluted with cold water (100 mL), basified with dil. NaOH solution (pH ~ 12), extracted with DCM (50 mL x 3). Combined organic extracts, washed with brine, dried over Na₂SO₄, filtered and concentrated in vacuo to obtain the title compound. Yield: 0.38 g (55 %); ¹H – NMR (DMSO-*d*₆, 400 MHz) δ ppm: 1.23 – 1.28 (t, *J* = 6.8 Hz, 3H), 2.21 – 2.22 (d, *J* = 4.8 Hz, 3H), 2.55 (s, 3H), 4.11 – 4.16 (q, *J* = 6.8 Hz, 2H), 4.67 – 4.83 (m, 4H), 7.55 (s, 1H), 7.85 (s, 1H); Mass (m/z): 260.0 (M+H)⁺.

Step-4: 4,5-Dimethyl-7,8-dihydro-6H-1,3a,7-triaza-as-indacene hydrochloride

A mixture of concentrated hydrochloric acid (5 mL) and 4,5-dimethyl-6,8-dihydro-1,3a,7-triaza-as-indacene-7-carboxylic acid ethyl ester (0.38 g, 0.0014 mol) was refluxed for ~24 h. The reaction mixture was then concentrated to obtain the title compound. Yield: 0.32 g (100 %); ^1H – NMR (DMSO- d_6 , 400 MHz) δ ppm: 2.36 (s, 3H), 2.72 (s, 3H), 4.75 (s, 2H), 4.85 (s, 2H), 8.26 (s, 1H), 8.37 (s, 1H); Mass (m/z): 188.0 (M+H) $^+$.

Intermediate-11: 5-Azetidin-1-yl-7,8-dihydro-6H-2,3,4,7,8b-pentaaza-as-indacene hydrochloride

Step-1: 4-Azetidin-1-yl-2-chloro-5,7-dihydro-pyrrolo[3,4-d]pyrimidine-6-carboxylic acid tert-butyl ester

Azetidine hydrochloride (2.94 g, 0.031 mol) was added to a stirred solution of 2,4-dichloro-5,7-dihydro-pyrrolo[3,4-d]pyrimidine-6-carboxylic acid tert-butyl ester (7.6 g, 0.026 mol) in THF (250 mL) followed by addition of diisopropylethylamine (13.89 mL, 0.078 mol) under N_2 atmosphere and then the reaction mass stirred at RT for 16 h. The reaction mixture was concentrated to obtain a residual mass that was purified by column chromatography using 50 - 60 % ethyl acetate in hexanes to obtain title compound. Yield: 6.2 g (76%). ^1H – NMR (CDCl_3 , 400 MHz) δ ppm: 1.45 – 1.49 (m, 9H), 2.40 - 2.48 (m, 2H), 4.25 – 4.29 (m, 4H), 4.41 - 4.63 (m, 4H); Mass (m/z): 310.9, 312.8 (M+H) $^+$.

Step-2: 4-Azetidin-1-yl-2-hydrazino-5,7-dihydro-pyrrolo[3,4-d]pyrimidine-6-carboxylic acid tert-butyl ester

Hydrazine hydrate (0.02 mL, 0.0053 mol) was added to a stirred solution of 4-azetidin-1-yl-2-chloro-5,7-dihydro-pyrrolo[3,4-d]pyrimidine-6-carboxylic acid tert-butyl ester (1.1 g, 0.387 mol) in 1,4-dioxane (10 mL) and the reaction mixture was refluxed for 7 h during which solids precipitated. These solids were filtered and dried in vacuo to obtain the title compound. Yield: 0.3 g (88 %); ^1H – NMR (CDCl_3 , 400 MHz) δ ppm: 1.49 (m, 9H), 2.34 – 2.42 (m, 2H), 4.15 – 4.19 (m, 4H), 4.47 - 4.61 (m, 4H), 5.96 (s, 1H), 6.68 (bs, 2H); Mass (m/z): 307.36 (M+H) $^+$.

Step-3: 5-Azetidin-1-yl-6,8-dihydro-2,3,4,7,8b-pentaaza-as-indacene-7-carboxylic acid tert-butyl ester

Triethyl orthoformate (11.8 mL, 0.072 mol) was added to a stirred solution of 4-azetidin-1-yl-2-hydrazino-5,7-dihydro-pyrrolo[3,4-d]pyrimidine-6-carboxylic acid tert-butyl ester (1.1 g, 0.036 mol) in THF (20 mL) were heated in a sealed tube at 170 $^\circ\text{C}$ for 6 h then

at 100 °C for 16 h. The reaction mixture was cooled to RT and concentrated to get a residual mass that was purified by column chromatography using 4 - 6 % MeOH in DCM to obtain the title compound. Yield: 0.88 g (77%); ¹H – NMR (CDCl₃, 400 MHz) δ ppm: 1.49 – 1.54 (m, 9H), 2.45 -2.49 (m, 2H), 4.30 – 4.36 (m, 4H), 4.65 - 4.78 (m, 4H), 8.29 (s, 1H); Mass (m/z): 317.3, (M+H)⁺.

Step-4: 5-Azetidin-1-yl-7,8-dihydro-6H-2,3,4,7,8b-pentaaza-as-indacene hydrochloride

IPA.HCl (4.4 mL, 10 vol. to SM, 12% w/v solution) was added to a stirred solution of 5-azetidin-1-yl-6,8-dihydro-2,3,4,7,8b-pentaaza-as-indacene-7-carboxylic acid tert-butyl ester (0.88 g, 0.002 mol) in MeOH (10 mL) and the reaction mass was stirred at RT for 5 h. The reaction mixture was then concentrated in vacuo to obtain tittle compound. Yield: 0.52 g (74%). ¹H – NMR (CD₃OD, 400 MHz) δ ppm: 2.44 - 2.48 (m, 2H), 4.28 – 4.32 (m, 2H), 4.58 – 4.62 (m, 2H), 4.72 - 4.87 (m, 4H), 8.87 (s, 1H); Mass (m/z): 217.0 (M+H)⁺.

Intermediate-12: 5-Methyl-7,8-dihydro-6H-2,3,4,7,8b-pentaaza-as-indacene hydrochloride

Step-1: 2-Chloro-4-methyl-5,7-dihydro-pyrrolo[3,4-d]pyrimidine-6-carboxylic acid tert-butyl ester

Methylzinc chloride (17.2 mL, 0.034 mol, 2M solution in THF) was added to a stirred solution of 2,4-dichloro-5,7-dihydro-pyrrolo[3,4-d]pyrimidine-6-carboxylic acid tert-butyl ester (10 g, 0.034 mol) in THF (100 mL) followed by addition of Pd(dppf)Cl₂·CH₂Cl₂ (0.84 g, 0.001 mol) under N₂ atmosphere and then the reaction mixture was refluxed 4 h. The reaction mixture was cooled to RT and concentrated to obtain a residual mass that was purified by column chromatography using 20 - 25 % ethyl acetate in hexanes to obtain tittle compound. Yield: 3.5 g (37%). ¹H – NMR (CDCl₃, 400 MHz) δ ppm: 1.39 – 1.52 (m, 9H), 2.48 (s, 3H), 4.62– 4.68 (m, 4H); Mass (m/z): 270.0 (M+H)⁺.

Step-2: 2-Hydrazino-4-methyl-5,7-dihydro-pyrrolo[3,4-d]pyrimidine-6-carboxylic acid tert-butyl ester

Hydrazine hydrate (0.15 mL, 3.011 mol) was added to a stirred solution of 2-chloro-4-methyl-5,7-dihydro-pyrrolo[3,4-d]pyrimidine-6-carboxylic acid tert-butyl ester (0.27 g, 0.013 mol) in 1,4-dioxane (10 mL) and the reaction mixture was refluxed for 7 h during which solids precipitated. These solids were filtered and dried in vacuo to obtain the title

compound. Yield: 0.3 g (88 %); ^1H – NMR (CDCl_3 , 400 MHz) δ ppm: 1.47 – 1.52 (m, 9H), 2.31 (s, 3H), 4.48 – 4.54 (m, 4H), 6.27 (s, 1H), 6.38 (bs, 2H); Mass (m/z): 265.7, (M+H) $^+$.

Step-3: 5-Methyl-6,8-dihydro-2,3,4,7,8b-pentaaza-as-indacene-7-carboxylic acid tert-butyl ester

5 Triethyl orthoformate (1.8 mL, 0.011 mol) was added to stirred solution of 2-hydrazino-4-methyl-5,7-dihydro-pyrrolo[3,4-d]pyrimidine-6-carboxylic acid tert-butyl ester (0.15 g, 0.0005 moles) in THF (20 mL) were heated in a sealed tube at 170 °C for 6 h then at 100 °C for 16 h. The reaction mixture was cooled to RT and concentrated to get a residual mass that was purified by column chromatography using 4 - 6% MeOH in DCM to obtain
10 the title compound. Yield: 0.06 g (38%); ^1H – NMR (CDCl_3 , 400 MHz) δ ppm: 1.43 – 1.54 (m, 9H), 2.68 (s, 3H), 4.70 – 4.76 (m, 4H), 8.76 (s, 1H); Mass (m/z): 275.9 (M+H) $^+$.

Step-4: 5-Methyl-7,8-dihydro-6H-2,3,4,7,8b-pentaaza-as-indacene hydrochloride

IPA.HCl (3.5 mL, 10 vol. to SM, 12% w/v solution) was added to a stirred solution of 5-methyl-6,8-dihydro-2,3,4,7,8b-pentaaza-as-indacene-7-carboxylic acid tert-butyl ester
15 (0.06 g, 0.218 mol) in MeOH (50 mL) and the reaction mixture was stirred at RT for 5 h. The reaction mixture was then concentrated in vacuo to obtain tittle compound. Yield: 0.032 g (69 %). ^1H – NMR (CD_3OD , 400 MHz) δ ppm: 2.54 (s, 3H), 4.63 – 4.68 (m, 2H), 4.73 – 4.77 (m, 2H), 9.66 (s, 1H); Mass (m/z): 175.9 (M+H) $^+$.

Intermediate-13: 1-(2-Amino-4-methyl-5,7-dihydro-pyrrolo[3,4-d]pyrimidin-6-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone
20

Step-1: 2-Chloro-4-methyl-6,7-dihydro-5H-pyrrolo[3,4-d]pyrimidine hydrochloride

IPA.HCl (35 mL, 10 vol. to SM, 12% w/v solution) was added to a stirred solution of 2-chloro-4-methyl-5,7-dihydro-pyrrolo[3,4-d]pyrimidine-6-carboxylic acid tert-butyl ester (3.5 g, 0.013 mol) in MeOH (50 mL) and the reaction mixture was stirred at RT for 5h. The
25 reaction mixture was then concentrated in vacuo to obtain tittle compound. Yield: 2.5 gm. ^1H – NMR (CD_3OD , 400 MHz) δ ppm: 2.54 (s, 3H), 4.63– 4.68 (m, 2H), 4.73– 4.77 (m, 2H); Mass (m/z): 169.8 (M+H) $^+$.

Step-2: 1-(2-Chloro-4-methyl-5,7-dihydro-pyrrolo[3,4-d]pyrimidin-6-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone

30 HATU (4.38 g, 0.01 mol) was added to a stirred solution [1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-acetic acid (2.5 g, 0.009 mol) in DMF (20 mL) followed by

addition of 2-chloro-4-methyl-6,7-dihydro-5H-pyrrolo[3,4-d]pyrimidine hydrochloride (2.37 g, 0.01 mol) and diisopropylethylamine (6.79 mL, 0.038 mol) and the reaction mixture stirred at RT for 16 h. The reaction mixture then poured onto cold water, product extracted using DCM (100 mL x 3). The organic extracts were combined, washed with brine, dried over Na₂SO₄, filtered and concentrated in vacuo to obtain a residual mass that was purified by column chromatography using 1 – 2 % MeOH in DCM to obtain the title compound. Yield: 3.3 g; ¹H – NMR (DMSO-*d*₆, 400 MHz) δ ppm: 2.41 (s, 3H), 2.78 – 2.83 (m, 2H), 3.30 – 3.32 (m, 1H), 3.71 – 3.76 (m, 2H), 4.25 – 4.29 (m, 2H), 4.70 – 4.80 (m, 4H) 6.32 – 6.33 (m, 1H), 6.57 (s, 1H), 8.27 – 8.29 (m, 1H); Mass (m/z): 412.0 (M+H)⁺.

10 Step-3: 1-[2-(4-Methoxy-benzylamino)-4-methyl-5,7-dihydro-pyrrolo[3,4-d]pyrimidin-6-yl]-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone

Potassium fluoride (1.0 g, 0.020 mol) was added to a stirred mixture of 1-(2-chloro-4-methyl-5,7-dihydro-pyrrolo[3,4-d]pyrimidin-6-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone (2.8 g, 0.006 mol) and 4-methoxybenzylamine (2.7 g, 0.020 mol) in water (120 mL) and the reaction mixture was refluxed for overnight. The reaction mixture was cooled to RT and the product was extracted with ethyl acetate (50 mL x 3). The organic extracts were combined, washed with brine (50 mL), dried over Na₂SO₄ and concentrated in vacuo to get a residual mass that was purified by column chromatography using 2 - 3 % MeOH in DCM to obtain the title compound. Yield: 2.6 g; ¹H – NMR (CDCl₃, 400 MHz) δ ppm: 2.29 – 2.31 (d, *J* = 6.8 Hz, 3H), 2.75 – 2.81 (m, 2H), 3.30 – 3.31 (m, 1H), 3.71 – 3.73 (m, 2H), 3.75 – 3.79 (s, 3H) 4.24 – 4.29 (m, 2H), 4.54 – 4.70 (m, 6H) 5.29 – 5.33 (m, 1H), 6.31 – 6.32 (d, *J* = 5.6 Hz, 1H), 6.57 (s, 1H), 6.85 – 6.87 (d, *J* = 8.4 Hz, 2H), 7.26 – 7.27 (m, 2H), 8.27 – 8.28 (d, *J* = 5.6 Hz, 1H); Mass (m/z): 513.3 (M+H)⁺.

