

**ORGANIC COMPOUNDS AS MUSCARINIC M4 RECEPTOR POSITIVE
ALLOSTERIC MODULATORS (M4 PAMs)**

FIELD OF INVENTION

The present invention relates to the 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.

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.

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 a 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*).

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*).

Xanomeline, a M1/M4-preferring mAChR agonist, has shown to significantly reduce the behavioral symptoms in patients with Alzheimer's disease (AD) (*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 WO2021/099527, WO2018/234953, WO2018/066718, and WO2018/002760 disclose compounds that are muscarinic M4 receptor PAMs. WO2022/226078 discloses some of the reported M4 PAM compounds as a therapy for alcohol-related liver diseases. While several muscarinic M4 receptor PAMs have been disclosed in the literature till date, no muscarinic M4 receptor PAM compound has been 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 the treatment of disorders that are affected by the muscarinic M4 receptors.

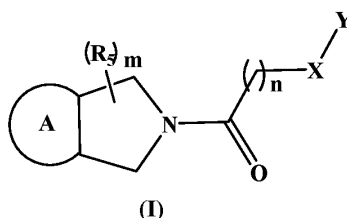
Literature suggests that compounds that acts on Muscarinic M2 receptor mediates cholinergic side effects such as bradycardia and hypotension (*Grauer et al., 2020 Brain Research; 1737:146814; Sundaram et al., 1989 Brain research, 477(1-2), 358-362; Mirza et al., 2003 CNS drug reviews, 9(2), 159-186*). Additionally there exists a similarity in allosteric binding pocket for M4 as well as M2 muscarinic acetylcholine receptors which pose key challenges in development of an M4 PAM with subtype selective against M2. Our

compounds exhibit minimal activity towards Muscarinic M2 receptor (*Wood et al., 2016 ACS medicinal chemistry letters, 8(2), 233–238; Butler et al., 2024 Journal of medicinal chemistry, 67(13), 10831–10847; Croy et al., 2014 Molecular pharmacology, 86(1), 106–115*).

- 5 The present invention discloses novel compounds that are muscarinic M4 receptor PAMs with desirable profiles. The compounds of this invention have potent affinity at M4, selectivity over muscarinic subtype receptors like M1, M2, M3 and M5, acceptable pharmacokinetic properties, good brain penetration, receptor occupancy and efficacy in animal models.

10 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,



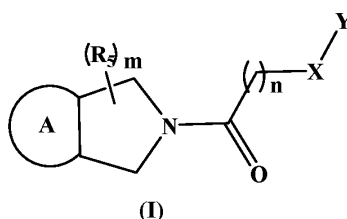
Wherein,

- 15 Ring A is a 9 to 12 membered heterocyclic ring, wherein the heterocycle is substituted with 0, 1, 2, or 3 groups independently selected from hydrogen, halogen, $-NH_2$, $-C_1-C_4$ alkyl, $-C_1-C_4$ haloalkyl, $-C_1-C_4$ hydroxyalkyl, $-C_1-C_4$ alkoxyalkyl, $-O-C_1-C_4$ alkyl, $-OC_1-C_4$ haloalkyl, $-NHC_1-C_4$ alkyl or $-R_5$ -Phenyl;
- X is selected from 3 to 7 membered cycloalkyl or 3 to 7 membered heterocycloalkyl,
- 20 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;
- Y 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
- 25 selected from the group consisting of hydrogen, deuterium, halogen, cyano, hydroxy, $-NH_2$, $-NHC_1-C_4$ alkyl, $-C_1-C_4$ alkyl, $-C_1-C_4$ haloalkyl, $-OC_1-C_4$ alkyl, $-OC_1-C_4$ haloalkyl, and $-C_3-C_7$ cycloalkyl;
- R_5 is selected from hydrogen, deuterium and $-C_1-C_4$ alkyl;

m is an integer selected from 0 to 2; and

n is an integer selected from 0 to 3.

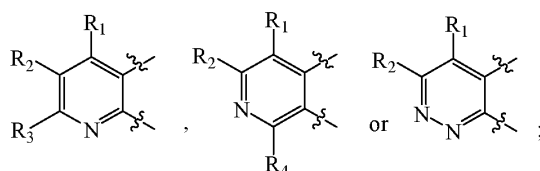
In another aspect, the present invention relates to a compound of formula (I), or an isotopic form, or a stereoisomer, or a pharmaceutically acceptable salt thereof,



5

wherein

A is a ring moiety selected from



“” is point of attachment;

- 10 R₁ and R₂ together with the carbon atoms to which they are attached form a 5 to 8 membered cycloalkyl or 5 to 8 membered heterocycloalkyl ring, wherein the cycloalkyl or heterocycloalkyl is optionally substituted with one or two groups independently selected from hydrogen, hydroxyl, -C₁-C₄alkyl or -R₅-phenyl;

- R₂ and R₃ together with the carbon atoms to which they are attached form a 5 to 8 membered cycloalkyl or 5 to 8 membered heterocycloalkyl ring, wherein the cycloalkyl or heterocycloalkyl is optionally substituted with one or two groups independently selected from hydrogen, hydroxyl, -C₁-C₄alkyl or -R₅-phenyl;

- When R₁ and R₂ form a ring, then R₃ is selected from hydrogen, -C₁-C₄hydroxyalkyl, -NH₂, -C₁-C₄alkyl or -C₁-C₄haloalkyl;

- 20 When R₂ and R₃ form a ring, then R₁ is selected from hydrogen, -C₁-C₄hydroxyalkyl, -NH₂, -C₁-C₄alkyl or -C₁-C₄haloalkyl;

R₄ is selected from hydrogen, -C₁-C₄hydroxyalkyl, NH₂, C₁-C₄alkyl, NH-C₁-C₄alkyl or C₁-C₄haloalkyl;

R₅ is selected from hydrogen, deuterium and C₁-C₄alkyl;

- 25 X is selected from 3 to 7 membered cycloalkyl or 3 to 7 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;

Y 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
5 selected from the group consisting of hydrogen, deuterium, halogen, cyano, hydroxy, -NH₂, -NHC₁-C₄alkyl, -C₁-C₄alkyl, -C₁-C₄haloalkyl, -OC₁-C₄alkyl, -OC₁-C₄haloalkyl, and -C₃-C₇cycloalkyl;

m is an integer selected from 0 to 2; and

n is an integer selected from 0 to 3.

10 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.

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
15 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 thereof a therapeutically effective amount of the compound of formula (I), or an isotopic form, or a stereoisomer, or a pharmaceutically acceptable salt thereof.

20 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.

DETAILED DESCRIPTION OF THE INVENTION

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

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

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

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-butyl.

5 The term, “-NHC₁-C₄alkyl” as used herein refers to -C₁-C₄alkyl as defined above, attached to the parent molecular moiety through an nitrogen atom. Examples of the -NHC₁-C₄alkyl include, but are not limited to, methylamine, ethylamine, propylamine, and butylamine.

10 The term, “-C₁-C₄hydroxyalkyl” as used herein refers to -C₁-C₄alkyl as defined above, wherein one or more hydrogens of the same or different carbon atoms are substituted with hydroxy group. Examples of -C₁-C₄hydroxyalkyl include, but are not limited to, hydroxymethyl, 2-hydroxyethyl, 2-hydroxypropyl, 3-hydroxypropyl, 1-(hydroxymethyl)-2-methylpropyl, 2-hydroxybutyl, 3-hydroxybutyl, 4-hydroxybutyl, 2,3-dihydroxypropyl, 1-(hydroxymethyl)-2-hydroxyethyl, 2,3-dihydroxybutyl, and 3,4-dihydroxybutyl.

15 The phrase “9 to 12 membered heterocyclic ring” as used herein refers to a fused bicyclic ring system containing 9 to 12 carbon atoms, in which atleast one of the carbon in the ring is replaced with heteroatom independently selected from N, O or S. Examples of 9 to 12 membered heterocyclic rings include, but are not limited to 6,7-dihydro-5H-cyclopenta[b]pyridine, 6,7-dihydro-5H-pyrrolo[3,4-b]pyridine, 6,7-dihydro-5H-cyclopenta[c]pyridazine, 5,6,7,8-tetrahydro-quinoline, 5,6,7,8-tetrahydro-[1,6]naphthyridine, 7,8-dihydro-5H-pyrano[4,3-b]pyridine, 5,7-dihydro-furo[3,4-b]pyridine, 3,4-dihydro-1H-pyrano[3,4-c]pyridine, 2,3-dihydro-1H-pyrido[2,3-b][1,4]oxazine, 2,3-dihydro-[1,4]dioxino[2,3-c]pyridine, 1,2,3,4-tetrahydro-2,7-naphthyridine, 2,3-dihydro-1H-pyrrolo[3,4-c]pyridine, 2,3-dihydrofuro[2,3-b]pyridine, 25 2,3-dihydrofuro[3,2-b]pyridine, 5,7-dihydrofuro[3,4-b]pyridine, 2,3-dihydrofuro[2,3-c]pyridine, 1,3-dihydrofuro[3,4-c]pyridine, 2,3-dihydrofuro[3,2-c]pyridine, 1,2,3,4-tetrahydro-2,6-naphthyridine, 5,6,7,8-tetrahydro-1,7-naphthyridine, 6,7-dihydro-5H-cyclopenta[c]pyridine, 5,6,7,8-tetrahydrocinnoline, 6,8-dihydro-5H-pyrano[3,4-c]pyridazine, 6,7-dihydro-5H-pyrrolo[3,4-c]pyridazine, 5,6,7,8-tetrahydropyrido[4,3-c]pyridazine, 5,6,7,8-tetrahydro-1,6-naphthyridine, 6,8-dihydro-5H-pyrano[3,4-b]pyridine, 30 7,8-dihydro-5H-pyrano[4,3-b]pyridine, and 7,8-dihydro-5H-pyrano[4,3-b]pyridine.

The phrase, “-C₃-C₈cycloalkyl or 3 to 8 membered cycloalkyl” as used herein refers to a saturated monocyclic hydrocarbon ring containing three to eight carbon atoms. Examples of -C₃-C₈cycloalkyl or 3 to 8 membered cycloalkyl group include, but are not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl and cyclooctyl.

5 The phrase, “3 to 8 membered heterocycloalkyl or C₃-C₈heterocycloalkyl” as used herein refers to heterocycloalkyl substituent containing a total of 3 to 8 ring atoms, at least one of which is a heteroatom selected from nitrogen, oxygen or sulfur. Examples of 3 to 8 membered heterocycloalkyl include but are not limited to aziridinyl, azetidiny, pyrrolidinyl, tetrahydrofuranyl, tetrahydrothienyl, tetrahydropyranyl, tetrahydrothiopyranyl, 10 piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, azepanyl and 1,4-oxazepanyl.

The phrase “-C₆-C₁₀aryl or 6 to 10 membered aryl” as used herein refers to aromatic hydrocarbon rings containing six to ten carbon atoms. Examples of -C₆-C₁₀aryl group include, but not limited to phenyl, indanyl, indenyl and naphthyl.

The phrase “-C₅-C₁₀heteroaryl or 5 to 10 membered heteroaryl” as used herein refers 15 to aromatic monocyclic or aromatic bicyclic ring systems containing five to ten carbon atoms in which at least one carbon atom is substituted with heteroatoms independently selected from N, O or S or at least two carbon atoms of one or both of the rings are replaced with a heteroatom independently selected from N, O, or S. Examples of -C₅-C₁₀heteroaryl include, but not limited to 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,4-thiadiazolyl, 1,3,4- 20 thiadiazolyl, triazolyl, tetrazolyl, triazinyl, furyl, imidazolyl, isoxazolyl, isothiazolyl, oxazolyl, pyrrolyl, pyrazolyl, thiazolyl, thienyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, benzodioxolyl, benzofuranyl, benzofurazanyl, benzimidazolyl, benzopyrazolyl, benzothiazolyl, benzotriazolyl, benzothiophenyl, benzoxazepinyl, benzooxazinonyl, benzooxazolonyl, benzoxazolyl, imidazopyridinyl, thienopyridinyl, furopyridinyl, 25 pyrrolopyridinyl, pyrazolopyridinyl, oxazolopyridinyl, thiazolopyridinyl, imidazopyrazinyl, imidazopyrimidinyl, thienopyrimidinyl, furopyrimidinyl, pyrrolopyrimidinyl, pyrazolopyrimidinyl, oxazolopyrimidinyl, thiazolopyrimidinyl, pyrazolotriazinyl, isoquinolyl, quinolyl, phthalazinyl, naphthyridinyl, quinoxaliny, quinazolinyl, and N-oxides thereof.

30 The term, “-C₁-C₄haloalkyl” as used herein refers to -C₁-C₄alkyl as defined above wherein one or more hydrogens of the same or different carbon atoms are substituted with

halogen atom. Examples of the $-C_1-C_4$ haloalkyl include, but are not limited to, fluoromethyl, 2-fluoroethyl, difluoromethyl and trifluoromethyl.

The term, “ $-OC_1-C_4$ alkyl” as used herein refers to $-C_1-C_4$ alkyl as defined above, attached to the parent molecular moiety through an oxygen atom. Examples of the $-OC_1-C_4$ alkyl include, but are not limited to, methoxy, ethoxy, propoxy, isopropoxy and butyloxy.

The term “ $-OC_1-C_4$ haloalkyl” as used herein refers to $-C_1-C_4$ haloalkyl as defined above that is bonded to the oxygen atom. Examples of the $-OC_1-C_4$ haloalkyl include, but are not limited to, $-OCH_2F$, $-OCHF_2$, and $-OCF_3$.

The term, “ $-C_1-C_4$ alkoxyalkyl” as used herein refers to $-C_1-C_4$ alkyl as defined above wherein one or more hydrogens of the same or different carbon atoms is substituted with $-OC_1-C_4$ alkyl group. Examples of $-C_1-C_4$ alkoxyalkyl group include, but are not limited to, methoxymethyl, ethoxymethyl, propoxymethyl and butoxymethyl.

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 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 or D) 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 , iodine such as ^{123}I , ^{124}I , ^{125}I and ^{131}I , and sulphur such as ^{35}S . Substitution with heavier isotopes, for example, replacing one or more key carbon-hydrogen 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 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, deuterated-cycloalkyl, deuterated-heterocyclyl, deuterated-aryl, deuterated-heteroaryl and the like. The term "deuterated-alkyl" refers to an $-C_1-C_4$ -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 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" as used herein refers to 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).

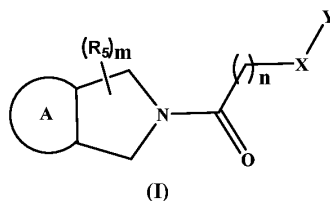
The phrase, "cognitive disorders" as used herein refers to diseases or disorders such as amnesia, dementia, amnesic disorder, dementia due to Alzheimer's diseases, dementia due to human immunodeficiency virus (HIV) disease, dementia due to Huntington's disease, dementia due to Parkinson's disease, Lewy body dementia, vascular dementia, frontotemporal dementia (FTD), 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, and 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,



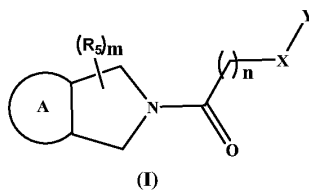
Wherein,

Ring A is a 9 to 12 membered heterocyclic ring, wherein the heterocycle is substituted with 0, 1, 2, or 3 groups independently selected from hydrogen, halogen, $-NH_2$, $-C_1-C_4$ alkyl, $-C_1-C_4$ haloalkyl, $-C_1-C_4$ hydroxyalkyl, $-C_1-C_4$ alkoxyalkyl, $O-C_1-C_4$ alkyl, $-OC_1-C_4$ haloalkyl, $-NHC_1-C_4$ alkyl or $-R_5$ -Phenyl;

X is selected from 3 to 7 membered cycloalkyl or 3 to 7 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;

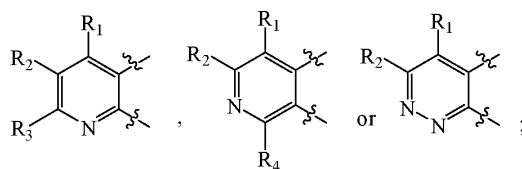
- 5 Y is selected from 6 to 10 membered aryl or 5 to 10 membered heteroaryl, wherein aryl and heteroaryl groups are optionally substituted with one to five substituents independently selected from the group consisting of hydrogen, deuterium, halogen, cyano, hydroxy, -NH₂, -NHC₁-C₄alkyl, -C₁-C₄alkyl, -C₁-C₄haloalkyl, -OC₁-C₄alkyl, -OC₁-C₄haloalkyl, and -C₃-C₇cycloalkyl;
- 10 R₅ is selected from hydrogen, deuterium and -C₁-C₄alkyl;
m is an integer selected from 0 to 2; and
n is an integer selected from 0 to 3.

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,



wherein

A is a ring moiety selected from



“” is point of attachment;

- 20 R₁ and R₂ together with the carbon atoms to which they are attached form a 5 to 8 membered cycloalkyl or 5 to 8 membered heterocycloalkyl ring, wherein the cycloalkyl or heterocycloalkyl is optionally substituted with one or two groups independently selected from hydrogen, hydroxyl, -C₁-C₄alkyl or -R₅-Phenyl;
- R₂ and R₃ together with the carbon atoms to which they are attached form a 5 to 8
- 25 membered cycloalkyl or 5 to 8 membered heterocycloalkyl ring, wherein the cycloalkyl or

heterocycloalkyl is optionally substituted with one or two groups independently selected from hydrogen, hydroxyl, -C₁-C₄alkyl or -R₅-Phenyl;

When R₁ and R₂ form a ring, then R₃ is selected from hydrogen, -C₁-C₄hydroxyalkyl, -NH₂, -C₁-C₄alkyl or -C₁-C₄haloalkyl;

- 5 When R₂ and R₃ form a ring, then R₁ is selected from hydrogen, -C₁-C₄hydroxyalkyl, -NH₂, -C₁-C₄alkyl or -C₁-C₄haloalkyl;

R₄ is selected from hydrogen, -C₁-C₄hydroxyalkyl, -NH₂, -C₁-C₄alkyl, -NH-C₁-C₄alkyl or -C₁-C₄haloalkyl; and

R₅ is selected from hydrogen, deuterium and -C₁-C₄alkyl.

- 10 X is selected from 3 to 7 membered cycloalkyl or 3 to 7 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;

Y is selected from 6 to 10 membered aryl or 5 to 10 membered heteroaryl, wherein aryl and

- 15 heteroaryl groups are optionally substituted with one to five substituents independently selected from the group consisting of hydrogen, deuterium, halogen, cyano, hydroxy, -NH₂, -NHC₁-C₄alkyl, C₁-C₄alkyl, C₁-C₄haloalkyl, -OC₁-C₄alkyl, -OC₁-C₄haloalkyl, and -C₃-C₇cycloalkyl;

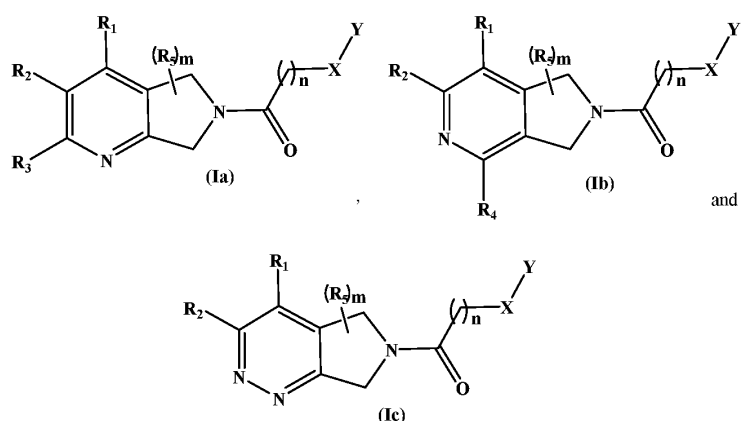
m is an integer selected from 0 to 2; and

- 20 n is an integer selected from 0 to 3.

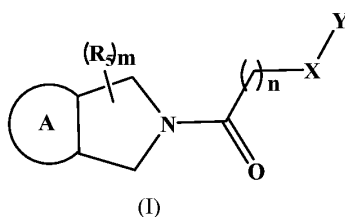
In certain embodiments, -R₅-Phenyl is selected from -C₁-C₄-phenyl; In certain embodiments, -R₅-Phenyl is -CH₂-phenyl.

- In certain embodiments X is cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, azetidiny, pyrrolidiny, tetrahydrofuranyl, tetrahydrothienyl, 25 tetrahydropyranyl, tetrahydrothiopyranyl, piperidiny, morpholiny, thiomorpholiny, piperaziny, azepanyl and 1,4-oxaazepanyl. In certain embodiments X is azetidiny, and pyrrolidiny.

- In certain embodiment, the compound of formula (I) is further defined by formula (Ia), (Ib) and (Ic) or an isotopic form, or a stereoisomer, or a pharmaceutically acceptable 30 salt thereof, wherein all indicated variables are as defined above embodiment,

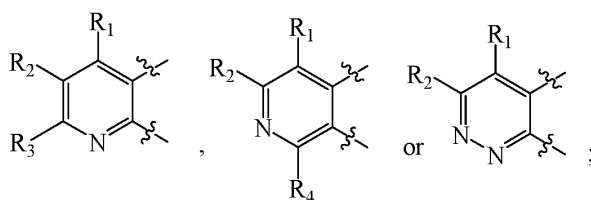


In another embodiment, the present invention relates to method of treating or preventing diseases or disorders mediated by muscarinic M4 receptors, comprising administering to a patient a therapeutically effective amount of a compound having the structure of formula (I), or an isotopic form, or a stereoisomer,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