25 Step-4: 1-(2-Amino-4-methyl-5,7-dihydro-pyrrolo[3,4-d]pyrimidin-6-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone

A stirred mixture of trifluoroacetic acid (50 ml, 20 vol) and 1-[2-(4-methoxy-benzylamino)-4-methyl-5,7-dihydro-pyrrolo[3,4-d]pyrimidin-6-yl]-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone (2.6 g, 0.005 mol) was refluxed for overnight and then the reaction mixture was concentrated to obtain a residual mass. The obtained mass was diluted with cold water (100 mL), basified with dil. NaOH solution and the product was extracted with ethyl acetate (100 mL x 3). The organic extracts were combined, washed with brine (100 mL), dried over Na₂SO₄ and concentrated in vacuo get obtain a residual mass that

was purified by column chromatography using 3 - 5 % MeOH in DCM to obtain the title compound. Yield: 1.28 g; ^1H - NMR (DMSO- d_6 , 400 MHz) δ ppm : 2.19 – 2.20 (d, J = 4.4 Hz, 3H), 2.80 – 2.83 (m, 2H), 3.10 (bs, 1H), 3.67 – 3.70 (t, 2H), 4.14 – 4.18 (m, 2H), 4.36 (s, 1H), 4.45 (s, 1H), 4.59 (s, 1H), 4.67 (s, 1H), 6.51 – 6.53 (m, 1H), 6.56 – 6.57 (m, 2H),
5 6.70 – 6.71 (s, 1H), 8.19 – 8.20 (d, J = 5.2 Hz, 1H); Mass (m/z): 393.0 (M+H) $^+$.

Intermediate-14: 1-(2-Hydrazino-4-methyl-5,7-dihydro-pyrrolo[3,4-d]pyrimidin-6-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone

Hydrazine hydrate (0.02 mL, 0.00036 mol) was added to a stirred solution of 1-(2-chloro-4-methyl-5,7-dihydro-pyrrolo[3,4-d]pyrimidin-6-yl)-2-[1-(2-trifluoromethyl-pyridin-
10 4-yl)-azetidin-3-yl]-ethanone (0.05 g, 0.00012 mol) in 1,4-dioxane (5 mL) and the reaction mixture was refluxed at 100 – 110 °C for 16 h. The reaction mixture was concentrated to obtain crude compound which was triturated with hexanes (3 mL x 2) to obtain the title compound. Yield: 0.035 g (71 %); Mass (m/z): 408.2, (M+H) $^+$.

Intermediate-15: 2-Methyl-7,8-dihydro-6H-1,4,7,8b-tetraaza-as-indacene

15 **Step-1: 5-Hydroxy-2-methyl-6,8-dihydro-1,4,7,8b-tetraaza-as-indacene-7-carboxylic acid ethyl ester**

5-Methyl-2H-pyrazol-3-ylamine (1.69 g, 0.017 mol) was added to a stirred solution of 4-oxo-pyrrolidine-1,3-dicarboxylic acid diethylester (4.0 g, 0.017 mol) in acetic acid (17.5 mL), and the reaction mixture was heated to 120 °C for 3 h. The reaction mixture was
20 cooled to RT, diluted with ethanol (35 mL) and diethyl ether (35 mL) under stirring for 30 min during which solids precipitated. These solids were filtered through a Buchner funnel, dried under high vacuum to obtain the title compound. Yield: 3.01 g (65 %); ^1H - NMR (400 MHz, DMSO- d_6): δ ppm 1.25 (t, J = 7.2 Hz, 3H), 2.28 (s, 3H), 4.13 (q, J = 7.2 Hz, 2H), 4.60 (d, J = 2.0 Hz, 4H), 6.02 (s, 1H), 12.81 (bs, 1H); Mass (m/z); 263.2 (M+H) $^+$

25 **Step-2: 5-Chloro-2-methyl-6,8-dihydro-1,4,7,8b-tetraaza-as-indacene-7-carboxylic acid ethyl ester**

To a stirred solution of 5-hydroxy-2-methyl-6,8-dihydro-1,4,7,8b-tetraaza-as-indacene-7-carboxylic acid ethyl ester (1.0 g, 0.0038 mol) in acetonitrile (0.2M 19.0 mL), POCl₃ (0.6 M, 6.4 mL) was added at RT. The reaction mixture was heated to reflux for 6 h,
30 and then cooled to RT, volatiles were removed under reduced pressure, reaction mass was diluted with ethylacetate, washed with water followed by brine solution, the organic layer

was dried over anhydrous Na₂SO₄ and the volatiles were removed under reduced pressure, to obtain the title compound. Yield: 0.51g, (54 %); ¹H - NMR (400 MHz, DMSO-*d*₆): δ ppm 1.28 (t, *J* = 1.6 Hz, 3H), 2.42 (s, 3H), 4.17 (q, *J* = 7.2 Hz, 2H), 4.64 – 4.72 (m, 4H), 6.63 (s, 1H); Mass (m/z); 281.2, 283.0 (M+H)⁺.

5 **Step-3: 2-Methyl-6,8-dihydro-1,4,7,8b-tetraaza-as-indacene-7-carboxylic acid ethyl ester**

To a stirred solution of 5-chloro-2-methyl-6,8-dihydro-1,4,7,8b-tetraaza-as-indacene-7-carboxylic acid ethyl ester (1.0 g, 0.0034 mol) in methanol (0.25 M, 14.3 mL), was added Pd/C (500.0 mg) at RT, was stirred for 12 h, under H₂ gas balloon, was filtered through a celite, volatiles were removed under reduced pressure, to obtain the title compound. Yield: 0.8 g (91.9 %); ¹H - NMR (400 MHz, DMSO-*d*₆): δ ppm 1.27 (t, *J* = 2.8 Hz, 3H), 2.42 (s, 3H), 4.16 (q, *J* = 4.4 Hz, 2H), 4.49 – 4.71 (m, 4H), 6.38 (s, 1H), 7.44 (s, 1H); Mass (m/z); 247.2 (M+H)⁺.

Step-4: 7,8-Dihydro-2-methyl-6H-pyrazolo[1,5-a]pyrrolo[3,4-e]pyrimidine

15 To a stirred solution of 2-methyl-6,8-dihydro-1,4,7,8b-tetraaza-as-indacene-7-carboxylic acid ethyl ester (1.0 g, 0.0036 mol) in Ethanol:water (1:1, 40 volumes), potassium hydroxide (9.10 g, 0.162 mol) was added at RT, the reaction mixture was heated to reflux for 12 h, and it was then cooled to RT, volatiles were removed under reduced pressure, reaction mixture was extracted with ethyl acetate, followed by brine solution, organic layer was dried over anhydrous Na₂SO₄, and the volatiles were removed under reduced pressure, to obtain the title compound. Yield: 0.41 g (58.0 %); ¹H - NMR (400 MHz, DMSO-*d*₆): δ ppm 1.84 (bs, 1H), 1.98 (s, 3H), 4.03 (d, *J* = 7.2 Hz, 4H), 7.57 (s, 1H), 6.34 (s, 1H); Mass (m/z); 175.3 (M+H)⁺.

Intermediate-16: 2,5-Dimethyl-7,8-dihydro-6H-1,4,7,8b-tetraaza-as-indacene

25 Methyl boronic acid (0.096 g, 0.001 mol), Pd(dppf)Cl₂•DCM (0.087 g, 0.0001 mol) and sodium carbonate (0.45 g, 0.004 mol), were added sequentially to a stirred solution of 5-chloro-2-methyl-6,8-dihydro-1,4,7,8b-tetraaza-as-indacene-7-carboxylic acid ethyl ester (0.3 g, 0.001 mol, Step-2 product of Intermediate-15) in 1,4-dioxane : H₂O (5:1). The reaction mixture was heated at 110 °C for 7 h. The reaction mixture was poured on to water and product was extracted using ethyl acetate (100 mL x 3). The organic extracts were combined, washed with brine (50 mL), dried over Na₂SO₄ and concentrated in vacuo to get

2,5-Dimethyl-6,8-dihydro-1,4,7,8b-tetraaza-as-indacene-7-carboxylic acid ethyl ester. This ester was converted to intermediate 16 by following step-4 of intermediate-15 procedure.

Yield: 0.15 g (53.0 %), Mass (m/z); 189.2 (M+H)⁺.

Intermediate-17: [1-(2-Trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-acetic acid

5 **Step-1: Azetidin-3-yl-acetic acid ethyl ester hydrochloride**

IPA.HCl (100 ml, 5 vol., 12% w/v solution) was added to stirred solution of ethoxycarbonylmethyl-azetidine-1-carboxylic acid tert-butyl ester (20 g, 0.0823 mol; prepared following experimental procedure in *ACS Medicinal Chemistry Letters* (2021), 12(10), 1585-1588) at RT and maintained for overnight and then reaction mixture was
10 concentrated in vacuo to obtain the title compound that was used as such for next step without further purification. Yield: 11.5 g (78%); Mass (m/z): 141.8 (M+H)⁺.

Step-2: [1-(2-Trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-acetic acid ethyl ester

Cesium fluoride (38.1 g, 0.250 mol), triethylamine (47 mL, 0.334 mol) were added sequentially to a stirred solution of azetidin-3-yl-acetic acid ethyl ester hydrochloride (15 g,
15 0.083mol) and 4-bromo-2-trifluoromethyl-pyridine (19 g, 0.083 mol) in DMSO (60 mL) and the reaction mixture was maintained for 4 h at 110 °C. The reaction mixture was then poured onto water and product was extracted using ethyl acetate (100 mL x 3). The organic extracts were combined, washed with brine (50 mL), dried over Na₂SO₄, filtered and concentrated in vacuo to obtain a residual mass that was purified by column chromatography using 15 – 25
20 % ethyl acetate in hexanes to obtain the title compound. Yield: 20 g (83 %): ¹H – NMR (CDCl₃, 400 MHz) δ ppm: 1.23 – 1.29 (m, 3H), 2.68 – 2.77 (m, 2H), 3.15 – 3.21 (m, 1H), 3.69 – 3.71 (m, 4H), 4.13 – 4.21 (m, 2H), 6.31– 6.32 (d, J = 5.6 Hz, 1H), 6.56 – 6.56 (d, J = 1 Hz, 1H), 8.27 – 8.28 (d, J = 5.6 Hz, 1H); Mass (m/z): 289.1 (M+H)⁺.

Step-3: [1-(2-Trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-acetic acid

25 Lithium hydroxide monohydrate (8.96 g, 0.109 mol) was added to a stirred solution of [1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-acetic acid ethyl ester (20 g, 0.071 mol) in THF (100 mL) and water (50 mL) and the reaction mixture was refluxed for 6 h at 55 - 60 °C. The reaction mixture was then concentrated to obtain a crude mass that was diluted with cold water (100 mL), washed with diethyl ether (50 mL x 3) and separated the aqueous
30 layer. The aqueous layer was acidified with acetic acid (pH ~ 4) during which solids precipitated. These solids were filtered and concentrated from DCM (100 mL) in vacuo to obtain the title compound. Yield: 10.5 g (56 %): ¹H – NMR (DMSO-*d*₆, 400 MHz) δ ppm:

2.64 – 2.66 (d, J = 8 Hz, 2H), 3.00 – 3.04 (m, 1H), 3.65 – 3.68 (m, 2H), 4.10 – 4.14 (m, 2H), 6.50 – 6.52 (m, 1H), 6.69 (s, 1H), 8.19 – 8.20 (d, J = 5.6 Hz, 1H), 12.26 (bs, 1H); Mass (m/z): 261.0 (M+H)⁺.

Intermediate-18: [1-(6-Trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-acetic acid

5 **Step-1: [1-(6-Trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-acetic acid ethyl ester**

Pd₂dba₃ (0.72 g, 0.0007 mol), BINAP (0.82 g, 0.001 mol) followed by Cs₂CO₃ (25.8 g, 0.079 mol) were added sequentially to a stirred solution of azetidin-3-yl-acetic acid ethyl ester hydrochloride (6.0 g, 0.0265 mol, step-1 of intermediate-17) and 5-bromo-2-trifluoromethyl-pyridine (5.7 g, 0.036 mol) in toluene (60 mL) and the reaction mixture was
10 refluxed under N₂ atmosphere for 16 h. The reaction mixture was then poured on to water and product was extracted using DCM (50 mL x 3). The organic extracts were combined, washed with brine (50 mL), dried over Na₂SO₄, filtered and concentrated in vacuo to obtain a residual mass that was purified by column chromatography using 15 25 % ethyl acetate in hexanes to obtain the title compound. Yield: 2.9 g (20 %); ¹H – NMR (CDCl₃, 400 MHz) δ ppm: 1.19 – 1.29 (m, 3H), 2.68 – 2.75 (m, 2H), 3.14 – 3.19 (m, 1H), 3.68 – 3.71 (m, 4H),
15 4.13 – 4.20 (m, 2H), 6.68 – 6.70 (dd, J = 8.8, 2.4 Hz, 1H), 7.44 – 7.46 (dd, J = 8.8 Hz, 1H), 7.83 – 7.84 (s, 1H); Mass (m/z): 289.1 (M+H)⁺.

Step-2: [1-(6-Trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-acetic acid

[1-(6-Trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-acetic acid (intermediate-18) was
20 prepared from [1-(6-Trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-acetic acid ethyl ester (step-1 compound) by following the procedure as described in step-3 of intermediate-17 with some non-critical variations. Yield: 1.5 g (55 %); ¹H – NMR (DMSO-*d*₆, 400 MHz) δ ppm: 2.64 – 2.66 (s, 2H), 3.01 – 3.03 (m, 1H), 3.64 – 3.67 (m, 2H), 4.09 – 4.13 (m, 2H),
6.87 – 6.90 (dd, J = 8.8, 8.4 Hz, 1H), 7.56 – 7.59 (dd, J = 8.8, Hz, 1H), 7.87 (s, 1H), 11.12
25 (bs, 1H); Mass (m/z): 261.0 (M+H)⁺.

Intermediate-19: (1-Pyridin-3-yl)-azetidin-3-yl)-acetic acid

(1-Pyridin-3-yl)-azetidin-3-yl)-acetic acid was prepared by following the procedure as described in step-3 of intermediate-17 with some non-critical variations to obtain the crude compound. The resulting crude compound was triturated with a hot solution of ethyl
30 acetate:n-hexane (7:3, 10 volumes) and the resulting solids were filtered in vacuo and dried. Yield: 0.62 g, (31%); ¹H – NMR (DMSO-*d*₆, 400 MHz) δ ppm: 2.62 – 2.64 (d, 2H), 2.95 – 3.01 (m, 1H), 3.51 – 3.54 (m, 2H), 3.98 – 4.02 (t, J = 7.6 Hz, 2H), 6.77 – 6.80 (m, 1H), 7.12

– 7.15 (m, 1H), 7.78 – 7.79 (d, $J = 2.4$ Hz, 1H), 7.88 – 7.89 (m, 1H); Mass (m/z): 193.1 (M+H)⁺

Intermediate-20: [1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-acetic acid

[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-acetic acid was prepared by following the procedure as described in step 1 of Example 12 on page 110 of WO2018/002760 with some non-critical variations. Yield: Quantitative; ¹H – NMR (DMSO-*d*₆, 400 MHz) δ ppm: 2.64 – 2.66 (d, 2H), 2.98 – 3.05 (m, 1H), 3.62 – 3.65 (m, 2H), 4.07 – 4.11 (t, $J = 8.2$ Hz, 2H), 6.42 – 6.44 (m, 1H), 6.54 – 6.55 (d, $J = 2.4$ Hz, 1H), 6.58 – 6.85 (t, $J = 55.2$ Hz, 1H), 8.14 – 8.16 (d, $J = 5.6$ Hz, 1H), 12.25 (bs, 1H); Mass (m/z): 243.0 (M+H)⁺.

Intermediate-21: [1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-acetic acid

[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-acetic acid was prepared by following the procedure as described in the synthesis of intermediate-17 with some non-critical variations. ¹H – NMR (DMSO-*d*₆, 400 MHz) δ ppm: 2.58 – 2.60 (d, 2H), 2.86 – 2.93 (m, 1H), 3.70 – 3.74 (m, 2H), 3.78 (s, 3H), 4.14 – 4.18 (t, $J = 8.2$ Hz, 2H), 6.22 (s, 1H), 7.65 (s, 1H), 12.16 (bs, 1H); Mass (m/z): 256.4, 258.8 (M+H)⁺

Intermediate-22: 2-(1-(Pyridin-4-yl)azetidin-3-yl)acetic acid

2-(1-(Pyridin-4-yl)azetidin-3-yl)acetic acid was prepared by following the procedure given in the reference *J. Med. Chem.* 2024, 67, 13, 10831–10847 (supporting information). ¹H NMR (400 MHz, CD₃OD) δ 7.97 – 8.06 (m, 2H), 6.31 – 6.41 (m, 2H), 4.10 – 4.20 (m, 2H), 3.69 (dd, $J = 5.52, 8.53$ Hz, 2H), 3.06 – 3.20 (m, 1H), 2.54 (d, $J = 7.53$ Hz, 2H); Mass (m/z): 193.10.

Intermediate-23: Lithium [1-(3-trifluoromethyl-phenyl)-azetidin-3-yl]-acetate

Lithium [1-(3-trifluoromethyl-phenyl)-azetidin-3-yl]-acetate was prepared by following the procedures given for intermediate 24, page 86, reference WO2024130066 with some non-critical variations. Mass (m/z): 260.1

Intermediate-24: 1-(2-Trifluoromethyl-pyridin-4-yl)-pyrrolidine-3(R)-carboxylic acid

Step-1: 1-(2-Trifluoromethyl-pyridin-4-yl)-3(R)-pyrrolidine carboxylic acid ethyl ester

1-(2-Trifluoromethyl-pyridin-4-yl)-3(R)-pyrrolidine carboxylic acid ethyl ester was obtained by following the procedure given in step-2 of intermediate-17 with some non-critical variations. Yield: Quantitative; Mass (m/z): 274.6 (M+H)⁺.

Step-2: 1-(2-Trifluoromethyl-pyridin-4-yl)-3(R)-pyrrolidine carboxylic acid

1-(2-Trifluoromethyl-pyridin-4-yl)-3(R)-pyrrolidine carboxylic acid was obtained by following the procedure given in step-3 of intermediate-17 with some non-critical variations. Yield: 7.5 g (52 %); ^1H – NMR (DMSO- d_6 , 400 MHz) δ ppm: 2.13 – 2.25 (m, 2H), 3.17 – 3.22 (m, 1H), 3.33 – 3.35 (m, 2H), 3.37 – 3.56 (m, 2H), 6.66 – 6.67 (d, J = 4.0 Hz, 1H), 6.82
5 (s, 1H), 8.20 – 8.21 (d, J = 6.0 Hz, 1H), 11.05 (bs, 1H); Mass (m/z): 260.9 (M+H) $^+$.

Intermediate-25: 1-Pyridin-3-yl-pyrrolidine-3(R)-carboxylic acid

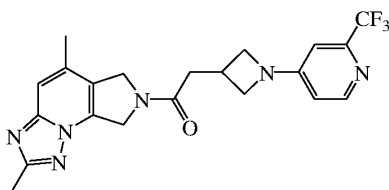
Step-1: 1-Pyridin-3-yl-pyrrolidine-3(R)-carboxylic acid ethyl ester

1-Pyridin-3-yl-pyrrolidine-3(R)-carboxylic acid ethyl ester was obtained by following the procedure given in step-1 of intermediate-18 with some non-critical variations.
10 Yield: Quantitative; Mass (m/z): 221.3 (M+H) $^+$.

Step-2: 1-Pyridin-3-yl-pyrrolidine-3(R)-carboxylic acid

1-Pyridin-3-yl-pyrrolidine-3(R)-carboxylic acid was obtained by following the procedure given in step-3 of intermediate-17 with some non-critical variations. Yield: 49%;
 ^1H – NMR (DMSO- d_6 , 400 MHz) δ ppm: 2.01 – 2.06 (m, 1H), 2.09 – 2.16 (m, 1H), 2.75 –
15 2.80 (m, 1H), 3.15 – 3.31 (m, 4H), 6.80 – 6.83 (m, 1H), 7.09 – 7.13 (m, 1H), 7.76 – 7.78 (dd, J = 1.2, 4.8 Hz, 1H), 7.86 – 7.86 (d, J = 2.8 Hz, 1H); Mass (m/z): 193.4 (M+H) $^+$.

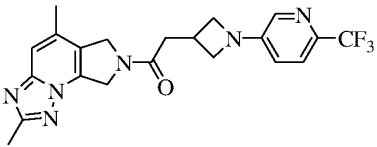
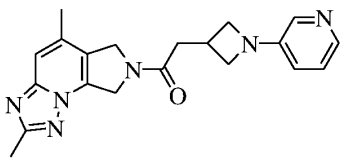
Example-1: 1-(2,5-Dimethyl-6,8-dihydro-1,3,7,8b-tetraaza-as-indacen-7-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone

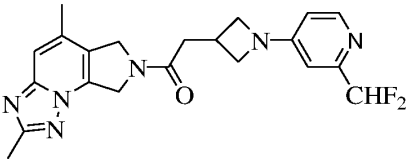
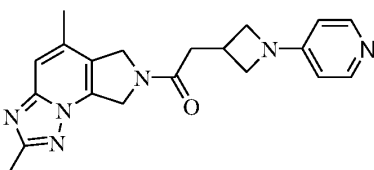
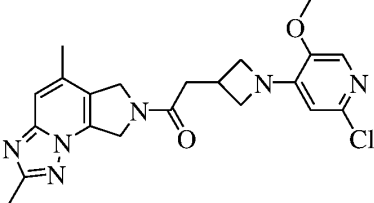


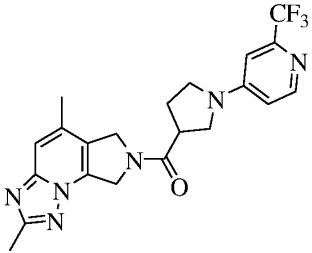
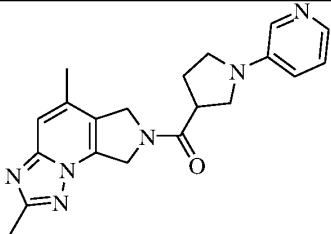
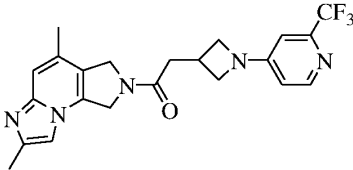
20 HATU (0.061g, 0.00016 mol) was added to a stirred solution of [1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-acetic acid (0.038 g, 0.00014 mol, intermediate-17) in DMF (3 mL) followed by the addition of 2,5-dimethyl-7,8-dihydro-6H-1,3,7,8b-tetraaza-as-indacene hydrochloride (0.030 g, 0.00013 mol, intermediate-1) and diisopropylethylamine (0.094 mL, 0.00053 mol) and the reaction mass stirred at RT for 12 h. The reaction mixture was poured
25 onto cold water (50 mL) and product extracted using DCM (15 mL x 3). The organic extracts were combined, washed with brine (15 mL), dried over Na₂SO₄, filtered and concentrated in vacuo to get a residual mass that was purified by column chromatography using 2 - 4 % MeOH in DCM to obtain the title compound. Yield: 0.030 g (52 %); ^1H – NMR (DMSO- d_6 , 400 MHz) δ ppm: 2.37 (s, 3H), 2.47 (3H), 2.89 – 2.93 (m, 2H), 3.12 –

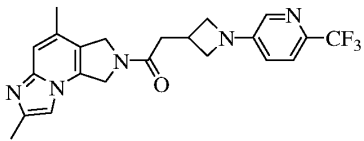
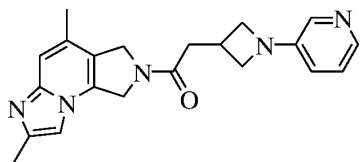
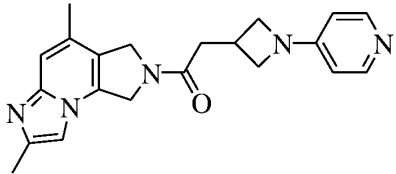
3.15 (m, 1H), 3.70 – 3.74 (m, 2H), 4.17 – 4.21 (m, 2H), 4.71 – 5.21 (m, 4H), 6.53 – 6.54 (d, $J = 5.2$ Hz, 1H), 6.72 (s, 1H), 7.50 – 7.51 (d, $J = 4.8$ Hz, 1H), 8.20 – 8.21 (d, $J = 5.6$ Hz, 1H); Mass (m/z): 431.0 (M+H)⁺.

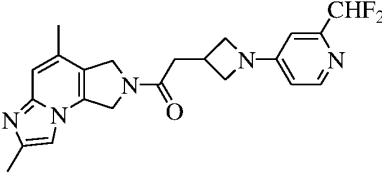
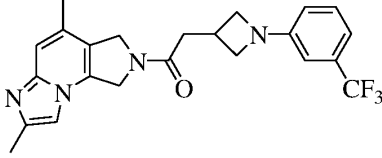
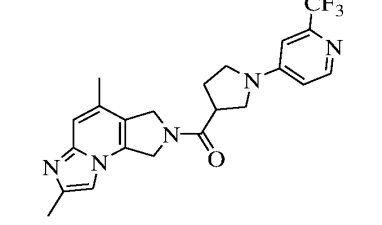
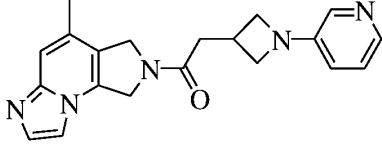
The below Example numbers 2 to 44 were prepared by following the experimental procedure of preparation as described in the Example-1 using suitable intermediates (synthesized above or commercially procured) with some non-critical variations.

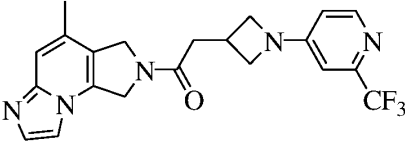
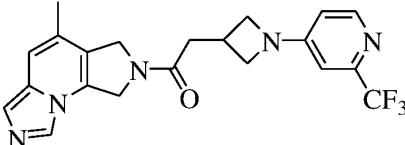
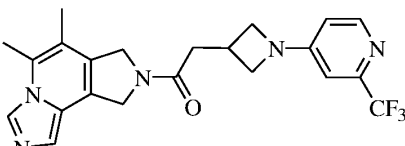
Example No.	Chemical structure and IUPAC Name	Characterization Data
2	 1-(2,5-Dimethyl-6,8-dihydro-1,3,7,8b-tetraaza-as-indacen-7-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone	¹ H – NMR (DMSO- <i>d</i> ₆ , 400 MHz) δ ppm: 2.37 – 2.38 (d, 3H), 2.47 (s, 3H), 2.90 – 2.94 (t, 2H), 3.15 (m, 1H), 3.69 – 3.73 (t, 2H), 4.16 – 4.20 (t, 2H), 4.71 (s, 1H), 4.93 (s, 2H), 5.21 (s, 1H), 6.90 – 6.92 (d, $J = 8$ Hz, 1H), 7.50 – 7.51 (d, $J = 4$ Hz, 1H), 7.57 – 7.60 (d, $J = 8.8$ Hz, 1H), 7.89 (s, 1H); Mass (m/z): 431.0 (M+H) ⁺ .
3	 1-(2,5-Dimethyl-6,8-dihydro-1,3,7,8b-tetraaza-as-indacen-7-yl)-2-(1-pyridin-3-yl)-azetidin-3-yl-ethanone	¹ H – NMR (DMSO- <i>d</i> ₆ , 400 MHz) δ ppm: 2.38 – 2.38 (d, $J = 6.4$ Hz, 3H), 2.46 – 2.47 (d, $J = 2.4$ Hz, 3H), 2.87 – 2.91 (t, 2H), 3.09 – 3.13 (m, 1H), 3.57 – 3.60 (t, $J = 6.6$ Hz, 2H), 4.05 – 4.08 (t, $J = 7.6$ Hz, 2H), 4.71 (s, 1H), 4.93 (s, 2H), 5.21 (s, 1H), 6.80 – 6.83 (m, 1H), 7.13 – 7.17 (m, 1H), 7.50 – 7.51 (d, $J = 3.6$ Hz, 1H), 7.81 – 7.81 (d, $J = 2.0$ Hz, 1H), 7.89 – 7.90 (d, $J = 4.4$ Hz, 1H); Mass (m/z): 363.0 (M+H) ⁺ .
4		¹ H – NMR (CDCl ₃ , 400 MHz) δ ppm: 2.42 (s, 3H), 2.60 – 2.61 (d, $J = 5.2$