Wherein

A is a ring moiety selected from:



~~~~~ is point of attachment;

$R_1$  and  $R_2$  together with the carbon atoms to which they are attached form a 5 to 8 membered cycloalkyl or 5 to 8 membered heterocycloalkyl ring, wherein the cycloalkyl or heterocycloalkyl is optionally substituted with one or two groups independently selected from hydrogen, hydroxyl,  $-C_1-C_4$ alkyl or  $-R_5$ -Phenyl;

$R_2$  and  $R_3$  together with the carbon atoms to which they are attached form a 5 to 8 membered cycloalkyl or 5 to 8 membered heterocycloalkyl ring, wherein the cycloalkyl or

heterocycloalkyl is optionally substituted with one or two groups independently selected from hydrogen, hydroxyl, -C<sub>1</sub>-C<sub>4</sub>alkyl or -R<sub>5</sub>-Phenyl;

When R<sub>1</sub> and R<sub>2</sub> form a ring, then R<sub>3</sub> is selected from hydrogen, -C<sub>1</sub>-C<sub>4</sub>hydroxyalkyl, -NH<sub>2</sub>, -C<sub>1</sub>-C<sub>4</sub>alkyl or -C<sub>1</sub>-C<sub>4</sub>haloalkyl;

- 5 When R<sub>2</sub> and R<sub>3</sub> form a ring, then R<sub>1</sub> is selected from hydrogen, -C<sub>1</sub>-C<sub>4</sub>hydroxyalkyl, -NH<sub>2</sub>, -C<sub>1</sub>-C<sub>4</sub>alkyl or -C<sub>1</sub>-C<sub>4</sub>haloalkyl;

R<sub>4</sub> is selected from hydrogen, -C<sub>1</sub>-C<sub>4</sub>hydroxyalkyl, -NH<sub>2</sub>, -C<sub>1</sub>-C<sub>4</sub>alkyl, -NH-C<sub>1</sub>-C<sub>4</sub>alkyl or -C<sub>1</sub>-C<sub>4</sub>haloalkyl;

- X is selected from 3 to 7 membered cycloalkyl or 3 to 7 membered heterocycloalkyl ring,  
10 wherein cycloalkyl and heterocycloalkyl are optionally substituted with one to five substituents independently selected from the group consisting of hydrogen, halogen, deuterium, cyano, -OC<sub>1</sub>-C<sub>4</sub>alkyl, and -C<sub>1</sub>-C<sub>4</sub>haloalkyl;

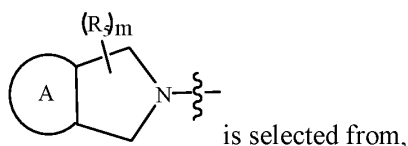
- Y is selected from 6 to 10 membered aryl or 5 to 10 membered heteroaryl, wherein aryl and heteroaryl groups are optionally substituted with one to five substituents independently  
15 selected from the group consisting of hydrogen, deuterium, halogen, cyano, hydroxy, -NH<sub>2</sub>, -NHC<sub>1</sub>-C<sub>4</sub>alkyl, -C<sub>1</sub>-C<sub>4</sub>alkyl, -C<sub>1</sub>-C<sub>4</sub>haloalkyl, -OC<sub>1</sub>-C<sub>4</sub>alkyl, -OC<sub>1</sub>-C<sub>4</sub>haloalkyl, and -C<sub>3</sub>-C<sub>7</sub>cycloalkyl;

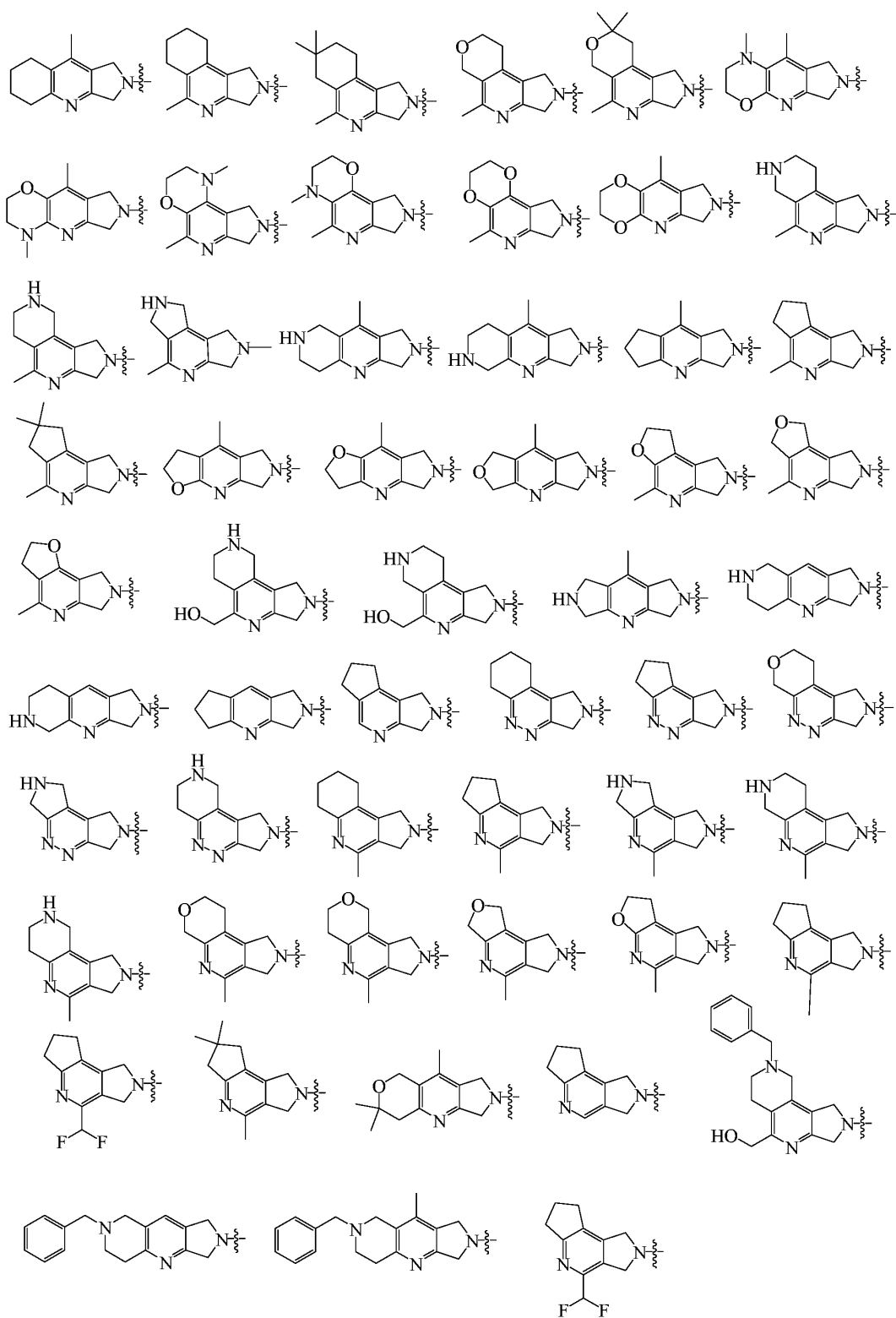
R<sub>5</sub> is selected from hydrogen, deuterium and -C<sub>1</sub>-C<sub>4</sub>alkyl;

m is an integer selected from 0 to 2; and

- 20 n is an integer selected from 0 to 3.

In another embodiment, the ring





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:

- 1-(8-Methyl-3,5,6,7-tetrahydro-1*H*-2,4-diaza-s-indacen-2-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone;
- 1-(8-Methyl-3,5,6,7-tetrahydro-1*H*-2,4-diaza-s-indacen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 1-(8-Methyl-3,5,6,7-tetrahydro-1*H*-2,4-diaza-s-indacen-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone;
- 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(8-methyl-3,5,6,7-tetrahydro-1*H*-2,4-diaza-s-indacen-2-yl)-ethanone;
- 1-(8-Methyl-3,5,6,7-tetrahydro-1*H*-2,4-diaza-s-indacen-2-yl)-2-(1-pyridin-4-yl-azetidin-3-yl)-ethanone;
- 1-(8-Methyl-3,5,6,7-tetrahydro-1*H*-2,4-diaza-s-indacen-2-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone;
- 1-(8-Methyl-3,5,6,7-tetrahydro-1*H*-2,4-diaza-s-indacen-2-yl)-2-(1-pyrimidin-5-yl-azetidin-3-yl)-ethanone;
- 2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(8-methyl-3,5,6,7-tetrahydro-1*H*-2,4-diaza-s-indacen-2-yl)-ethanone;
- (8-Methyl-3,5,6,7-tetrahydro-1*H*-2,4-diaza-s-indacen-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone;
- (8-Methyl-3,5,6,7-tetrahydro-1*H*-2,4-diaza-s-indacen-2-yl)-(1-pyridin-3-yl-pyrrolidin-3(R)-yl)-methanone;
- (8-Methyl-3,5,6,7-tetrahydro-1*H*-2,4-diaza-s-indacen-2-yl)-[1-(6-trifluoromethyl-pyridin-3-yl)-pyrrolidin-3(R)-yl]-methanone;
- [1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(8-methyl-3,5,6,7-tetrahydro-1*H*-2,4-diaza-s-indacen-2-yl)-methanone;
- 2-[1-(2-Trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(5,7,7-trimethyl-3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-ethanone;
- 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(5,7,7-trimethyl-3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-ethanone;

- 2-(1-Pyridin-3-yl-azetidin-3-yl)-1-(5,7,7-trimethyl-3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-ethanone;
- [1-(2-Trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(5,7,7-trimethyl-3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-methanone;
- 5 [1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(5,7,7-trimethyl-3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-methanone;
- 1-(3,5,6,7-Tetrahydro-1*H*-2,4-diaza-s-indacen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(3,5,6,7-tetrahydro-1*H*-2,4-diaza-s-indacen-2-yl)-ethanone;
- 10 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(3,5,6,7-tetrahydro-1*H*-2,4-diaza-s-indacen-2-yl)-ethanone;
- (3,5,6,7-Tetrahydro-1*H*-2,4-diaza-s-indacen-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone;
- 15 [1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(3,5,6,7-tetrahydro-1*H*-2,4-diaza-s-indacen-2-yl)-methanone;
- 2-(1-Pyridin-3-yl-azetidin-3-yl)-1-(3,5,6,7-tetrahydro-1*H*-2,4-diaza-s-indacen-2-yl)-ethanone;
- (3,6,7,8-Tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone;
- 20 [1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-methanone;
- (1-Pyridin-3-yl-pyrrolidin-3(R)-yl)-(3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-methanone;
- 25 1-(3,6,7,8-Tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-ethanone;
- 2-(1-Pyridin-3-yl-azetidin-3-yl)-1-(3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-ethanone;
- 30 2-(1-Pyrimidin-5-yl-azetidin-3-yl)-1-(3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-ethanone;

- 1-(3,6,7,8-Tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone;  
2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-ethanone;
- 5 1-(3,6,7,8-Tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone;  
1-(4-Methyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;  
2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(4-methyl-3,6,7,8-tetrahydro-1*H*-2,5-
- 10 diaza-as-indacen-2-yl)-ethanone;  
1-(4-Methyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-2-(1-pyridin-3-yl)-azetidin-3-yl)-ethanone;  
(4-Methyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone;
- 15 [1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(4-methyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-methanone;  
(4-Methyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-[1-(6-trifluoromethyl-pyridin-3-yl)-pyrrolidin-3(R)-yl]-methanone;  
1-(4-Methyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-2-[1-(6-trifluoromethyl-
- 20 pyridin-3-yl)-azetidin-3-yl]-ethanone;  
1-(4-Methyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone;  
1-(4-Methyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-2-(1-pyrimidin-5-yl)-azetidin-3-yl)-ethanone;
- 25 2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(4-methyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-ethanone;  
1-(4-Methyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-2-(1-pyridin-4-yl)-azetidin-3-yl)-ethanone;  
1-(4-Difluoromethyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-2-[1-(2-
- 30 trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;  
2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(4-difluoromethyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-ethanone;

- 1-(4-Difluoromethyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone;
- 1-(4-Difluoromethyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone;
- 5 1-(4-Difluoromethyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-2-(1-pyrimidin-5-yl-azetidin-3-yl)-ethanone;
- 1-(4-Difluoromethyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone;
- 2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(4-difluoromethyl-3,6,7,8-
- 10 tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-ethanone;
- (4-Difluoromethyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone;
- [1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(4-difluoromethyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-methanone;
- 15 1-(9-Methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-*b*]quinolin-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 1-(9-Methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-*b*]quinolin-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone;
- 1-(9-Methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-*b*]quinolin-2-yl)-2-(1-pyridin-3-yl-azetidin-
- 20 3-yl)-ethanone;
- 2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(9-methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-*b*]quinolin-2-yl)-ethanone;
- (9-Methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-*b*]quinolin-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone;
- 25 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(9-methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-*b*]quinolin-2-yl)-ethanone;
- 2-[1-(2-Trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(5,7,7-trimethyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-*c*]isoquinolin-2-yl)-ethanone;
- 2-(1-Pyridin-3-yl-azetidin-3-yl)-1-(5,7,7-trimethyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-
- 30 *c*]isoquinolin-2-yl)-ethanone;
- 2-[1-(6-Trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-1-(5,7,7-trimethyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-*c*]isoquinolin-2-yl)-ethanone;

- [1-(2-Trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(5,7,7-trimethyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-c]isoquinolin-2-yl)-methanone;
- [1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(5,7,7-trimethyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-c]isoquinolin-2-yl)-methanone;
- 5 1-(1,3,6,7,8,9-Hexahydro-pyrrolo[3,4-c]cinnolin-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 1-(1,3,6,7,8,9-Hexahydro-pyrrolo[3,4-c]cinnolin-2-yl)-2-(1-pyridin-3-yl)-azetidin-3-yl)-ethanone;
- 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(1,3,6,7,8,9-hexahydro-pyrrolo[3,4-c]cinnolin-2-yl)-ethanone;
- 10 c]cinnolin-2-yl)-ethanone;
- 1-(1,3,6,7,8,9-Hexahydro-pyrrolo[3,4-c]cinnolin-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone;
- 1-(1,3,6,7,8,9-Hexahydro-pyrrolo[3,4-c]cinnolin-2-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone;
- 15 (1,3,6,7,8,9-Hexahydro-pyrrolo[3,4-c]cinnolin-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone;
- [1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(1,3,6,7,8,9-hexahydro-pyrrolo[3,4-c]cinnolin-2-yl)-methanone;
- 1-(4-Methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacen-6-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 20 pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 1-(4-Methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacen-6-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone;
- 1-(4-Methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacen-6-yl)-2-(1-pyridin-3-yl)-azetidin-3-yl)-ethanone;
- 25 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(4-methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacen-6-yl)-ethanone;
- 2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(4-methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacen-6-yl)-ethanone;
- 1-(4-Methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacen-6-yl)-2-(1-pyrimidin-5-yl)-azetidin-3-yl)-ethanone;
- 30 1-(4-Methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacen-6-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone;



- (4-Methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacen-6-yl)-[1-(6-trifluoromethyl-pyridin-3-yl)-pyrrolidin-3(R)-yl]-methanone;
- (4-Methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacen-6-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone;
- 5 [1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(4-methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacen-6-yl)-methanone;
- (4-Methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacen-6-yl)-(1-pyridin-3-yl-pyrrolidin-3(R)-yl)-methanone;
- 1-(8-Methyl-5,7-dihydro-1*H*,3*H*-2-oxa-4,6-diaza-s-indacen-6-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone;
- 10 1-(8-Methyl-5,7-dihydro-1*H*,3*H*-2-oxa-4,6-diaza-s-indacen-6-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 1-(8-Methyl-5,7-dihydro-1*H*,3*H*-2-oxa-4,6-diaza-s-indacen-6-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone;
- 15 1-(8-Methyl-5,7-dihydro-1*H*,3*H*-2-oxa-4,6-diaza-s-indacen-6-yl)-2-(1-pyridin-4-yl-azetidin-3-yl)-ethanone;
- 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(8-methyl-5,7-dihydro-1*H*,3*H*-2-oxa-4,6-diaza-s-indacen-6-yl)-ethanone;
- 2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(8-methyl-5,7-dihydro-1*H*,3*H*-2-oxa-4,6-diaza-s-indacen-6-yl)-ethanone;
- 20 oxa-4,6-diaza-s-indacen-6-yl)-ethanone;
- 1-(8-Methyl-5,7-dihydro-1*H*,3*H*-2-oxa-4,6-diaza-s-indacen-6-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone;
- 1-(8-Methyl-5,7-dihydro-1*H*,3*H*-2-oxa-4,6-diaza-s-indacen-6-yl)-2-(1-pyrimidin-5-yl-azetidin-3-yl)-ethanone;
- 25 (8-Methyl-5,7-dihydro-1*H*,3*H*-2-oxa-4,6-diaza-s-indacen-6-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone;
- [1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(8-methyl-5,7-dihydro-1*H*,3*H*-2-oxa-4,6-diaza-s-indacen-6-yl)-methanone;
- 2-[1-(2-Trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(6,6,9-trimethyl-3,5,6,8-tetrahydro-1*H*-7-oxa-2,4-diaza-cyclopenta[*b*]naphthalen-2-yl)-ethanone;
- 30 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(6,6,9-trimethyl-3,5,6,8-tetrahydro-1*H*-7-oxa-2,4-diaza-cyclopenta[*b*]naphthalen-2-yl)-ethanone;

- 2-(1-Pyridin-3-yl-azetidin-3-yl)-1-(6,6,9-trimethyl-3,5,6,8-tetrahydro-1*H*-7-oxa-2,4-diaza-cyclopenta[b]naphthalen-2-yl)-ethanone;
- 2-(1-Pyridin-4-yl-azetidin-3-yl)-1-(6,6,9-trimethyl-3,5,6,8-tetrahydro-1*H*-7-oxa-2,4-diaza-cyclopenta[b]naphthalen-2-yl)-ethanone;
- 5 2-[1-(6-Trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-1-(6,6,9-trimethyl-3,5,6,8-tetrahydro-1*H*-7-oxa-2,4-diaza-cyclopenta[b]naphthalen-2-yl)-ethanone;
- 2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(6,6,9-trimethyl-3,5,6,8-tetrahydro-1*H*-7-oxa-2,4-diaza-cyclopenta[b]naphthalen-2-yl)-ethanone;
- 2-(1-Pyrimidin-5-yl-azetidin-3-yl)-1-(6,6,9-trimethyl-3,5,6,8-tetrahydro-1*H*-7-oxa-2,4-diaza-cyclopenta[b]naphthalen-2-yl)-ethanone;
- 10 2-[1-(5-Trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-1-(6,6,9-trimethyl-3,5,6,8-tetrahydro-1*H*-7-oxa-2,4-diaza-cyclopenta[b]naphthalen-2-yl)-ethanone;
- [1-(2-Trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(6,6,9-trimethyl-3,5,6,8-tetrahydro-1*H*-7-oxa-2,4-diaza-cyclopenta[b]naphthalen-2-yl)-methanone;
- 15 [1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(6,6,9-trimethyl-3,5,6,8-tetrahydro-1*H*-7-oxa-2,4-diaza-cyclopenta[b]naphthalen-2-yl)-methanone;
- 2-[1-(2-Trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(5,8,8-trimethyl-3,6,8,9-tetrahydro-1*H*-7-oxa-2,4-diaza-cyclopenta[a]naphthalen-2-yl)-ethanone;
- 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(5,8,8-trimethyl-3,6,8,9-tetrahydro-1*H*-7-oxa-2,4-diaza-cyclopenta[a]naphthalen-2-yl)-ethanone;
- 20 1-(1,3,5,6,7,8-Hexahydro-pyrrolo[3,4-b]quinolin-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 1-(1,3,5,6,7,8-Hexahydro-pyrrolo[3,4-b]quinolin-2-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone;
- 30 1-(1,3,5,6,7,8-Hexahydro-pyrrolo[3,4-b]quinolin-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone;

- 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b]quinolin-2-yl)-ethanone;  
 (1,3,5,6,7,8-Hexahydro-pyrrolo[3,4-b]quinolin-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone;
- 5 [1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b]quinolin-2-yl)-methanone;  
 1-(3,6,7,8-Tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;  
 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-
- 10 indacen-2-yl)-ethanone;  
 1-(3,6,7,8-Tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone;  
 2-(1-Pyrimidin-5-yl)-azetidin-3-yl)-1-(3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-ethanone;
- 15 2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-ethanone;  
 1-(3,6,7,8-Tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone;  
 (3,6,7,8-Tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-
- 20 pyrrolidin-3(R)-yl]-methanone;  
 [1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-methanone;  
 (3,6,7,8-Tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-[1-(6-trifluoromethyl-pyridin-3-yl)-pyrrolidin-3(R)-yl]-methanone;
- 25 2-(1-Pyridin-4-yl)-azetidin-3-yl)-1-(3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-ethanone;  
 2-(1-Pyridin-3-yl)-azetidin-3-yl)-1-(3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-ethanone;  
 1-(8-Benzyl-5-hydroxymethyl-1,3,6,7,8,9-hexahydro-2,4,8-triaza-cyclopenta[a]naphthalen-
- 30 2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;  
 1-(5-hydroxymethyl-1,3,6,7,8,9-hexahydro-2,4,8-triaza-cyclopenta[a]naphthalen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;

- 1-(7-Benzyl-9-methyl-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 1-(9-Methyl-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 5 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(9-methyl-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-2-yl)-ethanone;
- 1-(9-Methyl-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-2-yl)-2-(1-pyridin-3-yl)-azetidin-3-yl)-ethanone;
- 1-(9-Methyl-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone;
- 10 1-(9-Methyl-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-2-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone;
- 1-(9-Methyl-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-2-yl)-2-(1-pyrimidin-5-yl)-azetidin-3-yl)-ethanone;
- 15 2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(9-methyl-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-2-yl)-ethanone;
- (9-Methyl-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone;
- [1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(9-methyl-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-2-yl)-methanone;
- 20 1-(6-Benzyl-9-methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b][1,7]naphthyridin-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 1-(9-Methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b][1,7]naphthyridin-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 25 1-(9-Methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b][1,7]naphthyridin-2-yl)-2-(1-pyridin-3-yl)-azetidin-3-yl)-ethanone;
- 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(9-methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b][1,7]naphthyridin-2-yl)-ethanone;
- 1-(9-Methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b][1,7]naphthyridin-2-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone;
- 30 1-(9-Methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b][1,7]naphthyridin-2-yl)-2-(1-pyrimidin-5-yl)-azetidin-3-yl)-ethanone;

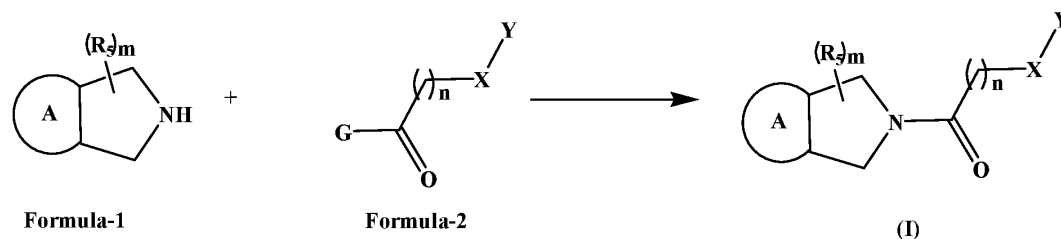
- 2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(9-methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b][1,7]naphthyridin-2-yl)-ethanone;  
(9-Methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b][1,7]naphthyridin-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone;
- 5 (9-Methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b][1,7]naphthyridin-2-yl)-[1-(6-trifluoromethyl-pyridin-3-yl)-pyrrolidin-3(R)-yl]-methanone;  
[1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(9-methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b][1,7]naphthyridin-2-yl)-methanone;  
1-(7-Benzyl-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 10 1-(1,3,5,6,7,8-Hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;  
2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-2-yl)-ethanone;
- 15 1-(1,3,5,6,7,8-Hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-2-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone;  
1-(5-Methyl-1,3,6,7,8,9-hexahydro-2,4,7-triaza-cyclopenta[a]naphthalen-2-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone hydrochloride;  
1-(5-Methyl-1,3,6,7,8,9-hexahydro-2,4,7-triaza-cyclopenta[a]naphthalen-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone hydrochloride;
- 20 1-(5-Methyl-1,3,6,7,8,9-hexahydro-2,4,7-triaza-cyclopenta[a]naphthalen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone hydrochloride;  
2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(5-methyl-1,3,6,7,8,9-hexahydro-2,4,7-triaza-cyclopenta[a]naphthalen-2-yl)-ethanone hydrochloride;
- 25 1-(5-Methyl-1,3,6,7,8,9-hexahydro-2,4,7-triaza-cyclopenta[a]naphthalen-2-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone hydrochloride;  
1-(5-Methyl-1,3,6,7,8,9-hexahydro-2,4,7-triaza-cyclopenta[a]naphthalen-2-yl)-2-(1-pyrimidin-5-yl-azetidin-3-yl)-ethanone hydrochloride;  
2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(5-methyl-1,3,6,7,8,9-hexahydro-
- 30 2,4,7-triaza-cyclopenta[a]naphthalen-2-yl)-ethanone hydrochloride;  
1-(5-Methyl-1,3,6,7,8,9-hexahydro-2,4,7-triaza-cyclopenta[a]naphthalen-2-yl)-2-(1-pyridin-4-yl-azetidin-3-yl)-ethanone hydrochloride;

- (5-Methyl-1,3,6,7,8,9-hexahydro-2,4,7-triaza-cyclopenta[a]naphthalen-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone hydrochloride;  
[1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(5-methyl-1,3,6,7,8,9-hexahydro-2,4,7-triaza-cyclopenta[a]naphthalen-2-yl)-methanone hydrochloride;
- 5 1-(5-Methyl-1,3,6,7,8,9-hexahydro-2,4,8-triaza-cyclopenta[a]naphthalen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone hydrochloride;  
1-(5-Methyl-1,3,6,7,8,9-hexahydro-2,4,8-triaza-cyclopenta[a]naphthalen-2-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone hydrochloride;  
2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(5-methyl-1,3,6,7,8,9-hexahydro-
- 10 2,4,8-triaza-cyclopenta[a]naphthalen-2-yl)-ethanone hydrochloride;  
1-(5-Methyl-1,3,6,7,8,9-hexahydro-2,4,8-triaza-cyclopenta[a]naphthalen-2-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone hydrochloride;  
1-(5-Methyl-1,3,6,7,8,9-hexahydro-2,4,8-triaza-cyclopenta[a]naphthalen-2-yl)-2-(1-pyrimidin-5-yl-azetidin-3-yl)-ethanone hydrochloride;
- 15 2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(5-methyl-1,3,6,7,8,9-hexahydro-2,4,8-triaza-cyclopenta[a]naphthalen-2-yl)-ethanone hydrochloride;  
(5-Methyl-1,3,6,7,8,9-hexahydro-2,4,8-triaza-cyclopenta[a]naphthalen-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone hydrochloride;  
[1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(5-methyl-1,3,6,7,8,9-hexahydro-
- 20 2,4,8-triaza-cyclopenta[a]naphthalen-2-yl)-methanone hydrochloride;  
1-(5-methyl-3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;  
1-(5-Methyl-3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone;
- 25 1-(5-Methyl-3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone;  
2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(5-methyl-3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-ethanone;  
1-(5-Methyl-3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-2-[1-(5-trifluoromethyl-
- 30 pyrimidin-2-yl)-azetidin-3-yl]-ethanone;  
2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(5-methyl-3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-ethanone;

- 1-(5-Methyl-3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-2-(1-pyrimidin-5-yl-azetidin-3-yl)-ethanone;  
(5-Methyl-3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone;
- 5 [1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(5-methyl-3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-methanone;  
(5-Methyl-3, 6, 7, 8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-(1-pyridin-3-yl-pyrrolidin-3(R)-yl)-methanone;
- 10 1-(5-Methyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-*c*]isoquinolin-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;  
1-(5-Methyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-*c*]isoquinolin-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone;  
1-(5-Methyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-*c*]isoquinolin-2-yl)-2-(1-pyrimidin-5-yl-azetidin-3-yl)-ethanone;
- 15 1-(5-Methyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-*c*]isoquinolin-2-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone;  
2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(5-methyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-*c*]isoquinolin-2-yl)-ethanone;  
1-(5-Methyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-*c*]isoquinolin-2-yl)-2-(1-pyridin-3-yl-
- 20 azetidin-3-yl)-ethanone;  
2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(5-methyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-*c*]isoquinolin-2-yl)-ethanone;  
(5-Methyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-*c*]isoquinolin-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone;
- 25 [1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(5-methyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-*c*]isoquinolin-2-yl)-methanone; or  
[1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(5-methyl-3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-methanone.

### Experimental procedure

- 30 The below scheme depicts a general process for the preparation of the compound of formula (I), wherein ring A, R<sub>5</sub>, X, Y, m and n are as defined herein above. Further G is a leaving group selected from -OH, -OCH<sub>3</sub> or halogen.

**Scheme:****Preparation of the compound of formula (I)**

5            A compound of formula-1 is reacted with a compound of formula-2 in a suitable solvent selected from DMF, THF or DCM in the presence of coupling agent selected from HATU, TBTU, or pyBop and a base such as triethylamine, or Hunig's base at room temperature for 4 to 24 h. The obtained reaction mixture was extracted with suitable organic solvent, washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated in vacuo to get a

10    residual mass that was purified by chromatographic technique to obtain the compound of formula (I).

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

          The compound of formula (I) can optionally be converted into its pharmaceutically acceptable salt by reaction with the appropriate acid or base. Suitable pharmaceutically

15    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.

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

20            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 in the reduction process. The metal catalyst may be rhodium, ruthenium, indium and
- 25            the like. The chiral ligands may preferably be chiral phosphines.



- 5 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 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.
- 10 d. The mixture of stereoisomers may be resolved by conventional methods such as microbial resolution, resolving the diastereomeric salts formed with chiral acids or 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.

15 In another embodiment, the suitable pharmaceutically acceptable salt includes 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).

20 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.

25 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.

30 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.

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.

5 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.

10 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 the treatment of diseases or disorders selected from psychiatric disorders, neurological disorders, pain disorders, sleep disorders, or cognitive disorders.

15 In some embodiments, 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), schizophrenia, substance use disorders and other psychotic disorders.

20 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 persisting delirium, or any other diseases with psychotic features.

25 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).

30 In some embodiments, the cognitive disorders are selected from the group consisting 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

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 treatment of schizophrenia includes treatment of positive  
5 symptoms of schizophrenia and/or negative symptoms of schizophrenia.

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

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

15 In some embodiments, cognitive impairment in schizophrenia include but are not 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,  
20 suspiciousness/persecution and hostility.

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

25 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  
30 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.

5           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.

10           The following abbreviations are used herein

|    |                                 |   |                                                                                         |
|----|---------------------------------|---|-----------------------------------------------------------------------------------------|
|    | AMP                             | : | Adenosine monophosphate                                                                 |
|    | BINAP                           | : | 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl                                             |
|    | Boc                             | : | Tert-butyloxycarbonyl                                                                   |
|    | CDCl <sub>3</sub>               | : | Deuterated chloroform                                                                   |
| 15 | Cs <sub>2</sub> CO <sub>3</sub> | : | Cesium carbonate                                                                        |
|    | DAST                            | : | Diethylaminosulfur Trifluoride                                                          |
|    | DCM                             | : | Dichloromethane                                                                         |
|    | DIBAL-H                         | : | Diisobutylaluminium hydride                                                             |
|    | DMAP                            | : | 4-(Dimethylamino)pyridine                                                               |
| 20 | DMF                             | : | <i>N, N</i> –Dimethyl formamide                                                         |
|    | DMSO                            | : | Dimethylsulfoxide                                                                       |
|    | E <sub>max</sub>                | : | Maximal effect or receptor activity                                                     |
|    | EC <sub>50</sub>                | : | Half maximal effective concentration                                                    |
|    | EtOAc                           | : | Ethyl acetate                                                                           |
| 25 | 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                                       |
| 30 | IPA                             | : | Isopropyl alcohol                                                                       |
|    | MeOH                            | : | Methanol                                                                                |

|    |                                  |   |                                                                           |
|----|----------------------------------|---|---------------------------------------------------------------------------|
|    | mL                               | : | Millilitre                                                                |
|    | mol                              | : | Mole                                                                      |
|    | Na <sub>2</sub> CO <sub>3</sub>  | : | Sodium carbonate                                                          |
|    | NaH                              | : | Sodium hydride                                                            |
| 5  | Na <sub>2</sub> SO <sub>4</sub>  | : | Sodium sulphate                                                           |
|    | POCl <sub>3</sub>                | : | phosphorous oxychloride                                                   |
|    | ppm                              | : | parts per million                                                         |
|    | psi                              | : | Pound per square inch                                                     |
|    | Pd(dppf)Cl <sub>2</sub>          | : | 1,1'-Bis(diphenylphosphino)ferrocene)palladium(II)                        |