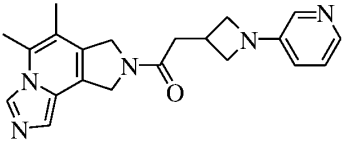
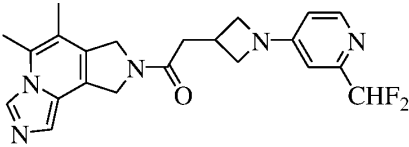
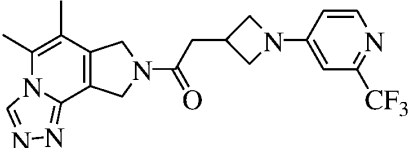
	 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(2,5-dimethyl-6,8-dihydro-1,3,7,8b-tetraaza-as-indacen-7-yl)-ethanone	Hz 3H), 2.84 – 2.88 (m, 2H), 3.30 – 3.35 (m, 1H), 3.72 – 3.75 (m, 2H), 4.25 – 4.30 (m, 2H), 4.84 – 4.86 (m, 2H), 5.14 – 5.16 (m, 2H), 6.29 – 6.30 (d, $J = 5.6$ Hz, 1H), 6.51 – 7.65 (m, 2H), 7.41 – 7.42 (m, 1H), 8.22 – 8.23 (d, $J = 5.6$ Hz, 1H); Mass (m/z): 413.1 (M+H)⁺.
5	 1-(2,5-Dimethyl-6,8-dihydro-1,3,7,8b-tetraaza-as-indacen-7-yl)-2-(1-pyridin-4-yl)-azetidin-3-yl)-ethanone	Mass (m/z): 363.3 (M+H)⁺.
6	 2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(2,5-dimethyl-6,8-dihydro-1,3,7,8b-tetraaza-as-indacen-7-yl)-ethanone	¹H – NMR (DMSO-<i>d</i>₆, 400 MHz) δ ppm: 2.22 – 2.23 (d, $J = 4.0$ Hz, 3H), 2.50 (s, 3H), 2.85 – 2.89 (t, $J = 7.2$ Hz, 2H), 3.78 – 3.79 (m, 3H), 3.75 (s, 3H), 4.21 – 4.25 (t, $J = 8.0$ Hz, 2H), 4.70 (s, 1H), 4.92 (s, 2H), 5.20 (s, 1H), 6.24 – 6.25 (s, 1H), 7.50 – 7.51 (d, $J = 4.0$ Hz, 1H), 7.66 (s, 1H); Mass (m/z): 426.9, 428.8 (M+H)⁺.

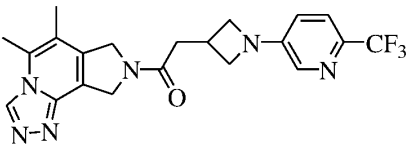
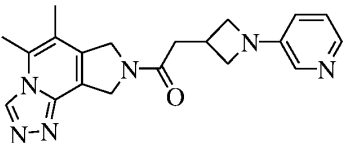
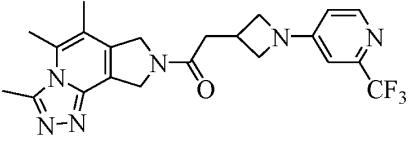
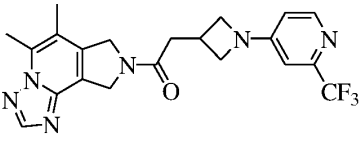
7	 (2,5-Dimethyl-6,8-dihydro-1,3,7,8b-tetraaza-as-indacen-7-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone	¹ H – NMR (DMSO- <i>d</i> ₆ , 400 MHz) δ ppm: 2.12 – 2.13 (d, <i>J</i> = 4.0 Hz, 3H), 2.32 (s, 3H), 3.12 – 3.15 (m, 2H), 3.42– 3.44 (m, 2H), 3.52 – 3.63 (m, 2H), 3.71 – 3.75 (m, 1H), 4.68 (s, 1H), 4.97 (s, 2H), 5.19 (s, 1H), 6.70 – 6.71 (d, <i>J</i> = 4.8 Hz, 1H), 6.87 (s, 1H), 7.50 – 7.53 (d, <i>J</i> = 4.4 Hz, 1H), 8.22 (s, 1H); Mass (m/z): 431.2 (M+H) ⁺ .
8	 (2,5-Dimethyl-6,8-dihydro-1,3,7,8b-tetraaza-as-indacen-7-yl)-(1-pyridin-3-yl-pyrrolidin-3(R)-yl)-methanone	Mass (m/z): 363.1 (M+H) ⁺ .
9	 1-(4,7-Dimethyl-1,3-dihydro-2,6,8a-triaza-as-indacen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone	¹ H – NMR (DMSO- <i>d</i> ₆ , 400 MHz) δ ppm: 2.28 – 2.30 (d, <i>J</i> = 6.0 Hz, 3H), 2.32 (s, 3H), 2.88 – 2.90 (m, 2H), 3.15 – 3.18 (m, 1H), 3.70 – 3.74 (t, <i>J</i> = 6.0 Hz, 2H), 4.17 – 4.21 (t, <i>J</i> = 8.0 Hz, 2H), 4.64 – 5.04 (m, 4H), 6.53 – 6.54 (d, <i>J</i> = 4.8 Hz, 1H), 6.72 (s, 1H), 7.23 (s, 1H), 7.45 – 7.54 (m, 1H), 8.20 – 8.21 (d, <i>J</i> = 5.6 Hz, 1H); Mass (m/z): 430.2 (M+H) ⁺ .

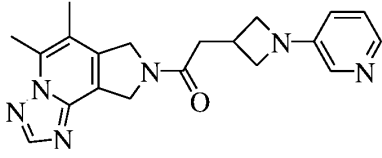
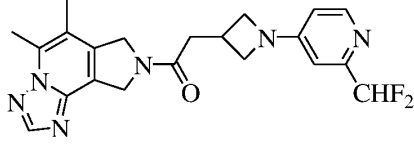
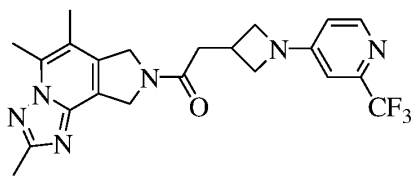
10	 1-(4,7-Dimethyl-1,3-dihydro-2,6,8a-triaza-as-indacen-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone	¹ H – NMR (DMSO- <i>d</i> ₆ , 400 MHz) δ ppm: 2.28 – 2.30 (d, <i>J</i> = 6.0 Hz, 3H), 2.32 (s, 3H), 2.80 – 2.86 (m, 2H), 3.13 – 3.16 (m, 1H), 3.69 – 3.73 (t, <i>J</i> = 6.4 Hz, 2H), 4.16 – 4.20 (t, <i>J</i> = 7.6 Hz, 2H), 4.64 – 5.05 (m, 4H), 6.90 – 6.92 (d, <i>J</i> = 8.8 Hz, 1H), 7.23 (s, 1H), 7.45 – 7.60 (m, 2H), 7.90 (s, 1H); Mass (m/z): 430.2 (M+H) ⁺ .
11	 1-(4,7-Dimethyl-1,3-dihydro-2,6,8a-triaza-as-indacen-2-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone	¹ H – NMR (DMSO- <i>d</i> ₆ , 400 MHz) δ ppm: 2.29 – 2.30 (d, <i>J</i> = 6.0 Hz, 3H), 2.32 (s, 3H), 2.86 – 2.89 (m, 2H), 3.09 – 3.16 (m, 1H), 3.57 – 3.60 (m, 2H), 4.04 – 4.08 (t, <i>J</i> = 7.6 Hz, 2H), 4.65 (s, 1H), 4.82 (s, 1H), 4.86 – 4.87 (d, <i>J</i> = 2.4 Hz, 1H), 5.05 (s, 1H), 6.79 – 6.82 (m, 1H), 7.13 – 7.16 (m, 1H), 7.24 (s, 1H), 7.55 (s, 1H), 7.80 – 7.81 (d, <i>J</i> = 4.0 Hz, 1H), 7.88 – 7.90 (d, <i>J</i> = 4.4 Hz, 1H); Mass (m/z): 362.3 (M+H) ⁺ .
12	 1-(4,7-Dimethyl-1,3-dihydro-2,6,8a-triaza-as-indacen-2-yl)-2-(1-pyridin-4-yl-azetidin-3-yl)-ethanone	¹ H – NMR (DMSO- <i>d</i> ₆ , 400 MHz) δ ppm: 2.28 – 2.30 (d, <i>J</i> = 6.0 Hz, 3H), 2.32 (s, 3H), 2.89 – 2.91 (m, 2H), 3.19 – 3.21 (m, 1H), 3.75 – 3.79 (m, 2H), 3.97 – 4.01 (m, 2H), 4.74 – 5.10 (m, 4H), 6.41 – 6.43 (d, <i>J</i> = 5.6 Hz, 2H), 7.41 (s, 1H), 7.69 (s, 1H), 8.12 – 8.14 (d, <i>J</i> = 5.4 Hz, 2H); Mass (m/z): 362.3 (M+H) ⁺ .

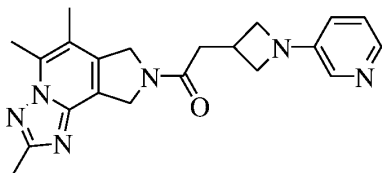
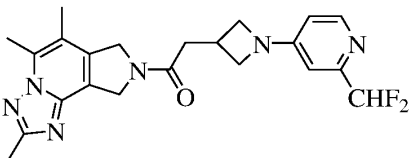
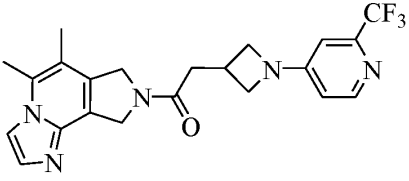
13	 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(4,7-dimethyl-1,3-dihydro-2,6,8a-triaza-as-indacen-2-yl)-ethanone	Mass (m/z): 412.2 (M+H) ⁺ .
14	 1-(4,7-Dimethyl-1,3-dihydro-2,6,8a-triaza-as-indacen-2-yl)-2-[1-(3-trifluoromethyl-phenyl)-azetidin-3-yl]-ethanone	Mass (m/z): 428.5 (M+H) ⁺ .
15	 (4,7-Dimethyl-1,3-dihydro-2,6,8a-triaza-as-indacen-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone	¹ H – NMR (CDCl ₃ , 400 MHz) δ ppm: 2.36 (s, 3H), 2.40 – 2.44 (m, 2H), 2.48 (s, 3H), 3.46 – 3.53 (m, 2H), 3.63 – 3.75 (m, 3H), 4.83 (s, 1H), 4.94 (s, 2H), 5.05 (s, 1H), 6.50 – 6.51 (d, <i>J</i> = 4.0 Hz, 1H), 6.77 – 6.78 (d, <i>J</i> = 4.0 Hz, 1H), 7.11 (s, 1H), 7.34 (s, 1H), 8.31 – 8.32 (d, <i>J</i> = 5.6 Hz, 1H); Mass (m/z): 430.2 (M+H) ⁺ .
16	 1-(4-Methyl-1,3-dihydro-2,6,8a-triaza-as-indacen-2-yl)-2-(1-(pyridin-4-yl)-azetidin-3-yl)-ethanone	¹ H – NMR (DMSO- <i>d</i> ₆ , 400 MHz) δ ppm: 2.32 – 2.33 (d, <i>J</i> = 2.4 Hz, 3H), 2.87– 2.90 (m, 2H), 3.10 – 3.14 (m, 1H), 3.57 – 3.60 (t, <i>J</i> = 6.8 Hz, 2H), 4.05 – 4.09 (t, <i>J</i> = 7.6 Hz, 2H), 4.67 (s, 1H), 4.89 (s, 2H), 5.11 (s, 1H),

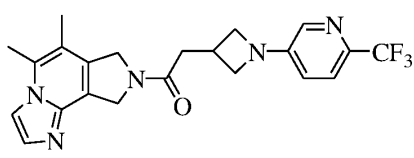
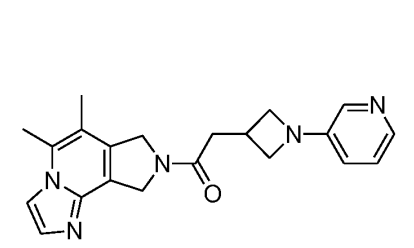
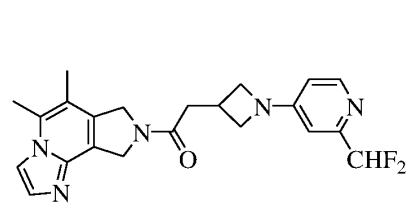
	pyridin-3-yl-azetidin-3-yl)-ethanone	6.80 – 6.83(m, 1H), 7.13 – 7.17 (m, 1H), 7.38 (s, 1H), 7.59 – 7.60 (m, 1H), 7.81 – 7.82, (d, $J = 2.8$ Hz, 1H) 7.85 (s, 1H) 7.89 – 7.90, (d, $J = 4.4$ Hz, 1H); Mass (m/z): 348.0 (M+H) ⁺ .
17	 1-(4-Methyl-1,3-dihydro-2,6,8a-triaza-as-indacen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone	¹ H – NMR (CDCl ₃ , 400 MHz) δ ppm: 2.36 (s, 3H), 2.87–2.89 (m, 2H), 3.10 – 3.25 (m, 1H), 3.74 – 3.76 (m, 2H), 4.27 – 4.31 (t, $J = 8.0$ Hz, 2H), 4.81 – 4.84 (m, 4H), 6.33 – 6.34 (m, 1H), 6.59 – 6.59 (d, $J = 2.0$ Hz, 1H), 7.31 (s, 1H), 7.44 (s, 1H), 7.69 (s, 1H), 8.28 – 8.29, (d, $J = 5.6$ Hz, 1H); Mass (m/z): 415.9 (M+H) ⁺ .
18	 1-(4-Methyl-1,3-dihydro-2,7,8a-triaza-as-indacen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone	¹ H – NMR (DMSO- <i>d</i> ₆ , 400 MHz) δ ppm: 2.24 (s, 3H), 2.88 – 2.90 (m, 2H), 3.13 – 3.17 (m, 1H), 3.71 – 3.74 (m, 2H), 4.17 – 4.21 (t, $J = 8.4$ Hz, 2H), 4.61 (s, 1H), 4.83 – 4.87 (m, 3H), 6.53 – 6.55 (d, $J = 5.6$ Hz, 1H), 6.73 (s, 1H), 7.37–7.41 (m, 2H), 8.20 – 8.22 (d, $J = 5.6$ Hz, 1H), 8.37 (s, 1H); Mass (m/z): 415.7 (M+H) ⁺ .
19	 1-(4,5-Dimethyl-6,8-dihydro-2,3a,7-triaza-as-indacen-7-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone	¹ H – NMR (DMSO- <i>d</i> ₆ , 400 MHz) δ ppm: 2.23 – 2.24 (s, 3H), 2.57 (s, 3H), 2.84 – 2.87 (m, 2H), 3.33 – 3.36 (m, 1H), 3.73 – 3.78 (m, 2H), 4.26 – 4.30 (t, $J = 8$ Hz, 2H), 4.75 (s, 2H), 4.92 – 4.94 (s, 2H), 6.32 – 6.34 (dd, $J = 2.0$, 5.6 Hz, 1H), 6.58 (s, 1H), 7.33 – 7.39 (s, 1H), 8.01 – 8.08 (s, 1H), 8.27 – 8.29 (d, $J = 5.6$ Hz, 1H); Mass (m/z):

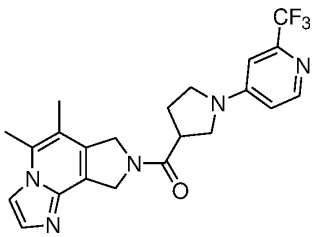
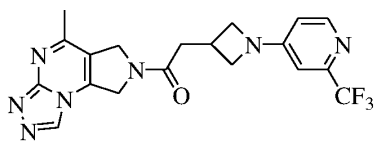
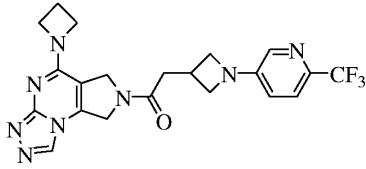
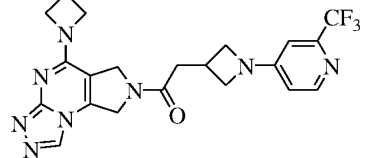
		430.2 (M+H) ⁺ .
20	 1-(4,5-Dimethyl-6,8-dihydro-2,3a,7-triaza-as-indacen-7-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone	¹ H – NMR (DMSO- <i>d</i> ₆ , 400 MHz) δ ppm: 2.19 – 2.20 (d, <i>J</i> = 3.6 Hz, 3H), 2.56 (s, 3H), 2.87 – 2.88 (d, <i>J</i> = 7.6 Hz, 2H), 3.10 – 3.14 (m, 1H), 3.59 – 3.61 (m, 2H), 4.07 – 4.11 (t, <i>J</i> = 7.6 Hz, 2H), 4.61 (s, 1H), 4.75 (s, 1H), 4.82 – 4.83 (s, 1H), 4.97 (s, 1H), 6.93 – 6.95 (d, <i>J</i> = 8.4 Hz, 1H), 7.24 – 7.28 (m, 1H), 7.42 (m, 1H), 7.84 – 7.85 (d, <i>J</i> = 2.8 Hz, 1H), 7.92 – 7.93 (d, <i>J</i> = 3.6 Hz, 1H) 8.39 – 8.41 (d, <i>J</i> = 7.2 Hz, 1H); Mass (m/z): 362.1 (M+H) ⁺ .
21	 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(4,5-dimethyl-6,8-dihydro-2,3a,7-triaza-as-indacen-7-yl)-ethanone	¹ H – NMR (DMSO- <i>d</i> ₆ , 400 MHz) δ ppm: 2.19 – 2.28 (s, 3H), 2.54 (s, 3H), 2.88– 2.89 (m, 2H), 3.29 – 3.32 (m, 1H), 3.68 – 3.70 (m, 2H), 4.13 – 4.15 (m, 2H), 4.61 (s, 1H), 4.75 (s, 1H), 4.82 (s, 1H), 4.97 (s, 1H), 6.44 – 6.45 (d, <i>J</i> = 4.4 Hz, 1H), 6.57 (s, 1H), 6.58 – 6.85 (t, <i>J</i> = 55.2 Hz, 1H), 7.31– 7.32 (m, 1H), 8.15 – 8.16 (d, <i>J</i> = 5.6 Hz, 1H), 8.33 (s, 1H); Mass (m/z): 412.1 (M+H) ⁺ .
22	 1-(4,5-Dimethyl-6,8-dihydro-1,2,3a,7-tetraaza-as-indacen-7-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone	¹ H – NMR (CDCl ₃ , 400 MHz) δ ppm: 2.29 (s, 3H), 2.66 (s, 3H), 2.86 – 2.87 (m, 2H), 3.31 – 3.36 (m, 1H), 3.74 – 3.79 (m, 2H), 4.26 – 4.30 (t, <i>J</i> = 8.0 Hz, 2H), 4.82 – 4.84 (t, <i>J</i> = 2.8 Hz, 2H), 5.17 – 5.18 (m, 2H) 6.33 – 6.34 (m, 1H), 6.59 – 6.59 (d, <i>J</i> = 2.4 Hz, 1H), 8.27 – 8.29, (d, <i>J</i> = 5.6 Hz, 1H),

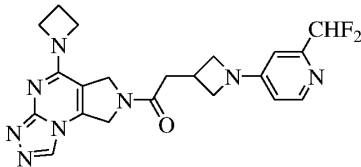
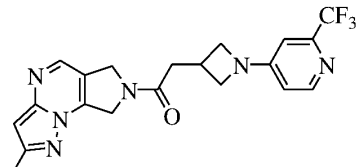
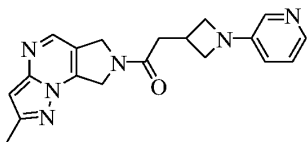
		8.78 (s, 1H); Mass (m/z): 431.3 (M+H) ⁺ .
23	 1-(4,5-Dimethyl-6,8-dihydro-1,2,3a,7-tetraaza-as-indacen-7-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone	¹ H – NMR (CDCl ₃ , 400 MHz) δ ppm: 2.29 (s, 3H), 2.66 (s, 3H), 2.86 – 2.89 (m, 2H), 3.32 – 3.34 (m, 1H), 3.74 – 3.77 (m, 2H), 4.25 – 4.29 (m, 2H), 4.83 (s, 2H), 5.19 (s, 2H) 6.70 – 6.73 (dd, <i>J</i> = 2.4, 8.4 Hz, 1H), 7.45 – 7.47 (d, <i>J</i> = 8.0 Hz, 1H), 7.86 – 7.87 (d, <i>J</i> = 2.0 Hz, 1H), 8.78 (s, 1H); Mass (m/z): 430.9 (M+H) ⁺ .
24	 1-(4,5-Dimethyl-6,8-dihydro-1,2,3a,7-tetraaza-as-indacen-7-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone	¹ H – NMR (CDCl ₃ , 400 MHz) δ ppm: 2.22 – 2.23 (d, <i>J</i> = 4.4 Hz, 3H), 2.64 (s, 3H), 2.89 – 2.91 (m, 2H), 3.07 – 3.11 (m, 1H), 3.57 – 3.59 (m, 2H), 3.97 – 4.06 (m, 2H), 4.70 – 4.71 (m, 2H), 4.87 – 4.89 (m, 2H), 6.80 – 6.82 (m, 1H), 7.13 – 7.17 (m, 1H), 7.81 – 7.89 (m, 2H), 8.49 – 8.52 (m, 1H); Mass (m/z): 362.9 (M+H) ⁺ .
25	 2-[1-(2-Trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(3,4,5-trimethyl-6,8-dihydro-1,2,3a,7-tetraaza-as-indacen-7-yl)-ethanone	Mass (m/z): 444.5 (M+H) ⁺ .
26	 1-(5,6-Dimethyl-7,9-dihydro-1,2,3a,7-tetraaza-as-indacen-7-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone	¹ H – NMR (CDCl ₃ , 400 MHz) δ ppm: 2.34 (s, 3H), 2.81 (s, 3H), 2.87 – 2.88 (m, 2H), 3.10 – 3.12 (m, 1H), 3.74 – 3.79 (m, 2H), 4.26 – 4.32 (t, <i>J</i> = 7.4 Hz, 2H), 4.88 (s, 2H), 5.13 (s, 2H)

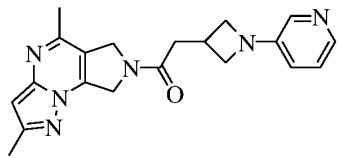
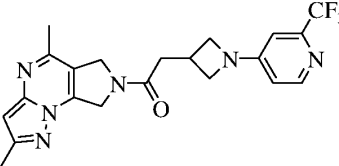
	pyrrolo[3,4-c][1,2,4]triazolo[1,5-a]pyridin-8-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone	6.33 – 6.34 (m, 1H), 6.58 – 6.59 (d, J = 2.0 Hz, 1H), 8.27 – 8.34 (m, 2H); Mass (m/z): 431.2 (M+H) ⁺ .
27	 1-(5,6-Dimethyl-7,9-dihydro-pyrrolo[3,4-c][1,2,4]triazolo[1,5-a]pyridin-8-yl)-2-(1-pyridin-3-yl)-azetidin-3-yl)-ethanone	¹ H – NMR (CDCl ₃ , 400 MHz) δ ppm: 2.34 (s, 3H), 2.81 (s, 3H), 2.86 – 2.88 (m, 2H), 3.26 – 3.30 (m, 1H), 3.65 – 3.70 (m, 2H), 4.19 – 4.23 (m, 2H), 4.88 – 4.88 (m, 2H), 5.14 (s, 2H), 6.79 – 6.81 (d, J = 6.8 Hz, 1H), 7.19 – 7.21 (m, 1H), 7.86 – 7.87 (m, 1H), 7.98 – 7.99 (m, 1H), 8.31 – 8.34 (d, J = 8.8 Hz, 1H); Mass (m/z): 363.0 (M+H) ⁺ .
28	 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(5,6-dimethyl-7,9-dihydro-pyrrolo[3,4-c][1,2,4]triazolo[1,5-a]pyridin-8-yl)-ethanone	¹ H – NMR (DMSO- <i>d</i> ₆ , 400 MHz) δ ppm: 2.29 – 2.30 (d, J = 4.0 Hz, 3H), 2.73 (s, 3H), 2.88 – 2.90 (m, 2H), 3.14 – 3.17 (m, 1H), 3.67 – 3.71 (m, 2H), 4.13 – 4.18 (m, 2H), 4.77 – 4.87 (m, 2H), 4.99 – 5.12 (m, 2H), 6.44 – 6.45 (d, J = 5.6 Hz, 1H), 6.57 – 6.72 (m, 2H), 8.15 – 8.16 (d, J = 5.6 Hz, 1H), 8.46 – 8.46 (d, J = 1.2 Hz, 1H); Mass (m/z): 412.1 (M+H) ⁺ .
29	 2-[1-(2-Trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(2,5,6-trimethyl-7,9-dihydro-pyrrolo[3,4-c][1,2,4]triazolo[1,5-a]pyridin-8-yl)-ethanone	¹ H – NMR (DMSO- <i>d</i> ₆ , 400 MHz) δ ppm: 2.26 – 2.27 (d, J = 4.0 Hz, 3H), 2.33 – 2.34 (d, J = 4.0 Hz, 3H), 2.68 (s, 3H), 2.89 – 2.91 (m, 2H), 3.09 – 3.13 (m, 1H), 3.52 – 3.59 (m, 2H), 4.17 – 4.21 (d, J = 8.0 Hz, 2H), 4.74 (s, 1H), 4.83 (s, 1H), 4.96 (s, 1H), 5.07 (s, 1H), 6.52 – 6.54 (dd, J = 2.4,

	yl)-ethanone	5.6 Hz, 1H), 6.71 – 6.72 (d, J = 2.4 Hz, 1H), 8.20 – 8.21 (d, J = 5.2 Hz, 1H); Mass (m/z): 445.1 (M+H) ⁺ .
30	 2-(1-Pyridin-3-yl-azetidin-3-yl)-1-(2,5,6-trimethyl-7,9-dihydro-pyrrolo[3,4-c][1,2,4]triazolo[1,5-a]pyridin-8-yl)-ethanone	¹ H – NMR (CDCl ₃ , 400 MHz) δ ppm: 2.30 (s, 3H), 2.61 (s, 3H), 2.76 (s, 3H), 2.85 – 2.88 (m, 2H), 3.24 – 3.27 (m, 1H), 3.66 – 3.69 (m, 2H), 4.17 – 4.21 (m, 2H), 4.85 (s, 2H), 5.09 (s, 2H), 6.73 – 6.74 (m, 1H), 7.06 – 7.09 (dd, J = 2.4, 8.4 Hz, 1H), 7.25 – 7.27 (d, J = 8.0 Hz, 1H), 7.34 – 7.35 (d, J = 2.4 Hz, 1H); Mass (m/z): 377.1 (M+H) ⁺ .
31	 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(2,5,6-trimethyl-7,9-dihydro-pyrrolo[3,4-c][1,2,4]triazolo[1,5-a]pyridin-8-yl)-ethanone	Mass (m/z): 427.1 (M+H) ⁺ .
32	 1-(4,5-Dimethyl-6,8-dihydro-1,3a,7-triaza-as-indacen-7-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone	¹ H – NMR (DMSO- <i>d</i> ₆ , 400 MHz) δ ppm: 2.22 – 2.24 (d, J = 8 Hz, 3H), 2.56 (s, 3H), 2.89 – 2.94 (m, 2H), 3.13 – 3.16 (m, 1H), 3.68 – 3.74 (m, 2H), 4.17 – 4.20 (m, 2H), 4.69 (s, 1H), 4.82 (s, 1H), 4.91 (s, 1H), 5.06 (s, 1H), 6.53 – 6.54 (d, J = 4 Hz, 1H), 6.71 (s, 1H), 7.56 (s, 1H), 7.86 (s, 1H), 8.20 – 8.21 (d, J = 5.6 Hz, 1H); Mass (m/z): 430.2 (M+H) ⁺ .