| 10 | dichloride                       | : |                                                                           |
|    | Pd <sub>2</sub> dba <sub>3</sub> | : | Tris(dibenzylideneacetone)dipalladium                                     |
|    | Pd/C                             | : | Palladium on carbon                                                       |
|    | pyBop                            | : | (Benzotriazol-1-yloxy)tripyrrolidinophosphonium<br>hexafluorophosphate    |
| 15 | RM                               | : | Reaction Mixture                                                          |
|    | RT                               | : | Room Temperature                                                          |
|    | THF                              | : | Tetrahydrofuran                                                           |
|    | TBTU                             | : | 2-(1H-Benzotriazole-1-yl)-1,1,3,3-tetramethylaminium<br>tetrafluoroborate |

## 20 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.

### 25 Preparation of Intermediates:

#### Intermediate-1: 8-Methyl-1,2,3,5,6,7-hexahydro-2,4-diaza-s-indacene hydrochloride

##### Step 1: 2-Methoxycarbonyl-4-methyl-6,7-dihydro-5H-cyclopenta[b]pyridine-3-carbonitrile

30 Pd(dppf)Cl<sub>2</sub>.CH<sub>2</sub>Cl<sub>2</sub> complex (14.7 g, 0.018 mol) was added to a stirred solution of 2-chloro-4-methyl-6,7-dihydro-5H-cyclopenta[b]pyridine-3-carbonitrile (25 g, 0.129 mol, prepared as per the procedure disclosed in step-2 of example 21 on page 79 of

WO2020160134) and triethylamine (56.0 mL, 0.388 mol) in methanol (450 mL) and the contents were heated at 70 °C under 50 psi pressure of carbon monoxide in an autoclave for 4 h. The reaction mixture was cooled to RT, filtered and concentrated to get a residual mass that was purified by column chromatography using 45 – 65 % ethyl acetate in hexanes to  
5 obtain the title compound. Yield: 21.9 g (78 %); <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz) δ ppm: 2.19 – 2.27 (m, 2H), 2.54 (s, 3H), 2.99 – 3.02 (t, *J* = 7.60 Hz, 2H), 3.16 – 3.20 (t, *J* = 8.0 Hz, 2H), 4.05 (s, 3H); Mass (m/z): 216.9 (M+H)<sup>+</sup>.

**Step 2: 8-Methyl-1,5,6,7-tetrahydro-2H-2,4-diaza-s-indacen-3-one**

Pd/C (10.0 g) was added to a solution of 2-methoxycarbonyl-4-methyl-6,7-dihydro-5H-cyclopenta[b]pyridine-3-carbonitrile (21 g, 0.097 mol) in methanol (100 mL) and acetic  
10 acid (75 ml, 5 vol) the reaction mixture was stirred under 50 psi pressure of H<sub>2</sub> (gas) in an autoclave for 6 h. The reaction mixture then filtered and concentrated to get a residual mass that was purified by column chromatography using 2 - 5 % MeOH in DCM to obtain the title compound. Yield: 17.6 g (96 %); <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz) δ ppm: : 2.07 – 2.24  
15 (m, 2H), 2.28 (s, 3H), 2.93 – 2.97 (t, *J* = 7.20 Hz, 2H), 3.11 – 3.15 (t, *J* = 7.60 Hz, 2H), 4.35 (s, 2H), 7.33 (s, 1H); Mass (m/z): 189.0 (M+H)<sup>+</sup>.

**Step 3: 8-Methyl-3-oxo-3,5,6,7-tetrahydro-1H-2,4-diaza-s-indacene-2-carboxylic acid tert-butyl ester**

Boc anhydride (53.1 g, 0.234 mol) was added to a stirred solution of 8-methyl-1,5,6,7-tetrahydro-2H-2,4-diaza-s-indacen-3-one (17.6 g, 0.093 mol) and DMAP ( 1.710 g, 0.014  
20 mol) in DCM (100 mL) at RT and maintained for 16 h. The reaction mixture was then poured into water (100 mL) and product was extracted using DCM (50 mL x 3). The organic extracts were combined, washed with brine (50 mL), dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated in vacuo to obtain a residual mass that was purified by column  
25 chromatography using 1.5 – 2.5 % MeOH in DCM to obtain the title compound. Yield: 25.0 g (95 %); <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz) δ ppm: 1.61 (s, 9H), 2.18 – 2.23 (m, 2H), 2.29 (s, 3H), 2.94 – 2.97 (t, *J* = 7.60 Hz, 2H), 3.12 – 3.14 (t, *J* = 8.00 Hz, 2H), 4.62 (s, 2H); Mass (m/z): 288.9 (M+H)<sup>+</sup>.

**Step 4: 3-Hydroxy-8-methyl-3,5,6,7-tetrahydro-1H-2,4-diaza-s-indacene-2-carboxylic acid tert-butyl ester**  
30

DIBAL-H (174 mL, 0.086 mol) was added to a stirred solution of 8-methyl-3-oxo-3,5,6,7-tetrahydro-1*H*-2,4-diaza-s-indacene-2-carboxylic acid tert-butyl ester (25 g, 0.043 mol) in THF (350 mL) at 0 °C - 10 °C. The reaction mixture further stirred at RT for 4 h. Sodium sulphate decahydrate (10 g) and ethyl acetate (250 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: 20.2 g; Mass (m/z): 291.1 (M+H)<sup>+</sup>.

**Step 5: 8-Methyl-3,5,6,7-tetrahydro-1*H*-2,4-diaza-s-indacene-2-carboxylic acid tert-butyl ester**

Sodium cyanoborohydride (13.1 g, 0.208 mol) was added to a stirred solution of 3-hydroxy-8-methyl-3,5,6,7-tetrahydro-1*H*-2,4-diaza-s-indacene-2-carboxylic acid tert-butyl ester (20.2 g, 0.069 mol) in acetic acid (100 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 1.5 - 3 % MeOH in DCM to obtain the title compound. Yield: 5.89 g (31 %); <sup>1</sup>H - NMR (CDCl<sub>3</sub>, 400 MHz) δ ppm: 1.53 (s, 9H), 2.08 – 2.14 (m, 2H), 2.16 – 2.17 (d, *J* = 3.60 Hz, 3H), 2.83 – 2.87 (t, *J* = 7.60 Hz, 2H), 2.98 – 3.01 (t, *J* = 7.60 Hz, 2H), 4.56 (s, 1H), 4.61 (s, 2H), 4.67 (s, 1H); Mass (m/z): 275.1 (M+H)<sup>+</sup>.

**Step 6: 8-Methyl-1,2,3,5,6,7-hexahydro-2,4-diaza-s-indacene hydrochloride**

IPA.HCl (58 mL, 10 vol., 12% w/v solution) was added to a stirred solution of 8-methyl-3,5,6,7-tetrahydro-1*H*-2,4-diaza-s-indacene-2-carboxylic acid tert-butyl ester (5.8 g, 0.021 mol) in methanol (60 mL) and the reaction mixture was maintained at 45 °C - 50 °C for 3 h and then the reaction mixture was concentrated in vacuo to obtain the title compound (intermediate-1). Yield: 3.81 (77 %); <sup>1</sup>H - NMR (CD<sub>3</sub>OD, 400 MHz) δ ppm: 2.19 – 2.52 (m, 2H), 2.29 – 2.31 (d, *J* = 8.80 Hz, 3H), 2.94 – 2.97 (t, *J* = 7.60 Hz, 2H), 3.09 – 3.13 (t, *J* = 8.00 Hz, 2H), 4.66 (s, 2H), 4.68 (s, 2H); Mass (m/z): 175.0 (M+H)<sup>+</sup>.

**Intermediate-2: 9-Methyl-2,3,5,6,7,8-hexahydro-1*H*-pyrrolo[3,4-*b*]quinoline hydrochloride**

**Step-1: 4-Methyl-2-oxo-1,2,5,6,7,8-hexahydro-quinoline-3-carbonitrile**

Ethyl cyanoacetate (69 g, 0.612 mol) was added to a stirred solution of cyclohexanone (30 g, 0.306 mol), acetaldehyde (20.2 g, 0.459 mol) and ammonium acetate (70.7 g, 0.918 mol) in ethanol (300 mL) at RT and then refluxed for 16 h. The reaction mixture was concentrated to obtain a crude mass. This mass was diluted with cold water (100 mL) and

product was extracted using DCM (250 mL x 3). The organic extracts were combined, washed with brine (50 mL), dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated in vacuo to obtain a residual mass that was purified by column chromatography using 5 – 6 % MeOH in DCM to obtain the title compound. Yield: 20.0 g (35 %); <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ ppm: 1.66 – 1.70 (m, 4H), 2.27 (s, 3H), 2.34 – 2.36 (t, *J* = 5.6 Hz, 2H), 2.54 – 2.55 (t, *J* = 5.2 Hz, 2H), 12.09 (bs, 1H); Mass (m/z): 189.1 (M+H)<sup>+</sup>.

**Step-2: 2-Chloro-4-methyl-5,6,7,8-tetrahydro-quinoline-3-carbonitrile**

POCl<sub>3</sub> (80 ml, 4 vol. to SM) was added to stirred solution of 4-methyl-2-oxo-1,2,5,6,7,8-hexahydro-quinoline-3-carbonitrile (20 g, 0.163 mol) at RT and then refluxed for 16 h. The reaction mixture was concentrated to get a residual mass which was diluted with water (100 mL), basified with saturated Na<sub>2</sub>CO<sub>3</sub> solution during which solids precipitated. These solids were filtered and concentrated from DCM to obtain the title compound. Yield: 9.5 g (43 %); <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz) δ ppm: 1.84 – 1.88 (m, 4H), 2.45 (s, 3H), 2.62 – 2.65 (m, 2H), 2.91 – 2.94 (m, 2H); Mass (m/z): 206.7, 207.5 (M+H)<sup>+</sup>.

**Step-3: 3-Cyano-4-methyl-5,6,7,8-tetrahydro-quinoline-2-carboxylic acid methyl ester**

3-Cyano-4-methyl-5,6,7,8-tetrahydro-quinoline-2-carboxylic acid methyl ester was prepared by using the procedure as described in step-1 of intermediate-1 with some non-critical variations. Yield: 9 g (90 %); <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz) δ ppm: 1.88 – 1.92 (m, 4H), 2.52 (s, 3H), 2.74 – 2.75 (m, 2H), 3.02 – 3.05 (m, 2H), 4.04 (s, 3H); Mass (m/z): 231.1 (M+H)<sup>+</sup>.

**Step-4: 9-Methyl-1,2,5,6,7,8-hexahydro-pyrrolo[3,4-b]quinolin-3-one**

9-Methyl-1,2,5,6,7,8-hexahydro-pyrrolo[3,4-b]quinolin-3-one was prepared by using the procedure as described in step-2 of intermediate-1 with some non-critical variations. Yield: 6.1 g (75 %); <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ ppm: 1.80 – 1.81 (m, 4H), 2.18 (s, 3H), 2.71 – 2.74 (t, *J* = 4.6 Hz, 2H), 2.88 – 2.90 (t, *J* = 3.8 Hz, 2H), 4.28 (s, 2H), 8.72 (bs, 1H); Mass (m/z): 202.7 (M+H)<sup>+</sup>.

**Step-5: 9-Methyl-3-oxo-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b]quinoline-2-carboxylic acid tert-butyl ester**

9-Methyl-3-oxo-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b]quinoline-2-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: 8.0 g (87 %); <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ ppm:



1.53 (s, 9H), 1.80 – 1.81 (m, 4H), 2.21 (s, 3H), 2.74 – 2.75 (m, 2H), 2.89 – 2.90 (m, 2H), 4.69 (s, 2H); Mass (m/z): 303.3 (M+H)<sup>+</sup>.

**Step-6: 3-Hydroxy-9-methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b]quinoline-2-carboxylic acid tert-butyl ester**

- 5 3-Hydroxy-9-methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b]quinoline-2-carboxylic acid tert-butyl ester was prepared by using the procedure as described in step-4 of intermediate-1 with some non-critical variations. Yield: 3.6 g (90 %); Mass (m/z): 305.1 (M+H)<sup>+</sup>.

**Step-7: 9-Methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b]quinoline-2-carboxylic acid tert-butyl ester:**

- 10 9-Methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b]quinoline-2-carboxylic acid tert-butyl ester was prepared by using the procedure as described in step-5 of intermediate-1 with some non-critical variations. Yield: 2.1 g (61 %); <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz) δ ppm: 1.52 (s, 9H), 1.86 – 1.88 (m, 4H), 2.14 – 2.16 (d, *J* = 6.4 Hz, 3H), 2.64 – 2.66 (m, 2H), 2.92 – 2.94 (m, 2H), 4.58 – 4.67 (m, 4H); Mass (m/z): 289.1 (M+H)<sup>+</sup>.

- 15 **Step-8: 9-Methyl-2,3,5,6,7,8-hexahydro-1H-pyrrolo[3,4-b]quinoline hydrochloride**

- 9-Methyl-2,3,5,6,7,8-hexahydro-1H-pyrrolo[3,4-b]quinoline hydrochloride was prepared by using the procedure as described in step-6 of intermediate-1 with some non-critical variations. Yield: 1.4 g (92 %); <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ ppm: 1.79 – 1.80 (m, 4H), 2.26 (s, 3H), 2.69 – 2.70 (m, 2H), 2.92 – 2.93 (m, 2H), 4.59 (bs, 4H), 10.41 (bs, 2H);  
20 Mass (m/z): 188.8 (M+H)<sup>+</sup>.

**Intermediate-3: 4-Methyl-3,5,6,7-tetrahydro-2H-1-oxa-6,8-diaza-s-indacene hydrochloride**

**Step-1: Trifluoro-methanesulfonic acid 5-cyano-4-methyl-2,3-dihydro-furo[2,3-b]pyridin-6-yl ester**

- 25 Trifluoro methanesulfonic anhydride (10.57 g, 0.0375 mol) was added to a stirred solution of 6-hydroxy-4-methyl-2,3-dihydro-furo[2,3-b]pyridine-5-carbonitrile (5.5 g, 0.031 mol; reference *Aust. J. Chem.* 9(2), 1956, 244-251.) and triethylamine (4.7 g, 0.046 mol) in DCM at 0 °C - 5 °C for 1 h. The reaction mixture was diluted with cold water (25 mL) and product was extracted using DCM (50 mL x 3). The organic extracts were combined, washed with  
30 brine (25 mL), dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated in vacuo to obtain a residual mass that was purified by column chromatography using 10 - 15 % ethyl acetate in hexanes to

obtain the title compound. Yield: 8.5 g (88%);  $^1\text{H}$  – NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  ppm: 2.48 (s, 3H), 3.25 – 3.30 (t,  $J$  = 8.4 Hz, 2H), 4.82 – 4.86 (t,  $J$  = 8.8 Hz, 2H); Mass (m/z): 308.8 ( $\text{M}+\text{H}$ ) $^+$ .

**Step-2: 5-Cyano-4-methyl-2,3-dihydro-furo[2,3-b]pyridine-6-carboxylic acid methyl ester**

5-Cyano-4-methyl-2,3-dihydro-furo[2,3-b]pyridine-6-carboxylic acid methyl ester was prepared from trifluoro-methanesulfonic acid 5-cyano-4-methyl-2,3-dihydro-furo[2,3-b]pyridin-6-yl ester by using the procedure as described in step-1 of intermediate-1 with some non-critical variations. Yield: 3.5 g (47 %);  $^1\text{H}$  – NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  ppm: 2.51 (s, 3H), 3.30 – 3.34 (t,  $J$  = 8.4 Hz, 2H), 4.01 (s, 3H), 4.78 – 4.82 (t,  $J$  = 8.8 Hz, 2H); Mass (m/z): 219.1 ( $\text{M}+\text{H}$ ) $^+$ .

**Step-3: 4-Methyl-2,3,5,6-tetrahydro-1-oxa-6,8-diaza-s-indacen-7-one**

4-Methyl-2,3,5,6-tetrahydro-1-oxa-6,8-diaza-s-indacen-7-one was prepared from 5-cyano-4-methyl-2,3-dihydro-furo[2,3-b]pyridine-6-carboxylic acid methyl ester by using the procedure as described in step-2 of intermediate-1 with some non-critical variations. Yield: 2.4 g (80 %);  $^1\text{H}$  – NMR ( $\text{DMSO}-d_6$ , 400 MHz)  $\delta$  ppm: 2.23 (s, 3H), 3.22 – 3.26 (t,  $J$  = 8.6 Hz, 2H), 4.22 (s, 2H), 4.61 – 4.66 (t,  $J$  = 8.6 Hz, 2H), 8.68 (bs, 1H); Mass (m/z): 191.0 ( $\text{M}+\text{H}$ ) $^+$ .

**Step-4: 4-Methyl-7-oxo-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacene-6-carboxylic acid tert-butyl ester**

4-Methyl-7-oxo-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacene-6-carboxylic acid tert-butyl ester was prepared from 4-methyl-2,3,5,6-tetrahydro-1-oxa-6,8-diaza-s-indacen-7-one by using the procedure as described in step-3 of intermediate-1 with some non-critical variations. Yield: 3.0 g (83 %);  $^1\text{H}$  – NMR ( $\text{DMSO}-d_6$ , 400 MHz)  $\delta$  ppm: 1.52 (s, 9H), 2.26 (s, 3H), 3.22 – 3.24 (m, 2H), 4.63 – 4.66 (m, 4H); Mass (m/z): 291.1 ( $\text{M}+\text{H}$ ) $^+$ .

**Step-5: 7-Hydroxy-4-methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacene-6-carboxylic acid tert-butyl ester**

7-Hydroxy-4-methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacene-6-carboxylic acid tert-butyl ester was prepared from 4-methyl-7-oxo-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacene-6-carboxylic acid tert-butyl ester by using the procedure as described in step-4 of

intermediate-1 with some non-critical variations. Yield: 3.1 g (91 %); Mass (m/z): 293.1 (M+H)<sup>+</sup>.

**Step-6: 4-Methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacene-6-carboxylic acid tert-butyl ester**

- 5 4-Methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacene-6-carboxylic acid tert-butyl ester was prepared from 7-hydroxy-4-methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacene-6-carboxylic acid tert-butyl ester by using the procedure as described in step-5 of intermediate-1 with some non-critical variations. Yield: 1.6 g (62 %); <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz) δ ppm: 1.52 (s, 9H), 2.17 (s, 3H), 3.14 – 3.18 (t, *J* = 8.6 Hz, 2H), 3.30 – 3.34 (t, *J* = 8.6 Hz, 2H), 4.50 – 4.56 (m, 4H); Mass (m/z): 277.0 (M+H)<sup>+</sup>.
- 10

**Step-7: 4-Methyl-3,5,6,7-tetrahydro-2H-1-oxa-6,8-diaza-s-indacene hydrochloride**

- 4-Methyl-3,5,6,7-tetrahydro-2H-1-oxa-6,8-diaza-s-indacene hydrochloride was prepared from 4-methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacene-6-carboxylic acid tert-butyl ester by using the procedure as described in step-6 of intermediate-1 with some non-critical variations. Yield: 1.6 g (62 %); <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz) δ ppm: 2.16 (s, 3H), 2.91 – 2.94 (t, *J* = 7.2 Hz, 2H), 3.68 – 3.72 (t, *J* = 7.2 Hz, 2H), 4.30 – 4.31 (d, *J* = 3.6 Hz, 4H), 9.97 (bs, 2H); Mass (m/z): 177.2 (M+H)<sup>+</sup>.
- 15

**Intermediate-4: 8-Methyl-3,5,6,7-tetrahydro-1H-2-oxa-4,6-diaza-s-indacene**

**Step-1: 4-Methyl-2-oxo-1,2,5,7-tetrahydro-furo[3,4-b]pyridine-3-carbonitrile**

- 20 2-Hydroxy-4-methyl-5,7-dihydro-furo[3,4-b]pyridine-3-carbonitrile was prepared by using the procedure as described in step-1 of intermediate-2 using suitable starting materials with some non-critical variations. Yield: 7.7 g (20 %); <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ ppm: 2.28 (s, 3H), 4.85 – 4.88 (m, 4H), 7.1 (bs, 1H); Mass (m/z): 176.9 (M+H)<sup>+</sup>.

**Step-2: 2-Chloro-4-methyl-5,7-dihydro-furo[3,4-b]pyridine-3-carbonitrile**

- 25 2-Chloro-4-methyl-5,7-dihydro-furo[3,4-b]pyridine-3-carbonitrile was prepared from 2-hydroxy-4-methyl-5,7-dihydro-furo[3,4-b]pyridine-3-carbonitrile by using the procedure as described in step-2 of intermediate-2 with some non-critical variations. Yield: 1.0 g (10 %); <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz) δ ppm: 2.49 (s, 3H), 5.07 – 5.15 (m, 4H); Mass (m/z): 194.9, 197.0 (M+H)<sup>+</sup>.

- 30 **Step-3: 3-Cyano-4-methyl-5,7-dihydro-furo[3,4-b]pyridine-2-carboxylic acid methyl ester**

3-Cyano-4-methyl-5,7-dihydro-furo[3,4-b]pyridine-2-carboxylic acid methyl ester was prepared from 2-chloro-4-methyl-5,7-dihydro-furo[3,4-b]pyridine-3-carbonitrile by using the procedure as described in step-1 of intermediate-1 with some non-critical variations. Yield: 0.31 g (55 %); <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz) δ ppm: 2.55 (s, 3H), 4.08 (s, 3H), 5.18 – 5.23 (m, 4H); Mass (m/z): 219.1 (M+H)<sup>+</sup>.

**Step-4: 8-Methyl-1,3,6,7-tetrahydro-2-oxa-4,6-diaza-s-indacen-5-one**

8-Methyl-1,3,6,7-tetrahydro-2-oxa-4,6-diaza-s-indacen-5-one was prepared from 3-cyano-4-methyl-5,7-dihydro-furo[3,4-b]pyridine-2-carboxylic acid methyl ester by using the procedure as described in step-2 of intermediate-1 with some non-critical variations. Yield: 0.15 g (50 %); <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ ppm: 2.30 (s, 3H), 4.39 (s, 2H), 5.16 – 5.22 (m, 4H), 6.61 (bs, 1H); Mass (m/z): 190.8 (M+H)<sup>+</sup>.

**Step-5: 8-Methyl-3,5,6,7-tetrahydro-1H-2-oxa-4,6-diaza-s-indacene**

Borane-dimethyl sulfide complex (2M solution in THF; 1.5 mL, 2.63 mmol) was added dropwise to a solution of 8-methyl-1,3,6,7-tetrahydro-2-oxa-4,6-diaza-s-indacen-5-one (0.1 g, 0.52 mmol) in tetrahydrofuran (15 mL) at 0 °C. The reaction mixture was stirred under reflux for 18 h, then it was cooled to 0 °C and quenched via slow addition of methanol (6 mL), followed by adding aqueous hydrochloric acid (6 M, 10 mL). The resulting mixture was allowed to stir under reflux for 3 hours and then cooled to RT. The pH of the solution was adjusted to 9-10 via addition of 2M aqueous sodium hydroxide solution, and product extracted with ethyl acetate (3 x 50 mL). The organic extracts were combined, washed with brine (50 mL), dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated in vacuo to obtain a residual mass that was purified by column chromatography using 5 % MeOH in DCM to obtain the title compound. Yield: 50 mg (50 %); <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ ppm: 2.12 (s, 3H), 4.02 – 4.08 (m, 4H), 4.89 – 5.04 (m, 4H), 6.94 (bs, 1H); Mass (m/z): 177.0 (M+H)<sup>+</sup>.

**Intermediate-5: 6,6,9-Trimethyl-1,2,3,5,6,8-hexahydro-7-oxa-2,4-diaza-cyclopenta[b]naphthalene hydrochloride**

**Step-1: 4,7,7-Trimethyl-2-oxo-1,5,7,8-tetrahydro-2H-pyrano[4,3-b]pyridine-3-carbonitrile**

4,7,7-Trimethyl-2-oxo-1,5,7,8-tetrahydro-2H-pyrano[4,3-b]pyridine-3-carbonitrile was prepared by using the procedure as described in step-1 of intermediate-2 with some non-

critical variations. Yield: 1.03 g (19.6%);  $^1\text{H}$  – NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  ppm: 1.33 (s, 6H), 2.34 (s, 3H), 2.68 (s, 2H), 4.52 (s, 2H), 12.19 (bs, 1H); Mass (m/z): 219.0 ( $\text{M}+\text{H}$ ) $^+$ .

**Step-2: Trifluoro-methanesulfonic acid 3-cyano-4,7,7-trimethyl-7,8-dihydro-5H-pyrano[4,3-b]pyridin-2-yl ester**

5 Trifluoro-methanesulfonic acid 3-cyano-4,7,7-trimethyl-7,8-dihydro-5H-pyrano[4,3-b]pyridin-2-yl ester was prepared from 4,7,7-trimethyl-2-oxo-1,5,7,8-tetrahydro-2H-pyrano[4,3-b]pyridine-3-carbonitrile by using the procedure as described in step-1 of intermediate-3 with some non-critical variations. Yield: 0.55 g (36.9 %);  $^1\text{H}$  – NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  ppm: 1.32 (s, 6H), 2.46 (s, 3H), 2.90 (s, 2H), 4.73 (s, 2H); Mass (m/z):  
10 350.8 ( $\text{M}+\text{H}$ ) $^+$ .

**Step-3: 3-Cyano-4,7,7-trimethyl-7,8-dihydro-5H-pyrano[4,3-b]pyridine-2-carboxylic acid methyl ester**

3-Cyano-4,7,7-trimethyl-7,8-dihydro-5H-pyrano[4,3-b]pyridine-2-carboxylic acid methyl ester was prepared from trifluoro-methanesulfonic acid 3-cyano-4,7,7-trimethyl-7,8-dihydro-5H-pyrano[4,3-b]pyridin-2-yl ester by using the procedure as described in step-1 of  
15 intermediate-1 with some non-critical variations. Yield: 0.033 g (37 %);  $^1\text{H}$  – NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  ppm: 1.32 (s, 6H), 2.48 (s, 3H), 3.01 (s, 2H), 4.06 (s, 3H), 4.80 (s, 2H); Mass (m/z): 261.0 ( $\text{M}+\text{H}$ ) $^+$ .

**Step-4: 6,6,9-Trimethyl-1,2,5,8-tetrahydro-6H-7-oxa-2,4-diaza-cyclopenta[b]naphthalen-3-one**

6,6,9-Trimethyl-1,2,5,8-tetrahydro-6H-7-oxa-2,4-diaza-cyclopenta[b]naphthalen-3-one was prepared from 3-cyano-4,7,7-trimethyl-7,8-dihydro-5H-pyrano[4,3-b]pyridine-2-carboxylic acid methyl ester by using the procedure as described in step-2 of intermediate-1 with some non-critical variations. Yield: 0.12 g (48 %);  $^1\text{H}$  – NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  ppm: 1.32 (s,  
25 6H), 2.21 (s, 3H), 3.04 (s, 2H), 4.40 (s, 2H), 4.84 (s, 2H), 6.38 (bs, 1H); Mass (m/z): 233.0 ( $\text{M}+\text{H}$ ) $^+$ .

**Step-5: 6,6,9-Trimethyl-3-oxo-3,5,6,8-tetrahydro-1H-7-oxa-2,4-diaza-cyclopenta[b]naphthalene-2-carboxylic acid tert-butyl ester**

6,6,9-Trimethyl-3-oxo-3,5,6,8-tetrahydro-1H-7-oxa-2,4-diaza-cyclopenta[b]naphthalene-2-carboxylic acid tert-butyl ester was prepared from 6,6,9-trimethyl-1,2,5,8-tetrahydro-6H-7-oxa-2,4-diaza-cyclopenta[b]naphthalen-3-one by using the procedure as described in step-3  
30 of intermediate-1 with some non-critical variations. Yield: 0.1 g (58%);  $^1\text{H}$  – NMR ( $\text{CDCl}_3$ ,

400 MHz)  $\delta$  ppm: 1.32 (s, 6H), 1.49 (s, 9H), 2.22 (s, 3H), 3.03 (s, 2H), 4.66 (s, 2H), 4.83 (s, 2H); Mass (m/z): 333.1 (M+H)<sup>+</sup>.

**Step-6: 3-Hydroxy-6,6,9-trimethyl-3,5,6,8-tetrahydro-1H-7-oxa-2,4-diaza-cyclopenta[b]naphthalene-2-carboxylic acid tert-butyl ester**

5 3-Hydroxy-6,6,9-trimethyl-3,5,6,8-tetrahydro-1H-7-oxa-2,4-diaza-cyclopenta[b]naphthalene-2-carboxylic acid tert-butyl ester was prepared from 6,6,9-trimethyl-3-oxo-3,5,6,8-tetrahydro-1H-7-oxa-2,4-diaza-cyclopenta[b]naphthalene-2-carboxylic acid tert-butyl ester by using the procedure as described in step-4 of intermediate-1 with some non-critical variations. Yield: 0.1 g, Mass (m/z): 335.1 (M+H)<sup>+</sup>;

10 **Step-7: 6,6,9-Trimethyl-3,5,6,8-tetrahydro-1H-7-oxa-2,4-diaza-cyclopenta[b]naphthalene-2-carboxylic acid tert-butyl ester**

6,6,9-Trimethyl-3,5,6,8-tetrahydro-1H-7-oxa-2,4-diaza-cyclopenta[b]naphthalene-2-carboxylic acid tert-butyl ester was prepared from 3-hydroxy-6,6,9-trimethyl-3,5,6,8-tetrahydro-1H-7-oxa-2,4-diaza-cyclopenta[b]naphthalene-2-carboxylic acid tert-butyl ester  
15 by using the procedure as described in step-5 of intermediate-1 with some non-critical variations. Yield: 0.37 mg (39%); <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  ppm: 1.25 (s, 6H), 1.51 (s, 9H), 2.09 (s, 3H), 2.85 (bs, 2H), 4.60 – 4.68 (m, 4H), 4.74 (s, 2H); Mass (m/z): 319.1 (M+H)<sup>+</sup>.

20 **Step-8: 6,6,9-Trimethyl-1,2,3,5,6,8-hexahydro-7-oxa-2,4-diaza-cyclopenta[b]naphthalene hydrochloride**

6,6,9-Trimethyl-1,2,3,5,6,8-hexahydro-7-oxa-2,4-diaza-cyclopenta[b]naphthalene hydrochloride was prepared from 3-hydroxy-6,6,9-trimethyl-3,5,6,8-tetrahydro-1H-7-oxa-2,4-diaza-cyclopenta[b]naphthalene-2-carboxylic acid tert-butyl ester by using the procedure as described in step-6 of intermediate-1 with some non-critical variations. Yield:  
25 24 mg (77%). <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 400 MHz)  $\delta$  ppm: 1.21 (s, 6H), 2.12 (s, 3H), 2.75 (s, 2H), 4.43 – 4.45 (m, 2H), 4.54 – 4.57 (m, 2H), 4.71 (s, 2H), 7.52 (bs, 1H), 9.52 (bs, 1H); Mass (m/z): 219.0 (M+H)<sup>+</sup>.

**Intermediate-6: 5,7,7-Trimethyl-2,3,6,7,8,9-hexahydro-1H-pyrrolo[3,4-c]isoquinoline hydrochloride**

30 **Step-1: 3-Chloro-1,7,7-trimethyl-5,6,7,8-tetrahydro-isoquinoline-4-carbonitrile**  
Pd(PPh<sub>3</sub>)<sub>4</sub> (0.045 g, 0.000039 mol) was added to stirred mixture of 1,3-dichloro-7,7-dimethyl-5,6,7,8-tetrahydro-isoquinoline-4-carbonitrile (1 g, 0.0039 mol, prepared as per

the procedure disclosed in preparation 3 on page 31 of WO2010081692), methylboronic acid (0.25 g, 0.0043 mol) and potassium carbonate (1.62 g, 0.011 mol) in 1,4-dioxane (25 mL) and the reaction mixture was refluxed for overnight. The reaction mixture was cooled to RT, poured on to water (100 mL) and product extracted using ethyl acetate (50 mL x 3).

- 5 The organic extracts were combined, washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated in vacuo to obtain title compound.

**Step 2: 5,7,7-Trimethyl-2,3,6,7,8,9-hexahydro-1H-pyrrolo[3,4-c]isoquinoline hydrochloride**

- 10 5,7,7-Trimethyl-2,3,6,7,8,9-hexahydro-1H-pyrrolo[3,4-c]isoquinoline hydrochloride was prepared by following the procedure as described in step-1 to step-6 of intermediate-1 using suitable starting materials with some non-critical variations. <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ ppm: 1.05 (s, 6H), 1.81 – 1.84 (m, 2H), 2.49 (s, 3H), 2.57 – 2.62 (m, 4H), 4.51, (s, 1H), 4.56 (s, 1H), 4.59 (s, 1H), 4.65 (s, 1H), 10.31(bs, 2H); Mass (m/z): 217.0 (M+H)<sup>+</sup>.

- 15 **Intermediate-7: 5,7,7-Trimethyl-1,2,3,6,7,8-hexahydro-2,4-diaza-as-indacene hydrochloride**

- 1,3-Dichloro-6,7-dihydro-6,6-dimethyl-5H-cyclopenta[c]pyridine-4-carbonitrile (commercially procured) was reacted by following the step 1 of intermediate 6 to obtain 3-chloro-1,6,6-trimethyl-5,7-dihydro-cyclopenta[3,4-c]pyridine-4-carbonitrile that was further reacted by following the procedure as described in step-1 to step-6 of intermediate-1 with  
20 some non-critical variations to obtain the title compound. <sup>1</sup>H – NMR (CD<sub>3</sub>OD, 400 MHz) δ ppm: 1.12 (s, 6H), 2.55 (s, 2H), 2.60 (s, 3H), 2.67 (s, 2H), 4.78 – 4.85 (m, 4H); Mass (m/z): 203.1 (M+H)<sup>+</sup>.

**Intermediate-8: 5,8,8-Trimethyl-1,2,3,6,8,9-hexahydro-7-oxa-2,4-diaza-cyclopenta[a]naphthalene hydrochloride**

- 25 **Step-1:** 5,8,8-Trimethyl-1,2,3,6,8,9-hexahydro-7-oxa-2,4-diaza-cyclopenta[a]naphthalene hydrochloride was prepared from 3,3,8-Trimethyl-6-oxo-3,4,6,7-tetrahydro-1H-pyrano[3,4-c]pyridine-5-carbonitrile (prepared as per the procedure of compound 6a in reference *Current Organic Chemistry*, 2021, 25 (11), 1704-1714 ) by following the procedure as described in Step-2 to step-8 of intermediate-5 using suitable starting materials with some  
30 non-critical variations to obtain the title compound. <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ ppm: 1.19 (s, 6H), 2.41 (s, 3H), 2.59 (s, 2H), 4.41 – 4.44 (m, 2H), 4.52 – 4.54 (m, 2H), 4.69 (s, 2H), 7.59 (bs, 1H), 9.34 (bs, 1H); Mass (m/z): 219.1 (M+H)<sup>+</sup>.

**Intermediate-9: 1,2,3,5,6,7-Hexahydro-2,4-diaza-s-indacene hydrochloride****Step-1: 3-Cyano-6,7-dihydro-5H-cyclopenta[b]pyridine -2-carboxylic acid methyl ester**

3-Cyano-6,7-dihydro-5H-cyclopenta[b]pyridine-2-carboxylic acid methyl ester was prepared from 2-chloro-6,7-dihydro-5H-cyclopenta[b]pyridine-3-carbonitrile (5.5 g, 0.030 mol, prepared as per the procedure disclosed in step-3 of example 81 on page 238 of WO2022155419) by using the procedure as described in step-1 of intermediate-1 with some non-critical variations. Yield: 4.1 g (66 %); <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz) δ ppm: 2.23 – 2.27 (m, 2H), 3.05 – 3.09 (t, *J* = 7.2 Hz, 2H), 3.16 – 3.20 (t, *J* = 7.8 Hz, 2H), 4.06 (s, 3H), 7.90 (s, 1H); Mass (m/z): 202.8 (M+H)<sup>+</sup>.

**Step-2: 1,5,6,7-Tetrahydro-2H-2,4-diaza-s-indacen-3-one**

1,5,6,7-Tetrahydro-2H-2,4-diaza-s-indacen-3-one was prepared from 3-cyano-6,7-dihydro-5H-cyclopenta[b]pyridine-2-carboxylic acid methyl ester by using the procedure as described in step-2 of intermediate-1 with some non-critical variations. Yield: 0.22 g (22 %); <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ ppm: 2.09 – 2.13 (m, 2H), 2.94 – 2.98 (m, 4H), 4.30 (s, 2H), 7.79 (s, 1H), 8.74 (bs, 1H); Mass (m/z): 175.1 (M+H)<sup>+</sup>.

**Step-3: 3,5,6,7-Tetrahydro-1H-2,4-diaza-s-indacene-2-carboxylic acid tert-butyl ester**

Borane-dimethyl sulfide complex (2M solution in THF; 1.43 mL, 0.0028 mol) was added dropwise to a solution of 1,5,6,7-tetrahydro-2H-2,4-diaza-s-indacen-3-one (0.1 g, 0.00057 mol) in tetrahydrofuran (15 mL) at 0 °C. The reaction mixture was stirred under reflux for 18 h, then cooled to 0 °C and quenched via slow addition of methanol (6 mL), followed by adding aqueous hydrochloric acid (6 M, 10 mL). The resulting mixture was allowed to stir under reflux for 3 hours and then cooled to room temperature. The pH of the solution was adjusted to 9-10 via addition of 2M aqueous sodium hydroxide solution. Di-tert-butyl dicarbonate (0.25 g, 0.0011 mol) was added to the reaction mixture and stirred at room temperature for 16 hours. The reaction mixture was diluted with water (50 mL) and extracted with ethyl acetate (3 x 50 mL). The organic extracts were combined, washed with brine (50 mL), dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated in vacuo to obtain a residual mass that was purified by column chromatography using 1.5 – 2.5 % MeOH in DCM to obtain the title compound. Yield: 35 mg (23 %); <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz) δ ppm: 1.51 (s, 9H), 2.11 – 2.19 (m, 2H), 2.90 – 2.94 (m, 2H), 2.97 – 3.01 (m, 2H), 4.61 – 4.67 (m, 4H), 7.38 (s, 1H); Mass (m/z): 261.0 (M+H)<sup>+</sup>.

**Step-4: 1,2,3,5,6,7-Hexahydro-2,4-diaza-s-indacene hydrochloride**



1,2,3,5,6,7-Hexahydro-2,4-diaza-s-indacene hydrochloride was prepared from 3,5,6,7-tetrahydro-1*H*-2,4-diaza-s-indacene-2-carboxylic acid tert-butyl ester by using the procedure as described in step-6 of intermediate-1 with some non-critical variations. Yield: 25 mg (94 %); <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ ppm: 2.04 – 2.12 (m, 2H), 2.87 – 2.91 (m, 4H), 4.38 – 4.50 (m, 4H), 7.63 (s, 1H), 9.79 (bs, 2H); Mass (m/z): 160.8 (M+H)<sup>+</sup>.

**Intermediate-10: 1,2,3,6,7,8-Hexahydro-2,4-diaza-as-indacene**

**Step-1: 4-Cyano-6,7-dihydro-5*H*-cyclopenta[c]pyridine-3-carboxylic acid methyl ester**

4-Cyano-6,7-dihydro-5*H*-cyclopenta[c]pyridine-3-carboxylic acid methyl ester was prepared from 3-chloro-6,7-dihydro-5*H*-cyclopenta[c]pyridine-4-carbonitrile (1.79 g, 0.01 mol, prepared as per the procedure disclosed in step-2 of example 24 on page 82 of WO2020160134) by using the procedure as described in step-1 of intermediate-1 with some non-critical variations. Yield: 1.6 g (80 %); <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz) δ ppm: 2.24 – 2.32 (m, 2H), 3.10 – 3.14 (t, *J* = 7.6 Hz, 2H), 3.21 – 3.24 (t, *J* = 7.6 Hz, 2H), 4.06 (s, 3H), 8.69 (s, 1H); Mass (m/z): 203.0 (M+H)<sup>+</sup>.

**Step-2: 1,6,7,8-Tetrahydro-2*H*-2,4-diaza-as-indacen-3-one**

1,6,7,8-Tetrahydro-2*H*-2,4-diaza-as-indacen-3-one was prepared by using the procedure as described in step-2 of intermediate-1 with some non-critical variations. Yield: 0.35 g (26 %);

<sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ ppm: 2.17 – 2.31 (m, 2H), 2.92 – 2.96 (t, *J* = 7.6 Hz, 2H), 3.02 – 3.57 (t, *J* = 7.6 Hz, 2H) 4.32 (s, 2H), 8.60 (s, 1H), 8.88 (bs, 1H); Mass (m/z): 175.1 (M+H)<sup>+</sup>.

**Step-3: 1,2,3,6,7,8-Hexahydro-2,4-diaza-as-indacene**

1,2,3,6,7,8-Hexahydro-2,4-diaza-as-indacene was prepared by using the procedure as described in step-5 of intermediate-4 with some non-critical variations. Yield: 150 mg (23 %); <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz) δ ppm: 1.99 – 2.07 (m, 2H), 2.76 – 2.79 (t, *J* = 7.2 Hz, 2H), 2.84 – 2.88 (t, *J* = 7.6 Hz, 2H), 3.98 – 4.06 (m, 4H), 6.35 (bs, 1H), 8.22 (s, 1H); Mass (m/z): 161.1 (M+H)<sup>+</sup>.

**Intermediate-11: 2,3,5,6,7,8-Hexahydro-1*H*-pyrrolo[3,4-*b*]quinoline hydrochloride**

**Step 1:** 2,3,5,6,7,8-Hexahydro-1*H*-pyrrolo[3,4-*b*]quinoline hydrochloride was prepared from 2-hydroxy-5,6,7,8-tetrahydroquinoline-3-carbonitrile (prepared as per the procedure disclosed in step-2 of example 10 on page 128 of WO2022155419) by using the procedure

as described in step-1 to step-4 of intermediate-9 with some non-critical variations. Mass (m/z): 175.1 (M+H)<sup>+</sup>.

**Intermediate-12: 2,3,6,7,8,9-Hexahydro-1H-pyrrolo[3,4-c]cinnoline hydrochloride**

**Step-1: Cyano-acetic acid (2-oxo-cyclohexylidene)-hydrazide**

- 5 1,2-Cyclohexane-dione (43.5 g, 0.38 mol) was added dropwise to a stirred mixture of 2-cyanoacetohydrazide (35 g, 0.35 mol) in absolute ethanol (300 mL) at 0 °C – 10 °C and then the reaction mixture was stirred at RT for 18 h during which solids precipitated. These solids were filtered, washed with absolute ethanol (50 mL x 2), and the filtrate was concentrated in vacuo to obtain the title compound. Yield: 37.2 g (54 %); <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ ppm: 1.62 – 1.66 (m, 2H), 2.10 – 2.13 (m, 2H), 2.41 – 2.44 (m, 2H), 2.49 – 2.51 (m, 2H), 4.31 (s, 2H), 7.38 (s, 1H); Mass (m/z): 192.1 (M-H)<sup>+</sup>.