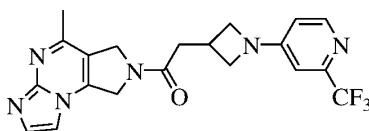
33	 1-(4,5-Dimethyl-6,8-dihydro-1,3a,7-triaza-as-indacen-7-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone	¹ H – NMR (DMSO- <i>d</i> ₆ , 400 MHz) δ ppm: 2.24 (s, 3H), 2.57 (s, 3H), 2.89 – 2.94 (m, 2H), 3.14 – 3.16 (m, 1H), 3.72 – 3.74 (m, 2H), 4.16 – 4.20 (t, <i>J</i> = 7.6 Hz, 2H), 4.70 (s, 1H), 4.83 (s, 1H), 4.92 (s, 1H), 5.07 (s, 1H), 6.89 – 6.91 (d, <i>J</i> = 8.4 Hz, 1H), 7.57 – 7.59 (m, 2H), 7.87 – 7.89 (d, <i>J</i> = 7.6 Hz, 2H); Mass (m/z): 430.1 (M+H) ⁺ .
34	 1-(4,5-Dimethyl-6,8-dihydro-1,3a,7-triaza-as-indacen-7-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone	¹ H – NMR (DMSO- <i>d</i> ₆ , 400 MHz) δ ppm: 2.24 (s, 3H), 2.57 (s, 3H), 2.87 – 2.91 (t, <i>J</i> = 8.0 Hz, 2H), 3.10 – 3.13 (m, 1H), 3.57 – 3.61 (m, 2H), 4.05 – 4.08 (m, 2H), 4.67 – 4.70 (m, 1H), 4.80 – 4.83 (m, 1H), 4.92 (s, 1H), 5.06 (s, 1H), 6.81 – 6.83 (d, <i>J</i> = 8.0, 1H), 7.14 – 7.17 (m, 1H), 7.59 – 7.60 (d <i>J</i> = 5.2 Hz, 1H), 7.81 (s, 1H), 7.87 – 7.89 (d, <i>J</i> = 5.6 Hz, 2H) Mass (m/z): 362.2 (M+H) ⁺ .
35	 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(4,5-dimethyl-6,8-dihydro-1,3a,7-triaza-as-indacen-7-yl)-ethanone	¹ H – NMR (DMSO- <i>d</i> ₆ , 400 MHz) δ ppm: 2.24 – 2.25 (d, <i>J</i> = 4.0 Hz, 3H), 2.57 (s, 3H), 2.89 – 2.94 (m, 2H), 3.12 – 3.16 (m, 1H), 3.67 – 3.72 (m, 2H), 4.14 – 4.18 (m, 2H), 4.70 (s, 1H), 4.83 (s, 1H), 4.92 (s, 1H), 5.07 (s, 1H), 6.44 – 6.46 (m, 1H), 6.57 – 6.72 (m, 2H), 7.60 – 7.62 (d, <i>J</i> = 8.4 Hz, 1H) 7.88 – 7.90 (d, <i>J</i> = 8.4 Hz, 1H), 8.15 – 8.16 (d, <i>J</i> = 5.6 Hz, 1H); Mass (m/z): 412.1 (M+H) ⁺ .

36	 (4,5-Dimethyl-6,8-dihydro-1,3a,7-triaza-as-indacen-7-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone	¹ H – NMR (DMSO- <i>d</i> ₆ , 400 MHz) δ ppm: 2.19 – 2.20 (d, <i>J</i> = 4.2 Hz 3H), 2.32 – 2.36 (m, 2H), 2.58 (s, 3H), 3.44 – 3.45 (m, 1H), 3.49 – 3.50 (m, 2H), 3.60 – 3.63 (m, 2H), 4.74 (s, 1H), 4.86 (s, 1H), 5.05 – 5.07 (m, 1H), 5.18 (s, 1H), 6.70 – 6.71 (d, <i>J</i> = 4.0 Hz, 1H), 6.87 (s, 1H), 7.57 – 7.58 (d, <i>J</i> = 4.8 Hz, 1H), 7.87 (s, 1H), 8.22 (s 1H); Mass (m/z): 430.3 (M+H) ⁺ .
37	 (5-Methyl-6,8-dihydro-2,3,4,7,8b-pentaaza-as-indacen-7-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone	¹ H – NMR (CDCl ₃ , 400 MHz) δ ppm: 2.86 (s, 3H), 2.58 – 2.61 (m, 2H), 3.15 – 3.18 (m, 2H), 3.32 – 3.34 (m, 1H), 4.27 – 4.31 (m, 2H), 4.70 – 4.94 (m, 4H), 6.33 – 6.34 (d, <i>J</i> = 5.2 Hz, 1H), 6.59 (s, 1H), 7.80 – 7.81 (d, <i>J</i> = 7.2 Hz, 1H), 8.49 (s, 1H); Mass (m/z): 417.7 (M+H) ⁺ .
38	 1-(5-Azetidin-1-yl-6,8-dihydro-2,3,4,7,8b-pentaaza-as-indacen-7-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone	¹ H – NMR (DMSO- <i>d</i> ₆ , 400 MHz) δ ppm: 1.23 – 1.25 (m, 4H), 2.32 – 2.40 (m, 2H), 2.83 – 2.89 (m, 2H), 3.12 – 3.17 (m, 1H), 3.67 – 3.70 (t, <i>J</i> = 6.4 Hz, 2H), 4.15 – 4.19 (t, <i>J</i> = 5.6 Hz, 2H), 4.68 (s, 1H), 4.0 (s, 1H), 4.90 (s, 1H), 5.04 (s, 1H), 6.89 – 6.91 (d, <i>J</i> = 8.4 Hz, 1H), 7.58 – 7.60 (d, <i>J</i> = 8.4 Hz, 1H), 7.89 (s, 1H), 8.80 – 8.86 (m, 1H); Mass (m/z): 458.8 (M+H)
39		¹ H – NMR (DMSO- <i>d</i> ₆ , 400 MHz) δ ppm: 2.32 – 2.38 (m, 2H), 2.83 – 2.88 (m, 2H), 3.11 – 3.16 (m, 1H), 3.68 – 3.71 (t, <i>J</i> = 6.0 Hz, 2H), 4.16 – 4.18

	1-(5-Azetidin-1-yl-6,8-dihydro-2,3,4,7,8b-pentaaza-as-indacen-7-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone	(m, 2H), 4.26 – 4.27 (m, 4H), 4.67 (s, 1H), 4.80 (s, 1H), 4.90 (s, 1H), 5.04 (s, 1H), 6.53 – 6.54 (bs, 1H), 6.72 (s, 1H) 8.20 – 8.21 (d, $J = 5.6$ Hz, 1H), 8.86 (s, 1H); Mass (m/z): 459.0, (M+H) ⁺ .
40	 1-(5-Azetidin-1-yl-6,8-dihydro-2,3,4,7,8b-pentaaza-as-indacen-7-yl)-2-[1-(2-difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone	¹ H – NMR (DMSO- <i>d</i> ₆ , 400 MHz) δ ppm: 2.32 – 2.38 (m, 2H), 2.82 – 2.88 (m, 2H), 3.09 – 3.11 (m, 1H), 3.16 – 3.17 (d, $J = 5.2$ Hz, 1H), 3.64 – 3.68 (t, $J = 6.4$ Hz, 2H), 4.07 – 4.17 (m, 3H), 4.25 – 4.29 (m, 2H), 4.68 (s, 1H), 4.80 (s, 1H), 4.90 (s, 1H), 5.04 (s, 1H), 6.44 – 6.45 (m, 1H), 6.56 – 6.56 (m, 1H), 6.58 – 6.86 (t, $J = 55.2$ Hz, 1H) 8.15 – 8.16 (d, $J = 5.2$ Hz, 1H), 8.80 – 8.86 (m, 1H); Mass (m/z): 441.1 (M+H) ⁺ .
41	 1-(2-Methyl-6,8-dihydro-1,4,7,8b-tetraaza-as-indacen-7-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone	¹ H – NMR (400 MHz, CDCl ₃): δ 2.52 (s, 3H), 2.84 (d, $J = 7.6$ Hz, 2H), 3.34 – 3.31 (m, 1H), 3.77 – 3.72 (m, 2H), 4.30 (t, $J = 8.0$ Hz, 2H), 4.78 (d, $J = 2.8$ Hz, 2H), 4.89 (d, $J = 3.2$ Hz, 2H), 6.34 – 6.32 (d, $J = 2.0$ Hz, 1H), 6.44 (d, $J = 5.2$ Hz, 1H), 6.58 (d, $J = 2.0$ Hz, 1H), 8.29 (d, $J = 5.6$ Hz, 1H), 8.53 (d, $J = 12.4$ Hz, 1H); Mass (m/z); 417.1 (M+H) ⁺
42	 1-(2-Methyl-6,8-dihydro-1,4,7,8b-	¹ H – NMR (CDCl ₃ , 400 MHz) δ ppm: 2.53 (s, 3H), 2.85 – 2.88 (m, 2H), 3.31 – 3.34 (m, 1H), 3.73 – 3.78 (m, 2H), 4.17 – 4.22 (m, 2H), 4.79 (s, 2H), 4.83 (s, 2H), 6.32 – 6.34 (d, J

	tetraaza-as-indacen-7-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone	=4.4 Hz, 1H), 6.73 – 6.75 (d, J = 8.4 Hz, 1H), 7.10 – 7.13 (m, 1H), 7.86 – 7.87 (d, J = 2.8 Hz, 1H), 8.00 (s, 1H), 8.29 (s, 1H); Mass (m/z): 349.20 (M+H) ⁺ .
43	 1-(2,5-Dimethyl-6,8-dihydro-1,4,7,8b-tetraaza-as-indacen-7-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone	¹ H – NMR (CDCl ₃ , 400 MHz) δ ppm: 2.53 (s, 3H), 2.83 (s, 3H), 2.85 – 2.88 (m, 2H), 3.28 – 3.29 (m, 1H), 3.73 – 3.78 (m, 2H), 4.17 – 4.22 (m, 2H), 4.79 (s, 2H), 4.83 (s, 2H), 6.43 – 6.45 (d, J = 4.4 Hz, 1H), 6.73 – 6.75 (d, J = 8.4 Hz, 1H), 7.10 – 7.13 (m, 1H), 7.86 – 7.87 (d, J = 2.8 Hz, 1H), 8.00 (s, 1H); Mass (m/z): 363.20 (M+H) ⁺ .
44	 1-(2,5-Dimethyl-6,8-dihydro-1,4,7,8b-tetraaza-as-indacen-7-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone	¹ H – NMR (CDCl ₃ , 400 MHz) δ ppm: 2.61 (s, 3H), 2.80 (s, 3H), 2.84 – 2.85 (m, 2H), 3.33 – 3.34 (m, 1H), 3.73 – 3.78 (m, 2H), 4.26 – 4.31 (m, 2H), 4.78 (s, 2H), 4.83 (s, 2H), 6.32 – 6.34 (m, 1H), 6.43 – 6.45 (d, J = 4.8 Hz, 1H), 6.58 – 6.58 (d, J = 2.0 Hz, 1H), 8.28 (s, 1H); Mass (m/z): 431.2 (M+H) ⁺ .

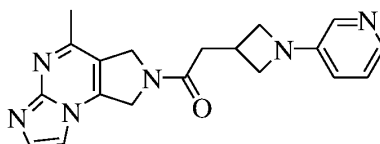
Example-45: 1-(4-Methyl-1,3-dihydro-2,5,6,8a-tetraaza-as-indacen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone



Chloroacetaldehyde (9.3 mL, 0.001 moles, 50% w/v solution) was added to a stirred
 5 mixture of 1-(2-amino-4-methyl-5,7-dihydro-pyrrolo[3,4-d]pyrimidin-6-yl)-2-[1-(2-

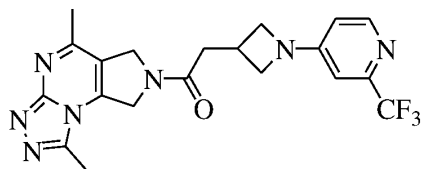
trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone (0.6 g, 0.001 moles, Intermediate-13) in water (50 mL) and the reaction mixture was refluxed for overnight. The reaction mixture was cooled to RT, basified with saturated Na₂CO₃ solution and product extracted with ethyl acetate (100 mL x 3). The organic extracts were combined, washed with brine (100 mL),
 5 dried over Na₂SO₄ and concentrated in vacuo to get a residual mass that was purified by column chromatography using 3 - 5 % MeOH in DCM to obtain the title compound. Yield: 0.21 g; ¹H – NMR (DMSO-*d*₆, 400 MHz) δ ppm: 2.64 (s, 3H), 2.88 – 2.90 (m, 2H), 3.13 – 3.14 (m, 1H), 3.70 – 3.73 (m, 2H), 4.17– 4.20 (m, 2H), 4.63 (s, 1H), 4.70 (s, 1H), 4.89 (s, 1H), 4.94 (s, 1H), 6.53 – 6.54 (d, *J* = 4.8 Hz, 1H), 6.72 (s, 1H), 7.71 (s, 1H), 7.89 – 7.70 (s,
 10 1H), 8.20 – 8.21 (d, *J* = 5.2 Hz, 1H); Mass (m/z): 417.0 (M+H)⁺.

Example-46: 1-(4-Methyl-1,3-dihydro-2,5,6,8a-tetraaza-as-indacen-2-yl)-2-(1-pyridin-3-yl)-azetidin-3-yl)-ethanone



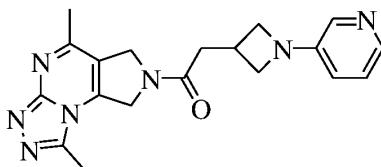
Example-46 was prepared by following the procedure as described for example-45
 15 using suitable intermediates with some non-critical variations. Mass (m/z): 349.40 (M+H)⁺.

Example 47: 1-(1,5-Dimethyl-6,8-dihydro-2,3,4,7,8b-pentaaza-as-indacen-7-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone



Triethylorthoacetate (2 mL) was added to a stirred solution of 1-(2-hydrazino-4-methyl-5,7-dihydro-pyrrolo[3,4-d]pyrimidin-6-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone (0.035 g, 0.085 mmol, Intermediate-14) in THF (10 mL) in a sealed tube and the reaction mixture was heated at 170 °C for 6 h, then at 100 °C for 16 h. The reaction mixture was cooled to RT and concentrated to get a residual mass that was purified by column chromatography using 8 - 10 % MeOH in DCM to obtain the title compound.
 20 Yield: 0.0126 g (32%); ¹H – NMR (DMSO-*d*₆, 400 MHz) δ ppm: 2.76 – 2.80 (m, 2H), 2.90 (s, 3H), 3.16 (s, 3H), 3.27 – 3.32 (m, 1H), 3.65 – 3.71 (m, 2H), 4.16 – 4.18 (m, 2H), 4.60 – 4.87 (m, 4H), 6.53 (m, 1H), 6.72 (m, 1H), 8.20 (m, 1H); Mass (m/z): 432.2, (M+H)⁺.

Example-48: 1-(1,5-Dimethyl-6,8-dihydro-2,3,4,7,8b-pentaaza-as-indacen-7-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone



Example-48 was prepared by following the procedure as described for example-47
5 using suitable intermediate with some non-critical variations. Mass (m/z): 364.42 (M+H)⁺.

Example-49: Determination of allosteric potency EC₅₀ values for Muscarinic M4 receptor

The compounds were tested for their ability to activate the muscarinic M4 receptor. Experimental procedures and results are provided below.

10 Experimental procedures

A. CRE-Luc reporter assay - A CHO-K1 cell line (Chinese hamster ovary (CHO) K1 (ATCC CCL-61) was purchased from ATCC), engineered to stably express recombinant human muscarinic M4 receptor and pCRE-Luc reporter system was used for cell-based assay. The assay offers a non-radioactive based approach to determine binding of a
15 compound to GPCRs. In this specific assay, the level of intracellular cyclic AMP which is modulated by activation or inhibition of the receptor is measured. The recombinant cells harbor luciferase reporter gene under the control of cyclic AMP response element.

The above cells were grown in 96 well clear bottom white plates in Hams F12 medium containing 10% fetal bovine serum (FBS, was purchased from ThermoFisher
20 Scientific). Prior to the addition of compounds or standard agonist, cells were serum starved overnight. Increasing concentrations of test compounds were added along with EC₂₀ of acetylcholine and forskolin (1 μM) in Opti-MEM medium to the cells.

The incubation was continued at 37°C in CO₂ incubator for 4 h. After removal of medium, cells were lysed using lysis buffer, detection reagent was added and luciferase
25 activity was measured in a Luminometer. The reference agonist (10 μM) in the presence of forskolin (1 μM) stimulated luciferase activity was assigned a value of 100 % while basal luciferase activity i.e. only forskolin (1 μM) in the absence of a reference agonist was assigned a value of 0 %. Rest of the luminescent values obtained for compounds at various doses were calculated with reference to stimulated after correcting for basal luciferase

activities. Compound activity (%) vs compound concentration was plotted and dose response curves were analyzed using a 4-parameter logistic fit model of GraphPad Prism software. EC₅₀ values of the compounds were defined as the concentration required in stimulating the luciferase activity by 50 % in presence of EC₂₀ of acetylcholine and the results are provided in table 1A as EC₅₀.

Table 1A: Allosteric potency EC₅₀ values for Muscarinic M4 receptor

Human Muscarinic M4 receptor			
Example No.	PAM EC ₅₀ (nM)	Example No.	PAM EC ₅₀ (nM)
1	9	25	84
2	43	26	5
3	16	32	22
4	14	34	44
9	20	37	140
10	48	38	201
11	31	40	62
19	4	41	113
20	11	45	158
24	207		

B. Glosensor cAMP assay - A HEK293 cell line (human embryonic kidney cells (HEK-293) (ATCC CRL-1573) was purchased from ATCC), engineered to transiently express recombinant human muscarinic M4 receptor and pGloSensor-22F cAMP was used for Glosensor cAMP assay. The assay offers a non-radioactive based approach to determine binding of a compound to GPCRs, uses genetically encoded biosensor variants with cAMP binding domains fused to mutant forms of Photinus pyralis luciferase. Upon binding to cAMP, conformational changes occur that promote large increases in light output. Following pre-equilibration with substrate, cells transiently or stably expressing a biosensor variant can be used to assay GPCR function using a live-cell, nonlytic assay format, enabling facile kinetic measurements of cAMP accumulation or turnover in living cells.

The above cells were grown in 96 well clear bottom white plates in Dulbecco's Modified Eagle Medium containing Glutamax and 10 % fetal bovine serum (FBS, was purchased from ThermoFisher Scientific) at 37 °C in CO₂ incubator for overnight. Prior to

the addition of compounds or standard agonist, cells were pre-equilibrated with substrate in CO₂ independent medium containing 10% FBS for 2 h at RT. Increasing concentrations of test compounds were added along with EC₂₀ of acetylcholine and isoprenaline (0.1 µM) in CO₂ independent medium containing 10 % FBS to the cells.

- 5 The incubation was continued at room temperature for 12 minutes. After incubation, luciferase activity was measured in a Luminometer. The reference agonist (10 µM) in the presence of isoprenaline stimulated luciferase activity was assigned a value of 100 % while basal luciferase activity i.e., only isoprenaline in the absence of a reference agonist was assigned a value of 0 %. Rest of the luminescent values obtained for compounds at various
- 10 doses were calculated with reference to stimulated after correcting for basal luciferase activities. Compound activity (%) vs compound concentration was plotted and dose response curves were analyzed using a 4-parameter logistic fit model of GraphPad Prism software. EC₅₀ values of the compounds were defined as the concentration required in stimulating the luciferase activity by 50 % in presence of EC₂₀ of acetylcholine and the
- 15 results are provided in table 1B as EC₅₀.

Table 1B: Allosteric potency EC₅₀ values for Muscarinic M4 receptor

Human Muscarinic M4 receptor	
Example No.	PAM EC₅₀ (nM)
1	12
2	34
3	10
4	3
9	54
19	9
20	32
26	24
32	34
34	69

Example-50: Rodent pharmacokinetic study

- Male Wistar rats (250 ± 50 grams) were used as experimental animals. Animals were housed individually in polypropylene cages. Two days prior to study, male Wistar rats were
- 20 anesthetized with isoflurane for surgical placement of jugular vein catheter. Rats were administered with test compound at a dose of 5 mg/kg and 2 mL/kg as dose volume. Rats received food and water *ad libitum* during acclimatization, surgical recovery and study.

Formulation for intraperitoneal administration was prepared using 5 % v/v DMSO + 5 % v/v Solutol HS15 + 90 % v/v Water for injection as vehicle. The dose formulations were prepared freshly on the day of dosing.

Post dosing, 200 μ L of blood sample was collected at each time point through the jugular vein and replenished with an equivalent volume of normal saline. The collected blood sample was transferred into a labeled eppendorf tube containing 10 μ L of sodium heparin (1000 IU/mL) as an anticoagulant. Blood samples were collected at 0.08, 0.25, 0.5, 1, 2, 3, 5, 7 and 24 h post-dose. Blood was centrifuged at 4,000 revolutions per minute (rpm) for 10 min. Plasma was separated and stored frozen at -80 °C until analysis. The concentrations of the test compounds were quantified in plasma by qualified LC-MS/MS method using a suitable extraction technique. Study samples were analyzed using calibration samples in the batch and quality control samples spread across the batch.

Pharmacokinetic parameters C_{max} , T_{max} , AUC_{0-t} , $t_{1/2}$ were calculated using a standard non-compartmental model by using Phoenix WinNonlin 8.1 version Software package. The pharmacokinetic profile of the test compounds is given in the table-2 below:

Table 2: Pharmacokinetic profile of the compounds of the present invention

Example No.	C_{max} (ng/mL)	T_{max} (h)	AUC_{0-t} (ng.h/mL)	$t_{1/2}$ (h)
1	2500 $\pm$ 137	0.25	16333 $\pm$ 1601	3.81 $\pm$ 0.37
2	1711 $\pm$ 31	5.50	11975 $\pm$ 499	9.71
3	1189 $\pm$ 174	0.25	1675 $\pm$ 290	1.88 $\pm$ 1.53
4	1167 $\pm$ 318	0.25	6135 $\pm$ 1730	4.45 $\pm$ 0.69
10	2567 $\pm$ 989	0.83	21133 $\pm$ 9603	5.94 $\pm$ 1.72

Example-51: Antagonism of amphetamine induced hyperlocomotion

Male Wistar rats of 230-250 g weight were used. The body weights of the rats were recorded. Rats were randomized according to their body weights. Animals were brought to the laboratory 1 h prior to acclimatizing to the laboratory conditions. The open field is a black colored arena of 51 x 51 x 51 cm enclosed by black plastic walls of same dimensions. Rats were habituated to the open field arena for a period of 30 minutes. Animals were administered respective treatments (vehicle or test compounds) based on the brain exposures. After the habituation period, animals were challenged with amphetamine (0.5

mg/kg, *s.c.*) or vehicle. Then the animals were placed in open field arenas and distance traveled by rats was tracked for 120 minutes using Videomot software. Data was analyzed using GraphPad prism. The results of the test compounds are given in the table 3 below:

Table-3: Antipsychotic like activity of the compounds of the present invention

Example No.	Percent Rerversal		Inference
	3 mg/kg, <i>i.p.</i>	10 mg/kg, <i>i.p.</i>	
2	62	90	Active
3	44	65	Active

5 Example-52: Receptor Occupancy Study in Rats

Male Wistar rats (250 ± 50 grams) were used as experimental animals. Animals were housed individually in polypropylene cages and acclimatized to the experimental condition for 4 days. On the day of the experiment, rats were administered with vehicle (10 mL/Kg) or test compound (3, 10 or 30 mg/Kg) intraperitoneally. At T_{max} of the test compound, all rats were intravenously administered with MK-6884, 3 μ g/Kg (tracer), through lateral tail vein. After 5 minutes of tracer administration, rats were killed by cervical dislocation, brain was separated from the skull, splashed with ice cold water, and two brain regions (striatum and cerebellum) were isolated and transferred into respective pre-labeled/weighed microcentrifuge tubes and stored on dry ice or -80°C until processed for tracer extraction and analysis using LC-MS/MS based method. Study samples were analyzed for tracer concentrations with calibration samples in the batch and quality control samples spread across the batch.

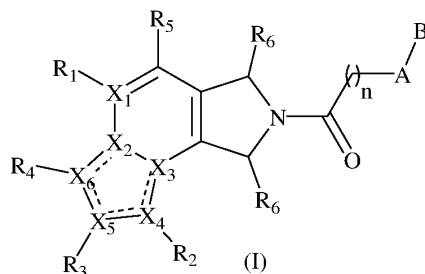
Receptor occupancy in striatum was calculated using ratio method based on the tracer.

20 **Table 4:** Receptor occupancy of test compounds of the present invention

Example No.	Receptor Occupancy (%)	
	10 mg/kg, <i>i.p.</i>	30 mg/kg, <i>i.p.</i>
2	36.2 ± 4.5	63.4 ± 1.3
3	50.0 ± 3.9	79.6 ± 3.4
4	33.9 ± 7.3	66.7 ± 9.7

We claim:

1. A compound of formula (I)



or an isotopic form, or a stereoisomer, or a pharmaceutically acceptable salt thereof,

5 wherein,

--- can be each independently a single bond or a double bond;

X₁ is N or C, provided that when X₁ is N then R₁ is absent;

X₂, X₃, X₄, X₅ and X₆ are independently selected from N or C, provided that at least one of X₂, X₃, X₄, X₅ and X₆ is C; and provided that when X₄, X₅, or X₆ is N then R₂, R₃, or R₄ is
10 absent;

R₁ when present is selected from hydrogen, halogen, cyano, C₁-C₄alkyl, -OC₁-C₄alkyl, C₁-C₄haloalkyl, C₃-C₇cycloalkyl, or C₁-C₄alkoxyalkyl;

R₂ when present is selected from hydrogen, deuterium, halogen, C₁-C₄alkyl, -OC₁-C₄alkyl, C₁-C₄haloalkyl, C₃-C₇cycloalkyl, -CH₂OH, or C₁-C₄alkoxyalkyl;

15 R₃ when present is selected from hydrogen, deuterium, halogen, C₁-C₄alkyl, -OC₁-C₄alkyl, C₁-C₄haloalkyl, C₃-C₇cycloalkyl, -CH₂OH, or C₁-C₄alkoxyalkyl;

R₄ when present is selected from hydrogen, deuterium, halogen, C₁-C₄alkyl, -OC₁-C₄alkyl, C₁-C₄haloalkyl, C₃-C₇cycloalkyl, -CH₂OH, or C₁-C₄alkoxyalkyl;

R₅ is selected from hydrogen, halogen, -NH₂, -NHCH₃, C₁-C₄alkyl, C₁-C₄alkoxyalkyl, C₃-C₇cycloalkyl, or C₄-C₁₀heterocycloalkyl;
20 C₇cycloalkyl, or C₄-C₁₀heterocycloalkyl;

R₆ is independently selected from hydrogen or C₁-C₄alkyl;

A is selected from 3 to 7 membered cycloalkyl or 4 to 10 membered heterocycloalkyl, wherein cycloalkyl and heterocycloalkyl are optionally substituted with one to five substituents independently selected from the group consisting of hydrogen, halogen, deuterium, cyano, -OC₁-C₄alkyl, and C₁-C₄haloalkyl;
25

B is selected from 6 to 10 membered aryl or 5 to 10 membered heteroaryl, wherein aryl and heteroaryl groups are optionally substituted with one to five substituents independently

selected from the group consisting of hydrogen, deuterium, halogen, cyano, hydroxy, -NH₂, NHCH₃, C₁-C₄alkyl, C₁-C₄haloalkyl, -OC₁-C₄alkyl, -OC₁-C₄haloalkyl, and C₃-C₇cycloalkyl; and

n is an integer from 0 to 3.