- 10

**Step-2: 3-Oxo-2,3,5,6,7,8-hexahydro-cinnoline-4-carbonitrile**

- Granular potassium carbonate (52.9 g, 0.38 mol) was added to a stirred mixture of cyano-acetic acid (2-oxo-cyclohexylidene)-hydrazide (37 g, 0.19 mol) in absolute ethanol (300 mL) at RT and then refluxed for 6 h. The reaction mixture was cooled to RT, filtered through hyflow and residue was washed with absolute ethanol (50 mL x 3). The filtrate was concentrated in vacuo to obtain the title compound as dark mass. Yield: quantitative; <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ ppm: 1.54 – 1.63 (m, 2H), 1.67 – 1.72 (m, 2H), 2.50 – 2.54 (m, 2H), 2.68 – 2.70 (m, 2H), 7.38 (s, 1H); Mass (m/z): 176.1 (M+H)<sup>+</sup>.
- 15

**Step-3: 3-Chloro-5,6,7,8-tetrahydro-cinnoline-4-carbonitrile**

20

- POCl<sub>3</sub> (175 mL, 5 vol.to SM) was added slowly dropwise to 3-oxo-2,3,5,6,7,8-hexahydro-cinnoline-4-carbonitrile (35 g, 0.2 mol) at 0 °C – 10 °C under stirring and then the reaction mixture was refluxed for 4 - 5 h. The reaction mixture was cooled to RT and concentrated in vacuo to obtain a residual mass that was diluted with water (500 mL) and 10 % methanol in DCM (500 mL). This combined mixture was stirred for 15 minutes and filtered through hyflow. The organic layer was separated and aqueous layer was again extracted with 10 % methanol in DCM (250 mL x 250 mL). The combined organic extracts were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated in vacuo to obtain a residual mass that was purified by column chromatography using 30 - 50 % ethyl acetate in hexanes to obtain the title compound. Yield: 11.9 g (30 %); <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz) δ ppm: 1.90 – 2.02 (m, 4H), 3.02 – 3.05 (t, *J* = 6.8 Hz, 2H), 3.18 – 3.21 (t, *J* = 6.4 Hz, 2H); Mass (m/z): 194.1 (M+H)<sup>+</sup>.
- 25
- 30

**Step-4: 4-Cyano-5,6,7,8-tetrahydro-cinnoline-3-carboxylic acid methyl ester**

4-Cyano-5,6,7,8-tetrahydro-cinnoline-3-carboxylic acid methyl ester was prepared from 3-chloro-5,6,7,8-tetrahydro-cinnoline-4-carbonitrile by using the procedure as described in step-1 of intermediate-1 with some non-critical variations. Yield: 8 g (60 %); <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz) δ ppm: 1.94 – 2.03 (m, 4H), 3.08 – 3.11 (t, *J* = 6.4 Hz, 2H), 3.30 – 3.33, (t, *J* = 6.4 Hz, 2H), 4.12(s, 3H); Mass (m/z): 217.9 (M+H)<sup>+</sup>.

**Step-5: 1,2,6,7,8,9-Hexahydro-pyrrolo[3,4-c]cinnolin-3-one**

1,2,6,7,8,9-Hexahydro-pyrrolo[3,4-c]cinnolin-3-one was prepared from 4-cyano-5,6,7,8-tetrahydro-cinnoline-3-carboxylic acid methyl ester by using the procedure as described in step-2 of intermediate-1 with some non-critical variations. Yield: 6.5 g (86 %); <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz) δ ppm: 1.92 – 1.96 (m, 2H), 1.99–2.04 (m, 2H), 2.80– 2.83 (t, *J* = 6.4 Hz, 2H), 3.28 – 3.31, (t, *J* = 6.0 Hz, 2H), 4.43 (s, 2H), 7.84 (s, 1H); Mass (m/z): 190.2 (M+H)<sup>+</sup>.

**Step-6: 3-Oxo-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-c]cinnoline-2-carboxylic acid tert-butyl ester**

3-Oxo-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-c]cinnoline-2-carboxylic acid tert-butyl ester was prepared from 1,2,6,7,8,9-hexahydro-pyrrolo[3,4-c]cinnolin-3-one by using the procedure as described in step-3 of intermediate-1 with some non-critical variations. Yield: 9.9 g (100%); Mass (m/z): 290.1 (M+H)<sup>+</sup>.

**Step-7: 3-Hydroxy-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-c]cinnoline-2-carboxylic acid tert-butyl ester**

3-Hydroxy-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-c]cinnoline-2-carboxylic acid tert-butyl ester was prepared from 3-oxo-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-c]cinnoline-2-carboxylic acid tert-butyl ester by using the procedure as described in step-4 of intermediate-1 with some non-critical variations. Yield: 7.7 g (77%); Mass (m/z): 292.3 (M+H)<sup>+</sup>.

**Step-8: 1,3,6,7,8,9-Hexahydro-pyrrolo[3,4-c]cinnoline-2-carboxylic acid tert-butyl ester**

1,3,6,7,8,9-Hexahydro-pyrrolo[3,4-c]cinnoline-2-carboxylic acid tert-butyl ester was prepared from 3-hydroxy-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-c]cinnoline-2-carboxylic acid tert-butyl ester by using the procedure as described in step-5 of intermediate-1 with some non-critical variations. Yield: 0.89 g (10%); Mass (m/z): 276.1 (M+H)<sup>+</sup>.

**Step-9: 2,3,6,7,8,9-Hexahydro-1*H*-pyrrolo[3,4-c]cinnoline hydrochloride**

2,3,6,7,8,9-Hexahydro-1*H*-pyrrolo[3,4-*c*]cinnolinewas prepared from 1,3,6,7,8,9-hexahydro-pyrrolo[3,4-*c*]cinnoline-2-carboxylic acid tert-butyl ester by using the procedure as described in step-6 of intermediate-1 with some non-critical variations. Yield: 0.45 g (65%); Mass (m/z): 176.0 (M+H)<sup>+</sup>.

5 **Intermediate-13: 1,2,3,6,7,8-Hexahydro-2,5-diaza-as-indacene hydrochloride**

**Step-1: 4-Oxo-3,4,5,6,7,8-hexahydro-1*H*-2,5-diaza-as-indacene-2-carboxylic acid tert-butyl ester**

A mixture of tert- butyl 3-cyano-4-oxopyrrolidine-1-carboxylate (5 g, 23.8 mmol) in cyclopentanone (20 mL) was added to polyohosphoric acid (100 g) at 100 °C, and the  
10 reaction mixture was stirred at 100 °C - 120 °C for 4 h. The reaction mixture was cooled to 15 °C, quenched by addition of water (1.5 L), and pH of the reaction mixture was adjusted to 10 – 11 using sodium hydroxide. Then di-tert-butyl dicarbonate (10.0 g, 45.8 mmol) was added to the reaction mixture at RT, stirred for 15 h and filtered. The solid cake was washed with water (50 mL x 3) followed by a mixture of tert butyl methy ether : n- hexane (40 mL  
15 x 3, 1:1) to afford the product as an off-white solid. Yield: 5 g (76 %); <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz) δ ppm: 1.50 (s, 9H), 2.12 – 2.20 (m, 2H), 2.65 – 2.68 (d, *J* = 7.2 Hz, 2H), 2.88 – 2.91 (d, *J* = 7.6 Hz, 2H), 4.49 – 4.54 (m, 4H), 12.19 (bs, 1H); Mass (m/z): 277.0 (M+H)<sup>+</sup>.

**Step-2: 4-Trifluoromethanesulfonyloxy-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacene-2-carboxylic acid tert-butyl ester**

20 Triflic anhydride (4.0 mL 0.023 mol) was added to a stirred solution of 4-oxo-3,4,5,6,7,8-hexahydro-1*H*-2,5-diaza-as-indacene-2-carboxylic acid tert-butyl ester (5.0 g, 0. 018 mol) and Et<sub>3</sub>N (4 mL, 0.027 mol) in DCM (50 mL) at 0 °C and maintained for 3 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 Na<sub>2</sub>SO<sub>4</sub>,  
25 filtered and concentrated in vacuo to obtain a residual mass that was purified by column chromatography using 15 - 20 % ethyl acetate in hexanes to obtain the title compound. Yield: 0.72 g (10 %); <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz) δ ppm: 1.52 (s, 9H), 2.21 – 2.24 (m, 2H), 2.85 – 2.89 (d, *J* = 7.6 Hz, 2H), 2.99 – 3.03 (d, *J* = 7.6 Hz, 2H), 4.61 – 4.73 (m, 4H); Mass (m/z): 409.0 (M+H)<sup>+</sup>.

30 **Step-3: 3,6,7,8-Tetrahydro-1*H*-2,5-diaza-as-indacene-2-carboxylic acid tert-butyl ester**

Triphenylphosphine (0.049 g, 0.00018 mol), palladium(II) acetate (0.014 g, 0.000063 mol), triethylamine (0.52 mL, 0.0037 mol) and formic acid (0.096 mL, 0.0025 mol) were added

sequentially to a stirred solution of 4-trifluoromethanesulfonyloxy-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacene-2-carboxylic acid tert-butyl ester (0.5 g, 0.0012 mol) in DMF (3 mL) and the RM was stirred at 60 °C – 70 °C for 3-4 h. After completion of reaction, the reaction mixture was cooled to RT, poured on to water (15 mL) and the product was  
 5 extracted with ethyl acetate (10 mL x 3). The organic extracts were combined, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated in vacuo to obtain a residual mass that was purified by column chromatography using 15-20 % ethyl acetate in hexanes to obtain the title compound. Yield: 0.24 g (75 %); Mass (m/z): 261.3 (M+H)<sup>+</sup>.

**Step-4: 1,2,3,6,7,8-Hexahydro-2,5-diaza-as-indacene hydrochloride**

10 1,2,3,6,7,8-Hexahydro-2,5-diaza-as-indacene hydrochloride was prepared from 3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacene-2-carboxylic acid tert-butyl ester by using the procedure as described in step-6 of intermediate-1 with some non-critical variations. Yield: 3.81 (77 %); <sup>1</sup>H – NMR (CD<sub>3</sub>OD, 400 MHz) δ ppm: 2.20 – 2.23 (t, *J* = 7.6 Hz, 2H), 2.98 – 3.02 (t, *J* = 7.2 Hz, 2H), 3.12 – 3.16 (t, *J* = 8.0 Hz, 2H), 4.63 – 4.66 (m, 4H), 8.56 (s, 1H),  
 15 10.4 (bs, 2H);; Mass (m/z): 161.0 (M+H)<sup>+</sup>.

**Intermediate-14: 4-Methyl-1,2,3,6,7,8-hexahydro-2,5-diaza-as-indacene hydrochloride**

**Step-1: 4-Methyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacene-2-carboxylic acid tert-butyl ester**

Bis(diphenylphosphino)ferrocene]dichloropalladium(II) (0.06 g, 0.000073 mol), methylzinc  
 20 chloride solution 2.0 M in THF, (0.47 mL, 0.0029 mol) were added sequentially to a stirred solution of 4-trifluoromethanesulfonyloxy-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacene-2-carboxylic acid tert-butyl ester (0.3 g, 0.0007 mol) in THF (5 mL) and the RM was stirred at 60 °C – 70 °C for 3-4 h. After completion of reaction, the reaction mixture was cooled to RT and concentrated in vacuo to obtain a residual mass that was purified by column  
 25 chromatography using 3 % methanol in DCM to obtain the title compound. Yield: 0.19 g (95 %); <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ ppm: 1.47 (s, 9H), 2.14 – 2.18 (m, 2H), 2.49 (s, 3H), 2.89 – 2.92 (d, *J* = 7.2 Hz, 2H), 3.04 – 3.07 (d, *J* = 7.6 Hz, 2H), 4.63 – 4.69 (m, 4H); Mass (m/z): 275.0 (M+H)<sup>+</sup>.

**Step 2: 4-Methyl-1,2,3,6,7,8-hexahydro-2,5-diaza-as-indacene hydrochloride**

30 4-Methyl-1,2,3,6,7,8-hexahydro-2,5-diaza-as-indacene hydrochloride was prepared from 4-methyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacene-2-carboxylic acid tert-butyl ester by using the procedure as described in step-6 of intermediate-1 with some non-critical

variations. Yield: 0.1g (83%);  $^1\text{H}$  – NMR ( DMSO- $d_6$ , 400 MHz)  $\delta$  ppm: 2.16 – 2.23 (m, 2H), 2.57 ( s, 3H), 2.94 – 2.98 ( d,  $J$  = 7.6 Hz , 2H), 3.11 – 3.14 ( d,  $J$  = 7.6 Hz , 2H), 4.63 – 4.69 (m, 4H); Mass (m/z): 175.0 (M+H) $^+$ .

**Intermediate 15: 4-Difluoromethyl-1,2,3,6,7,8-hexahydro-2,5-diaza-as-indacene hydrochloride**

5 4-Trifluoromethanesulfonyloxy-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacene-2-carboxylic acid tert-butyl ester (step-2 of intermediate-13) was reacted by following steps 1 and 2 of preparation P6, page 76 and steps 1 and 2 of preparation P7, page 78 of WO2018234953 with some non-critical variations to obtain 4-difluoromethyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacene-2-carboxylic acid tert-butyl ester that was reacted in a similar manner to  
10 step-6 of intermediate-1 with some non-critical variations to obtain the title compound.  $^1\text{H}$  - NMR (CD $_3$ OD, 400 MHz)  $\delta$  ppm: 2.17 – 2.21(m, 2H), 2.65 – 2.71 (m, 2H), 2.91 – 3.01 (m, 2H), 4.59 – 4.71 (m, 4H), 6.46 – 6.72 (t,  $J$  = 55.2 Hz, 1H); Mass (m/z): 211.1 (M+H) $^+$ .

**Intermediate-16: 5-Methyl-1,2,3,6,7,8-hexahydro-2,4-diaza-as-indacene hydrochloride and 8-methyl-1,2,3,5,6,7-hexahydro-2,4-diaza-s-indacene hydrochloride**

**Step-1: 3-Methoxycarbonyl-1-methyl-6,7-dihydro-5*H*-cyclopenta[c]pyridine-4-carbonitrile and 2-methoxycarbonyl-4-methyl-6,7-dihydro-5*H*-cyclopenta[b]pyridine-3-carbonitrile**

Pd(dppf)Cl $_2$ .CH $_2$ Cl $_2$  complex (33.1 g, 0.040 mol) was added to a stirred solution of 3-chloro-1-methyl-3,5,6,7-tetrahydro-2*H*-cyclopenta[c]pyridine-4-carbonitrile (56 g, 0.290  
20 mol, prepared as per the procedure disclosed in step-2 of example 190 on page 363 of WO2022155419) and Et $_3$ N (125.5 mL, 0.870 mol) in methanol (650 mL) and the contents were heated at 70  $^\circ\text{C}$  under 50 psi pressure of carbon monoxide in an autoclave for 4 h. The reaction mixture was cooled to RT, filtered and concentrated to get a residual mass that was  
25 purified by column chromatography using 40 – 50 % ethyl acetate in hexanes to obtain the title compound. Yield: 42.3 g (67.7 %); Mass (m/z): 217.0 (M+H) $^+$ .

**Step-2: 5-Methyl-1,6,7,8-tetrahydro-2*H*-2,4-diaza-as-indacen-3-one and 8-methyl-1,5,6,7-tetrahydro-2*H*-2,4-diaza-s-indacen-3-one**

A mixture of 5-methyl-1,6,7,8-tetrahydro-2*H*-2,4-diaza-as-indacen-3-one and 8-methyl-  
30 1,5,6,7-tetrahydro-2*H*-2,4-diaza-s-indacen-3-one was prepared by using the procedure as described in step-2 of intermediate-1 with some non-critical variations. Yield: 24.1 g (66 %); Mass (m/z): 188.9 (M+H) $^+$ .

**Step-3: 5-Methyl-3-oxo-3,6,7,8-tetrahydro-1H-2,4-diaza-as-indacene-2-carboxylic acid tert-butyl ester and 8-methyl-3-oxo-3,5,6,7-tetrahydro-1H-2,4-diaza-s-indacene-2-carboxylic acid tert-butyl ester**

A mixture of 5-methyl-3-oxo-3,6,7,8-tetrahydro-1H-2,4-diaza-as-indacene-2-carboxylic acid tert-butyl ester and 8-methyl-3-oxo-3,5,6,7-tetrahydro-1H-2,4-diaza-s-indacene-2-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: 32.0 g (88 %); Mass (m/z): 289.0 (M+H)<sup>+</sup>.

**Step-4: 3-Hydroxy-5-methyl-3,6,7,8-tetrahydro-1H-2,4-diaza-as-indacene-2-carboxylic acid tert-butyl ester and 3-hydroxy-8-methyl-3,5,6,7-tetrahydro-1H-2,4-diaza-s-indacene-2-carboxylic acid tert-butyl ester**

A mixture of 3-hydroxy-5-methyl-3,6,7,8-tetrahydro-1H-2,4-diaza-as-indacene-2-carboxylic acid tert-butyl ester and 3-hydroxy-8-methyl-3,5,6,7-tetrahydro-1H-2,4-diaza-s-indacene-2-carboxylic acid tert-butyl ester was prepared by using the procedure as described in step-4 of intermediate-1 with some non-critical variations. Yield: 30.7 g (95 %); Mass (m/z): 291.0 (M+H)<sup>+</sup>.

**Step-5: 5-Methyl-3,6,7,8-tetrahydro-1H-2,4-diaza-as-indacene-2-carboxylic acid tert-butyl ester and 8-Methyl-3,5,6,7-tetrahydro-1H-2,4-diaza-s-indacene-2-carboxylic acid tert-butyl ester**

A mixture of 5-methyl-3,6,7,8-tetrahydro-1H-2,4-diaza-as-indacene-2-carboxylic acid tert-butyl ester and 8-methyl-3,5,6,7-tetrahydro-1H-2,4-diaza-s-indacene-2-carboxylic acid tert-butyl ester was prepared by using the procedure as described in step-5 of intermediate-1 with some non-critical variations. Yield: 7.7 g (26%); Mass (m/z): 275.1 (M+H)<sup>+</sup>.

**Step-6: 5-Methyl-1,2,3,6,7,8-hexahydro-2,4-diaza-as-indacene hydrochloride and 8-Methyl-1,2,3,5,6,7-hexahydro-2,4-diaza-s-indacene hydrochloride**

A mixture of 5-methyl-1,2,3,6,7,8-hexahydro-2,4-diaza-as-indacene hydrochloride and 8-methyl-1,2,3,5,6,7-hexahydro-2,4-diaza-s-indacene hydrochloride was prepared by using the procedure as described in step-6 of intermediate-1 with some non-critical variations. Yield: 7.7 g (26%); Mass (m/z): 174.7 (M+H)<sup>+</sup>.

**Intermediate-17: 5-Methyl-2,3,6,7,8,9-hexahydro-1H-pyrrolo[3,4-c]isoquinoline hydrochloride and 9-methyl-2,3,5,6,7,8-hexahydro-1H-pyrrolo[3,4-b]quinoline hydrochloride**

**Step-1: 1-Methyl-3-oxo-2,3,5,6,7,8-hexahydro-isoquinoline-4-carbonitrile and 4-methyl-2-oxo-1,2,5,6,7,8-hexahydro-quinoline-3-carbonitrile**

2-Cyanoacetamide (6 g 0.071 mol) was added to a stirred solution of 2-acetyl cyclohexanone (10 g, 0.071 mol) and piperidine (12.14 g, 0.071 mol) at RT then heated at  
5 70 °C - 80 °C for 16 h. The reaction mixture was cooled to RT and concentrated to obtain a crude mass. This mass was triturated with hexanes (3 x 50 mL) during which solids separated. These solids were filtered and dried in vacuo to obtain the title compound as a mixture of isomers. Yield: 13.4 g (100%); Mass (m/z): 188.8 (M+H)<sup>+</sup>.

**Step-2: 3-Chloro-1-methyl-5,6,7,8-tetrahydro-isoquinoline-4-carbonitrile and 2-chloro-4-methyl-5,6,7,8-tetrahydro-quinoline-3-carbonitrile**

A mixture of 3-chloro-1-methyl-5,6,7,8-tetrahydro-isoquinoline-4-carbonitrile and 2-chloro-4-methyl-5,6,7,8-tetrahydro-quinoline-3-carbonitrile was prepared by using the procedure as described in step-2 of intermediate-2 with some non-critical variations. Yield: 14.7 g (100 %); Mass (m/z): 206.9, 209.0 (M+H)<sup>+</sup>.

**Step-3: 3-Cyano-4-methyl-5,6,7,8-tetrahydro-quinoline-2-carboxylic acid methyl ester and 4-cyano-1-methyl-5,6,7,8-tetrahydro-isoquinoline-3-carboxylic acid methyl ester**

A mixture of 3-cyano-4-methyl-5,6,7,8-tetrahydro-quinoline-2-carboxylic acid methyl ester and 4-cyano-1-methyl-5,6,7,8-tetrahydro-isoquinoline-3-carboxylic acid methyl ester was prepared by using the procedure as described in step-1 of intermediate-1 with some non-critical variations. Yield: 9 g (90 %); Mass (m/z): 231.1 (M+H)<sup>+</sup>.

**Step-4: 5-Methyl-1,2,6,7,8,9-hexahydro-pyrrolo[3,4-c]isoquinolin-3-one and 9-methyl-1,2,5,6,7,8-hexahydro-pyrrolo[3,4-b]quinolin-3-one**

A mixture of 5-methyl-1,2,6,7,8,9-hexahydro-pyrrolo[3,4-c]isoquinolin-3-one and 9-methyl-1,2,5,6,7,8-hexahydro-pyrrolo[3,4-b]quinolin-3-one as described in step-2 of intermediate-1 with some non-critical variations. Yield: 6.1 g (75 %); Mass (m/z): 203.4 (M+H)<sup>+</sup>.

**Step-5: 5-Methyl-3-oxo-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-c]isoquinoline-2-carboxylic acid tert-butyl ester and 9-methyl-3-oxo-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b]quinoline-2-carboxylic acid tert-butyl ester**

A mixture of 5-methyl-3-oxo-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-c]isoquinoline-2-carboxylic acid tert-butyl ester and 9-methyl-3-oxo-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b]quinoline-2-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: 8.0 g (87 %); Mass (m/z): 303.1 (M+H)<sup>+</sup>.

**Step-6: 3-Hydroxy-5-methyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-c]isoquinoline-2-carboxylic acid tert-butyl ester and 3-hydroxy-9-methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b]quinoline-2-carboxylic acid tert-butyl ester**

A mixture of 3-hydroxy-5-methyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-c]isoquinoline-2-carboxylic acid tert-butyl ester ester and 3-hydroxy-9-methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b]quinoline-2-carboxylic acid tert-butyl ester by using the procedure as described in step-4 of intermediate-1 with some non-critical variations. Yield: 3.6 g (90 %); Mass (m/z): 304.9 (M+H)<sup>+</sup>.

**Step-7: 5-Methyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-c]isoquinoline-2-carboxylic acid tert-butyl ester and 9-methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b]quinoline-2-carboxylic acid tert-butyl ester**

A mixture of 5-methyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-c]isoquinoline-2-carboxylic acid tert-butyl ester and 9-methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b]quinoline-2-carboxylic acid tert-butyl ester by using the procedure as described in step-5 of intermediate-1 with some non-critical variations. Yield: 2.1 g (61 %); Mass (m/z): 289.2 (M+H)<sup>+</sup>.

**Step-8: 5-Methyl-2,3,6,7,8,9-hexahydro-1H-pyrrolo[3,4-c]isoquinoline hydrochloride and 9-methyl-2,3,5,6,7,8-hexahydro-1H-pyrrolo[3,4-b]quinoline hydrochloride**

A mixture of 5-methyl-2,3,6,7,8,9-hexahydro-1H-pyrrolo[3,4-c]isoquinoline hydrochloride and 9-methyl-2,3,5,6,7,8-hexahydro-1H-pyrrolo[3,4-b]quinoline hydrochloride was prepared from by using the procedure as described in step-6 of intermediate-1 with some non-critical variations. Yield: 1.4 g (92 %); Mass (m/z): 189.1 (M+H)<sup>+</sup>.

**Intermediate-18: 7-Benzyl-9-methyl-2,3,5,6,7,8-hexahydro-1H-2,4,7-triaza-cyclopenta[b]naphthalene hydrochloride**

**Step-1: 6-Benzyl-4-methyl-2-oxo-1,2,5,6,7,8-hexahydro-[1,6]naphthyridine-3-carbonitrile**

A solution of ethyl cyanoacetate (41.8 g, 0.370 moles), 1-benzyl-piperidin-4-one (70 g, 0.370 mol), acetaldehyde (16.2 g, 0.370 mol) and pyrrolidine (2.62 g, 0.037 mol) in DMSO (500 mL) stirred at RT for 1h. After added ammonium acetate (42.7 g, 0.555 mol) and stirred for 30 minutes at RT. Again added remaining pyrrolidine (31.55 g, 0.444 mol) at 0 °C – 5 °C slowly. Reaction mixture was heated to reflux for 16 h, after RM quenched into

ice-cold water (3.5 L), solids were precipitated and collected by filtration. Solids were dissolved in DCM (500 mL) and washed with cold water (2 X 100 mL), brine solution (2 X 100 mL) dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated in vacuo to obtain a residual mass that was purified by column chromatography using 2.5 – 3.5 % MeOH in DCM to obtain the title compound. Yield: 32 g (31 %); <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz) δ ppm: <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ ppm: 2.20 (s, 3H), 2.49 – 2.50 (m, 2H), 2.61 (s, 4H), 3.67 (s, 2H), 7.25 – 7.36 (m, 5H), 12.23 (bs, 1H); Mass (m/z): 280.0 (M+H)<sup>+</sup>.

**Step-2: 6-Benzyl-2-chloro-4-methyl-5,6,7,8-tetrahydro-[1,6]naphthyridine-3-carbonitrile**

6-Benzyl-2-chloro-4-methyl-5,6,7,8-tetrahydro-[1,6]naphthyridine-3-carbonitrile was prepared by following the procedure described in intermediate 2 on page 56 of WO 2023285583 using suitable intermediates with some non-critical variations. Yield: 5.5 g (39 %); <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ ppm: 2.35 (s, 3H), 2.69 – 2.72 (t, *J* = 5.8 Hz, 2H), 2.91 – 2.93 (t, *J* = 5.8 Hz, 2H), 3.60 (s, 2H), 3.74 (s, 2H), 7.28 – 7.36 (m, 5H); Mass (m/z): 297.8 (M+H)<sup>+</sup>.

**Step-3: 6-Benzyl-3-cyano-4-methyl-5,6,7,8-tetrahydro-[1,6]naphthyridine-2-carboxylic acid methyl ester**

6-Benzyl-3-cyano-4-methyl-5,6,7,8-tetrahydro-[1,6]naphthyridine-2-carboxylic acid methyl ester was prepared from 6-benzyl-2-chloro-4-methyl-5,6,7,8-tetrahydro-[1,6]naphthyridine-3-carbonitrile by using the procedure as described in step-1 of intermediate-1 with some non-critical variations. Yield: 5.0 g (84 %); <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ ppm: 2.39 (s, 3H), 2.74 – 2.76 (t, *J* = 5.6 Hz, 2H), 2.97 – 2.98 (t, *J* = 5.6 Hz, 2H), 3.70 (s, 2H), 3.76 (s, 2H), 3.91 (s, 3H), 7.28 – 7.39 (m, 5H); Mass (m/z): 321.6 (M+H)<sup>+</sup>.

**Step-4: 7-Benzyl-9-methyl-1,2,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-3-one**

7-Benzyl-9-methyl-1,2,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-3-one was prepared from 6-benzyl-3-cyano-4-methyl-5,6,7,8-tetrahydro-[1,6]naphthyridine-2-carboxylic acid methyl ester by using the procedure as described in step-2 of intermediate-1 with some non-critical variations. Yield: 0.11 g (24 %); <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ ppm: 2.13 (s, 3H), 2.74 – 2.76 (m, 2H), 2.97 – 3.01 (m, 2H), 3.67 (s, 2H), 3.75 (s, 2H), 4.24 – 4.30 (m, 2H), 7.29 – 7.38 (m, 5H), 8.79 (bs, 1H); Mass (m/z): 294.0 (M+H)<sup>+</sup>.

**Step-5: 7-Benzyl-9-methyl-3-oxo-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalene-2-carboxylic acid tert-butyl ester**

7-Benzyl-9-methyl-3-oxo-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalene-2-carboxylic acid tert-butyl ester was prepared from 7-benzyl-9-methyl-1,2,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-3-one by using the procedure as described in step-3 of intermediate-1 with some non-critical variations. Yield: 0.1 g (76 %); <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz) δ ppm: 1.56 (s, 9H), 2.17 (s, 3H), 2.82 – 2.85 (t, *J* = 5.8 Hz, 2H), 3.17 – 3.20 (t, *J* = 5.8 Hz, 2H), 3.68 (s, 2H), 3.77 (s, 2H), 4.63 (s, 2H), 7.26 – 7.38 (m, 5H); Mass (m/z): 393.9 (M+H)<sup>+</sup>.

**Step-6: 7-Benzyl-3-hydroxy-9-methyl-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalene-2-carboxylic acid tert-butyl ester**

7-Benzyl-3-hydroxy-9-methyl-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalene-2-carboxylic acid tert-butyl ester was prepared from 7-benzyl-9-methyl-3-oxo-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalene-2-carboxylic acid tert-butyl ester by using the procedure as described in step-4 of intermediate-1 with some non-critical variations. Yield: 0.1 g (95 %); Mass (m/z): 396.1 (M+H)<sup>+</sup>.

**Step-7: 7-Benzyl-9-methyl-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalene-2-carboxylic acid tert-butyl ester**

7-Benzyl-9-methyl-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalene-2-carboxylic acid tert-butyl ester was prepared from 7-benzyl-3-hydroxy-9-methyl-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalene-2-carboxylic acid tert-butyl ester by using the procedure as described in step-5 of intermediate-1 with some non-critical variations. Yield: 55 mg (57 %); <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz) δ ppm: 1.52 (s, 9H), 2.06 (s, 3H), 2.78 – 2.81 (m, 2H), 3.00 – 3.02 (m, 2H), 3.58 (s, 2H), 3.75 (s, 2H), 4.57 – 4.66 (m, 4H), 7.28 – 7.38 (m, 5H); Mass (m/z): 380.0 (M+H)<sup>+</sup>.

**Step-8: 7-Benzyl-9-methyl-2,3,5,6,7,8-hexahydro-1H-2,4,7-triaza-cyclopenta[b]naphthalene hydrochloride**

7-Benzyl-9-methyl-2,3,5,6,7,8-hexahydro-1H-2,4,7-triaza-cyclopenta[b]naphthalene hydrochloride was prepared from 7-benzyl-9-methyl-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalene-2-carboxylic acid tert-butyl ester by using the procedure as described in step-6 of intermediate-1 with some non-critical variations. Yield: 40 mg (88 %); <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ ppm: 2.54 (s, 3H), 2.96 – 3.00 (m, 2H), 3.29 – 3.32

(m, 2H), 4.28 – 4.30 (m, 2H), 4.44 – 4.45 (m, 2H), 4.56 – 4.57 (m, 4H), 7.48 – 7.50 (m, 3H), 7.67 – 7.72 (m, 2H), 10.22 (bs, 1H), 11.86 (bs, 1H); Mass (m/z): 280.0 (M+H)<sup>+</sup>.

**Intermediate-19: 5-Methyl-1,2,3,6,8,9-hexahydro-2,4,7-triaza-cyclopenta[a]naphthalene-7-carboxylic acid tert-butyl ester**

5 **Step-1: 5-Cyano-8-methyl-6-oxo-3,4,6,7-tetrahydro-1H-[2,7]naphthyridine-2-carboxylic acid tert-butyl ester**

KOH powder (1.28 g, 0.022 mol) was added to a stirred solution of 3-acetyl-4-oxo-piperidine-1-carboxylic acid tert-butyl ester (5 g, 0.02 mol) and cyanoacetamide (1.91 g, 0.022 mol) and the resulting mixture stirred at 60 - 65 °C for 5 h, The reaction mixture then  
10 cooled to RT and concentrated in vacuo to obtain a residual mass that was purified by column chromatography using 2 - 5 % MeOH in DCM to obtain the title compound. Yield: 2.8 g (47%); <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ ppm: 1.42 (s, 9H), 2.23 (s, 3H), 2.78 – 2.81 (t, *J* = 6.0 Hz, 2H), 3.51 – 3.53 (t, *J* = 6.0 Hz, 2H), 4.20 (s, 2H), 12.50 (bs, 1H); Mass (m/z): 290.0 (M+H)<sup>+</sup>.

15 **Step-2: 5-Cyano-8-methyl-6-trifluoromethanesulfonyloxy-3,4-dihydro-1H-[2,7]naphthyridine-2-carboxylic acid tert-butyl ester**

Triflic anhydride (1.64 mL, 0.0058 mol) was added to a stirred solution of 5-cyano-8-methyl-6-oxo-3,4,6,7-tetrahydro-1H-[2,7]naphthyridine-2-carboxylic acid tert-butyl ester (1.4 g, 0.0048 mol) and triethyl amine (1.47 mL, 0.014 mol) in DCM (25 mL) at 0 - 5 °C  
20 and stirred for 4 h. The reaction mixture was poured on to water (25 mL), extracted with DCM (25 mL x 3). The organic extracts were combined, dried over Na<sub>2</sub>SO<sub>4</sub>, 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: 0.9 g (44 %); <sup>1</sup>H – NMR (CDCl<sub>3</sub>-*d*<sub>6</sub>, 400 MHz) δ ppm: 1.50 (s, 9H), 2.52 (s, 3H), 3.04 – 3.07 (t, *J* = 5.6 Hz, 2H), 3.70 – 3.73 (t, *J* = 5.6 Hz, 2H), 4.53 (s, 2H); Mass (m/z): 421.9 (M+H)<sup>+</sup>.

**Step-3: 5-Cyano-8-methyl-3,4-dihydro-1H-[2,7]naphthyridine-2,6-dicarboxylic acid 2-tert-butyl ester 6-methyl ester**

5-Cyano-8-methyl-3,4-dihydro-1H-[2,7]naphthyridine-2,6-dicarboxylic acid 2-tert-butyl ester 6-methyl ester was prepared from 5-cyano-8-methyl-6-trifluoromethanesulfonyloxy-3,4-dihydro-1H-[2,7]naphthyridine-2-carboxylic acid tert-butyl ester by using the procedure  
30 as described in step-1 of intermediate-1 with some non-critical variations. Yield: 0.5 g (71 %); <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz) δ ppm: 1.51 (s, 9H), 2.61 (s, 3H), 3.08 – 3.11 (t, *J* = 6.0

Hz, 2H), 3.71 – 3.74 (t,  $J = 6.0$  Hz, 2H), 4.06 (s, 3H), 4.58 (s, 2H); Mass (m/z): 332.0 (M+H)<sup>+</sup>.

**Step-4: 5-Methyl-3-oxo-1,2,3,6,8,9-hexahydro-2,4,7-triaza-cyclopenta[a]naphthalene-7-carboxylic acid tert-butyl ester**

5 5-Methyl-3-oxo-1,2,3,6,8,9-hexahydro-2,4,7-triaza-cyclopenta[a]naphthalene-7-carboxylic acid tert-butyl ester was prepared from 5-cyano-8-methyl-3,4-dihydro-1H-[2,7]naphthyridine-2,6-dicarboxylic acid 2-tert-butyl ester 6-methyl ester by using the procedure as described in step-2 of intermediate-1 with some non-critical variations. Yield: 0.3 g (65 %); <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  ppm: 1.51 (s, 9H), 2.60 (s, 3H), 2.73 – 2.82  
10 (t,  $J = 6.0$  Hz, 2H), 3.72 – 3.75 (t,  $J = 6.0$  Hz, 2H), 4.35 (s, 2H), 4.59 (s, 2H), 6.57 (bs, 1H); Mass (m/z): 304.1 (M+H)<sup>+</sup>

**Step-5: 5-Methyl-1,2,3,6,8,9-hexahydro-2,4,7-triaza-cyclopenta[a]naphthalene-7-carboxylic acid tert-butyl ester**

Borane dimethylsulfide complex (2M in THF, 4.5 mL, 0.009 mol) was added dropwise to a  
15 solution of 5-methyl-3-oxo-1,2,3,6,8,9-hexahydro-2,4,7-triaza-cyclopenta[a]naphthalene-7-carboxylic acid tert-butyl ester (0.55 g, 0.0018 mol) at 0 °C. The reaction mixture was stirred under reflux for 18 h, then it was cooled to 0 °C and quenched via slow addition of methanol (2.5 mL) followed by water (10 mL). Then product extracted with ethyl acetate (3 x 50 mL). The organic extracts were combined, washed with brine (25 mL), dried over  
20 Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated in vacuo to obtain a residual mass that was purified by column chromatography using 2 - 5 % MeOH in DCM to obtain the title compound. Yield: 0.17 g (32 %); <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  ppm: 1.50 (s, 9H), 2.45 (s, 3H), 2.66 – 2.68 (m, 2H), 3.49 – 3.74 (m, 4H), 4.44 – 4.59 (m, 4H), 10.31 (bs, 1H); Mass (m/z): 290.1 (M+H)<sup>+</sup>.

25 **Intermediate 20: 5-Methyl-1,2,3,6,7,9-hexahydro-2,4,8-triaza-cyclopenta[a]naphthalene-8-carboxylic acid tert-butyl ester**

5-Methyl-1,2,3,6,7,9-hexahydro-2,4,8-triaza-cyclopenta[a]naphthalene-8-carboxylic acid tert-butyl ester was synthesized by following step-1 to step-5 of intermediate-19 using suitable starting materials with some non-critical variations. Mass (m/z): 290.3 (M+H)<sup>+</sup>.

30 **Intermediate-21: 7-Benzyl-2,3,5,6,7,8-hexahydro-1H-2,4,7-triaza-cyclopenta[b]naphthalenehydrochloride**

**Step-1: 6-Benzyl-2-oxo-1,2,5,6,7,8-hexahydro-[1,6]naphthyridine-3-carbonitrile**

DMF.DMA (14 mL, 0.015 mol) was added to a stirred solution of 1-benzyl-4-piperidine (20 g, 0.015 mol) in toluene (100 mL) and the reaction mixture was heated to 105 °C for 16 h. The reaction mixture was cooled to RT and concentrated to obtain a pale red oil that was dissolved in DMF (80 mL) and cooled to 0 °C. NaH (60% dispersion in mineral oil, 7.6 g, 0.190 mol) followed by cyano acetamide (8.8 g, 0.105 mol) were added to above reaction mixture at 0 – 5 °C and the reaction mixture was stirred at RT for 16 h. The reaction mixture was diluted with water (100 mL) and product was extracted using DCM (100 mL x 3). The organic extracts were combined, washed with brine (50 mL x 2), dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated in vacuo to obtain a residual mass that was purified by column chromatography using 2 - 5 % MeOH in DCM to obtain the title compound. Yield: 8.5 g (88%); <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ ppm: 2.51 – 2.66 (m, 2H), 3.26 – 3.28 (m, 2H), 3.61 – 3.63 (m, 2H), 4.26 – 4.28 (m, 2H), 7.26 – 7.36 (m, 6H), 7.89 (s, 1H); Mass (m/z): 265.7 (M+H)<sup>+</sup>.

**Step-2: 6-Benzyl-2-chloro-5,6,7,8-tetrahydro-[1,6]naphthyridine-3-carbonitrile**

6-Benzyl-2-chloro-5,6,7,8-tetrahydro-[1,6]naphthyridine-3-carbonitrile was prepared from 6-benzyl-2-oxo-1,2,5,6,7,8-hexahydro-[1,6]naphthyridine-3-carbonitrile by using the procedure as described in step-2 of intermediate-18 with some non-critical variations. Yield: 0.8 g (23 %); <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz) δ ppm: 2.84 – 2.87 (t, *J* = 6.0 Hz, 2H), 3.06 – 3.09 (t, *J* = 6.0 Hz, 2H), 3.59 – 3.61 (m, 2H), 3.72 – 3.73 (m, 2H), 7.26 – 7.35 (m, 5H), 7.37 (s, 1H); Mass (m/z): 283.9 (M+H)<sup>+</sup>.

**Step-3: 6-Benzyl-3-cyano-5,6,7,8-tetrahydro-[1,6]naphthyridine-2-carboxylic acid methyl ester**

6-Benzyl-3-cyano-5,6,7,8-tetrahydro-[1,6]naphthyridine-2-carboxylic acid methyl ester was prepared from 6-benzyl-2-chloro-5,6,7,8-tetrahydro-[1,6]naphthyridine-3-carbonitrile by using the procedure as described in step-1 of intermediate-1 with some non-critical variations. Yield: 0.62 (69.8 %); <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz) δ ppm: 2.89 – 2.92 (m, 2H), 3.18 – 3.20 (m, 2H), 3.68 – 3.70 (m, 2H), 3.73 – 3.75 (m, 2H), 4.05 (s, 3H), 7.26 – 7.36 (m, 5H), 7.73 (s, 1H); Mass (m/z): 307.7 (M+H)<sup>+</sup>.

**Step-4: 7-Benzyl-1,2,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-3-one**

7-Benzyl-1,2,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-3-one was prepared from 6-benzyl-3-cyano-5,6,7,8-tetrahydro-[1,6]naphthyridine-2-carboxylic acid methyl ester by using the procedure as described in step-2 of intermediate-1 with some non-critical

variations. Yield: 0.25g (43 %);  $^1\text{H}$  – NMR (DMSO- $d_6$ , 400 MHz)  $\delta$  ppm: 2.80 – 2.83 (t,  $J$  = 6.0 Hz, 2H), 2.99 – 3.02 (t,  $J$  = 6.0 Hz, 2H), 3.30 – 3.37 (m, 2H), 3.67 – 3.70 (m, 2H), 4.29 (s, 2H), 7.27 – 7.38 (m, 5H), 7.68 (s, 1H), 8.80 (s, 1H); Mass (m/z): 279.9 (M+H) $^+$ .

**Step-5: 7-Benzyl-3-oxo-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalene-2-carboxylic acid tert-butyl ester**

7-Benzyl-3-oxo-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalene-2-carboxylic acid tert-butyl ester was prepared from 7-benzyl-1,2,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-3-one by using the procedure as described in step-3 of intermediate-1 with some non-critical variations. Yield: 0.25 g (70 %);  $^1\text{H}$  – NMR (CDCl $_3$ , 400 MHz)  $\delta$  ppm: 1.60 (s, 9H), 2.88 – 2.91 (t,  $J$  = 12.4 Hz, 2H), 3.20 – 3.23 (t,  $J$  = 11.6 Hz, 2H), 3.72 – 3.74 (m, 4H), 4.67 (s, 2H), 7.33 – 7.37 (m, 5H), 7.42 (s, 1H); Mass (m/z): 380.0 (M+H) $^+$ .

**Step-6: 7-Benzyl-3-hydroxy-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalene-2-carboxylic acid tert-butyl ester**

7-Benzyl-3-hydroxy-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalene-2-carboxylic acid tert-butyl ester was prepared from 7-benzyl-3-oxo-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalene-2-carboxylic acid tert-butyl ester by using the procedure as described in step-4 of intermediate-1 with some non-critical variations. Yield: 0.22g (99 %); Mass (m/z): 382.1 (M+H) $^+$ .

**Step 7: 7-Benzyl-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalene-2-carboxylic acid tert-butyl ester**

7-Benzyl-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalene-2-carboxylic acid tert-butyl ester was prepared from 7-benzyl-3-hydroxy-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalene-2-carboxylic acid tert-butyl ester by using the procedure as described in step-5 of intermediate-1 with some non-critical variations. Yield: 0.05 g (15 %);  $^1\text{H}$  – NMR (CDCl $_3$ , 400 MHz)  $\delta$  ppm: 1.51 (s, 9H), 2.90 – 2.92 (m, 2H), 3.06 – 3.15 (m, 2H), 3.66 – 3.68 (m, 2H), 3.76 – 3.80 (m, 2H), 4.60 – 4.75 (m, 4H), 7.26 – 7.38 (m, 6H); Mass (m/z): 365.8(M+H) $^+$ .

**Step-8: 7-Benzyl-2,3,5,6,7,8-hexahydro-1H-2,4,7-triaza-cyclopenta[b]naphthalenehydrochloride**

7-Benzyl-2,3,5,6,7,8-hexahydro-1H-2,4,7-triaza-cyclopenta[b]naphthalenehydrochloride was prepared from 7-benzyl-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalene-

2-carboxylic acid tert-butyl ester by using the procedure as described in step-6 of intermediate-1 with some non-critical variations. Yield: 3.81 (77 %);  $^1\text{H}$  – NMR ( $\text{CD}_3\text{OD}$ , 400 MHz)  $\delta$  ppm: 3.08 – 3.21 (m, 2H), 4.40 – 4.42 (m, 2H), 4.46 – 4.48 (m, 4H), 4.60 – 4.75 (m, 4H), 7.44– 7.51 (m, 5H), 7.61 (s, 1H); Mass (m/z): 266.0 (M+H) $^+$ .

5 **Intermediate-22: (8-Benzyl-2,3,6,7,8,9-hexahydro-1H-2,4,8-triaza-cyclopenta[a]naphthalen-5-yl)-methanol hydrochloride**

**Step-1: 6-Benzyl-4-cyano-5,6,7,8-tetrahydro-[2,6]naphthyridine-1,3-dicarboxylic acid dimethyl ester**

A stirred solution of 6-benzyl-1,3-dichloro-5,6,7,8-tetrahydro-[2,6]naphthyridine-4-carbonitrile (20 g, 0.063 mol, prepared as per the procedure disclosed in intermediate 2 on page 56 of WO2023285583) was reacted with carbon monoxide by using the procedure as described in step-1 of intermediate-1 with some non-critical variations to obtain the title compound. Yield: 11.0 g (47 %);  $^1\text{H}$  – NMR ( $\text{DMSO}-d_6$ , 400 MHz)  $\delta$  ppm: 2.74 – 2.76 (t,  $J$  = 5.6 Hz, 2H), 3.04 – 3.06 (t,  $J$  = 5.6 Hz, 2H), 3.77 (s, 2H), 3.85 (s, 2H), 3.91 (s, 3H), 3.93 (s, 3H), 7.28 – 7.37 (m, 5H); Mass (m/z): 366.2 (M+H) $^+$ .

**Step-2: 8-Benzyl-3-oxo-2,3,6,7,8,9-hexahydro-1H-2,4,8-triaza-cyclopenta[a]naphthalene-5-carboxylic acid methyl ester**

8-Benzyl-3-oxo-2,3,6,7,8,9-hexahydro-1H-2,4,8-triaza-cyclopenta[a]naphthalene-5-carboxylic acid methyl ester was prepared from 6-benzyl-4-cyano-5,6,7,8-tetrahydro-[2,6]naphthyridine-1,3-dicarboxylic acid dimethyl ester by using the procedure as described in step-2 of intermediate-1 with some non-critical variations. Yield: 1.6 g (80 %, as such crude proceeded next step); Mass (m/z): 338.2 (M+H) $^+$ .

**Step-3: 8-Benzyl-3-oxo-1,3,6,7,8,9-hexahydro-2,4,8-triaza-cyclopenta[a]naphthalene-2,5-dicarboxylic acid 2-tert-butyl ester 5-methyl ester**

8-Benzyl-3-oxo-1,3,6,7,8,9-hexahydro-2,4,8-triaza-cyclopenta[a]naphthalene-2,5-dicarboxylic acid 2-tert-butyl ester 5-methyl ester was prepared from 8-benzyl-3-oxo-2,3,6,7,8,9-hexahydro-1H-2,4,8-triaza-cyclopenta[a]naphthalene-5-carboxylic acid methyl ester by using the procedure as described in step-3 of intermediate-1 with some non-critical variations. Yield: 0.9 g (45 %);  $^1\text{H}$  – NMR ( $\text{DMSO}-d_6$ , 400 MHz)  $\delta$  ppm: 1.53 (s, 9H), 2.68 – 2.71 (t,  $J$  = 5.8 Hz, 2H), 3.03 – 3.06 (t,  $J$  = 5.6 Hz, 2H), 3.73 – 3.77 (m, 4H), 3.89 (s, 3H), 4.74 (s, 2H), 7.29 – 7.39 (m, 5H); Mass (m/z): 438.3 (M+H) $^+$ .



**Step- 4: 8-Benzyl-3-hydroxy-5-hydroxymethyl-1,3,6,7,8,9-hexahydro-2,4,8-triaza-cyclopenta[a]naphthalene-2-carboxylic acid tert-butyl ester**

Lithium borohydride (1.97 mL, 4M in THF, 0.0078 mol) was added to a stirred solution of 8-benzyl-3-oxo-1,3,6,7,8,9-hexahydro-2,4,8-triaza-cyclopenta[a]naphthalene-2,5-

- 5 dicarboxylic acid 2-tert-butyl ester 5-methyl ester (2.3 g, 0.005 mole) in THF (50 mL) at 0 °C – 5 °C and maintained at RT for 2 h. The reaction mass was cooled to 0 °C – 5 °C and water (1mL) was added followed by addition of ethyl acetate (75 mL) and stirred for 1 h at RT. The reaction mixture was filtered through hyflow and the organic layer was separated. The organic layer was dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated in vacuo to obtain the  
10 title compound. Yield: 1.9 g (90 %); Mass (m/z): 412.2 (M+H)<sup>+</sup>.

**Step- 5: 8-Benzyl-5-hydroxymethyl-1,3,6,7,8,9-hexahydro-2,4,8-triaza-cyclopenta[a]naphthalene-2-carboxylic acid tert-butyl ester**

8-Benzyl-5-hydroxymethyl-1,3,6,7,8,9-hexahydro-2,4,8-triaza-cyclopenta[a]naphthalene-2-carboxylic acid tert-butyl ester was prepared from 8-benzyl-3-hydroxy-5-hydroxymethyl-

- 15 1,3,6,7,8,9-hexahydro-2,4,8-triaza-cyclopenta[a]naphthalene-2-carboxylic acid tert-butyl ester by using the procedure as described in step-5 of intermediate-1 with some non-critical variations. Yield: 0.6 g (22 %); <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz) δ ppm: 1.53 (s, 9H), 2.64 – 2.66 (m, 2H), 2.77 – 2.82 (m, 2H), 3.48 – 3.48 (d, J = 2.8 Hz, 2H), 3.70 – 3.72 (m, 3H), 4.48 – 4.50 (m, 2H), 4.67 – 4.69 (m, 4H), 7.28 – 7.37 (m, 5H); Mass (m/z): 396.2 (M+H)<sup>+</sup>.

- 20 **Step-6: (8-Benzyl-2,3,6,7,8,9-hexahydro-1H-2,4,8-triaza-cyclopenta[a]naphthalen-5-yl)-methanol hydrochloride**

(8-Benzyl-2,3,6,7,8,9-hexahydro-1H-2,4,8-triaza-cyclopenta[a]naphthalen-5-yl)-methanol hydrochloride was prepared by using the procedure as described in step-6 of intermediate-1 with some non-critical variations. Yield: 0.28 g (84 %); Mass (m/z): 295.3 (M+H)<sup>+</sup>.

- 25 **Intermediate-23: [1-(2-Trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-acetic acid**

**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 3-ethoxycarbonylmethyl-azetidine-1-carboxylic acid tert-butyl ester (20 g, 0.0823 mol; prepared by following the experimental procedure in *ACS Medicinal Chemistry Letters*  
30 2021, 12(10), 1585-1588) at RT and maintained for overnight and then reaction mixture was 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)<sup>+</sup>.

**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, 0.083 mol) 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 EtOAc (100 mL x 3). The organic extracts were combined, washed with brine (50 mL), dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated in vacuo to obtain a residual mass that was purified by column chromatography using 15 - 25 % EtOAc in hexane to obtain the title compound. Yield: 20 g (83 %): <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 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* = 1.0 Hz, 1H), 8.27 – 8.28 (d, *J* = 5.6 Hz, 1H); Mass (m/z): 289.1 (M+H)<sup>+</sup>.

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

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 °C – 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 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 %): <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 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)<sup>+</sup>.

**Intermediate-24: [1-(6-Trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-acetic acid****Step-1: [1-(6-Trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-acetic acid ethyl ester**

Pd<sub>2</sub>dba<sub>3</sub> (0.72 g, 0.0007 mol), BINAP (0.82 g, 0.001 mol) followed by Cs<sub>2</sub>CO<sub>3</sub> (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-23) and 5-bromo-2-trifluoromethyl-pyridine (5.7 g, 0.036 mol) in toluene (60 mL) and the reaction mixture was refluxed under nitrogen 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 Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated in vacuo to obtain a residual mass that was purified by column chromatography using 15 - 25 % EtOAc in hexane to obtain the title compound. Yield: 2.9 g (20 %); <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 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), 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)<sup>+</sup>.

#### 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-24) was prepared from [1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-acetic acid ethyl ester (step-1 compound) by using the procedure as described for step-3 of intermediate-23 with some non-critical variations. Yield: 1.5 g (55 %); <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 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 (bs, 1H); Mass (m/z): 261.0 (M+H)<sup>+</sup>.

#### Intermediate-25: (1-Pyridin-3-yl)-azetidin-3-yl)-acetic acid

Intermediate-25 was prepared by following the experimental procedure given in step-1 and step-2 of intermediate-24 with some non-critical variations using suitable starting material. <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz) δ ppm: 2.57 – 2.59 (d, *J* = 7.6 Hz, 2H), 2.95 – 2.99 (m, 1H), 3.49 – 3.53 (t, *J* = 6.80 Hz, 2H), 3.97 – 4.00 (t, *J* = 7.60 Hz, 2H), 6.77 – 6.79 (m, 1H), 7.11 – 7.15 (m, 1H), 7.77 – 7.78 (d, *J* = 2.4 Hz, 1H), 7.96 – 7.97 (d, *J* = 2.4 Hz, 1H), 12.05 (bs, 1H); Mass (m/z): 193.1 (M+H)<sup>+</sup>.

#### Intermediate-26: [1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-acetic acid

##### Step-1: 4-Chloro-2-difluoromethyl-pyridine

DAST (13.65 g, 0.085 mol) was added to a stirred solution of 4-chloro-pyridine-2-carbaldehyde (10.0 g, 0.071 mol) in DCM (100 mL) at -35 °C to -40 °C and stirred for 4 h and then stirred at RT for 16 h. The reaction mixture was poured on to water and product was extracted using DCM (75 mL x 5). The organic extracts were combined, washed with brine (100 mL), dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated in vacuo to obtain the title compound. Yield: 9.0 g (77 %); <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz) δ ppm: 6.48 – 6.76 (m, 1H), 7.41 – 7.43 (m, 1H), 7.65 – 7.66 (d, *J* = 2.0 Hz, 1H), 8.55 – 8.57 (d, *J* = 5.2 Hz, 1H); Mass (m/z): 164.5 (M+H)<sup>+</sup>.

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

[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-acetic acid ethyl ester was prepared from 4-chloro-2-difluoromethyl-pyridine by using the procedure as described in step-2 of intermediate-23 with some non-critical variations. Yield: 4.0 g (48 %); <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz) δ ppm: 1.31 – 1.34 (m, 3H), 2.72 – 2.74 (d, 2H), 3.14 – 3.18 (m, 1H), 3.67 – 3.69 (m, 2H), 3.70 (s, 3H), 4.16 – 4.20 (t, *J* = 8.2 Hz, 2H), 6.26 – 6.28 (m, 1H), 6.36 – 6.64 (m, 1H), 8.21 – 8.23 (d, *J* = 5.6 Hz, 1H); Mass (m/z): 271.1 (M+H)<sup>+</sup>.

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

[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-acetic acid was prepared from [1-(2-difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-acetic acid ethyl ester by using the procedure as described in step-3 of intermediate-23 with some non-critical variations. Yield: Quantitative; <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 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)<sup>+</sup>.

**Intermediate-27: [1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-acetic acid****Step-1: [1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-acetic acid ethyl ester**

[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-acetic acid ethyl ester was prepared by using the procedure as described in step-2 of intermediate-23 with some non-critical variations. Mass (m/z): 284.5, 286.9 (M+H)<sup>+</sup>.

**Step-2: [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 from [1-(2-chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-acetic acid ethyl ester by using the procedure as described in step-3 of intermediate-23 with some non-critical variations. <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 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)<sup>+</sup>.

**Intermediate-28: [1-(5-Trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-acetic acid****Step-1: [1-(5-Trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-acetic acid ethyl ester**

[1-(5-Trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-acetic acid ethyl ester was prepared by using the procedure as described in step-2 of intermediate-23 with some non-critical variations. Mass (m/z): 290.2 (M+H)<sup>+</sup>

**Step-2: [1-(5-Trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-acetic acid**

[1-(5-Trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-acetic acid was prepared from [1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-acetic acid ethyl ester by using the procedure as described in step-3 of intermediate-23 with some non-critical variations. Yield: 0.6 g (52 %); <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ ppm: 2.65 – 2.67 (d, *J* = 8.0 Hz, 2H), 2.95 – 3.02 (m, 1H), 3.79 – 3.82 (m, 2H), 4.21 – 4.25 (m, 2H), 8.65 (s, 2H), 12.27 (s, 1H); Mass (m/z): 261.8, (M+H)<sup>+</sup>

**Intermediate-29: (1-Pyrimidin-5-yl)-azetidin-3-yl)-acetic acid****Step-1: (1-Pyrimidin-5-yl)-azetidin-3-yl)-acetic acid ethyl ester**

(1-Pyrimidin-5-yl)-azetidin-3-yl)-acetic acid ethyl ester was prepared by using the procedure as described in step-1 of intermediate-24 with some non-critical variations. Mass (m/z): 222.5 (M+H)<sup>+</sup>.

**Step-2: (1-Pyrimidin-5-yl)-azetidin-3-yl)-acetic acid**

(1-Pyrimidin-5-yl)-azetidin-3-yl)-acetic acid was prepared from (1-pyrimidin-5-yl)-azetidin-3-yl)-acetic acid ethyl ester by using the procedure as described in step-3 of intermediate-23 with some non-critical variations. Yield: 0.6 g (48 %); <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ ppm: 2.63 – 2.65 (d, *J* = 8.0 Hz, 2H), 2.98 – 3.00 (m, 1H), 3.60 – 3.62 (t, *J* = 6.4 Hz, 2H), 4.05 – 4.09 (t, *J* = 7.6 Hz, 2H), 8.00 (s, 2H), 8.51 (s, 1H), 12.25 (s, 1H); Mass (m/z): 193.9 (M+H)<sup>+</sup>.

**Intermediate-30: (1-Pyridin-4-yl)-azetidin-3-yl)-acetic acid****Step-1: (1-Pyridin-4-yl)-azetidin-3-yl)-acetic acid ethyl ester**

(1-Pyridin-4-yl)-azetidin-3-yl)-acetic acid ethyl ester was prepared by using the procedure as described in step-2 of intermediate-23 with some non-critical variations. Mass (m/z): 220.9 (M+H)<sup>+</sup>.

**Step-2: (1-Pyridin-4-yl)-azetidin-3-yl)-acetic acid**

(1-Pyridin-4-yl)-azetidin-3-yl)-acetic acid was prepared from (1-pyridin-4-yl)-azetidin-3-yl)-acetic acid ethyl ester by using the procedure as described in step-3 of intermediate-23 with some non-critical variations. Yield: 1.0 g (33 %); <sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>OD) δ 2.54 (d, *J* = 7.53 Hz, 2H), 3.06 – 3.20 (m, 1H), 3.69 (dd, *J* = 5.52, 8.53 Hz, 2H), 4.10 – 4.20 (m, 2H), 6.31 – 6.41 (m, 2H), 7.97 – 8.06 (m, 2H); Mass (m/z): 193.1 (M+H)<sup>+</sup>.

**Intermediate-31: 1-(2-Trifluoromethyl-pyridin-4-yl)-3(R)-pyrrolidine carboxylic acid**

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

1-(2-Trifluoromethyl-pyridin-4-yl)-3(R)-pyrrolidine carboxylic acid methyl ester was prepared from 4-bromo-2-trifluoromethyl-pyridine and pyrrolidine-3(R)-carboxylic acid methyl ester by following the procedure given in step-2 of intermediate 23 with some non-critical variations. Yield: Quantitative; Mass (m/z): 274.9 (M+H)<sup>+</sup>.

**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 23 with some non-critical variations. Yield: 7.5 g (52 %); <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 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 (s, 1H), 8.20 – 8.21 (d, *J* = 6.0 Hz, 1H), 11.91 (bs, 1H); Mass (m/z): 260.9 (M+H)<sup>+</sup>.

**Intermediate-32: 1-(6-Trifluoromethyl-pyridin-3-yl)-3(R)-pyrrolidine carboxylic acid****Step-1: 1-(6-Trifluoromethyl-pyridin-3-yl)-3(R)-pyrrolidine carboxylic acid methyl ester**

1-(6-Trifluoromethyl-pyridin-3-yl)-3(R)-pyrrolidine-3-carboxylic acid methyl ester was prepared from 5-bromo-2-trifluoromethyl-pyridine and pyrrolidine-3(R)-carboxylic acid methyl ester by using the procedure as described in step-1 of intermediate-24 with some non-critical variations. Mass (m/z): 275.2 (M+H)<sup>+</sup>.

**Step-2: 1-(6-Trifluoromethyl-pyridin-3-yl)-3(R)-pyrrolidine carboxylic acid**

1-(6-Trifluoromethyl-pyridin-3-yl)-3(R)-pyrrolidine carboxylic acid was prepared from 1-(6-trifluoromethyl-pyridin-3-yl)-3(R)-pyrrolidine carboxylic acid methyl ester by following the procedure given in step-3 of intermediate-23 with some non-critical variations. Yield: 2.1 g (67 %); <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ ppm: 2.14 – 2.17 (m, 2H), 3.18 – 3.25 (m, 1H), 3.39 – 3.58 (m, 2H), 3.37 – 3.56 (m, 2H), 6.99 – 7.02 (dd, *J* = 2.0, 8.8 Hz, 1H), 7.57 – 7.59 (d, *J* = 8.4 Hz, 1H), 8.04 (s, 1H), 11.05 (bs, 1H); Mass (m/z): 261.0 (M+H)<sup>+</sup>.

**Intermediate-33: 1-(2-Difluoromethyl-pyridin-4-yl)-3(R)-pyrrolidine carboxylic acid****Step-1: 1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidine-3(R)-carboxylic acid methyl ester**

1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidine-3(R)-carboxylic acid methyl ester was prepared from 4-chloro-2-difluoromethyl pyridine and pyrrolidine-3(R)-carboxylic acid

methyl ester by using the procedure as described in step-2 of intermediate-26 with some non-critical variations. Mass (m/z): 257.2 (M+H)<sup>+</sup>.

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

1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidine-3(R)-carboxylic acid was prepared by following the procedure given in step-3 of intermediate-23 with some non-critical variations. Yield: 1.9 g (61%); <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ ppm: 2.13 – 2.26 (m, 2H), 3.18 – 3.31 (m, 1H), 3.33 – 3.39 (m, 2H), 3.46 – 3.55 (m, 2H), 6.57 – 6.58 (d, *J* = 2.4 Hz, 1H), 6.69 – 6.70 (d, *J* = 2.4 Hz, 1H), 6.59 – 6.87 (m, 1H), 8.15 – 8.16 (d, *J* = 6.0 Hz, 1H), 12.34 (s, 1H); Mass (m/z): 242.9 (M+H)<sup>+</sup>.

**Intermediate-34: 1-Pyridin-3-yl-pyrrolidine-3(R)-carboxylic acid**

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

1-Pyridin-3-yl-pyrrolidine-3(R)-carboxylic acid methyl ester was prepared from 3-bromopyridine and pyrrolidine-3(R)-carboxylic acid methyl ester by using the procedure as described in step-1 of intermediate-25 with some non-critical variations. Mass (m/z): 207.2 (M+H)<sup>+</sup>.

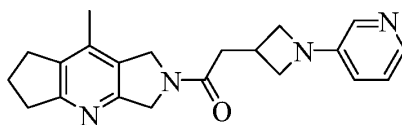
**Step-2: 1-Pyridin-3-yl-pyrrolidine-3(R)-carboxylic acid**

1-Pyridin-3-yl-pyrrolidine-3(R)-carboxylic acid was prepared from 1-Pyridin-3-yl-pyrrolidine-3(R)-carboxylic acid methyl ester by using the procedure as described in step-3 of intermediate-23 with some non-critical variations. Yield: 1.0 g (33 %); <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ ppm: 2.00 – 2.16 (m, 2H), 2.75 – 2.82 (m, 1H), 3.15 – 3.23 (m, 2H), 3.26 – 3.43 (m, 2H), 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 (s, 1H), 12.01 (bs, 1H); Mass (m/z): 193.1 (M+H)<sup>+</sup>.

**Intermediate-35: 6-Benzyl-9-methyl-2,3,5,6,7,8-hexahydro-1H-pyrrolo[3,4-b][1,7]naphthyridine hydrochloride**

**Step-1:** 6-Benzyl-9-methyl-2,3,5,6,7,8-hexahydro-1H-pyrrolo[3,4-b][1,7]naphthyridine hydrochloride was prepared by following step 1 – 8 of intermediate-18 with some non-critical variations using suitable starting materials. <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ ppm: 2.21 (s, 3H), 3.03 – 3.06 (m, 2H), 3.43 – 3.47 (m, 2H), 4.39 – 4.43 (m, 4H), 4.50 – 4.58 (m, 4H), 7.50 – 7.51 (m, 3H), 7.64 – 7.65 (m, 2H), 9.85 (bs, 1H), 11.24 (bs, 1H); Mass (m/z): 280.1 (M+H)<sup>+</sup>.

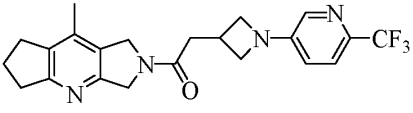
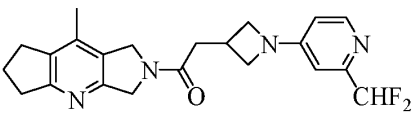
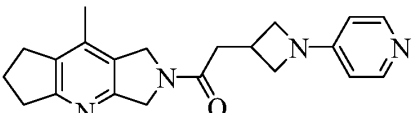
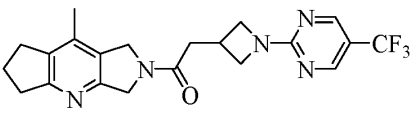
**Example-1: 1-(8-methyl-3,5,6,7-tetrahydro-1H-2,4-diaza-s-indacen-2-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone**

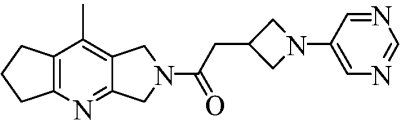
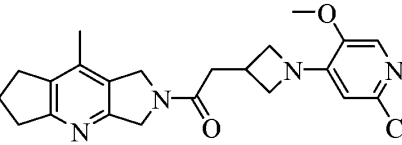
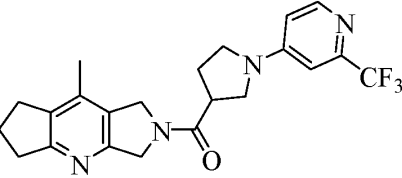


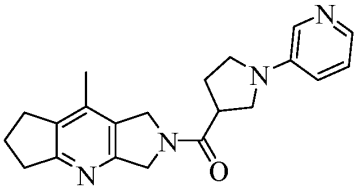
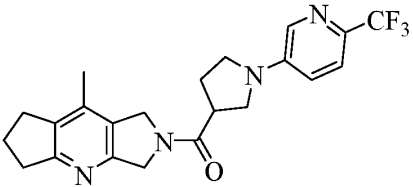
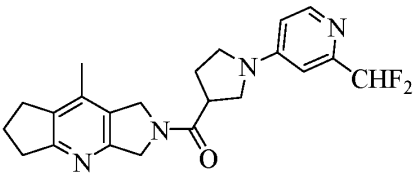
- HATU (5.94 g, 0.015 mol) was added to a stirred solution of (1-pyridin-3-yl-azetidin-3-yl)-acetic acid (2 g, 0.0104 mol, Intermediate-25) in DMF (10 mL), followed by the addition of 8-methyl-1,2,3,5,6,7-hexahydro-2,4-diaza-s-indacene hydrochloride (2.63 g, 0.012 mol, Intermediate-1) and diisopropylethylamine (7.3 mL, 0.041 mol) and the reaction mixture stirred at RT for 18 h. The reaction mixture was then poured onto cold water (25 mL) and product extracted using DCM (25 mL x 3). The organic extracts were combined, washed with brine (25 mL), dried over Na<sub>2</sub>SO<sub>4</sub>, filtered 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: 1.58 g (43 %); <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ ppm: 2.02–2.09 (m, 2H), 2.15 – 2.16 (d, *J* = 4.0 Hz, 3H), 2.81 – 2.90 (m, 6H), 3.07 – 3.11 (m, 1H), 3.55 – 3.58 (m, 2H), 4.03 – 4.06 (m, 2H), 4.52 (s, 1H), 4.57 (s, 1H), 4.75 (s, 1H), 4.80 (s, 1H), 6.78 – 6.81 (m, 1H), 7.12 – 7.15 (m, 1H), 7.79 – 7.80 (d, *J* = 2.8 Hz, 1H), 7.88 – 7.89 (d, *J* = 4.8 Hz, 1H); Mass (m/z): 349.0 (M+H)<sup>+</sup>.
- The following Example-2 to Example-124 were prepared by following the experimental procedure of preparation as described in the Example-1 using suitable intermediates (synthesized above) with some non-critical variations.

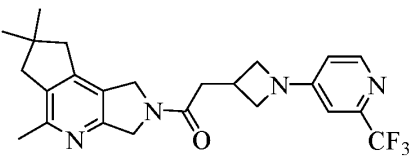
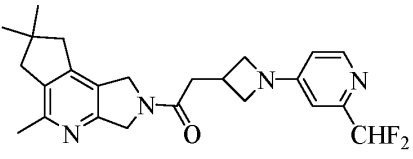
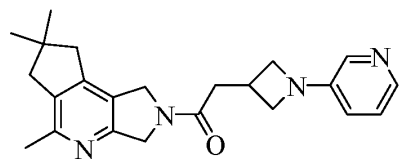
| Example | Chemical structure and IUPAC Name                                                                                             | Characterization Data                                                                                                                                                                                                                                                                                                                                                                  |
|---------|-------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 2       | <br>1-(8-Methyl-3,5,6,7-tetrahydro-1H-2,4-diaza-s-indacen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.04 – 2.15 (m, 2H), 2.15 – 2.16 (d, <i>J</i> = 3.6 Hz, 3H), 2.81 – 2.90 (m, 6H), 3.12 – 3.13 (m, 1H), 3.69 – 3.72 (m, 2H), 4.15 – 4.19 (m, 2H), 4.52 (s, 1H), 4.57 (s, 1H), 4.75 (s, 1H), 4.80 (s, 1H), 6.51 – 6.53 (m, 1H), 6.70 – 6.71 (d, <i>J</i> = 2.0 Hz, 1H), 8.19 – 8.21 (d, <i>J</i> = 5.6 Hz, 1H); Mass |

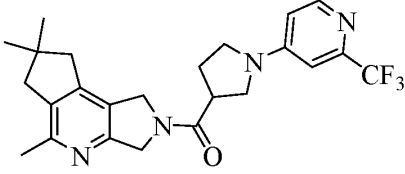
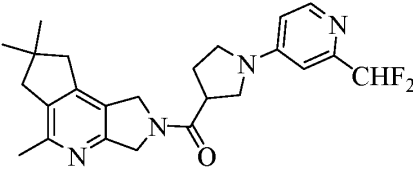
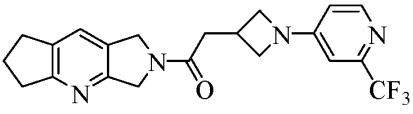


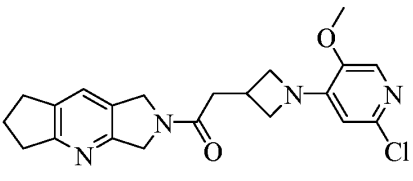
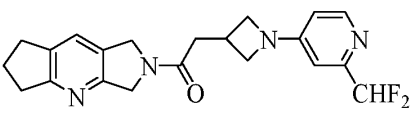
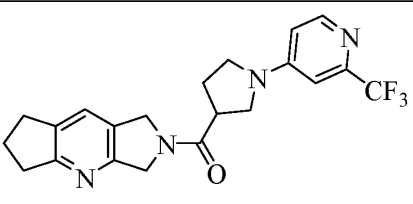
|   |                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|---|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|   |                                                                                                                                                                                                                      | (m/z): 416.9 (M+H) <sup>+</sup> .                                                                                                                                                                                                                                                                                                                                                                                                                              |
| 3 |  <p>1-(8-Methyl-3,5,6,7-tetrahydro-1H-2,4-diaza-s-indacen-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone</p>   | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.04 – 2.08 (m, 2H), 2.16 – 2.17 (d, <i>J</i> = 4.0 Hz, 3H), 2.81 – 2.90 (m, 6H), 3.12 – 3.16 (m, 1H), 3.68 – 3.71 (t, <i>J</i> = 5.6 Hz, 2H), 4.14 – 4.18 (t, <i>J</i> = 8.0 Hz, 2H), 4.53 (s, 1H), 4.57 (s, 1H), 4.75 (s, 1H), 4.80 (s, 1H), 6.88 – 6.91 (m, 1H), 7.57 – 7.59 (d, <i>J</i> = 8.8 Hz, 1H), 7.88 – 7.89 (d, <i>J</i> = 2.0 Hz, 1H); Mass (m/z): 416.9 (M+H) <sup>+</sup> . |
| 4 |  <p>2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(8-methyl-3,5,6,7-tetrahydro-1H-2,4-diaza-s-indacen-2-yl)-ethanone</p>   | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.04 – 2.07 (m, 2H), 2.15 – 2.17 (d, <i>J</i> = 4.8 Hz, 3H), 2.81 – 2.91 (m, 6H), 3.09 – 3.12 (m, 1H), 3.65 – 3.69 (m, 2H), 4.12 – 4.16 (t, <i>J</i> = 8.0 Hz, 2H), 4.52 (s, 1H), 4.57 (s, 1H), 4.75 (s, 1H), 4.80 (s, 1H), 6.44 – 6.45 (d, <i>J</i> = 2.0 Hz, 1H), 6.55 – 6.58 (m, 2H), 8.14 – 8.16 (d, <i>J</i> = 5.6 Hz, 1H); Mass (m/z): 399.3 (M+H) <sup>+</sup> .                    |
| 5 |  <p>1-(8-Methyl-3,5,6,7-tetrahydro-1H-2,4-diaza-s-indacen-2-yl)-2-(1-pyridin-4-yl)-azetidin-3-yl)-ethanone</p>                    | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.04 – 2.08 (m, 2H), 2.16 – 2.17 (d, <i>J</i> = 3.6 Hz, 3H), 2.81 – 2.90 (m, 6H), 3.61 – 3.76 (m, 1H), 4.09 – 4.23 (m, 4H), 4.52 (s, 1H), 4.57 (s, 1H), 4.75 (s, 1H), 4.80 (s, 1H), 6.46 – 6.48 (m, 2H), 8.12 – 8.14 (m, 2H); Mass (m/z): 349.0 (M+H) <sup>+</sup> .                                                                                                                       |
| 6 |  <p>1-(8-Methyl-3,5,6,7-tetrahydro-1H-2,4-diaza-s-indacen-2-yl)-2-[1-(3-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone</p> | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 2.15 – 2.18 (m, 2H), 2.20 (s, 3H), 2.79 – 2.89 (m, 4H), 2.99 – 3.04                                                                                                                                                                                                                                                                                                                                  |

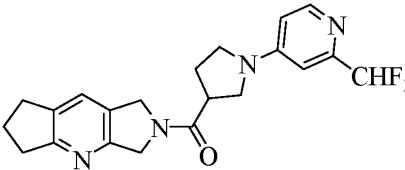
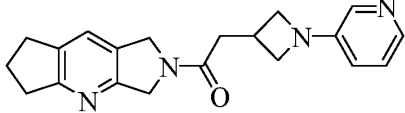
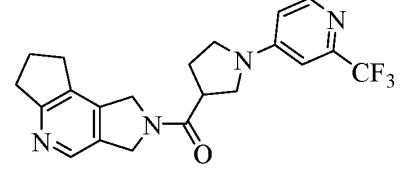
|   |                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                           |
|---|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|   | 1-(8-Methyl-3,5,6,7-tetrahydro-1 <i>H</i> -2,4-diaza-s-indacen-2-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone                                                                                         | (m, 2H), 3.25 – 3.29 (m, 1H), 3.91 – 3.96 (m, 2H), 4.42 – 4.47 (m, 2H), 4.72 – 4.77 (m, 4H), 8.47 (s, 2H); Mass (m/z): 418.6 (M+H) <sup>+</sup> .                                                                                                                                                                                                                                                                                         |
| 7 |  <p>1-(8-Methyl-3,5,6,7-tetrahydro-1<i>H</i>-2,4-diaza-s-indacen-2-yl)-2-(1-pyrimidin-5-yl)-azetidin-3-yl-ethanone</p>                      | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.04 – 2.08 (m, 2H), 2.16 – 2.17 (d, <i>J</i> = 3.2 Hz, 3H), 2.81 – 2.90 (m, 6H), 3.01 – 3.25 (m, 1H), 3.63 – 3.66 (t, <i>J</i> = 6.0 Hz, 2H), 4.12 – 4.14 (t, <i>J</i> = 6.8 Hz, 2H), 4.52 (s, 1H), 4.57 (s, 1H), 4.75 (s, 1H), 4.80 (s, 1H), 8.01 – 8.02 (d, <i>J</i> = 0.8 Hz, 2H), 8.50 – 8.51 (d, <i>J</i> = 0.4 Hz, 1H); Mass (m/z): 349.8 (M+H) <sup>+</sup> . |
| 8 |  <p>2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(8-methyl-3,5,6,7-tetrahydro-1<i>H</i>-2,4-diaza-s-indacen-2-yl)-ethanone</p> | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.04 – 2.08 (m, 2H), 2.16 – 2.17 (d, <i>J</i> = 2.0 Hz, 3H), 2.32 – 2.33 (m, 2H), 2.66 – 2.67 (m, 2H), 2.80 – 3.16 (m, 6H), 3.74 – 3.78 (m, 3H), 4.19 – 4.24 (m, 1H), 4.52 (s, 1H), 4.56 (s, 1H), 4.74 (s, 1H), 4.80 (s, 1H), 6.22 – 6.24 (m, 1H), 7.65 (s, 1H); Mass (m/z): 413.0 (M+H) <sup>+</sup> .                                                               |
| 9 |  <p>(8-Methyl-3,5,6,7-tetrahydro-1<i>H</i>-2,4-diaza-s-indacen-2-yl)-[1-(2-(trifluoromethyl)-pyridin-4-yl)-azetidin-3-yl]-ethanone</p>    | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 2.15 – 2.19 (m, 2H), 2.21 (s, 3H), 2.36 – 2.41 (m, 2H), 2.86 – 2.90 (t, <i>J</i> = 7.4 Hz, 2H), 3.00 – 3.03 (t, <i>J</i> = 7.2 Hz, 2H), 3.42 – 3.49 (m, 2H), 3.62 – 3.70 (m, 3H), 4.75 – 4.81 (m, 2H), 4.87 – 4.89 (m, 2H), 6.48 – 6.50                                                                                                                                         |

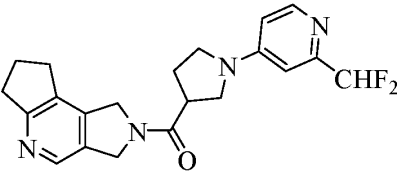
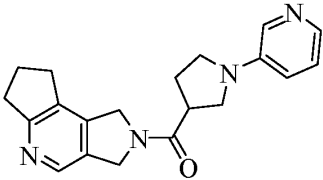
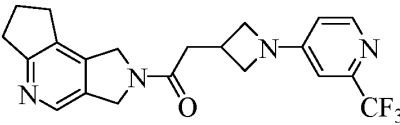
|    |                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
|----|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|    | trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone                                                                                                                                                            | (m, 1H), 6.75 – 6.76 (d, $J$ = 2.4 Hz, 1H), 8.29 – 8.30 (d, $J$ = 5.6 Hz, 1H); Mass (m/z): 416.8 (M+H) <sup>+</sup> .                                                                                                                                                                                                                                                                                                                                   |
| 10 |  <p>(8-Methyl-3,5,6,7-tetrahydro-1H-2,4-diaza-s-indacen-2-yl)-(1-pyridin-3-yl-pyrrolidin-3(R)-yl)-methanone</p>                       | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 2.13 – 2.15 (m, 2H), 2.21 (s, 3H), 2.35 – 2.40 (m, 2H), 2.86 – 2.90 (t, $J$ = 7.4 Hz, 2H), 3.00 – 3.03 (t, $J$ = 7.0 Hz, 2H), 3.40 – 3.43 (m, 2H), 3.53 – 3.59 (m, 1H), 3.62 – 3.65 (m, 2H), 4.76 – 4.81 (m, 2H), 4.87 – 4.89 (m, 2H), 6.84 – 6.87 (m, 1H), 7.12 – 7.15 (m, 1H), 7.95 – 7.97 (d, $J$ = 4.8 Hz, 1H), 8.01 – 8.01 (d, $J$ = 2.8 Hz, 1H); Mass (m/z): 349.1 (M+H) <sup>+</sup> . |
| 11 |  <p>(8-Methyl-3,5,6,7-tetrahydro-1H-2,4-diaza-s-indacen-2-yl)-[1-(6-trifluoromethyl-pyridin-3-yl)-pyrrolidin-3(R)-yl]-methanone</p> | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.03 – 2.09 (m, 2H), 2.17 – 2.18 (d, $J$ = 4.8 Hz, 3H), 2.33 – 2.36 (m, 2H), 2.82 – 2.91 (m, 4H), 3.38 – 3.68 (m, 4H), 3.69 – 3.70 (m, 1H), 4.57 (s, 1H), 4.88 (s, 1H), 4.91 (s, 1H), 4.96 (s, 1H), 7.01 – 7.04 (dd, $J$ = 2.4, 8.8 Hz, 1H), 7.58 – 7.61 (dd, $J$ = 2.0, 8.8 Hz, 1H), 8.06 (s, 1H); Mass (m/z): 417.0 (M+H) <sup>+</sup> .                                          |
| 12 |  <p>[1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(8-methyl-3,5,6,7-tetrahydro-1H-2,4-diaza-s-indacen-2-yl)-methanone</p>  | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 2.13 – 2.21 (m, 2H), 2.26 (s, 3H), 2.35 – 2.41 (m, 2H), 2.86 – 2.90 (t, $J$ = 7.6 Hz, 2H), 3.00 – 3.04 (t, $J$ = 7.6 Hz, 2H), 3.41 – 3.47 (m, 2H), 3.61 – 3.71 (m, 3H), 4.72 (s, 1H), 4.81 (s, 1H), 4.87 – 4.89 (m, 2H), 6.39 – 6.46                                                                                                                                                          |

|    |                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                 |