- 5 2. The compound of formula (I) or an isotopic form, or a stereoisomer, or a pharmaceutically acceptable salt thereof according to preceding embodiments, wherein the compound is selected from:
 - 1-(2,5-Dimethyl-6,8-dihydro-1,3,7,8b-tetraaza-as-indacen-7-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
 - 10 1-(2,5-Dimethyl-6,8-dihydro-1,3,7,8b-tetraaza-as-indacen-7-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone;
 - 1-(2,5-Dimethyl-6,8-dihydro-1,3,7,8b-tetraaza-as-indacen-7-yl)-2-(1-pyridin-3-yl)-azetidin-3-yl)-ethanone;
 - 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(2,5-dimethyl-6,8-dihydro-1,3,7,8b-tetraaza-as-indacen-7-yl)-ethanone;
 - 15 1-(2,5-Dimethyl-6,8-dihydro-1,3,7,8b-tetraaza-as-indacen-7-yl)-2-(1-pyridin-4-yl)-azetidin-3-yl)-ethanone;
 - 2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(2,5-dimethyl-6,8-dihydro-1,3,7,8b-tetraaza-as-indacen-7-yl)-ethanone;
 - 20 (2,5-Dimethyl-6,8-dihydro-1,3,7,8b-tetraaza-as-indacen-7-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone;
 - (2,5-Dimethyl-6,8-dihydro-1,3,7,8b-tetraaza-as-indacen-7-yl)-(1-pyridin-3-yl)-pyrrolidin-3(R)-yl)-methanone;
 - 1-(4,7-Dimethyl-1,3-dihydro-2,6,8a-triaza-as-indacen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
 - 25 1-(4,7-Dimethyl-1,3-dihydro-2,6,8a-triaza-as-indacen-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone;
 - 1-(4,7-Dimethyl-1,3-dihydro-2,6,8a-triaza-as-indacen-2-yl)-2-(1-pyridin-3-yl)-azetidin-3-yl)-ethanone;
 - 30 1-(4,7-Dimethyl-1,3-dihydro-2,6,8a-triaza-as-indacen-2-yl)-2-(1-pyridin-4-yl)-azetidin-3-yl)-ethanone;

- 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(4,7-dimethyl-1,3-dihydro-2,6,8a-triaza-as-indacen-2-yl)-ethanone;
- 1-(4,7-Dimethyl-1,3-dihydro-2,6,8a-triaza-as-indacen-2-yl)-2-[1-(3-trifluoromethyl-phenyl)-azetidin-3-yl]-ethanone;
- 5 (4,7-Dimethyl-1,3-dihydro-2,6,8a-triaza-as-indacen-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone;
- 1-(4-Methyl-1,3-dihydro-2,6,8a-triaza-as-indacen-2-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone;
- 1-(4-Methyl-1,3-dihydro-2,6,8a-triaza-as-indacen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 10 1-(4-Methyl-1,3-dihydro-2,7,8a-triaza-as-indacen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 1-(4,5-Dimethyl-6,8-dihydro-2,3a,7-triaza-as-indacen-7-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 15 1-(4,5-Dimethyl-6,8-dihydro-2,3a,7-triaza-as-indacen-7-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone;
- 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(4,5-dimethyl-6,8-dihydro-2,3a,7-triaza-as-indacen-7-yl)-ethanone;
- 1-(4,5-Dimethyl-6,8-dihydro-1,2,3a,7-tetraaza-as-indacen-7-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 20 1-(4,5-Dimethyl-6,8-dihydro-1,2,3a,7-tetraaza-as-indacen-7-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone;
- 1-(4,5-Dimethyl-6,8-dihydro-1,2,3a,7-tetraaza-as-indacen-7-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone;
- 25 2-[1-(2-Trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(3,4,5-trimethyl-6,8-dihydro-1,2,3a,7-tetraaza-as-indacen-7-yl)-ethanone;
- 1-(5,6-Dimethyl-7,9-dihydro-pyrrolo[3,4-c][1,2,4]triazolo[1,5-a]pyridin-8-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 1-(5,6-Dimethyl-7,9-dihydro-pyrrolo[3,4-c][1,2,4]triazolo[1,5-a]pyridin-8-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone;
- 30 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(5,6-dimethyl-7,9-dihydro-pyrrolo[3,4-c][1,2,4]triazolo[1,5-a]pyridin-8-yl)-ethanone;

- 2-[1-(2-Trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(2,5,6-trimethyl-7,9-dihydro-pyrrolo[3,4-c][1,2,4]triazolo[1,5-a]pyridin-8-yl)-ethanone;
- 2-(1-Pyridin-3-yl)-azetidin-3-yl)-1-(2,5,6-trimethyl-7,9-dihydro-pyrrolo[3,4-c][1,2,4]triazolo[1,5-a]pyridin-8-yl)-ethanone;
- 5 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(2,5,6-trimethyl-7,9-dihydro-pyrrolo[3,4-c][1,2,4]triazolo[1,5-a]pyridin-8-yl)-ethanone;
- 1-(4,5-Dimethyl-6,8-dihydro-1,3a,7-triaza-as-indacen-7-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 1-(4,5-Dimethyl-6,8-dihydro-1,3a,7-triaza-as-indacen-7-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone;
- 10 1-(4,5-Dimethyl-6,8-dihydro-1,3a,7-triaza-as-indacen-7-yl)-2-(1-pyridin-3-yl)-azetidin-3-yl)-ethanone;
- 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(4,5-dimethyl-6,8-dihydro-1,3a,7-triaza-as-indacen-7-yl)-ethanone;
- 15 (4,5-Dimethyl-6,8-dihydro-1,3a,7-triaza-as-indacen-7-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone;
- 1-(5-Methyl-6,8-dihydro-2,3,4,7,8b-pentaaza-as-indacen-7-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 1-(5-Azetidin-1-yl-6,8-dihydro-2,3,4,7,8b-pentaaza-as-indacen-7-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone;
- 20 1-(5-Azetidin-1-yl-6,8-dihydro-2,3,4,7,8b-pentaaza-as-indacen-7-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 1-(5-Azetidin-1-yl-6,8-dihydro-2,3,4,7,8b-pentaaza-as-indacen-7-yl)-2-[1-(2-difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 25 1-(2-Methyl-6,8-dihydro-1,4,7,8b-tetraaza-as-indacen-7-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 1-(2-Methyl-6,8-dihydro-1,4,7,8b-tetraaza-as-indacen-7-yl)-2-(1-pyridin-3-yl)-azetidin-3-yl)-ethanone;
- 1-(2,5-Dimethyl-6,8-dihydro-1,4,7,8b-tetraaza-as-indacen-7-yl)-2-(1-pyridin-3-yl)-azetidin-3-yl)-ethanone;
- 30 1-(2,5-Dimethyl-6,8-dihydro-1,4,7,8b-tetraaza-as-indacen-7-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;

1-(4-Methyl-1,3-dihydro-2,5,6,8a-tetraaza-as-indacen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;

1-(4-Methyl-1,3-dihydro-2,5,6,8a-tetraaza-as-indacen-2-yl)-2-(1-pyridin-3-yl)-azetidin-3-yl)-ethanone;

- 5 1-(1,5-Dimethyl-6,8-dihydro-2,3,4,7,8b-pentaaza-as-indacen-7-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone; or
1-(1,5-Dimethyl-6,8-dihydro-2,3,4,7,8b-pentaaza-as-indacen-7-yl)-2-(1-pyridin-3-yl)-azetidin-3-yl)-ethanone.

3. The compound of formula (I) or an isotopic form, a stereoisomer, or a pharmaceutically acceptable salt thereof as claimed in claim 1 or claim 2, for use as a muscarinic M4 receptor positive allosteric modulator (M4 PAMs).

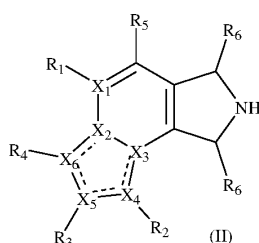
4. A pharmaceutical composition comprising the compound of formula (I) or an isotopic form, or a stereoisomer, or a pharmaceutically acceptable salt thereof as claimed in claim 1 or claim 2 and pharmaceutically acceptable excipients.

- 15 5. The pharmaceutical composition as claimed in claim 4, for use in the treatment of disease or disorder mediated by muscarinic M4 receptors, wherein said disease or disorder is selected from psychiatric disorders, neurological disorders, pain disorders, sleep disorders, or a cognitive disorders

6. A compound of formula (I) or an isotopic form, a stereoisomer, or a pharmaceutically acceptable salt thereof as claimed in claim 1 or claim 2, for use in the treatment of diseases or disorders mediated by muscarinic M4 receptors, wherein said disease or disorder is selected from psychiatric disorders, neurological disorders, pain disorders, sleep disorders, or cognitive disorders.

7. The compound for use as claimed in claim 6, wherein the psychiatric disorders are selected from the group consisting of, anxiety, personality disorders, depression, post-traumatic stress disorder (PTSD), obsessive-compulsive disorder (OCD), bipolar disorder, attention-deficit/hyperactivity disorder (ADHD), psychosis, schizophrenia, substance use disorders and psychotic disorders.

8. The compound for use as claimed in claim 6, wherein the neurological diseases or disorders are selected from the group consisting of Alzheimer's disease, Rett syndrome, Huntington's disease, vascular dementia, Parkinson's disease, and amyotrophic lateral sclerosis (ALS).
- 5 9. The compound for use as claimed in claim 6, wherein the cognitive disorders are selected from the group consisting of amnesia, dementia, amnesic disorder, dementia due to Alzheimer's disease, dementia due to HIV disease, dementia due to Huntington's disease, dementia due to Parkinson's disease, Lewy body dementia, vascular dementia, frontotemporal dementia, senile dementia, dementia associated with Down syndrome,
- 10 dementia associated with Tourette's syndrome, dementia associated with post-menopause, dementia in Creutzfeldt-Jakob disease, substance-induced persisting dementia, dementia in Pick's disease, dementia in Huntington's disease, traumatic brain injury, prion disease, HIV-associated neurocognitive disorders, mild cognitive impairment and any other diseases with cognitive symptoms.
- 15 10. The compound for use as claimed in claim 7, wherein the schizophrenia is selected from cognitive impairment in schizophrenia, positive symptoms of schizophrenia and/or negative symptoms of schizophrenia.
11. The compound for use as claimed in claim 7, wherein the psychotic disorders are selected from psychosis associated with Alzheimer's disease, psychosis associated with
- 20 Parkinson's disease, psychotic depression, psychosis associated with stroke, psychosis associated with epilepsy, psychosis associated with multiple sclerosis, psychosis associated with traumatic brain injury, substance-induced persisting delirium, or any other diseases with psychotic features.
12. A compound of Formula (II) or a pharmaceutically acceptable salt thereof:



25

wherein,

--- can be each independently a single bond or a double bond;

X_1 is selected from C or N;

X_2 is selected from C or N;

X_3 is selected from C or N;

5 X_4 is selected from C or N;

X_5 is selected from C or N;

X_6 is selected from C or N;

Provided that at least one of X_1, X_2, X_3, X_4, X_5 and X_6 is C; provided that when X_1, X_2, X_3, X_4, X_5 or X_6 is N then R_1, R_2, R_3 , or R_4 is absent;

10 R_1 when present is selected from hydrogen, halogen, C_1 - C_4 alkyl, $-OC_1$ - C_4 alkyl, C_1 - C_4 haloalkyl, C_3 - C_7 cycloalkyl, or C_4 - C_{10} heterocycloalkyl;

R_2 when present is selected from hydrogen, halogen, C_1 - C_4 alkyl, $-OC_1$ - C_4 alkyl, C_1 - C_4 haloalkyl, C_3 - C_7 cycloalkyl, or C_4 - C_{10} heterocycloalkyl;

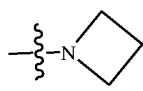
15 R_3 when present is selected from hydrogen, halogen, C_1 - C_4 alkyl, $-OC_1$ - C_4 alkyl, C_1 - C_4 haloalkyl, C_3 - C_4 cycloalkyl, or C_4 - C_{10} heterocycloalkyl;

R_4 when present is selected from hydrogen, halogen, C_1 - C_4 alkyl, $-OC_1$ - C_4 alkyl, C_1 - C_4 haloalkyl, C_3 - C_7 cycloalkyl, or C_4 - C_{10} heterocycloalkyl;

R_5 is selected from hydrogen, halogen, C_1 - C_4 alkyl, $-OC_1$ - C_4 alkyl, C_1 - C_4 haloalkyl, C_3 - C_7 cycloalkyl, or C_4 - C_{10} heterocycloalkyl; and

20 R_6 is selected from from hydrogen or C_1 - C_4 alkyl.

13. The compound of formula (II) or a pharmaceutically acceptable salt thereof as claimed in claim 12, wherein R_1 is selected from hydrogen, chloro, fluoro, methyl, ethyl, methoxy, ethoxy, CHF_2 , or CF_3 ; wherein R_2 is selected from hydrogen, chloro, fluoro, methyl, ethyl, methoxy, ethoxy, CHF_2 , or CF_3 ; wherein R_3 is selected from hydrogen, chloro, fluoro, methyl, ethyl, methoxy, ethoxy, CHF_2 , or CF_3 ; wherein R_4 is selected from hydrogen, chloro, fluoro, methyl, ethyl, methoxy, ethoxy, CHF_2 , or CF_3 ; wherein R_5 is selected from

hydrogen, chloro, fluoro, methyl, ethyl, methoxy, ethoxy, CHF_2 , CF_3 or ; wherein R_6 is selected from hydrogen, methyl or ethyl..