|----|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|    | 3,5,6,7-tetrahydro-1 <i>H</i> -2,4-diaza-s-indacen-2-yl)-methanone                                                                                                                                                                | (m, 2H), 6.71 – 6.72 (m, 1H), 8.22 – 8.24 (d, <i>J</i> = 6.0 Hz, 1H); Mass (m/z): 399.1 (M+H) <sup>+</sup> .                                                                                                                                                                                                                                                                                                                    |
| 13 |  <p>2-[1-(2-Trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(5,7,7-trimethyl-3,6,7,8-tetrahydro-1<i>H</i>-2,4-diaza-as-indacen-2-yl)-ethanone</p> | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 1.12 (s, 6H), 2.55 (s, 2H), 2.60 (s, 3H), 2.67 (s, 2H), 2.83 – 2.84 (d, <i>J</i> = 7.6 Hz, 2H), 3.02 – 3.04 (m, 1H), 3.69 – 3.71 (m, 2H), 4.12 – 4.15 (m, 2H), 4.51 (s, 1H), 4.56 (s, 1H), 4.73 (s, 1H), 4.79 (s, 1H), 6.52 – 6.53 (d, <i>J</i> = 4.4 Hz, 1H), 6.70 (s, 1H), 8.19 – 8.21 (d, <i>J</i> = 5.6 Hz, 1H); Mass (m/z): 445.3 (M+H) <sup>+</sup> . |
| 14 |  <p>2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(5,7,7-trimethyl-3,6,7,8-tetrahydro-1<i>H</i>-2,4-diaza-as-indacen-2-yl)-ethanone</p> | Mass (m/z): 427.5 (M+H) <sup>+</sup> .                                                                                                                                                                                                                                                                                                                                                                                          |
| 15 |  <p>2-(1-Pyridin-3-yl)-azetidin-3-yl]-1-(5,7,7-trimethyl-3,6,7,8-tetrahydro-1<i>H</i>-2,4-diaza-as-indacen-2-yl)-ethanone</p>                  | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 1.11 (s, 6H), 2.53 (s, 2H), 2.62 (s, 3H), 2.69 (s, 2H), 2.85 – 2.87 (d, <i>J</i> = 7.6 Hz, 2H), 3.02 – 3.04 (m, 1H), 3.69 – 3.71 (m, 2H), 4.14 – 4.17 (m, 2H), 4.53 (s, 1H), 4.55 (s, 1H), 4.73 (s, 1H), 4.76 (s, 1H), 6.69 – 6.71 (m, 1H), 7.09 – 7.11 (m, 1H), 7.85 – 7.86                                                                                |

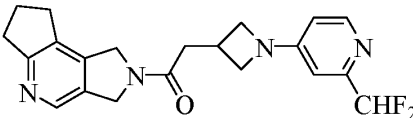
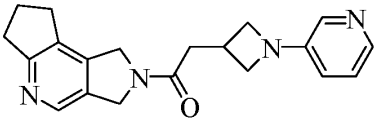
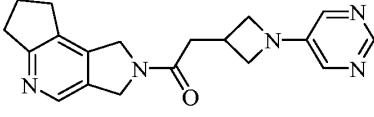
|    |                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                     |
|----|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|    |                                                                                                                                                                                                                              | (d, $J = 2.8$ Hz, 1H), 7.98 – 8.01 (m, 1H); Mass (m/z): 377.3 (M+H) <sup>+</sup> .                                                                                                                                                                                                                                                                                                  |
| 16 |  <p>[1-(2-Trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(5,7,7-trimethyl-3,6,7,8-tetrahydro-1H-2,4-diaza-as-indacen-2-yl)-methanone</p> | Mass (m/z): 445.5 (M+H) <sup>+</sup> .                                                                                                                                                                                                                                                                                                                                              |
| 17 |  <p>[1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(5,7,7-trimethyl-3,6,7,8-tetrahydro-1H-2,4-diaza-as-indacen-2-yl)-methanone</p> | Mass (m/z): 427.5 (M+H) <sup>+</sup> .                                                                                                                                                                                                                                                                                                                                              |
| 18 |  <p>1-(3,5,6,7-Tetrahydro-1H-2,4-diaza-s-indacen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone</p>                  | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) $\delta$ ppm: 2.03 – 2.10 (m, 2H), 2.84 – 2.90 (m, 6H), 3.13 – 3.15 (m, 1H), 3.68 – 3.72 (m 2H), 4.15 – 4.19 (t, $J = 8.2$ Hz, 2H), 4.53 – 4.58 (m, 2H), 4.75 – 4.80 (m, 2H), 6.51 – 6.53 (dd, $J = 2.4, 5.6$ Hz, 1H), 6.70 – 6.70 (d, $J = 2.4$ Hz, 1H), 7.57 – 7.58 (d, $J = 5.6$ Hz, 1H), 8.19 – 8.21 (d, $J = 5.6$ |

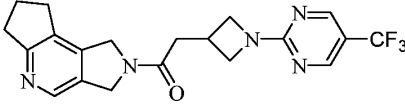
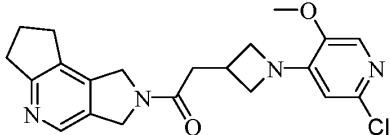
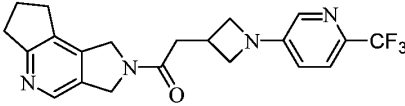
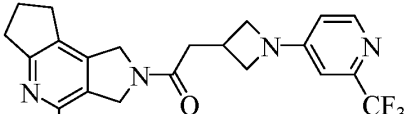
|    |                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
|----|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|    |                                                                                                                                                                                                               | Hz, 1H); Mass (m/z): 403.0 (M+H) <sup>+</sup> .                                                                                                                                                                                                                                                                                                                                                                                                                  |
| 19 |  <p>2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(3,5,6,7-tetrahydro-1H-2,4-diaza-s-indacen-2-yl)-ethanone</p>    | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.05 – 2.09 (m, 2H), 2.78 – 2.80 (m, 2H), 2.86 – 2.90 (m, 4H) 3.14 (m, 1H), 3.74 (m, 5H), 4.19 – 4.21 (t, <i>J</i> = 8.4 Hz, 2H), 4.52 (s, 1H), 4.58 (s, 1H), 4.74 (s, 1H), 4.80 (s, 1H), 6.23 (s, 1H), 7.57 – 7.58 (d, <i>J</i> = 4.4 Hz, 1H), 7.65 (s, 1H); Mass (m/z): 399.2 (M+H) <sup>+</sup> .                                                                                         |
| 20 |  <p>2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(3,5,6,7-tetrahydro-1H-2,4-diaza-s-indacen-2-yl)-ethanone</p>      | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.05 – 2.08 (m, 2H), 2.82 – 2.90 (m, 6H), 3.24 – 3.26 (m, 1H), 3.65 – 3.69 (m, 2H), 4.12 – 4.16 (t, <i>J</i> = 8.0 Hz, 2H), 4.53 (s, 1H), 4.59 (s, 1H), 4.75 (s, 1H), 4.80 (s, 1H), 6.42 – 6.44 (m, 1H), 6.55 – 6.55 (d, <i>J</i> = 2.0 Hz, 1H), 6.57 – 6.85 (m, 1H), 7.57 – 7.59 (d, <i>J</i> = 6.0 Hz, 1H), 8.14 – 8.16 (d, <i>J</i> = 5.2 Hz, 1H); Mass (m/z): 385.0 (M+H) <sup>+</sup> . |
| 21 |  <p>(3,5,6,7-Tetrahydro-1H-2,4-diaza-s-indacen-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone</p> | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.06 – 2.11 (m, 2H), 2.30 – 2.33 (m, 2H), 2.88 – 2.91 (m, 4H), 3.40 – 3.43 (m, 2H), 3.48 – 3.55 (m, 3H), 4.57 (s, 1H), 4.63 (s, 1H), 4.90 – 4.97 (m, 2H), 6.68 – 6.70 (m, 1H), 6.86 (s, 1H), 7.58 – 7.60 (d, <i>J</i> = 8.0 Hz, 1H), 8.21 – 8.22 (d, <i>J</i> = 5.6 Hz, 1H); Mass (m/z): 403.0 (M+H) <sup>+</sup> .                                                                          |

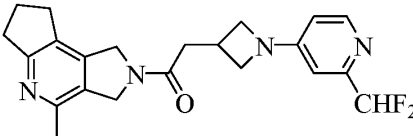
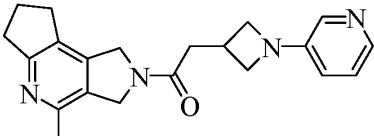
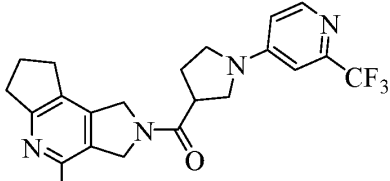
|    |                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
|----|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 22 |  <p>[1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(3,5,6,7-tetrahydro-1H-2,4-diaza-s-indacen-2-yl)-methanone</p>     | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.06 – 2.09 (m, 2H), 2.30 – 2.33 (m, 2H), 2.88 – 2.91 (m, 4H), 3.40 – 3.43 (m, 2H), 3.47 – 3.55 (m, 3H), 4.57 (s, 1H), 4.63 (s, 1H), 4.90 – 4.97 (m, 2H), 6.61 – 6.62 (m, 1H), 6.74 – 6.75 (m, 2H), 7.58 – 7.61 (d, <i>J</i> = 5.6 Hz, 1H), 8.16– 8.17 (d, <i>J</i> = 5.6 Hz, 1H); Mass (m/z): 385.0 (M+H) <sup>+</sup> .                                                                         |
| 23 |  <p>2-(1-Pyridin-3-yl-azetidin-3-yl)-1-(3,5,6,7-tetrahydro-1H-2,4-diaza-s-indacen-2-yl)-ethanone</p>                         | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.05 – 2.09 (m, 2H), 2.83 – 2.90 (m, 6H), 3.14 – 3.16 (m, 1H), 3.71 – 3.74 (m, 2H), 4.16 – 4.20 (t, <i>J</i> = 8.0 Hz, 2H), 4.53 – 4.59 (m, 2H), 4.76 – 4.80 (m, 2H), 7.42 – 7.44 (d, <i>J</i> = 8.4 Hz, 1H), 7.58 – 7.59 (d, <i>J</i> = 4.4 Hz, 1H), 7.67 – 7.71 (m, 1H), 7.98 – 7.99 (d, <i>J</i> = 2.4 Hz, 1H), 8.06 – 8.07 (d, <i>J</i> = 5.2 Hz, 1H); Mass (m/z): 335.2 (M+H) <sup>+</sup> . |
| 24 |  <p>(3,6,7,8-Tetrahydro-1H-2,5-diaza-as-indacen-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone</p> | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.06 – 2.12 (m, 2H), 2.86 – 2.93 (m, 4H), 3.39 – 3.44 (m, 2H), 3.50 – 3.54 (m, 4H), 3.66 – 3.69 (m, 1H), 4.63 (s, 1H), 4.69 (s, 1H), 4.96 – 5.02 (m, 2H), 6.69 – 6.70 (d, <i>J</i> = 5.6 Hz, 1H), 6.86 (s, 1H), 8.21 – 8.22 (d, <i>J</i> = 5.6 Hz, 1H), 8.31 – 8.32 (d, <i>J</i> = 7.2 Hz, 1H); Mass (m/z): 403.1 (M+H) <sup>+</sup> .                                                            |

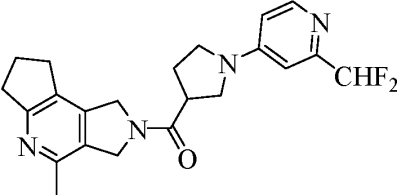
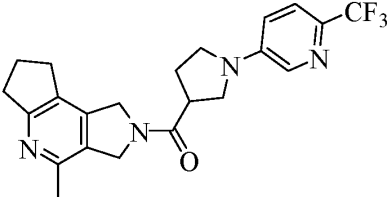
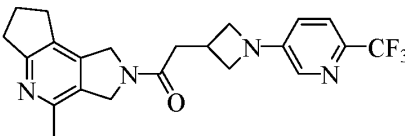
|    |                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
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| 25 |  <p>[1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(3,6,7,8-tetrahydro-1H-2,5-diaza-as-indacen-2-yl)-methanone</p>  | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.04 – 2.09 (m, 2H), 2.81 – 2.89 (m, 4H), 3.34 – 3.41 (m, 2H), 3.52 – 3.55 (m, 4H), 3.61 – 3.66 (m, 1H), 4.64 (s, 1H), 4.69 (s, 1H), 4.94 – 4.99 (m, 2H), 6.46 – 6.74 (t, <i>J</i> = 55.2 Hz, 1H), 6.69 – 6.70 (d, <i>J</i> = 5.6 Hz, 1H), 6.86 (s, 1H), 8.21 – 8.22 (d, <i>J</i> = 5.6 Hz, 1H), 8.31 (s, 1H); Mass (m/z): 385.2 (M+H) <sup>+</sup> .                                                                        |
| 26 |  <p>(1-Pyridin-3-yl-pyrrolidin-3(R)-yl)-(3,6,7,8-tetrahydro-1H-2,5-diaza-as-indacen-2-yl)-methanone</p>                    | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.06 – 2.11 (m, 2H), 2.66 – 2.68 (m, 2H), 2.86 – 2.93 (m, 4H), 3.12 – 3.18 (m, 2H), 3.38 – 3.43 (m, 2H), 4.45 – 4.47 (m, 1H), 4.63 (s, 1H), 4.68 (s, 1H), 4.96 (s, 1H), 5.01 (s, 1H), 7.16 – 7.19 (dd, <i>J</i> = 4.8, 8.4 Hz, 1H), 7.51 (s, 1H), 7.84 – 7.85 (dd, <i>J</i> = 4.0, 4.8 Hz, 1H), 7.95 – 7.96 (dd, <i>J</i> = 4.0, 4.8 Hz, 1H), 8.29 – 8.31 (d, <i>J</i> = 7.6 Hz, 1H); Mass (m/z): 335.2 (M+H) <sup>+</sup> . |
| 27 |  <p>1-(3,6,7,8-Tetrahydro-1H-2,5-diaza-as-indacen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone</p> | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.06 – 2.09 (m, 2H), 2.83 – 2.92 (m, 4H), 3.11 – 3.18 (m, 3H), 3.68 – 3.71 (m, 2H), 4.15 – 4.19 (m, 2H), 4.46 (s, 1H), 4.64 (s, 1H), 4.81 (s, 1H), 4.85 (s, 1H), 6.51 – 6.53 (dd, <i>J</i> = 2.0, 5.6 Hz, 1H), 6.70 – 6.71 (d, <i>J</i> = 2.0 Hz, 1H), 8.19 – 8.21 (d, <i>J</i> = 5.6 Hz, 1H), 8.31 (s, 1H); Mass (m/z):                                                                                                     |

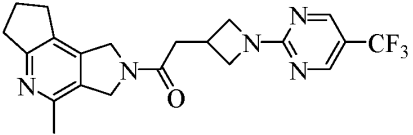
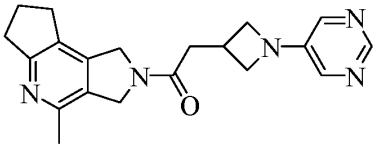
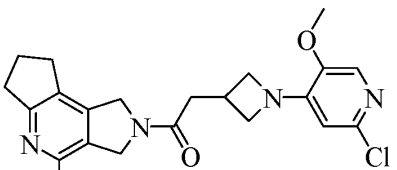


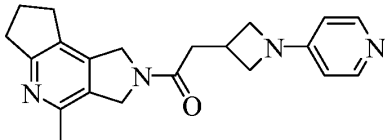
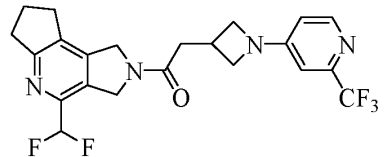
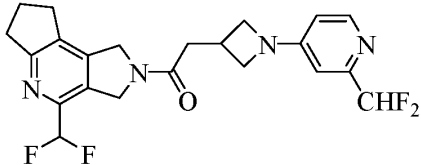
|    |                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|----|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|    |                                                                                                                                                                                                           | 402.9 (M+H) <sup>+</sup> .                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| 28 |  <p>2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(3,6,7,8-tetrahydro-1H-2,5-diaza-as-indacen-2-yl)-ethanone</p> | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.07 – 2.09 (m, 2H), 2.89 – 2.94 (m, 4H), 3.01 – 3.14 (m, 3H), 3.51 – 3.59 (m, 2H), 4.05 – 4.11 (m, 2H), 4.51 (s, 1H), 4.67 (s, 1H), 4.88 (s, 1H), 4.95 (s, 1H), 6.44 – 6.72 (t, <i>J</i> = 55.2 Hz, 1H), 6.47 – 6.49 (dd, <i>J</i> = 2.0, 5.6 Hz, 1H), 6.62 – 6.63 (d, <i>J</i> = 2.0 Hz, 1H), 8.11 – 8.12 (d, <i>J</i> = 5.6 Hz, 1H), 8.27 (s, 1H); Mass (m/z): 385.1 (M+H) <sup>+</sup> .                                              |
| 29 |  <p>2-(1-Pyridin-3-yl)-azetidin-3-yl]-1-(3,6,7,8-tetrahydro-1H-2,5-diaza-as-indacen-2-yl)-ethanone</p>                 | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.10 – 2.31 (m, 2H), 2.73 – 2.91 (m, 6H), 3.05 – 3.10 (m, 1H), 3.54 – 3.58 (t, <i>J</i> = 7.6 Hz, 2H), 4.03 – 4.06 (t, <i>J</i> = 7.6 Hz, 2H), 4.59 (s, 1H), 4.64 (s, 1H), 4.81 (s, 1H), 4.85 (s, 1H), 6.79 – 6.81 (m, 1H), 7.13 – 7.16 (dd, <i>J</i> = 4.8, 8.4 Hz, 1H), 7.80 – 7.80 (d, <i>J</i> = 2.4 Hz, 1H), 7.88 – 7.89 (d, <i>J</i> = 3.6 Hz, 1H), 8.28 – 8.30 (d, <i>J</i> = 10.4 Hz, 1H); Mass (m/z): 335.1 (M+H) <sup>+</sup> . |
| 30 |  <p>2-(1-Pyrimidin-5-yl)-azetidin-3-yl]-1-(3,6,7,8-tetrahydro-1H-2,5-diaza-as-indacen-2-yl)-ethanone</p>               | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.06 – 2.09 (m, 2H), 2.83 – 2.92 (m, 4H), 3.11 – 3.18 (m, 3H), 3.68 – 3.71 (m, 2H), 4.15 – 4.19 (m, 2H), 4.46 (s, 1H), 4.64 (s, 1H), 4.81 (s, 1H), 4.85 (s, 1H), 8.11 (s, 2H),                                                                                                                                                                                                                                                            |

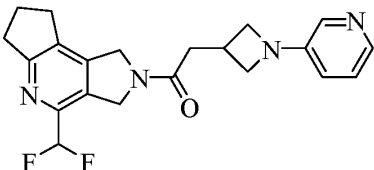
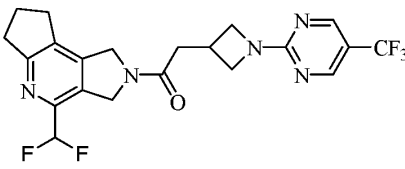
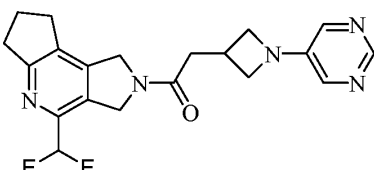
|    |                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                         |
|----|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|    |                                                                                                                                                                                                                       | 8.29 (s, 1H) 8.55 (s, 1H); Mass (m/z): 336.4 (M+H) <sup>+</sup> .                                                                                                                                                                                                                                       |
| 31 |  <p>1-(3,6,7,8-Tetrahydro-1H-2,5-diaza-as-indacen-2-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone</p>          | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.06 – 2.09 (m, 2H), 2.83 – 2.92 (m, 4H), 3.11 – 3.18 (m, 3H), 3.68 – 3.71 (m, 2H), 4.15 – 4.19 (m, 2H), 4.46 (s, 1H), 4.64 (s, 1H), 4.81 (s, 1H), 4.85 (s, 1H), 8.29 (s, 1H), 8.61 (s, 2H); Mass (m/z): 404.4 (M+H) <sup>+</sup> . |
| 32 |  <p>2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(3,6,7,8-tetrahydro-1H-2,5-diaza-as-indacen-2-yl)-ethanone</p>           | Mass (m/z): 399.9 (M+H) <sup>+</sup> .                                                                                                                                                                                                                                                                  |
| 33 |  <p>1-(3,6,7,8-Tetrahydro-1H-2,5-diaza-as-indacen-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone</p>          | Mass (m/z): 403.4 (M+H) <sup>+</sup> .                                                                                                                                                                                                                                                                  |
| 34 |  <p>1-(4-Methyl-3,6,7,8-tetrahydro-1H-2,5-diaza-as-indacen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone</p> | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.01 – 2.04 (m, 2H), 2.15 – 2.19 (m, 2H), 2.46 – 2.47 (d, <i>J</i> = 4.4 Hz, 3H), 2.80 – 2.88 (m, 2H), 2.99 – 3.03 (m, 2H), 3.33 (m, 1H), 3.69 – 3.76 (m, 2H), 4.25 – 4.29 (t, <i>J</i> = 8.4 Hz, 2H), 4.71 – 4.74 (m, 4H), 6.32 –  |

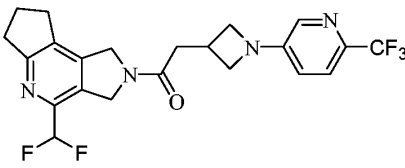
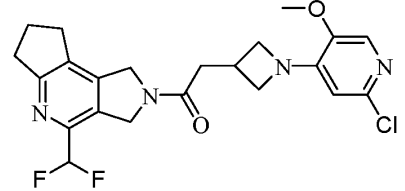
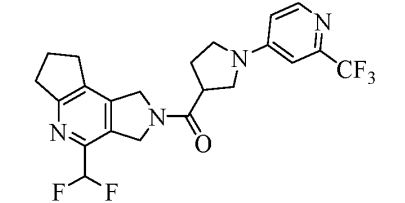
|    |                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                         |
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|    |                                                                                                                                                                                                                         | 6.34 (m, 1H), 6.57 – 6.58 (d, $J = 2.4$ Hz, 1H), 8.27 – 8.29 (d, $J = 5.6$ Hz, 1H); Mass (m/z): 417.0 (M+H) <sup>+</sup> .                                                                                                                                                                                                                                                                                                              |
| 35 |  <p>2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(4-methyl-3,6,7,8-tetrahydro-1H-2,5-diaza-as-indacen-2-yl)-ethanone</p>      | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) $\delta$ ppm: 2.15 – 2.22 (m, 2H), 2.45 – 2.46 (d, $J = 4$ Hz, 3H), 2.80 – 2.88 (m, 4H), 2.99 – 3.03 (t, $J = 7.6$ Hz, 2H), 3.31 (m, 1H), 3.72 – 3.75 (m, 2H), 4.24 – 4.28 (t, $J = 8.0$ Hz, 2H), 4.71 – 4.74 (m, 4H), 6.28 – 6.30 (m, 1H), 6.51 – 6.65 (m, 2H), 8.21 – 8.23 (d, $J = 5.6$ Hz, 1H); Mass (m/z): 398.8 (M+H) <sup>+</sup> .                                           |
| 36 |  <p>1-(4-Methyl-3,6,7,8-tetrahydro-1H-2,5-diaza-as-indacen-2-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone</p>                       | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) $\delta$ ppm: 2.13 – 2.21 (m, 2H), 2.45 – 2.46 (d, $J = 4$ Hz, 3H), 2.81 – 2.87 (m, 4H), 2.99 – 3.03 (t, $J = 7.6$ Hz, 2H), 3.25 – 3.30 (m, 1H), 3.49 – 3.64 (m, 2H), 4.17 – 4.21 (t, $J = 7.6$ Hz, 2H), 4.71 – 4.74 (m, 4H), 6.73 – 6.76 (m, 1H), 7.06 – 7.14 (m, 1H), 7.85 – 7.86 (d, $J = 2.4$ Hz, 1H), 7.99 – 8.00 (d, $J = 2.0$ Hz, 1H); Mass (m/z): 349.1 (M+H) <sup>+</sup> . |
| 37 |  <p>(4-Methyl-3,6,7,8-tetrahydro-1H-2,5-diaza-as-indacen-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone</p> | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) $\delta$ ppm: 2.16 – 2.20 (m, 2H), 2.38 – 2.44 (m, 2H), 2.45 – 2.47 (d, $J = 8$ Hz, 3H), 2.84 – 2.88 (d, $J = 7.2$ Hz, 3H), 3.00 – 3.03 (m, 2H), 3.22 – 3.28 (m, 1H), 3.43 – 3.49 (m, 2H), 3.61 – 3.64 (m, 2H), 4.75 – 4.87 (m, 4H), 6.49 – 6.51 (d, $J = 6.8$ Hz, 1H), 6.75                                                                                                         |

|    |                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|----|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|    |                                                                                                                                                                                                                             | – 6.75 (d, $J = 2.0$ Hz, 1H), 8.29 – 8.31 (d, $J = 6.0$ Hz, 1H); Mass (m/z): 417.0 (M+H) <sup>+</sup> .                                                                                                                                                                                                                                                                                                                            |
| 38 |  <p>[1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(4-methyl-3,6,7,8-tetrahydro-1H-2,5-diaza-as-indacen-2-yl)-methanone</p>        | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 2.16 – 2.20 (m, 2H), 2.38 – 2.44 (m, 2H), 2.45 – 2.46 (d, $J = 7.5$ Hz, 3H), 2.85 – 2.89 (d, $J = 7.5$ Hz, 2H), 3.00 – 3.05 (m, 2H), 3.24 – 3.28 (m, 1H), 3.40 – 3.45 (m, 2H), 3.63 – 3.66 (m, 2H), 4.75 – 4.82 (m, 4H), 6.53 – 6.55 (d, $J = 6.8$ Hz, 2H), 6.78 – 6.81 (d, $J = 2.2$ Hz, 1H), 8.30 – 8.33 (d, $J = 5.8$ Hz, 1H); Mass (m/z): 399.1 (M+H) <sup>+</sup> . |
| 39 |  <p>(4-Methyl-3,6,7,8-tetrahydro-1H-2,5-diaza-as-indacen-2-yl)-[1-(6-trifluoromethyl-pyridin-3-yl)-pyrrolidin-3(R)-yl]-methanone</p>     | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 2.14 – 2.22 (m, 2H), 2.36 – 2.46 (m, 2H), 2.45 – 2.47 (d, $J = 7.8$ Hz, 3H), 2.82 – 2.86 (d, $J = 7.4$ Hz, 2H), 3.00 – 3.04 (m, 2H), 3.22 – 3.29 (m, 1H), 3.43 – 3.49 (m, 2H), 3.63 – 3.66 (m, 2H), 4.74 – 4.88 (m, 4H), 6.32 – 6.45 (d, $J = 6.6$ Hz, 1H), 6.73 – 6.76 (d, $J = 2.0$ Hz, 1H), 8.28 – 8.33 (d, $J = 6.2$ Hz, 1H); Mass (m/z): 417.2 (M+H) <sup>+</sup> . |
| 40 |  <p>1-(4-Methyl-3,6,7,8-tetrahydro-1H-2,5-diaza-as-indacen-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-pyrrolidin-3(R)-yl]-methanone</p> | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.00 – 2.03 (m, 2H), 2.14 – 2.17 (m, 2H), 2.43 – 2.45 (d, $J = 4.2$ Hz, 3H), 2.78 – 2.80 (m, 2H), 3.00 – 3.04 (m, 2H), 3.28 (m, 1H), 3.59 – 3.68 (m, 2H), 4.21 – 4.25 (t, $J = 8.1$ Hz, 2H), 4.56 – 4.83 (m, 4H), 6.80 –                                                                                                                                       |

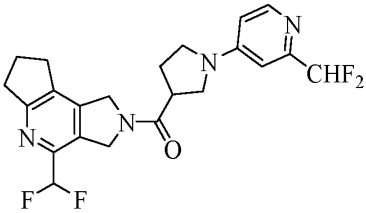
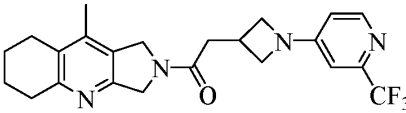
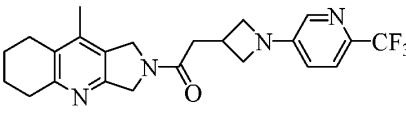
|    |                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                        |
|----|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|    | azetidin-3-yl]-ethanone                                                                                                                                                                                                | 6.88 (dd, $J = 2.4, 8.8$ Hz, 1H), 7.45 – 7.52 (d, $J = 8.8$ Hz, 1H), 7.83 – 7.88 (d, $J = 2.8$ Hz, 1H); Mass (m/z): 417.3 (M+H) <sup>+</sup> .                                                                                                                                                                                                                         |
| 41 |  <p>1-(4-Methyl-3,6,7,8-tetrahydro-1H-2,5-diaza-as-indacen-2-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone</p>  | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.03 – 2.05 (m, 2H), 2.16 – 2.19 (m, 2H), 2.46 – 2.48 (d, $J = 4.4$ Hz, 3H), 2.80 – 2.83 (m, 2H), 3.03 – 3.06 (m, 2H), 3.29 (m, 1H), 3.62 – 3.66 (m, 2H), 4.23 – 4.27 (t, $J = 8.6$ Hz, 2H), 4.51 – 4.84 (m, 4H), 8.65 (s, 2H); Mass (m/z): 418.3 (M+H) <sup>+</sup> .                             |
| 42 |  <p>1-(4-Methyl-3,6,7,8-tetrahydro-1H-2,5-diaza-as-indacen-2-yl)-2-(1-pyrimidin-5-yl)-azetidin-3-yl]-ethanone</p>                    | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.02 – 2.06 (m, 2H), 2.14 – 2.19 (m, 2H), 2.45 – 2.48 (d, $J = 4.4$ Hz, 3H), 2.81 – 2.83 (m, 2H), 3.08 – 3.09 (m, 2H), 3.27 (m, 1H), 3.65 – 3.66 (m, 2H), 4.25 – 4.29 (t, $J = 8.8$ Hz, 2H), 4.52 – 4.98 (m, 4H), 8.00 (s, 2H), 8.55 (s, 1H); Mass (m/z): 350.2 (M+H) <sup>+</sup> .               |
| 43 |  <p>2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(4-methyl-3,6,7,8-tetrahydro-1H-2,5-diaza-as-indacen-2-yl)-ethanone</p> | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.07 – 2.09 (m, 2H), 2.17 – 2.19 (m, 2H), 2.45 – 2.48 (d, $J = 4.3$ Hz, 3H), 2.87 – 2.89 (m, 2H), 3.05 – 3.07 (m, 2H), 3.28 (m, 1H), 3.59 – 3.65 (m, 2H), 3.89 (s, 3H), 4.19 – 4.24 (t, $J = 8.5$ Hz, 2H), 4.54 – 5.00 (m, 4H), 6.65 (s, 1H), 7.61 (s, 1H); Mass (m/z): 413.5 (M+H) <sup>+</sup> . |

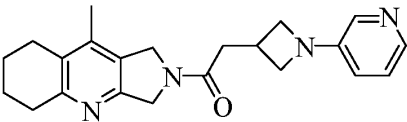
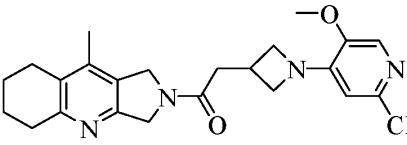
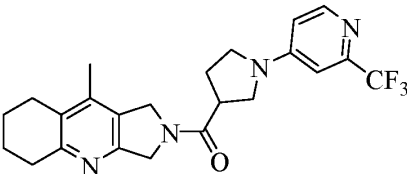
|    |                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                           |
|----|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 44 |  <p>1-(4-Methyl-3,6,7,8-tetrahydro-1H-2,5-diaza-as-indacen-2-yl)-2-(1-pyridin-4-yl-azetidin-3-yl)-ethanone</p>                              | <sup>1</sup> H – NMR ( DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.02 – 2.05 (m, 2H), 2.15 – 2.17 (m, 2H), 2.45 – 2.48 (d, <i>J</i> = 4.3 Hz, 3H), 2.79 – 2.83 (m, 2H), 3.06 – 3.08 (m, 2H), 3.29 (m, 1H), 3.62 – 3.66 (m, 2H), 4.22 – 4.27 (t, <i>J</i> = 8.6 Hz, 2H), 4.53 – 4.97 (m, 4H), 6.46 – 6.48 (m, 2H), 8.12 – 8.14 (m, 2H); Mass (m/z): 349.3 (M+H) <sup>+</sup> .                                         |
| 45 |  <p>1-(4-Difluoromethyl-3,6,7,8-tetrahydro-1H-2,5-diaza-as-indacen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone</p>  | <sup>1</sup> H – NMR ( DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.02 – 2.05 (m, 2H), 2.14 – 2.17 (m, 2H), 2.83 – 2.89 (m, 2H), 3.01 – 3.05 (m, 2H), 3.39 (m, 1H), 3.59 – 3.66 (m, 2H), 4.20 – 4.24 (t, <i>J</i> = 8.8 Hz, 2H), 4.73 – 4.75 (m, 4H), 6.32 – 6.34 (m, 1H), 6.55 – 6.57 (d, <i>J</i> = 2.4 Hz, 1H), 6.59 – 6.60 (m, 1H), 8.20 – 8.24 (d, <i>J</i> = 5.7 Hz, 1H); Mass (m/z): 453.3 (M+H) <sup>+</sup> . |
| 46 |  <p>2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(4-difluoromethyl-3,6,7,8-tetrahydro-1H-2,5-diaza-as-indacen-2-yl)-ethanone</p> | <sup>1</sup> H – NMR ( DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.04 – 2.06 (m, 2H), 2.14 – 2.18 (m, 2H), 2.82 – 2.88 (m, 2H), 3.01 – 3.06 (m, 2H), 3.39 (m, 1H), 3.59 – 3.66 (m, 2H), 4.20 – 4.24 (t, <i>J</i> = 8.8 Hz, 2H), 4.73 – 4.75 (m, 4H), 6.32 – 6.34 (m, 1H), 6.59 – 6.61 (d, <i>J</i> = 2.6 Hz, 1H), 6.63 – 6.66 (m, 2H), 8.16 – 8.19 (d, <i>J</i> = 5.4 Hz, 1H); Mass (m/z): 435.2 (M+H) <sup>+</sup> . |

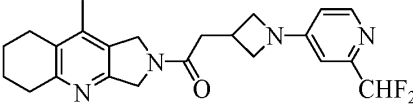
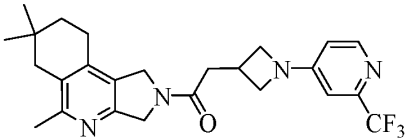
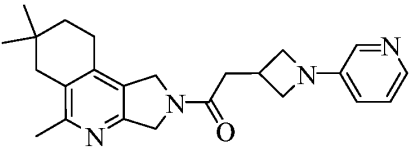
|    |                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                    |
|----|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 47 |  <p>1-(4-Difluoromethyl-3,6,7,8-tetrahydro-1H-2,5-diaza-as-indacen-2-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone</p>                        | <sup>1</sup> H - NMR (CD <sub>3</sub> OD, 400 MHz) δ ppm: 2.10 – 2.13 (m, 2H), 2.69 – 2.73 (m, 4H), 2.99 – 3.11 (m, 3H), 3.49 – 3.53 (m, 2H), 4.01 – 4.07 (m, 2H), 4.61 (s, 1H), 4.69 (s, 1H), 4.89 (s, 1H), 4.91 (s, 1H), 6.46 – 6.72 (t, <i>J</i> = 55.2 Hz, 1H), 6.83 – 6.86 (m, 1H), 7.17 – 7.20 (s, 1H), 7.81 – 7.82 (m, 1H), 7.89 – 7.90, (d, <i>J</i> = 4.4 Hz, 1H); Mass (m/z): 384.9 (M+H) <sup>+</sup> . |
| 48 |  <p>1-(4-Difluoromethyl-3,6,7,8-tetrahydro-1H-2,5-diaza-as-indacen-2-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone</p> | <sup>1</sup> H - NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.02 – 2.05 (m, 2H), 2.14 – 2.17 (m, 2H), 2.83 – 2.89 (m, 2H), 3.01 – 3.05 (m, 2H), 3.39 (m, 1H), 3.59 – 3.66 (m, 2H), 4.20 – 4.24 (t, <i>J</i> = 8.8 Hz, 2H), 4.73 – 4.75 (m, 2H), 6.32 – 6.34 (m, 1H), 6.55 – 6.57 (d, <i>J</i> = 2.4 Hz, 1H), 6.59 – 6.60 (m, 1H), 8.43 (s, 2H); Mass (m/z): 454.3 (M+H) <sup>+</sup> .                     |
| 49 |  <p>1-(4-Difluoromethyl-3,6,7,8-tetrahydro-1H-2,5-diaza-as-indacen-2-yl)-2-(1-pyrimidin-5-yl-azetidin-3-yl)-ethanone</p>                    | <sup>1</sup> H - NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.04 – 2.05 (m, 2H), 2.16 – 2.19 (m, 2H), 2.77 – 2.81 (m, 2H), 3.00 – 3.03 (m, 2H), 3.36 (m, 1H), 3.59 – 3.66 (m, 2H), 4.19 – 4.22 (t, <i>J</i> = 8.4 Hz, 2H), 4.73 – 4.75 (m, 4H), 6.65 – 6.69 (m, 1H), 8.03 – 8.04 (d, <i>J</i> = 0.9 Hz, 2H), 8.51 – 8.53 (d, <i>J</i> = 0.4 Hz, 1H); Mass (m/z): 386.4 (M+H) <sup>+</sup> .                |

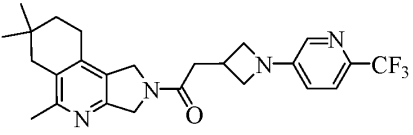
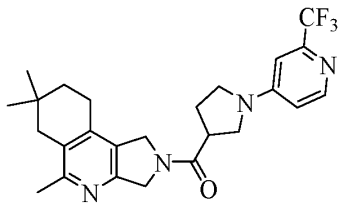
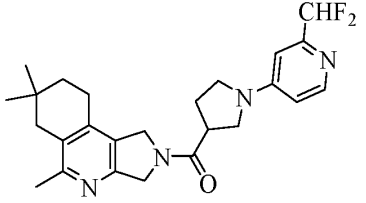
|    |                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                           |
|----|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 50 |  <p>1-(4-Difluoromethyl-3,6,7,8-tetrahydro-1H-2,5-diaza-as-indacen-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone</p>     | <sup>1</sup> H – NMR ( DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.02 – 2.05 (m, 2H), 2.14 – 2.17 (m, 2H), 2.83 – 2.89 (m, 2H), 3.01 – 3.05 (m, 2H), 3.39 (m, 1H), 3.59 – 3.66 (m, 2H), 4.20 – 4.24 (t, <i>J</i> = 8.8 Hz, 2H), 4.73 – 4.75 (m, 4H), 6.65 – 6.68 (m, 1H), 6.88 – 6.89 (m, 1H), 7.58 – 7.59 (d, <i>J</i> = 8.6 Hz, 1H), 7.86 – 7.87 (d, <i>J</i> = 2.3 Hz, 1H); Mass (m/z): 453.4 (M+H) <sup>+</sup> . |
| 51 |  <p>2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(4-difluoromethyl-3,6,7,8-tetrahydro-1H-2,5-diaza-as-indacen-2-yl)-ethanone</p>    | <sup>1</sup> H – NMR ( DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.04 – 2.07 (m, 2H), 2.16 – 2.18 (m, 2H), 2.82 – 2.86 (m, 2H), 3.04 – 3.06 (m, 2H), 3.39 (m, 1H), 3.61 – 3.66 (m, 2H), 3.74 (s, 3H), 4.21 – 4.24 (t, <i>J</i> = 8.8 Hz, 2H), 4.76 – 4.79 (m, 4H), 6.24 – 6.26 (m, 1H), 6.63 – 6.66 (m, 1H), 7.73 (s, 1H); Mass (m/z): 449.3 (M+H) <sup>+</sup> .                                                     |
| 52 |  <p>(4-Difluoromethyl-3,6,7,8-tetrahydro-1H-2,5-diaza-as-indacen-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone</p> | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.06 – 2.10 (m, 2H), 2.33 – 2.36 (m, 2H), 2.84 – 2.89 (m, 4H), 3.31 – 3.49 (m, 2H), 3.48 – 3.50 (m, 2H), 3.72 – 3.75 (m, 1H), 4.55 – 4.61 (m, 2H), 4.88 – 4.95 (m, 2H), 6.68 – 6.70 (m, 2H), 6.87 – 6.89 (m, 1H), 8.21 – 8.22 (d, <i>J</i> = 6.0 Hz, 1H); Mass (m/z): 453.1 (M+H) <sup>+</sup> .                                                      |

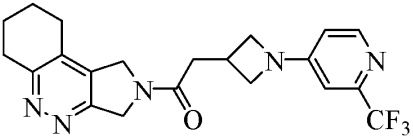
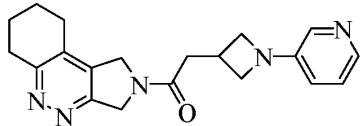
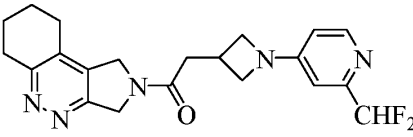


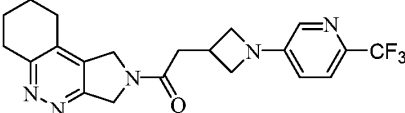
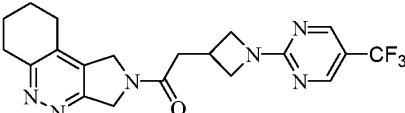
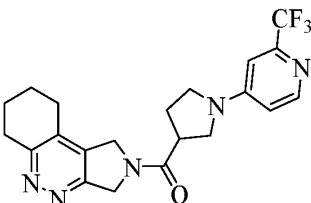
|    |                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                      |
|----|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 53 |  <p>[1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(4-difluoromethyl-3,6,7,8-tetrahydro-1H-2,5-diaza-as-indacen-2-yl)-methanone</p> | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.02 – 2.11 (m, 2H), 2.30 – 2.31 (m, 2H), , 2.80 – 2.91 (m, 4H), 3.33 – 3.42 (m, 2H), 3.45 – 3.50 (m, 2H), 3.70 – 3.72 (m, 1H), 4.55 – 4.61 (m, 2H), 4.86 – 4.95 (m, 2H), 6.58 – 6.62 (m, 2H), 6.65 – 6.71 (m, 1H), 6.87 – 6.89 (m, 1H), 8.24 – 8.25 (d, <i>J</i> = 6.2 Hz, 1H); Mass (m/z): 435.3 (M+H) <sup>+</sup> .                          |
| 54 |  <p>1-(9-Methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b]quinolin-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone</p>        | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 1.86 – 1.92 (m, 4H), 2.17 (s, 3H), 2.60 – 2.66 (m, 2H), 2.80 – 2.83 (m, 2H), 2.90 – 2.94 (m, 2H), 3.29 – 3.34 (m, 1H), 3.71 – 3.76 (m, 2H), 4.25 – 4.30 (m, 2H), 4.73 – 4.76 (m, 4H), 6.31 – 6.33 (m, 1H), 6.57 – 6.58 (d, <i>J</i> = 1.6 Hz, 1H), 8.26 – 8.28 (d, <i>J</i> = 5.6 Hz, 1H); Mass (m/z): 430.8 (M+H) <sup>+</sup> .                          |
| 55 |  <p>1-(9-Methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b]quinolin-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone</p>      | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 1.85 – 1.87 (m, 4H), 2.14 (s, 3H), 2.61 – 2.66 (m, 2H), 2.79 – 2.82 (m, 2H), 2.91 – 2.92 (m, 2H), 3.30 – 3.33 (m, 1H), 3.72 – 3.77 (m, 2H), 4.24 – 4.29 (m, 2H), 4.73 – 4.75 (m, 4H), 6.69 – 6.72 (dd, <i>J</i> = 2.4, 8.4 Hz, 1H), 7.44 – 7.46 (d, <i>J</i> = 8.4 Hz, 1H), 7.85 – 7.86 (d, <i>J</i> = 2.4 Hz, 1H); Mass (m/z): 431.0 (M+H) <sup>+</sup> . |

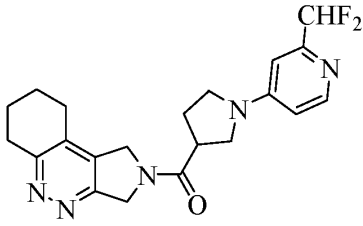
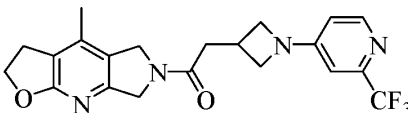
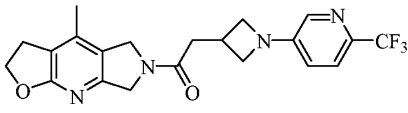
|    |                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
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| 56 |  <p>1-(9-Methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b]quinolin-2-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone</p>                         | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 1.77 – 1.78 (m, 4H), 2.11 – 2.11 (d, <i>J</i> = 2.4 Hz, 3H), 2.63 – 2.64 (m, 2H), 2.78 – 2.79 (m, 2H), 2.82 – 2.86 (t, <i>J</i> = 7.4 Hz, 2H), 3.09 – 3.12 (m, 1H), 3.59 – 3.63 (t, <i>J</i> = 6.6 Hz, 2H), 4.07 – 4.10 (t, <i>J</i> = 7.8 Hz, 2H), 4.51 (s, 1H), 4.58 (s, 1H), 4.73 (s, 1H), 4.81 (s, 1H), 6.96 – 6.98 (d, <i>J</i> = 8.0 Hz, 1H), 7.27 – 7.30 (m, 1H), 7.85 – 7.85 (d, <i>J</i> = 2.8 Hz, 1H), 7.93 – 7.95 (m, 1H); Mass (m/z): 363.0 (M+H) <sup>+</sup> . |
| 57 |  <p>2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(9-methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b]quinolin-2-yl)-ethanone</p>  | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 1.74 – 1.76 (m, 4H), 2.11 (s, 3H), 2.62 – 2.67 (m, 2H), 2.79 – 2.81 (m, 2H), 2.83 – 2.89 (m, 4H), 2.98 – 3.02 (m, 1H), 3.74 (s, 3H), 4.19 – 4.21 (t, <i>J</i> = 8.0 Hz, 2H), 4.49 – 4.57 (m, 2H), 4.72 – 4.80 (m, 2H), 6.23 (s, 1H), 7.65 (s, 1H); Mass (m/z): 427.0 (M+H) <sup>+</sup> .                                                                                                                                                                                    |
| 58 |  <p>(9-Methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b]quinolin-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone</p> | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 1.86 – 1.88 (m, 4H), 2.17 (s, 3H), 2.35 – 2.41 (m, 2H), 2.67 – 2.69 (m, 2H), 2.88 – 2.93 (m, 2H), 3.14 – 3.16 (m, 1H), 3.41 – 3.46 (m, 2H), 3.72 – 3.74 (m, 2H), 4.77 – 4.89 (m, 4H), 6.48 – 6.50 (m, 1H), 6.75 – 6.75 (d, <i>J</i> = 2.4 Hz, 1H), 8.28 – 8.30 (d, <i>J</i> = 6.0 Hz, 1H); Mass (m/z): 430.9                                                                                                                                                                           |

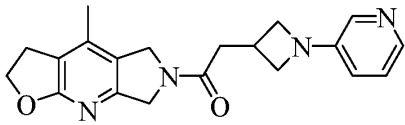
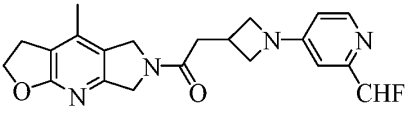
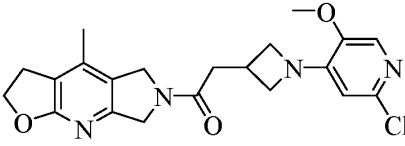
|    |                                                                                                                                                                                                                                  | (M+H) <sup>+</sup> .                                                                                                                                                                                                                                                                                                                                                                                                  |
|----|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 59 |  <p>2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(9-methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b]quinolin-2-yl)-ethanone</p>             | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 1.85 – 1.86 (m, 4H), 2.14 – 2.16 (d, <i>J</i> = 5.6 Hz, 3H), 2.65 – 2.66 (m, 2H), 2.78 – 2.81 (m, 2H), 2.91 – 2.93 (m, 2H), 3.31 – 3.34 (m, 1H), 3.73 – 3.78 (m, 2H), 4.25 – 4.30 (m, 2H), 4.73 – 4.75 (m, 4H), 6.29 – 6.30 (d, <i>J</i> = 5.6 Hz, 1H), 6.52 – 6.66 (m, 2H), 8.19 – 8.20 (d, <i>J</i> = 5.6 Hz, 1H); Mass (m/z): 413.1 (M+H) <sup>+</sup> . |
| 60 |  <p>2-[1-(2-Trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(5,7,7-trimethyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-c]isoquinolin-2-yl)-ethanone</p> | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 1.12 (s, 6H), 1.76 – 1.79 (m, 2H), 2.47 (s, 3H), 2.55 – 2.61 (m, 4H), 2.69 – 2.72 (m, 2H), 3.27 – 3.31 (m, 1H), 3.69 – 3.71 (m, 2H), 4.19 – 4.23 (m, 2H), 4.61 – 4.71 (m, 4H), 6.29 – 6.31 (d, <i>J</i> = 2.0 Hz, 1H), 6.56 – 6.56 (d, <i>J</i> = 2.0 Hz, 1H), 8.24 – 8.26 (d, <i>J</i> = 5.6 Hz, 1H); Mass (m/z): 459.3 (M+H) <sup>+</sup> .               |
| 61 |  <p>2-(1-Pyridin-3-yl-azetidin-3-yl)-1-(5,7,7-trimethyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-c]isoquinolin-2-yl)-ethanone</p>                    | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 1.12 (s, 6H), 1.76 – 1.79 (m, 2H), 2.47 (s, 3H), 2.55 – 2.61 (m, 4H), 2.69 – 2.72 (m, 2H), 3.27 – 3.31 (m, 1H), 3.69 – 3.71 (m, 2H), 4.19 – 4.23 (m, 2H), 4.61 – 4.71 (m, 4H), 6.71 – 6.73 (m, 1H), 7.11 – 7.13 (m, 1H), 7.86 – 7.87 (d, <i>J</i> = 2.8 Hz, 1H), 7.98 – 8.00 (m, 1H); Mass (m/z):                                                           |

|    |                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
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|    |                                                                                                                                                                                                                                    | 391.3 (M+H) <sup>+</sup> .                                                                                                                                                                                                                                                                                                                                                                                                                          |
| 62 |  <p>2-[1-(6-Trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-1-(5,7,7-trimethyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-c]isoquinolin-2-yl)-ethanone</p>    | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 1.11 (s, 6H), 1.77 – 1.79 (m, 2H), 2.49 (s, 3H), 2.56 – 2.63 (m, 4H), 2.67 – 2.71 (m, 2H), 3.29 – 3.31 (m, 1H), 3.67 – 3.70 (m, 2H), 4.17 – 4.21 (m, 2H), 4.59 – 4.69 (m, 4H), 6.69 – 6.72 (m, 1H), 7.43 – 7.45 (d, <i>J</i> = 8.8 Hz, 1H), 7.87 – 7.88 (d, <i>J</i> = 2.4 Hz, 1H); Mass (m/z): 459.3 (M+H) <sup>+</sup> .                                                                |
| 63 |  <p>[1-(2-Trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(5,7,7-trimethyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-c]isoquinolin-2-yl)-methanone</p> | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 1.21 (s, 6H), 1.73 – 1.78 (m, 2H), 1.84 – 1.87 (m, 2H), 2.37 (s, 3H), 2.47 – 2.53 (m, 2H), 2.66 – 2.67 (m, 2H), 3.38 – 3.44 (m, 1H), 3.49 – 3.70 (m, 4H), 4.54 (s, 1H), 4.56 (s, 1H), 4.87 – 4.91 (m, 2H), 6.68 – 6.70 (dd, <i>J</i> = 2.0, 5.6 Hz, 1H), 6.85 – 6.87 (t, <i>J</i> = 2.0 Hz, 1H), 8.21 – 8.22 (d, <i>J</i> = 5.6 Hz, 1H); Mass (m/z): 459.2 (M+H) <sup>+</sup> . |
| 64 |  <p>[1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(5,7,7-trimethyl-1,3,6,7,8,9-hexahydro-</p>                                          | Mass (m/z): 441.5 (M+H) <sup>+</sup> .                                                                                                                                                                                                                                                                                                                                                                                                              |

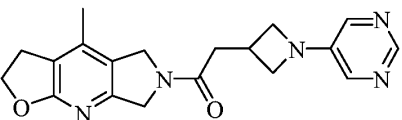
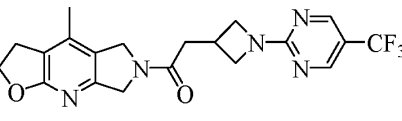
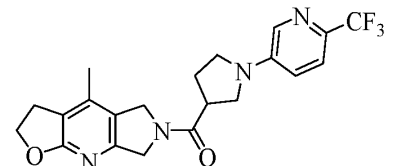
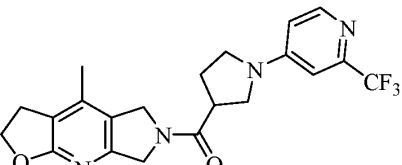
|    |                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                           |
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|    | pyrrolo[3,4-c]isoquinolin-2-yl)-methanone                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                           |
| 65 |  <p>1-(1,3,6,7,8,9-Hexahydro-pyrrolo[3,4-c]cinnolin-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone</p>  | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 1.77 – 1.85 (m, 4H), 2.64 – 2.72 (m, 2H), 2.73 – 2.84 (m, 2H), 2.85 – 2.86 (m, 2H), 2.88 – 3.10 (m, 1H), 3.17 – 3.37 (m, 2H), 3.69 – 4.11 (m, 2H), 4.62 (s, 1H), 4.75 (s, 1H), 4.86 (s, 1H), 5.00 (s, 1H), 6.52 – 6.54 (dd, <i>J</i> = 2.0, 5.6 Hz, 1H), 6.71 (s, 1H), 8.20 – 8.21 (d, <i>J</i> = 5.6 Hz, 1H); Mass (m/z): 418.2 (M+H) <sup>+</sup> . |
| 66 |  <p>1-(1,3,6,7,8,9-Hexahydro-pyrrolo[3,4-c]cinnolin-2-yl)-2-(1-pyridin-3-yl)-azetidin-3-yl)-ethanone</p>                    | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 1.77 – 1.86 (m, 4H), 2.60 – 2.73 (m, 2H), 2.82 – 2.88 (m, 2H), 2.99 – 3.00 (m, 2H), 3.06 – 3.18 (m, 1H), 3.48 – 3.60 (m, 2H), 4.03 – 4.07 (m, 2H), 4.62 (s, 1H), 4.75 (s, 1H), 4.86 (s, 1H), 5.00 (s, 1H), 6.80 – 6.82 (d, <i>J</i> = 9.2 Hz, 1H), 7.13 – 7.17 (m, 1H), 7.81 (s, 1H), 7.89 (s, 1H); Mass (m/z): 350.2 (M+H) <sup>+</sup> .            |
| 67 |  <p>2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(1,3,6,7,8,9-hexahydro-pyrrolo[3,4-c]cinnolin-2-yl)-ethanone</p> | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 1.68 – 1.72 (m, 4H), 2.18 – 2.20 (m, 2H), 2.68 – 2.72 (m, 2H), 2.78 – 2.81 (m, 2H), 2.83 – 2.85 (m, 1H), 3.22 – 3.45 (m, 2H), 3.58 – 4.09 (m, 2H), 4.56 (s, 1H), 4.68 (s, 1H), 4.75 (s, 1H), 4.92 (s, 1H), 6.38 – 6.43 (dd, <i>J</i> = 2.4, 6.0 Hz, 1H), 6.52 – 6.56 (m, 1H), 6.73 (s, 1H), 8.13 – 8.17 (d, <i>J</i> = 5.6 Hz, 1H); Mass (m/z):       |

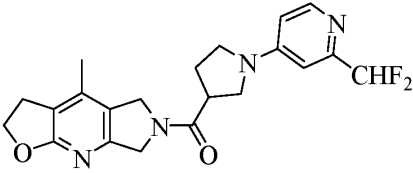
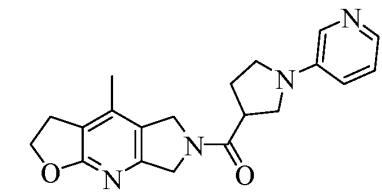
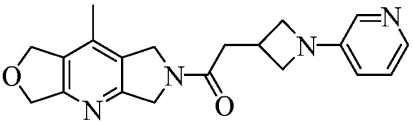
|    |                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                           |
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|    |                                                                                                                                                                                                                  | 400.4 (M+H) <sup>+</sup> .                                                                                                                                                                                                                                                                                                                                                                                                |
| 68 |  <p>1-(1,3,6,7,8,9-Hexahydro-pyrrolo[3,4-c]cinnolin-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone</p>     | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 1.75 – 1.83 (m, 4H), 2.62 – 2.70 (m, 2H), 2.75 – 2.81 (m, 2H), 2.83 – 2.86 (m, 2H), 2.90 – 3.11 (m, 1H), 3.13 – 3.28 (m, 2H), 3.65 – 4.09 (m, 2H), 4.58 (s, 1H), 4.72 (s, 1H), 4.84 (s, 1H), 4.96 (s, 1H), 6.87 – 6.91 (dd, <i>J</i> = 2.0, 8.8 Hz, 1H), 6.96 (s, 1H), 8.19 – 8.22 (d, <i>J</i> = 5.6 Hz, 1H); Mass (m/z): 418.4 (M+H) <sup>+</sup> . |
| 69 |  <p>1-(1,3,6,7,8,9-Hexahydro-pyrrolo[3,4-c]cinnolin-2-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone</p>   | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 1.73 – 1.84 (m, 4H), 2.63 – 2.75 (m, 2H), 2.77 – 2.80 (m, 2H), 2.82 – 2.84 (m, 2H), 2.90 – 3.15 (m, 1H), 3.14 – 3.26 (m, 2H), 3.65 – 4.09 (m, 2H), 4.58 (s, 1H), 4.78 (s, 1H), 4.86 (s, 1H), 4.96 (s, 1H), 8.54 (s, 2H); Mass (m/z): 419.3 (M+H) <sup>+</sup> .                                                                                       |
| 70 |  <p>(1,3,6,7,8,9-Hexahydro-pyrrolo[3,4-c]cinnolin-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone</p> | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 1.75 – 1.81 (m, 4H), 2.64 – 2.70 (m, 2H), 2.75 – 2.85 (m, 2H), 2.93 – 3.13 (m, 1H), 3.12 – 3.24 (m, 2H), 3.58 – 4.02 (m, 4H), 4.56 – 5.00 (m, 4H), 6.51 – 6.53 (m, 1H), 6.66 – 6.68 (d, <i>J</i> = 2.3 Hz, 1H), 8.28 – 8.30 (d, <i>J</i> = 6.2 Hz, 1H); Mass (m/z): 418.4 (M+H) <sup>+</sup> .                                                                  |

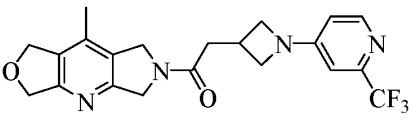
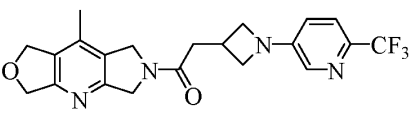
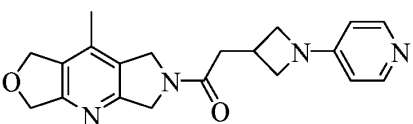
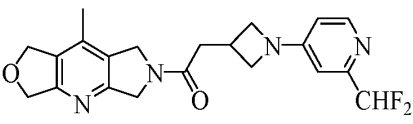
|    |                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                        |
|----|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 71 |  <p>[1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(1,3,6,7,8,9-hexahydro-pyrrolo[3,4-c]cinnolin-2-yl)-methanone</p>           | $^1\text{H}$ – NMR ( $\text{CDCl}_3$ , 400 MHz) $\delta$ ppm: 1.73 – 1.80 (m, 4H), 2.62 – 2.68 (m, 2H), 2.72 – 2.83 (m, 2H), 2.91 – 3.11 (m, 1H), 3.10 – 3.23 (m, 2H), 3.53 – 4.00 (m, 4H), 4.54 – 4.98 (m, 4H), 6.52 – 6.55 (m, 2H), 6.68 – 6.70 (m, 1H), 8.26 – 8.28 (d, $J$ = 6.0 Hz, 1H); Mass ( $m/z$ ): 400.1 ( $\text{M}+\text{H}$ ) <sup>+</sup> .                                                                             |
| 72 |  <p>1-(4-Methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacen-6-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone</p>   | $^1\text{H}$ – NMR ( $\text{CDCl}_3$ , 400 MHz) $\delta$ ppm: 2.19 – 2.20 (d, $J$ = 3.6 Hz, 3H), 2.77 – 2.81 (t, $J$ = 7.8 Hz, 2H), 3.15 – 3.18 (m, 2H), 3.28 – 3.32 (m, 1H), 3.71 – 3.77 (m, 2H), 4.24 – 4.29 (m, 2H), 4.65 – 4.69 (m, 6H), 6.31 – 6.33 (dd, $J$ = 2.4, 5.6 Hz, 1H), 6.57 – 6.57 (d, $J$ = 2.0 Hz, 1H), 8.26 – 8.28 (d, $J$ = 6.0 Hz, 1H); Mass ( $m/z$ ): 419.1 ( $\text{M}+\text{H}$ ) <sup>+</sup> .               |
| 73 |  <p>1-(4-Methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacen-6-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone</p> | $^1\text{H}$ – NMR ( $\text{CDCl}_3$ , 400 MHz) $\delta$ ppm: 2.19 – 2.20 (d, $J$ = 3.6 Hz, 3H), 2.78 – 2.82 (t, $J$ = 8.2 Hz, 2H), 3.16 – 3.20 (t, $J$ = 8.6 Hz, 2H), 3.29 – 3.33 (m, 1H), 3.71 – 3.76 (m, 2H), 4.23 – 4.28 (m, 2H), 4.65 – 4.69 (m, 6H), 6.69 – 6.71 (dd, $J$ = 2.4, 8.4 Hz, 1H), 7.44 – 7.46 (d, $J$ = 8.4 Hz, 1H), 7.85 – 7.86 (d, $J$ = 2.8 Hz, 1H); Mass ( $m/z$ ): 419.0 ( $\text{M}+\text{H}$ ) <sup>+</sup> . |

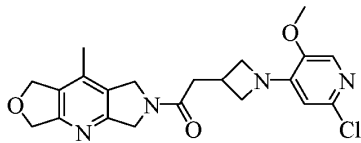
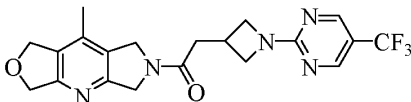
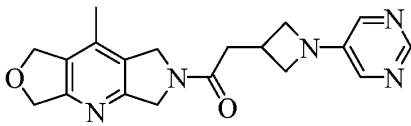
|    |                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
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| 74 |  <p>1-(4-Methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacen-6-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone</p>                        | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 2.19 – 2.20 (d, <i>J</i> = 3.2 Hz, 3H), 2.77 – 2.81 (m, 2H), 3.16 – 3.20 (t, <i>J</i> = 8.6 Hz, 2H), 3.25 – 3.30 (m, 1H), 3.63 – 3.67 (m, 2H), 4.16 – 4.20 (m, 2H), 4.67 – 4.69 (m, 6H), 6.74 – 6.77 (m, 1H), 7.12 – 7.15 (m, 1H), 7.81 (s, 1H), 7.95 – 7.96 (m, 1H); Mass (m/z): 351.0 (M+H) <sup>+</sup> .                                                                                                       |
| 75 |  <p>2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(4-methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacen-6-yl)-ethanone</p>     | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 2.19 – 2.20 (d, <i>J</i> = 3.6 Hz, 3H), 2.77 – 2.80 (m, 2H), 3.07 – 3.11 (m, 2H), 3.28 – 3.32 (m, 1H), 3.72 – 3.76 (m, 2H), 4.25 – 4.29 (t, <i>J</i> = 7.4 Hz, 2H), 4.65 – 4.71 (m, 6H), 6.29 – 6.31 (m, 1H), 6.52 – 6.66 (m, 2H), 8.19 – 8.20 (d, <i>J</i> = 6.0 Hz, 1H); Mass (m/z): 401.0 (M+H) <sup>+</sup> .                                                                                                  |
| 76 |  <p>2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(4-methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacen-6-yl)-ethanone</p> | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 2.16 – 2.16 (d, <i>J</i> = 3.6 Hz, 3H), 2.77 – 2.80 (t, <i>J</i> = 7.0 Hz, 2H), 2.97 – 3.01 (m, 1H), 3.13 – 3.17 (t, <i>J</i> = 8.6 Hz, 2H), 3.76 – 3.78 (m, 5H), 4.19 – 4.23 (t, <i>J</i> = 8.2 Hz, 2H), 4.43 – 4.50 (m, 2H), 4.56 – 4.60 (t, <i>J</i> = 8.6 Hz, 2H), 4.66 – 4.73 (m, 2H), 6.23 – 6.23 (d, <i>J</i> = 1.6 Hz, 1H), 6.65 – 6.65 (d, <i>J</i> = 1.2 Hz, 1H); Mass (m/z): 415.1 (M+H) <sup>+</sup> . |

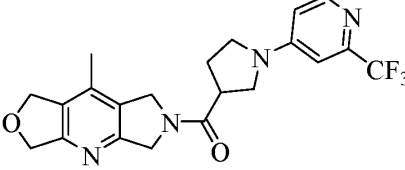
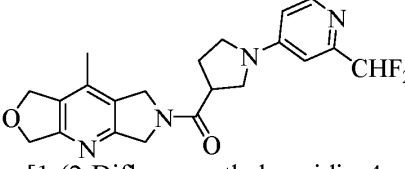
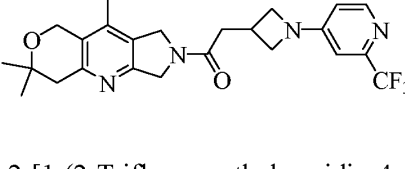
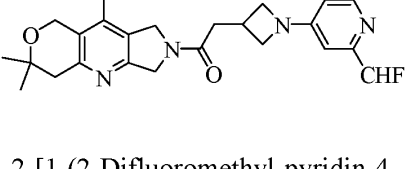


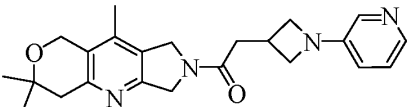
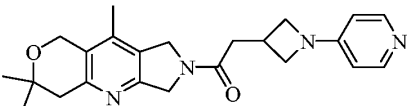
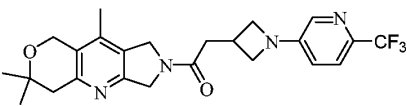
|    |                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
|----|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 77 |  <p>1-(4-Methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacen-6-yl)-2-(1-pyrimidin-5-yl-azetidin-3-yl)-ethanone</p>                       | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 2.19 – 2.20 (d, <i>J</i> = 3.2 Hz, 3H), 2.78 – 2.80 (m, 2H), 3.16 – 3.20 (t, <i>J</i> = 8.8 Hz, 2H), 3.28 – 3.32 (m, 2H), 3.69 – 3.74 (m, 3H), 4.23 – 4.25 (m, 2H), 4.65 – 4.69 (m, 4H), 7.94 (s, 2H), 8.62 (s, 1H); Mass (m/z): 352.0 (M+H) <sup>+</sup> .                                                                                                                                                    |
| 78 |  <p>1-(4-Methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacen-6-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone</p>   | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 2.19 (s, 3H), 2.77 – 2.81 (m, 2H), 3.16 – 3.20 (m, 2H), 3.26 – 3.27 (m, 1H), 3.90 – 3.95 (m, 2H), 4.42 – 4.46 (m, 2H), 4.65 – 4.69 (m, 6H), 8.47 (s, 2H); Mass (m/z): 420.1 (M+H) <sup>+</sup> .                                                                                                                                                                                                               |
| 79 |  <p>(4-Methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacen-6-yl)-[1-(6-trifluoromethyl-pyridin-3-yl)-pyrrolidin-3(R)-yl]-methanone</p> | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.18 – 2.19 (d, <i>J</i> = 3.6 Hz, 3H), 2.32 – 2.37 (m, 2H), 2.67–2.68 (m, 2H), 3.14 – 3.19 (t, <i>J</i> = 8.8 Hz, 2H), 3.47 – 3.50 (t, <i>J</i> = 7.2 Hz, 2H), 4.47 – 4.48 (m, 1H), 4.56 – 4.61 (m, 2H), 4.83 – 4.84 (m, 2H), 4.89 – 4.90 (m, 2H), 7.01 – 7.04 (dd, <i>J</i> = 2.8, 8.8 Hz, 1H), 7.58 – 7.61 (dd, <i>J</i> = 2.4, 8.8 Hz, 1H), 8.06 (s, 1H); Mass (m/z): 418.8 (M+H) <sup>+</sup> . |
| 80 |  <p>(4-Methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacen-6-yl)-[1-(3-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone</p> | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 2.21 (s, 3H), 2.35 – 2.40 (m, 2H), 3.17 – 3.21 (t, <i>J</i> = 8.6 Hz, 2H), 3.39 – 3.45 (m, 2H), 3.62 – 3.71 (m, 3H), 4.66 – 4.72 (m, 4H), 4.81 (s, 1H); Mass (m/z): 418.8 (M+H) <sup>+</sup> .                                                                                                                                                                                                                 |

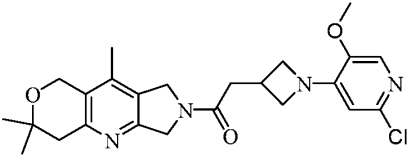
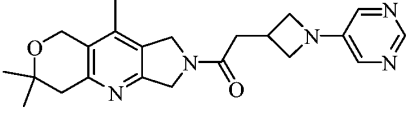
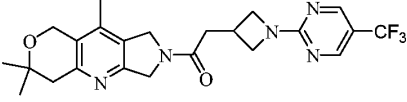
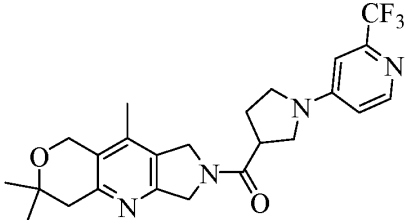
|    |                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                               |
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|    | oxa-6,8-diaza-s-indacen-6-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone                                                                                                                        | 2H), 6.48 – 6.50 (m, 1H), 6.75 – 6.75 (d, $J = 2.4$ Hz, 1H), 8.29 – 8.30 (d, $J = 6.0$ Hz, 1H); Mass (m/z): 418.8 (M+H) <sup>+</sup> .                                                                                                                                                                                                                        |
| 81 |  <p>[1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(4-methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacen-6-yl)-methanone</p> | Mass (m/z): 401.4 (M+H) <sup>+</sup> .                                                                                                                                                                                                                                                                                                                        |
| 82 |  <p>(4-Methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacen-6-yl)-(1-pyridin-3-yl-pyrrolidin-3(R)-yl)-methanone</p>                   | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 2.21 (m, 3H), 2.35 – 2.39 (m, 2H), 3.17 – 3.21 (t, $J = 8.4$ Hz, 2H), 3.40 – 3.45 (m, 2H), 3.51 – 3.56 (m, 1H), 3.61 – 3.64 (m, 2H), 4.64 – 4.76 (m, 4H), 4.81 (s, 2H), 6.84 – 6.86 (m, 1H), 7.11 – 7.14 (m, 1H), 7.96 – 8.01 (m, 2H); Mass (m/z): 351.1 (M+H) <sup>+</sup> .                       |
| 83 |  <p>1-(8-Methyl-5,7-dihydro-1H,3H-2-oxa-4,6-diaza-s-indacen-6-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone</p>                     | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 2.17 – 2.18 (d, $J = 4.8$ Hz, 3H), 2.83 – 2.85 (m, 2H), 3.15 – 3.24 (m, 1H), 3.56 – 3.60 (m, 2H), 4.03 – 4.09 (m, 2H), 4.59 – 4.63 (m, 2H), 4.82 – 4.86 (m, 2H), 4.93 – 5.08 (m, 4H), 6.83 – 6.86 (m, 1H), 7.17 – 7.20 (s, 1H), 7.81 – 7.82 (m, 1H), 7.89 – 7.90 (d, $J = 4.4$ Hz, 1H); Mass (m/z): |

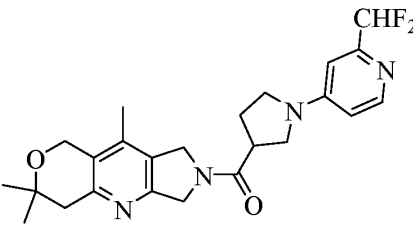
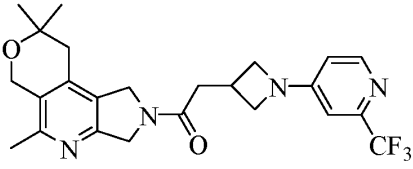
|    |                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                             |
|----|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|    |                                                                                                                                                                                                                       | 351.4 (M+H) <sup>+</sup> .                                                                                                                                                                                                                                                                                                                                                                                  |
| 84 |  <p>1-(8-Methyl-5,7-dihydro-1H,3H-2-oxa-4,6-diaza-s-indacen-6-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone</p>  | <sup>1</sup> H – NMR ( DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.17 – 2.18 (d, <i>J</i> = 4.8 Hz, 3H), 2.85 – 2.87 (m, 2H), 3.06 – 3.15 (m, 1H), 3.59 – 3.63 (m, 2H), 3.73 – 4.80 (m, 2H), 4.58 – 4.63 (m, 2H), 4.82 – 4.86 (m, 2H), 4.93 – 5.08 (m, 4H), 6.52 – 6.54 (d, <i>J</i> = 6.4 Hz, 1H), 6.66 – 6.71 (m, 1H), 8.19 – 8.21 (d, <i>J</i> = 5.6 Hz, 1H); Mass (m/z): 419.0 (M+H) <sup>+</sup> . |
| 85 |  <p>1-(8-Methyl-5,7-dihydro-1H,3H-2-oxa-4,6-diaza-s-indacen-6-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone</p> | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 2.19 – 2.20 (d, <i>J</i> = 3.6 Hz, 3H), 2.78 – 2.82 (m, 2H), 3.16 – 3.20 (m, 1H), 3.29 – 3.33 (m, 2H), 3.71 – 3.76 (m, 2H), 4.23 – 4.28 (m, 2H), 4.65 – 4.69 (m, 6H), 6.69 – 6.71 (dd, <i>J</i> = 2.4, 2.4 Hz, 1H), 7.44 – 7.46 (d, <i>J</i> = 8.4 Hz, 1H), 7.85 – 7.86 (d, <i>J</i> = 2.8 Hz, 1H); Mass (m/z): 419.0 (M+H) <sup>+</sup> .        |
| 86 |  <p>1-(8-Methyl-5,7-dihydro-1H,3H-2-oxa-4,6-diaza-s-indacen-6-yl)-2-(1-pyridin-4-yl-azetidin-3-yl)-ethanone</p>                    | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 2.18 – 2.21 (d, <i>J</i> = 4.2 Hz, 3H), 2.80 – 2.95 (m, 2H), 3.20 – 3.26 (m, 1H), 3.66 – 3.70 (m, 2H), 4.00 – 4.12 (m, 2H), 4.44 – 4.53 (m, 2H), 4.77 – 4.82 (m, 2H), 4.99 – 5.26 (m, 4H), 6.88 – 6.95 (m, 2H), 8.14 – 8.19 (m, 2H); Mass (m/z): 351.2 (M+H) <sup>+</sup> .                                                                       |
| 87 |  <p>1-(8-Methyl-5,7-dihydro-1H,3H-2-oxa-4,6-diaza-s-indacen-6-yl)-2-[1-(2-difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone</p> | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 2.21 – 2.21 (d, <i>J</i> = 2.8 Hz, 3H), 2.78 – 2.84 (m, 2H), 3.29 – 3.34 (m,                                                                                                                                                                                                                                                                      |

|    |                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                             |
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|    | 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(8-methyl-5,7-dihydro-1 <i>H</i> ,3 <i>H</i> -2-oxa-4,6-diaza-s-indacen-6-yl)-ethanone                                                                                           | 1H), 3.72 – 3.77 (m, 2H), 4.26 – 4.30 (m, 2H), 4.59 – 4.80 (m, 4H), 5.07 – 5.15 (m, 4H), 6.28 – 6.30 (d, <i>J</i> = 5.6 Hz, 1H), 6.51 – 6.65 (m, 2H), 8.21 – 8.22 (d, <i>J</i> = 5.6 Hz, 1H); Mass (m/z): 401.0 (M+H) <sup>+</sup> .                                                                                                                                        |
| 88 |  <p>2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(8-methyl-5,7-dihydro-1<i>H</i>,3<i>H</i>-2-oxa-4,6-diaza-s-indacen-6-yl)-ethanone</p>    | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 2.16 – 2.17 (d, <i>J</i> = 3.6 Hz, 3H), 2.86 – 2.93 (m, 2H), 3.19 – 3.25 (m, 1H), 3.52 – 3.61 (m, 2H), 3.63 – 3.69 (m, 5H), 4.56 – 4.66 (m, 2H), 4.76 – 4.88 (m, 2H), 5.00 – 5.12 (m, 4H), 6.53 – 6.53 (d, <i>J</i> = 1.6 Hz, 1H), 7.65 – 7.65 (d, <i>J</i> = 1.2 Hz, 1H); Mass (m/z): 415.1 (M+H) <sup>+</sup> . |
| 89 |  <p>1-(8-Methyl-5,7-dihydro-1<i>H</i>,3<i>H</i>-2-oxa-4,6-diaza-s-indacen-6-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone</p> | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 2.19 – 2.20 (d, <i>J</i> = 3.7 Hz, 3H), 2.62 – 2.71 (m, 2H), 3.03 – 3.15 (m, 1H), 3.62 – 3.73 (m, 2H), 3.82 – 3.99 (m, 2H), 4.45 – 4.56 (m, 2H), 4.66 – 4.78 (m, 2H), 5.09 – 5.12 (m, 4H), 8.53 (m, 2H); Mass (m/z): 420.2 (M+H) <sup>+</sup> .                                                                   |
| 90 |  <p>1-(8-Methyl-5,7-dihydro-1<i>H</i>,3<i>H</i>-2-oxa-4,6-diaza-s-indacen-6-yl)-2-(1-pyrimidin-5-yl)-azetidin-3-yl)-ethanone</p>                    | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 2.20 – 2.26 (d, <i>J</i> = 4.2 Hz, 3H), 2.59 – 2.65 (m, 2H), 3.13 – 3.19 (m, 1H), 3.55 – 3.63 (m, 2H), 3.71 – 3.80 (m, 2H), 4.55 – 4.80 (m, 4H), 4.98 – 5.09 (m, 4H), 8.03 – 8.05 (d, <i>J</i> = 0.9 Hz, 2H), 8.54 – 8.55 (d, <i>J</i> = 0.6 Hz, 1H); Mass (m/z): 352.1 (M+H) <sup>+</sup> .                      |

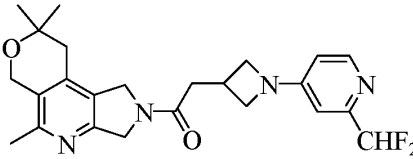
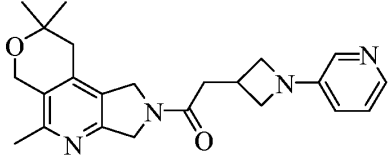
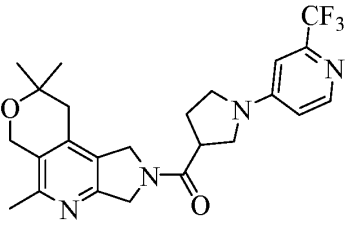
|    |                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                      |
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| 91 |  <p>(8-Methyl-5,7-dihydro-1H,3H-2-oxa-4,6-diaza-s-indacen-6-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone</p>                          | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 2.22 – 2.23 (d, <i>J</i> = 2.0 Hz, 3H), 2.37 – 2.42 (m, 2H), 3.38 (m, 1H), 3.41 – 3.50 (m, 2H), 3.62 – 3.71 (m, 2H), 4.67 – 4.94 (m, 4H), 5.16 – 5.30 (m, 4H), 6.48 – 6.50 (m, 1H), 6.75 – 6.76 (d, <i>J</i> = 2.4 Hz, 1H), 8.29 – 8.31 (d, <i>J</i> = 5.6 Hz, 1H); Mass (m/z): 419.8 (M+H) <sup>+</sup> . |
| 92 |  <p>[1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(8-methyl-5,7-dihydro-1H,3H-2-oxa-4,6-diaza-s-indacen-6-yl)-methanone</p>                           | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 2.23 (s, 3H), 2.23 – 2.27 (m, 2H), 3.18 – 3.32 (m, 2H), 3.44 – 3.49 (m, 2H), 3.62 (m, 1H), 4.66 – 4.72 (m, 4H), 4.93 – 5.08 (m, 4H), 6.29 – 6.31 (m, 1H), 6.52 – 6.66 (m, 2H), 8.19 – 8.20 (d, <i>J</i> = 6.0 Hz, 1H); Mass (m/z): 401.8 (M+H) <sup>+</sup> .                                              |
| 93 |  <p>2-[1-(2-Trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(6,6,9-trimethyl-3,5,6,8-tetrahydro-1H-7-oxa-2,4-diaza-cyclopenta[b]naphthalen-2-yl)-ethanone</p> | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 1.41 (s, 6H), 2.12 (d, <i>J</i> = 4.4 Hz, 3H), 2.79 – 2.88 (m, 4H), 3.28 – 3.32 (m, 1H), 3.72 – 3.77 (m, 2H), 4.25 – 4.29 (m, 2H), 4.75 – 4.77 (m, 6H), 6.31 – 6.33 (m, 1H), 6.57 – 6.58 (m, 1H), 8.27 – 8.28 (d, <i>J</i> = 5.6 Hz, 1H); Mass (m/z): 461.3 (M+H) <sup>+</sup> .                           |
| 94 |  <p>2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(6,6,9-trimethyl-3,5,6,8-tetrahydro-1H-7-oxa-2,4-diaza-cyclopenta[b]naphthalen-2-yl)-ethanone</p>  | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 1.39 (s, 6H), 2.11 (s, 3H), 2.74 – 2.86 (m, 4H), 3.24 – 3.31 (m, 1H), 3.69 – 3.73 (m, 2H), 4.45 – 4.53 (m, 2H), 4.76 – 4.79 (m, 6H), 6.31 – 6.33 (m, 1H), 6.57 – 6.58 (m, 1H), 8.27 – 8.28 (d, <i>J</i> = 5.6 Hz, 1H); Mass (m/z): 461.3 (M+H) <sup>+</sup> .                                              |

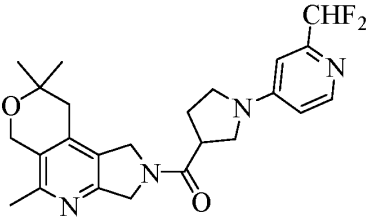
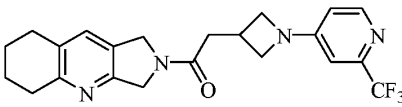
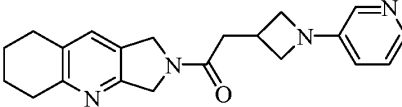
|    |                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                              |
|----|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|    | trimethyl-3,5,6,8-tetrahydro-1H-7-oxa-2,4-diazacyclopenta[b]naphthalen-2-yl)-ethanone                                                                                                                                                          | (m, 1H), 6.48 – 6.49 (d, $J = 2.4$ Hz, 1H), 6.30 – 6.57 (t, $J = 55.2$ Hz, 1H), 7.98 – 8.00 (d, $J = 6.0$ Hz, 1H); Mass (m/z): 443.5 (M+H) <sup>+</sup> .                                                                                                                                                                                                    |
| 95 |  <p>2-(1-(6,6,9-trimethyl-3,5,6,8-tetrahydro-1H-7-oxa-2,4-diazacyclopenta[b]naphthalen-2-yl)-3-yl)-1H-pyridin-3-yl)-azetidin-3-yl)-1-ethanone</p>             | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) $\delta$ ppm: 1.41 (s, 6H), 2.12 (s, 3H), 2.86 – 2.96 (m, 4H), 3.28 – 3.32 (m, 1H), 3.56 – 3.68 (m, 2H), 4.61 – 4.66 (m, 2H), 4.69 – 4.74 (m, 6H), 6.59 – 6.61 (d, $J = 8.0$ Hz, 1H), 6.98 – 6.99 (m, 1H), 7.06 – 7.08 (m, 1H), 7.78 – 7.79 (d, $J = 2.0$ Hz, 1H); Mass (m/z): 393.5 (M+H) <sup>+</sup> . |
| 96 |  <p>2-(1-(6,6,9-trimethyl-3,5,6,8-tetrahydro-1H-7-oxa-2,4-diazacyclopenta[b]naphthalen-2-yl)-3-yl)-1H-pyridin-4-yl)-azetidin-3-yl)-1-ethanone</p>            | Mass (m/z): 393.5 (M+H) <sup>+</sup> .                                                                                                                                                                                                                                                                                                                       |
| 97 |  <p>2-[1-(6-Trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-1-(6,6,9-trimethyl-3,5,6,8-tetrahydro-1H-7-oxa-2,4-diazacyclopenta[b]naphthalen-2-yl)-ethanone</p> | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) $\delta$ ppm: 1.42 (s, 6H), 2.13 (s, 3H), 2.80 – 2.89 (m, 4H), 3.29 – 3.33 (m, 1H), 3.65 – 3.68 (t, $J = 5.6$ Hz, 2H), 4.25 – 4.30 (m, 2H), 4.72 – 4.76 (m, 6H), 6.87 – 6.90 (dd, $J = 2.4, 8.8$ Hz, 1H), 7.57 – 7.58 (m, 1H), 7.87 – 7.88 (d, $J = 2.8$ Hz, 1H); Mass (m/z): 461.4 (M+H) <sup>+</sup> .  |

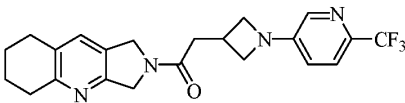
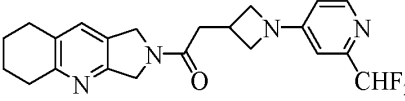
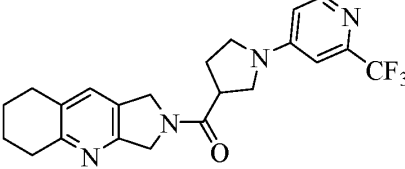
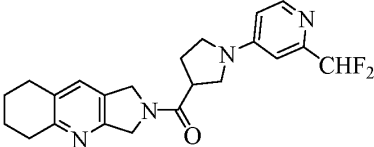
|     |                                                                                                                                                                                                                                                  |                                                                                                                                                                                                              |
|-----|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 98  |  <p>2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(6,6,9-trimethyl-3,5,6,8-tetrahydro-1H-7-oxa-2,4-diazacyclopenta[b]naphthalen-2-yl)-ethanone</p>    | Mass (m/z): 457.9 (M+H) <sup>+</sup> .                                                                                                                                                                       |
| 99  |  <p>2-(1-Pyrimidin-5-yl-azetidin-3-yl)-1-(6,6,9-trimethyl-3,5,6,8-tetrahydro-1H-7-oxa-2,4-diazacyclopenta[b]naphthalen-2-yl)-ethanone</p>                       | Mass (m/z): 394.4 (M+H) <sup>+</sup> .                                                                                                                                                                       |
| 100 |  <p>2-[1-(5-Trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-1-(6,6,9-trimethyl-3,5,6,8-tetrahydro-1H-7-oxa-2,4-diazacyclopenta[b]naphthalen-2-yl)-ethanone</p> | Mass (m/z): 462.3 (M+H) <sup>+</sup> .                                                                                                                                                                       |
| 101 |                                                                                                                                                               | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 1.41 (s, 6H), 2.12 (d, <i>J</i> = 4.4 Hz, 3H), 2.79 – 2.88 (m, 4H), 3.28 – 3.32 (m, 1H), 3.72 – 3.77 (m, 2H), 4.25 – 4.29 (m, 2H), 4.71 – 4.73 (m, |

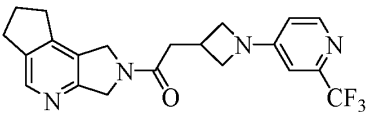
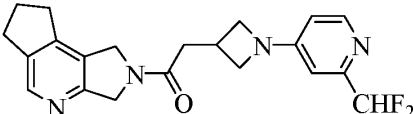
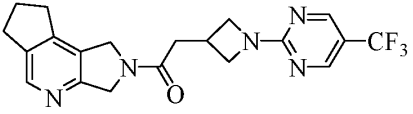
|     |                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                |
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|     | [1-(2-Trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(6,6,9-trimethyl-3,5,6,8-tetrahydro-1 <i>H</i> -7-oxa-2,4-diaza-cyclopenta[b]naphthalen-2-yl)-methanone                                                                                        | 2H), 4.75 – 4.79 (m, 4H); 6.68 – 6.69 (m, 1H), 6.88 (s, 1H), 8.21 – 8.22 (d, $J = 6.0$ Hz, 1H); Mass (m/z): 461.5 (M+H) <sup>+</sup> .                                                                                                                                                                                                         |
| 102 |  <p>[1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(6,6,9-trimethyl-3,5,6,8-tetrahydro-1<i>H</i>-7-oxa-2,4-diaza-cyclopenta[b]naphthalen-2-yl)-methanone</p>  | Mass (m/z): 443.5 (M+H) <sup>+</sup> .                                                                                                                                                                                                                                                                                                         |
| 103 |  <p>2-[1-(2-Trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(5,8,8-trimethyl-3,6,8,9-tetrahydro-1<i>H</i>-7-oxa-2,4-diaza-cyclopenta[a]naphthalen-2-yl)-ethanone</p> | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) $\delta$ ppm: 1.31 (s, 6H), 2.45 (s, 3H), 2.81 – 2.86 (m, 4H), 3.24 – 3.31 (m, 1H), 3.66 – 3.71 (m, 2H), 4.23 – 4.29 (m, 2H), 4.79 – 4.83 (m, 4H), 4.84 – 4.88 (m, 2H), 6.32 – 6.36 (m, 1H), 6.59 – 6.61 (m, 1H), 8.19 – 8.22 (d, $J = 5.4$ Hz, 1H); Mass (m/z): 461.3 (M+H) <sup>+</sup> . |
| 104 |                                                                                                                                                                                                                                                        | Mass (m/z): 443.5 (M+H) <sup>+</sup> .                                                                                                                                                                                                                                                                                                         |

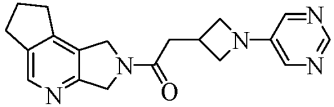
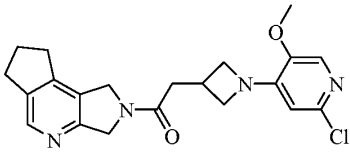
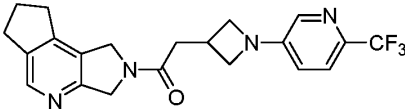
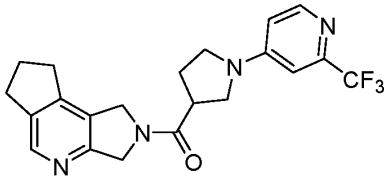


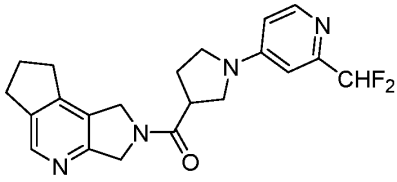
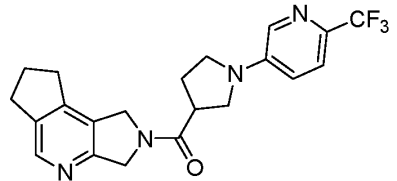
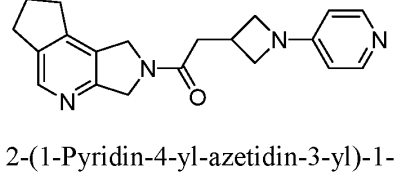
|     |                                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                   |
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|     |  <p>2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(5,8,8-trimethyl-3,6,8,9-tetrahydro-1H-7-oxa-2,4-diazacyclopenta[a]naphthalen-2-yl)-ethanone</p>      |                                                                                                                                                                                                                                                                                                                                                                   |
| 105 |  <p>2-(1-Pyridin-3-yl-azetidin-3-yl)-1-(5,8,8-trimethyl-3,6,8,9-tetrahydro-1H-7-oxa-2,4-diazacyclopenta[a]naphthalen-2-yl)-ethanone</p>                         | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 1.33 (s, 6H), 2.45 (s, 3H), 2.82 – 2.86 (m, 4H), 3.24 – 3.31 (m, 1H), 3.66 – 3.73 (m, 2H), 4.23 – 4.29 (m, 2H), 4.79 – 4.83 (m, 4H), 4.84 – 4.88 (m, 2H), 6.32 – 6.36 (m, 1H), 6.59 – 6.61 (m, 1H), 7.27 – 7.32 (m, 1H), 8.11 – 8.16 (d, <i>J</i> = 4.4 Hz, 1H); Mass (m/z): 393.4 (M+H) <sup>+</sup> . |
| 106 |  <p>[1-(2-Trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(5,8,8-trimethyl-3,6,8,9-tetrahydro-1H-7-oxa-2,4-diazacyclopenta[a]naphthalen-2-yl)-methanone</p> | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 1.31 (s, 6H), 2.45 (s, 3H), 2.81 – 2.86 (m, 4H), 3.15 – 3.19 (m, 1H), 3.66 – 3.71 (m, 2H), 4.23 – 4.29 (m, 2H), 4.79 – 4.83 (m, 6H), 6.36 – 6.39 (m, 1H), 6.69 – 6.71 (m, 1H), 8.23 – 8.26 (d, <i>J</i> = 5.4 Hz, 1H); Mass (m/z): 461.3 (M+H) <sup>+</sup> .                                           |

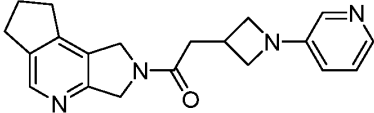
|     |                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                           |
|-----|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 107 |  <p>[1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(5,8,8-trimethyl-3,6,8,9-tetrahydro-1H-7-oxa-2,4-diazacyclopenta[a]naphthalen-2-yl)-methanone</p> | Mass (m/z): 443.5 (M+H) <sup>+</sup> .                                                                                                                                                                                                                                                                                                                                                                                    |
| 108 |  <p>1-(1,3,5,6,7,8-Hexahydro-pyrrolo[3,4-b]quinolin-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone</p>                                 | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 1.87 – 1.93 (m, 4H), 2.65 – 2.71 (m, 2H), 2.81 – 2.84 (m, 2H), 2.91 – 2.96 (m, 2H), 3.25 – 3.34 (m, 1H), 3.76 – 3.80 (m, 2H), 4.23 – 4.29 (m, 2H), 4.59 – 4.63 (m, 2H), 4.82 – 4.86 (m, 2H), 6.62 – 6.87 (m, 1H), 6.83 – 6.86 (m, 1H), 7.17 – 7.20 (s, 1H), 8.89 – 8.90 (d, <i>J</i> = 4.4 Hz, 1H); Mass (m/z): 417.0 (M+H) <sup>+</sup> .                      |
| 109 |  <p>1-(1,3,5,6,7,8-Hexahydro-pyrrolo[3,4-b]quinolin-2-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone</p>                                                    | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 1.88 – 1.92 (m, 4H), 2.65 – 2.71 (m, 2H), 2.81 – 2.87 (m, 2H), 2.91 – 2.96 (m, 2H), 3.25 – 3.34 (m, 1H), 3.86 – 3.90 (m, 2H), 4.23 – 4.29 (m, 2H), 4.59 – 4.66 (m, 2H), 4.82 – 4.86 (m, 2H), 6.69 – 6.87 (m, 1H), 6.82 – 6.86 (m, 1H), 7.19 – 7.22 (s, 1H), 7.81 – 7.82 (m, 1H), 8.89 – 8.94 (d, <i>J</i> = 5.6 Hz, 1H); Mass (m/z): 349.0 (M+H) <sup>+</sup> . |

|     |                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                     |
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| 110 |  <p>1-(1,3,5,6,7,8-Hexahydro-pyrrolo[3,4-b]quinolin-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone</p>     | $^1\text{H}$ – NMR ( $\text{CDCl}_3$ , 400 MHz) $\delta$ ppm: 1.88 – 1.93 (m, 4H), 2.65 – 2.71 (m, 2H), 2.81 – 2.84 (m, 2H), 2.90 – 2.96 (m, 2H), 3.25 – 3.31 (m, 1H), 3.76 – 3.80 (m, 2H), 4.23 – 4.29 (m, 2H), 4.59 – 4.63 (m, 2H), 4.82 – 4.86 (m, 2H), 6.62 – 6.77 (m, 1H), 6.82 – 6.86 (m, 1H), 7.27 – 7.30 (s, 1H), 8.89 – 8.90 (d, $J$ = 5.4 Hz, 1H); Mass (m/z): 417.0 (M+H) <sup>+</sup> . |
| 111 |  <p>2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b]quinolin-2-yl)-ethanone</p>      | Mass (m/z): 399.0 (M+H) <sup>+</sup> .                                                                                                                                                                                                                                                                                                                                                              |
| 112 |  <p>(1,3,5,6,7,8-Hexahydro-pyrrolo[3,4-b]quinolin-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone</p> | $^1\text{H}$ – NMR ( $\text{CDCl}_3$ , 400 MHz) $\delta$ ppm: 1.88 – 1.93 (m, 4H), 2.55 – 2.65 (m, 2H), 2.81 – 2.84 (m, 2H), 2.90 – 2.96 (m, 2H), 3.27 – 3.34 (m, 1H), 3.66 – 3.76 (m, 2H), 4.23 – 4.29 (m, 2H), 4.59 – 4.73 (m, 4H), 6.52 – 6.57 (m, 1H), 6.72 – 6.76 (m, 1H), 7.27 – 7.30 (s, 1H), 8.78 – 8.80 (d, $J$ = 5.2 Hz, 1H); Mass (m/z): 417.0 (M+H) <sup>+</sup> .                      |
| 113 |                                                                                                                               | Mass (m/z): 399.0 (M+H) <sup>+</sup> .                                                                                                                                                                                                                                                                                                                                                              |

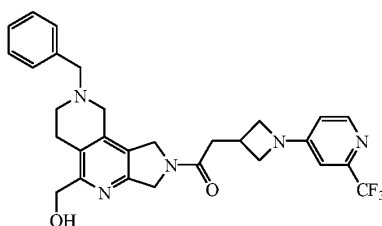
|     |                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                            |
|-----|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     | [1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b]quinolin-2-yl)-methanone                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                            |
| 114 |  <p>1-(3,6,7,8-Tetrahydro-1H-2,4-diaza-as-indacen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone</p>     | $^1\text{H}$ – NMR ( $\text{CDCl}_3$ , 400 MHz) $\delta$ ppm: 2.14 – 2.21 (m, 2H), 2.81 – 2.89 (m, 4H), 2.95 – 2.99 (t, $J$ = 6.8 Hz, 2H), 3.30 – 3.34 (m, 1H), 3.69 – 3.77 (m, 2H), 4.25 – 4.30 (m, 2H), 4.74 – 4.78 (m, 4H), 6.31 – 6.33 (m, 1H), 6.57 – 6.58 (d, $J$ = 2 Hz, 1H), 8.27 – 8.28 (d, $J$ = 5.6 Hz, 1H), 8.37 – 8.40 (d, $J$ = 12.8 Hz, 1H); Mass (m/z): 403.0 (M+H) $^+$ . |
| 115 |  <p>2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(3,6,7,8-tetrahydro-1H-2,4-diaza-as-indacen-2-yl)-ethanone</p>    | $^1\text{H}$ – NMR ( $\text{CDCl}_3$ , 400 MHz) $\delta$ ppm: 2.17 – 2.26 (m, 2H), 2.81 – 2.89 (m, 4H), 2.94 – 2.99 (t, $J$ = 7.6 Hz, 2H), 3.25 – 3.33 (m, 1H), 3.69 – 3.76 (m, 2H), 4.24 – 4.37 (m, 2H), 4.74 – 4.78 (m, 4H), 6.28 – 6.30 (m, 1H), 6.36 – 6.64 (m, 2H), 8.21 – 8.22 (d, $J$ = 6 Hz, 1H), 8.36 – 8.40 (d, $J$ = 12.4 Hz, 1H); Mass (m/z): 385.0 (M+H) $^+$ .               |
| 116 |  <p>1-(3,6,7,8-Tetrahydro-1H-2,4-diaza-as-indacen-2-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone</p> | $^1\text{H}$ – NMR ( $\text{CDCl}_3$ , 400 MHz) $\delta$ ppm: 2.11 – 2.19 (m, 2H), 2.78 – 2.83 (m, 4H), 2.90 – 2.97 (t, $J$ = 6.3 Hz, 2H), 3.33 – 3.37 (m, 1H), 3.69 – 3.77 (m, 2H), 4.28 – 4.39 (m, 2H), 4.73 – 4.79 (m, 4H), 8.27 – 8.28 (s, 1H), 8.48 (m, 2H); Mass (m/z): 404.3 (M+H) $^+$ .                                                                                           |

|     |                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                     |
|-----|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 117 |  <p>2-(1-Pyrimidin-5-yl-azetidin-3-yl)-1-(3,6,7,8-tetrahydro-1H-2,4-diazas-indacen-2-yl)-ethanone</p>                     | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 2.11 – 2.19 (m, 2H), 2.78 – 2.83 (m, 4H), 2.90 – 2.97 (t, <i>J</i> = 6.3 Hz, 2H), 3.33 – 3.37 (m, 1H), 3.69 – 3.77 (m, 2H), 4.28 – 4.39 (m, 2H), 4.73 – 4.79 (m, 4H), 7.93 (s, , 2H), 8.23 (s, 1H) 8.65 (s, 1H); Mass (m/z): 336.2 (M+H) <sup>+</sup> .                                                                                                   |
| 118 |  <p>2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(3,6,7,8-tetrahydro-1H-2,4-diazas-indacen-2-yl)-ethanone</p>  | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 2.16 – 2.19 (m, 2H), 2.71 – 2.80 (m, 4H), 2.96 – 2.99 (t, <i>J</i> = 6.6 Hz, 2H), 3.35 – 3.38 (m, 1H), 3.63 – 3.75 (m, 2H), 4.21 – 4.35 (m, 4H), 4.70 – 4.77 (m, 4H), 6.63 – 6.65 (s, 2H), 8.22 (s, 1H), 7.65 (s, 1H); Mass (m/z): 399.3 (M+H) <sup>+</sup> .                                                                                             |
| 119 |  <p>1-(3,6,7,8-Tetrahydro-1H-2,4-diazas-indacen-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone</p> | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 2.14 – 2.21 (m, 2H), 2.81 – 2.89 (m, 4H), 2.95 – 2.99 (t, <i>J</i> = 6.8 Hz, 2H), 3.30 – 3.34 (m, 1H), 3.69 – 3.77 (m, 2H), 4.25 – 4.30 (m, 2H), 4.74 – 4.78 (m, 4H), 6.33 – 6.38 (m, 1H), 6.66 – 6.71 (d, <i>J</i> = 2.6 Hz, 1H), 7.58 – 7.60 (d, <i>J</i> = 8.5 Hz, 1H), 8.28 – 8.31 (d, <i>J</i> = 5.4 Hz, 1H); Mass (m/z): 403.0 (M+H) <sup>+</sup> . |
| 120 |  <p>1-(3,6,7,8-Tetrahydro-1H-2,4-diazas-indacen-2-yl)-2-[1-(3-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone</p> | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 2.16 – 2.21 (m, 2H), 2.37 – 2.41 (m, 2H), 2.86 – 2.88 (m, 2H), 2.95 – 3.00 (m, 2H), 3.42 – 3.47 (m, 1H), 3.49 – 3.60 (m, 2H), 3.65 – 3.73                                                                                                                                                                                                                 |

|     |                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                        |
|-----|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     | (3,6,7,8-Tetrahydro-1H-2,4-diaza-as-indacen-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone                                                                                            | (m, 2H), 4.78 – 4.93 (m, 4H), 6.48 – 6.50 (m, 1H), 6.75 – 6.76 (d, $J = 2.4$ Hz, 1H), 8.29 – 8.30 (d, $J = 5.6$ Hz, 1H), 8.38 – 8.41 (d, $J = 13.2$ Hz, 1H); Mass (m/z): 403.0(M+H) <sup>+</sup> .                                                                                                                                                                                                     |
| 121 |  <p>[1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(3,6,7,8-tetrahydro-1H-2,4-diaza-as-indacen-2-yl)-methanone</p>    | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 2.14 – 2.20 (m, 2H), 2.37 – 2.43 (m, 2H), 2.85 – 2.89 (m, 2H), 2.95 – 3.04 (m, 2H), 3.42 – 3.49 (m, 1H), 3.49 – 3.62 (m, 2H), 3.67 – 3.75 (m, 2H), 4.79 – 4.94 (m, 4H), 6.48 – 6.50 (m, 2H), 6.77 – 6.78 (d, $J = 2.5$ Hz, 1H), 8.31 – 8.33 (d, $J = 5.7$ Hz, 1H), 8.37 – 8.43 (d, $J = 12.9$ Hz, 1H); Mass (m/z): 385.6(M+H) <sup>+</sup> . |
| 122 |  <p>(3,6,7,8-Tetrahydro-1H-2,4-diaza-as-indacen-2-yl)-[1-(6-trifluoromethyl-pyridin-3-yl)-pyrrolidin-3(R)-yl]-methanone</p> | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 2.14 – 2.22 (m, 2H), 2.36 – 2.42 (m, 2H), 2.81 – 2.89 (m, 2H), 2.95 – 3.03 (m, 2H), 3.43 – 3.49 (m, 1H), 3.54 – 3.60 (m, 2H), 3.68 – 3.70 (m, 2H), 4.73 – 4.94 (m, 4H), 6.49 – 6.52 (m, 1H), 6.66 – 6.68 (d, $J = 2.7$ Hz, 1H), 8.25 – 8.28 (d, $J = 5.8$ Hz, 1H), 8.33 – 8.36 (d, $J = 12.1$ Hz, 1H); Mass (m/z): 403.0(M+H) <sup>+</sup> . |
| 123 |  <p>2-(1-Pyridin-4-yl-azetidin-3-yl)-1-(3,6,7,8-tetrahydro-1H-2,4-diaza-as-indacen-2-yl)-ethanone</p>                       | Mass (m/z): 335.1 (M+H) <sup>+</sup> .                                                                                                                                                                                                                                                                                                                                                                 |

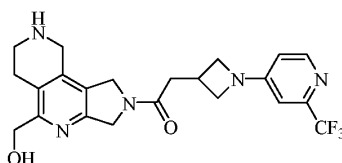
|     |                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                           |
|-----|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 124 |  <p>2-(1-(3-(pyridin-3-yl)azetidin-3-yl)-1-(3,6,7,8-tetrahydro-1H-2,4-diazas-indacen-2-yl)ethanone</p> | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 2.15 – 2.21 (m, 2H), 2.82 – 2.89 (m, 4H), 2.95 – 2.98 (t, <i>J</i> = 7.2 Hz, 2H), 3.25 – 3.28 (m, 1H), 3.64 – 3.69 (m, 2H), 4.17 – 4.21 (m, 2H), 4.74 – 4.78 (m, 4H), 6.72 – 6.75 (m, 1H), 7.05 – 7.12 (m, 1H), 7.85 – 7.86 (d, <i>J</i> = 2.8 Hz, 1H), 7.99 – 8.00 (d, <i>J</i> = 3.6 Hz, 1H), 8.36 – 8.39 (d, <i>J</i> = 12.0 Hz, 1H); Mass (m/z): 335.3 (M+H) <sup>+</sup> . |
|-----|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

**Example-125:** 1-(8-Benzyl-5-hydroxymethyl-1,3,6,7,8,9-hexahydro-2,4,8-triazacyclopenta[a]naphthalen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone



- 5 HATU (0.28 g, 0.00075) was added to a stirred solution of [1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-acetic acid (0.13 g, 0.0005 mol, Intermediate-23) in DMF (2 mL) followed by the addition of (8-benzyl-2,3,6,7,8,9-hexahydro-1H-2,4,8-triazacyclopenta[a]naphthalen-5-yl)-methanol hydrochloride (0.2 g, 0.0006 mol, Intermediate-22) and diisopropylethylamine (0.35 mL, 0.002 mol) and the reaction mixture stirred at RT for
- 10 18 h. The reaction mixture was then poured onto cold water (15 mL) and product extracted using DCM (15 mL x 3). The organic extracts were combined, washed with brine (15 mL), dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated in vacuo to get a residual mass that was purified by column chromatography using 5 - 6 % MeOH in DCM to obtain the title compound. Yield: 0.21 g (65 %); Mass (m/z): 538.1 (M+H)<sup>+</sup>.

- 15 **Example-126:** 1-(5-Hydroxymethyl-1,3,6,7,8,9-hexahydro-2,4,8-triazacyclopenta[a]naphthalen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone

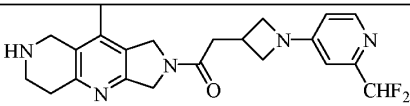
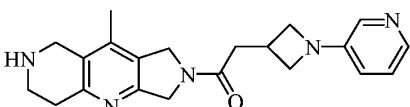
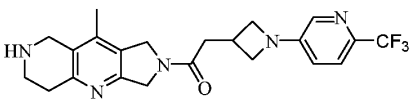
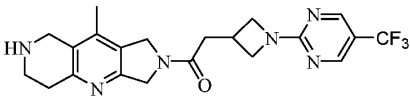


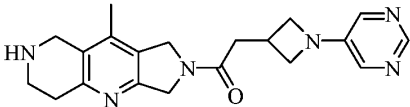
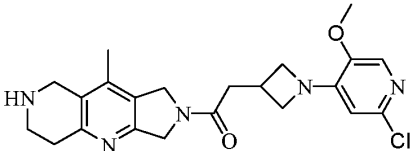
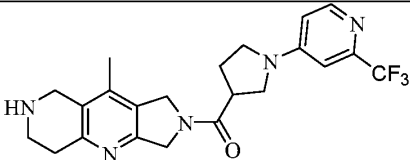
Pd/C (0.08 g) and ammonium formate (0.1 g, 0.0015 mol) were added to stirred solution of 1-(8-benzyl-5-hydroxymethyl-1,3,6,7,8,9-hexahydro-2,4,8-triaza-cyclopenta[a]naphthalen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone (0.085 g, 0.00015 mol, Example-1) in methanol (5 mL) and the reaction mixture was refluxed for 6 h. The reaction mixture was cooled to RT, filtered and filtrate was concentrated in vacuo to obtain residual mass that was purified by column chromatography using using 10 - 12 % MeOH in DCM to obtain the title compound. Yield: 15 mg (21 %), Mass (m/z): 448.2 (M+H)<sup>+</sup>.

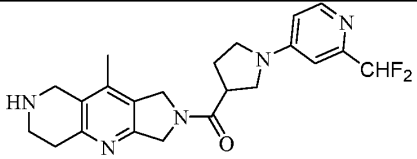
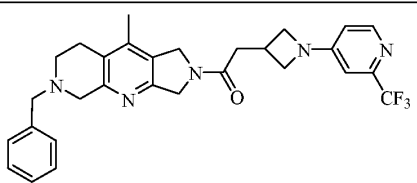
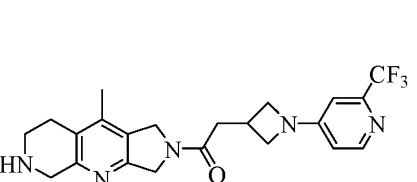
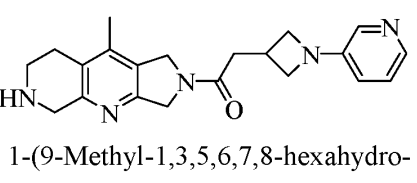
The following Example-127 to Example-150 were prepared by following the experimental procedure of preparation as described in the Example-125 and Example-126 using suitable intermediates (synthesized above) with some non-critical variations.

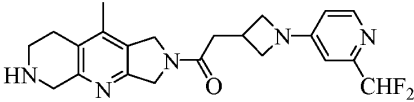
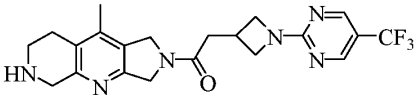
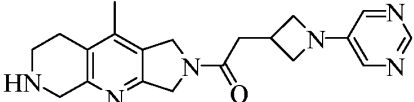
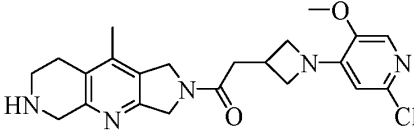
| Example | Chemical structure and IUPAC Name                                                                                                                          | Characterization Data                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|---------|------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 127     | <p>1-(7-Benzyl-9-methyl-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone</p> | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 2.07 – 2.09 (d, <i>J</i> = 6.8 Hz, 3H), 2.78 – 2.83 (d, <i>J</i> = 8.4 Hz, 2H), 2.93 – 2.95 (t, <i>J</i> = 5.2 Hz, 2H), 3.10 – 3.19 (m, 2H), 3.27 – 3.32 (m, 1H), 3.72 – 3.78 (m, 4H), 3.89 – 3.92 (m, 2H), 4.25 – 4.30 (m, 2H), 4.69 – 4.75 (m, 4H), 6.32 – 6.33 (m, 1H), 6.57 – 6.58 (m, 1H), 7.33 – 7.41 (m, 3H), 7.52 – 7.54 (m, 1H), 7.71 – 7.73 (m, 1H), 8.27 – 8.28 (d, <i>J</i> = 5.6 Hz, 1H); Mass (m/z): 522.3 (M+H) <sup>+</sup> . |
| 128     | <p>1-(9-Methyl-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone</p>          | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 2.10 – 2.11 (d, <i>J</i> = 6.8 Hz, 3H), 2.76 – 2.79 (d, <i>J</i> = 8.4 Hz, 2H), 2.94 – 2.96 (t, <i>J</i> = 5.2 Hz, 2H), 3.15 – 3.21 (m, 2H), 3.31 –                                                                                                                                                                                                                                                                                           |

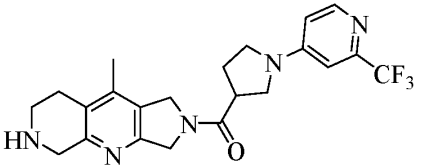
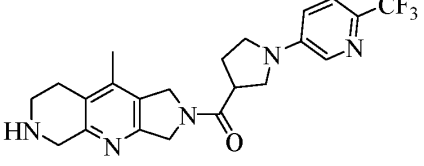
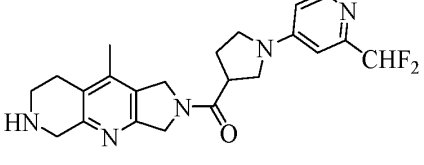
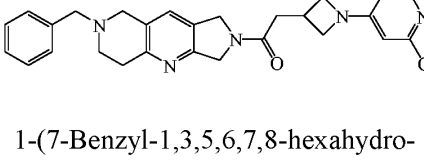


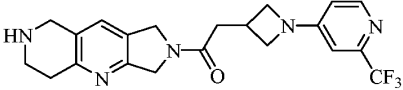
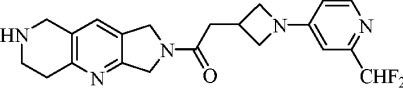
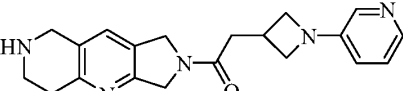
|     |                                                                                                                                                                                                                                       |                                                                                                                                                                                                                     |
|-----|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     | 2,4,7-triaza-cyclopenta[b]naphthalen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone                                                                                                                              | 3.35 (m, 1H), 3.75 – 3.91 (m, 4H), 3.93 – 3.96 (m, 2H), 4.71 – 4.76 (m, 4H), 6.29 – 6.31 (m, 1H), 6.57 – 6.58 (m, 1H), 8.27 – 8.28 (d, $J = 5.6$ Hz, 1H), 10.24 (bs, 1H);<br>Mass (m/z): 432.1 (M+H) <sup>+</sup> . |
| 129 |  <p>2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(9-methyl-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-2-yl)-ethanone</p>    | Mass (m/z): 414.4 (M+H) <sup>+</sup> .                                                                                                                                                                              |
| 130 |  <p>1-(9-Methyl-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-2-yl)-2-(1-pyridin-3-yl)-azetidin-3-yl)-ethanone</p>                     | Mass (m/z): 364.4 (M+H) <sup>+</sup> .                                                                                                                                                                              |
| 131 |  <p>1-(9-Methyl-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone</p> | Mass (m/z): 432.3 (M+H) <sup>+</sup> .                                                                                                                                                                              |
| 132 |  <p>1-(9-Methyl-1,3,5,6,7,8-hexahydro-2,4,7-triaza-</p>                                                                                            | Mass (m/z): 433.4 (M+H) <sup>+</sup> .                                                                                                                                                                              |

|            |                                                                                                                                                                                                                                        |                                        |
|------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|
|            | cyclopenta[b]naphthalen-2-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone                                                                                                                                          |                                        |
| <b>133</b> |  <p>1-(9-Methyl-1,3,5,6,7,8-hexahydro-2,4,7-triazacyclopenta[b]naphthalen-2-yl)-2-(1-pyrimidin-5-yl)-azetidin-3-yl)-ethanone</p>                      | Mass (m/z): 365.3 (M+H) <sup>+</sup> . |
| <b>134</b> |  <p>2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(9-methyl-1,3,5,6,7,8-hexahydro-2,4,7-triazacyclopenta[b]naphthalen-2-yl)-ethanone</p>   | Mass (m/z): 428.9 (M+H) <sup>+</sup> . |
| <b>135</b> |  <p>(9-Methyl-1,3,5,6,7,8-hexahydro-2,4,7-triazacyclopenta[b]naphthalen-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone</p> | Mass (m/z): 432.4 (M+H) <sup>+</sup> . |

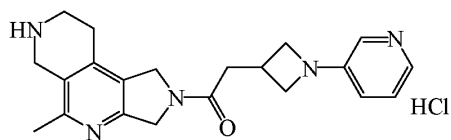
|     |                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                            |
|-----|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 136 |  <p>[1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(9-methyl-1,3,5,6,7,8-hexahydro-2,4,7-triazacyclopenta[b]naphthalen-2-yl)-methanone</p>     | Mass (m/z): 414.1 (M+H) <sup>+</sup> .                                                                                                                                                                                                                                                                                                                                                                                     |
| 137 |  <p>1-(6-Benzyl-9-methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b][1,7]naphthyridin-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone</p> | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 2.03 – 2.08 (m, 2H), 2.17 – 2.19 (d, <i>J</i> = 4.8 Hz, 3H), 2.80 – 2.85 (m, 4H), 3.29 – 3.33 (m, 1H), 3.74 – 3.79 (m, 6H), 4.26 – 4.30 (m, 2H), 4.74 – 4.77 (m, 4H), 6.33 – 6.35 (dd, <i>J</i> = 2.0, 5.6 Hz, 1H), 6.59 – 6.60 (d, <i>J</i> = 2.40 Hz, 1H), 7.31 – 7.41 (m, 5H), 8.28 – 8.30 (d, <i>J</i> = 5.6 Hz, 1H); Mass (m/z): 522.1 (M+H) <sup>+</sup> . |
| 138 |  <p>1-(9-Methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b][1,7]naphthyridin-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone</p>        | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 2.06 – 2.08 (m, 2H), 2.19 – 2.20 (d, <i>J</i> = 4.40 Hz, 3H), 2.75 – 2.82 (m, 4H), 3.46 – 3.49 (m, 1H), 3.70 – 3.77 (m, 4H), 4.25 – 4.32 (m, 2H), 4.75 – 4.78 (m, 4H), 6.32 – 6.34 (dd, <i>J</i> = 2.4, 5.6 Hz, 1H), 6.58 – 6.58 (d, <i>J</i> = 2.0 Hz, 1H), 8.27 – 8.29 (d, <i>J</i> = 6.0 Hz, 1H), 10.12 (bs, 1H); Mass (m/z): 432.1 (M+H) <sup>+</sup> .      |
| 139 |  <p>1-(9-Methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b][1,7]naphthyridin-2-</p>                                                                         | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 2.06 – 2.08 (m, 2H), 2.19 – 2.20 (d, <i>J</i> = 4.40 Hz, 3H), 2.75 – 2.82 (m, 4H), 3.46 – 3.49 (m, 1H), 3.70 – 3.77 (m, 4H), 4.25 – 4.32 (m, 2H), 4.75 – 4.78 (m, 4H), 6.77 –                                                                                                                                                                                    |

|     |                                                                                                                                                                                                                                   |                                                                                                                                                                     |
|-----|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     | yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone                                                                                                                                                                                     | 6.80 (dd, $J = 1.2, 6.8$ Hz, 1H), 7.15 – 7.18 (m, 1H), 7.77 – 7.78 (d, $J = 2.0$ Hz, 1H), 7.88 – 7.89 (d, $J = 4.0$ Hz, 1H); Mass (m/z): 364.1 (M+H) <sup>+</sup> . |
| 140 |  <p>2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(9-methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b][1,7]naphthyridin-2-yl)-ethanone</p>     | Mass (m/z): 414.1 (M+H) <sup>+</sup> .                                                                                                                              |
| 141 |  <p>1-(9-Methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b][1,7]naphthyridin-2-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone</p>  | Mass (m/z): 433.1 (M+H) <sup>+</sup> .                                                                                                                              |
| 142 |  <p>1-(9-Methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b][1,7]naphthyridin-2-yl)-2-(1-pyrimidin-5-yl-azetidin-3-yl)-ethanone</p>                    | Mass (m/z): 365.2 (M+H) <sup>+</sup> .                                                                                                                              |
| 143 |  <p>2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(9-methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b][1,7]naphthyridin-2-yl)-ethanone</p> | Mass (m/z): 428.1 (M+H) <sup>+</sup> .                                                                                                                              |

|     |                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                 |
|-----|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 144 |  <p>(9-Methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b][1,7]naphthyridin-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone</p>     | <sup>1</sup> H – NMR (CDCl <sub>3</sub> , 400 MHz) δ ppm: 2.10 – 2.12 (m, 2H), 2.21 – 2.22 (d, <i>J</i> = 4.40 Hz, 3H), 2.79 – 2.84 (m, 4H), 3.51 – 3.55 (m, 1H), 3.77 – 3.82 (m, 4H), 4.29 – 4.35 (m, 2H), 4.77 – 4.81 (m, 4H), 6.64 – 6.65 (d, <i>J</i> = 4.0 Hz, 1H), 6.85 (s, 1H), 8.21 – 8.22 (d, <i>J</i> = 6.0 Hz, 1H), 10.39 (bs, 1H); Mass (m/z): 432.1 (M+H) <sup>+</sup> .           |
| 145 |  <p>(9-Methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b][1,7]naphthyridin-2-yl)-[1-(6-trifluoromethyl-pyridin-3-yl)-pyrrolidin-3(R)-yl]-methanone</p>     | Mass (m/z): 432.0 (M+H) <sup>+</sup> .                                                                                                                                                                                                                                                                                                                                                          |
| 146 |  <p>[1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(9-methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b][1,7]naphthyridin-2-yl)-methanone</p>    | Mass (m/z): 412.2 (M+H) <sup>+</sup> .                                                                                                                                                                                                                                                                                                                                                          |
| 147 |  <p>1-(7-Benzyl-1,3,5,6,7,8-hexahydro-2,4,7-triazacyclopenta[b]naphthalen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone</p> | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.66 – 2.67 (t, <i>J</i> = 1.6 Hz, 2H), 2.82 – 2.85 (t, <i>J</i> = 7.2 Hz, 2H), 2.87 – 2.90 (m, 2H), 2.91 – 2.93 (m, 1H), 3.48 – 3.52 (m, 2H), 3.56 – 3.70 (m, 4H), 4.14 – 4.18 (t, <i>J</i> = 8.0 Hz, 2H), 4.52 – 4.57 (m, 2H), 4.75 – 4.79 (m, 2H), 6.51 – 6.53 (m, 1H), 6.70 (s, 1H), 7.27 – 7.36 (m, 5H), 7.47 (s, 1H), |

|            |                                                                                                                                                                                                                            |                                                                           |
|------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------|
|            |                                                                                                                                                                                                                            | 8.19 – 8.20 (d, $J = 5.6$ Hz, 1H); Mass (m/z): 508.1 (M+H) <sup>+</sup> . |
| <b>148</b> |  <p>1-(1,3,5,6,7,8-Hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone</p> | Mass (m/z): 418.1 (M+H) <sup>+</sup> .                                    |
| <b>149</b> |  <p>2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-2-yl)-ethanone</p>  | Mass (m/z): 400.3 (M+H) <sup>+</sup> .                                    |
| <b>150</b> |  <p>1-(1,3,5,6,7,8-Hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-2-yl)-2-(1-pyridin-3-yl)-azetidin-3-yl)-ethanone</p>                  | Mass (m/z): 350.4 (M+H) <sup>+</sup> .                                    |

**Example-151: 1-(5-Methyl-1,3,6,7,8,9-hexahydro-2,4,7-triaza-cyclopenta[a]naphthalen-2-yl)-2-(1-pyridin-3-yl)-azetidin-3-yl)-ethanone hydrochloride**



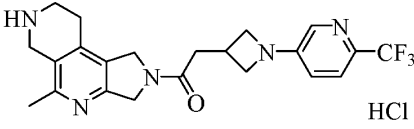
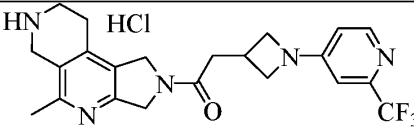
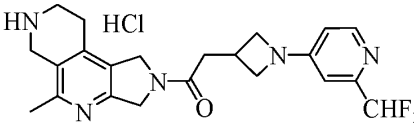
**Step 1: 5-Methyl-2-[2-(1-pyridin-3-yl-azetidin-3-yl)-acetyl]-1,2,3,6,8,9-hexahydro-2,4,7-triaza-cyclopenta[a]naphthalene-7-carboxylic acid tert-butyl ester**

HATU (0.16 g, 0.00041 mol) was added to a stirred solution of (1-pyridin-3-yl-azetidin-3-yl)-acetic acid (0.039 g, 0.0002 mol, intermediate-25) in DMF (2 mL) followed by the addition of 5-methyl-1,2,3,6,8,9-hexahydro-2,4,7-triaza-cyclopenta[a]naphthalene-7-carboxylic acid tert-butyl ester (0.1 g, 0.00034 mol, intermediate-19) and diisopropylethylamine (0.24 mL, 0.0013 mol) and the reaction mixture stirred at RT for 18 h. The reaction mixture was then poured onto cold water (10 mL) and product extracted using DCM (10 mL x 3). The organic extracts were combined, washed with brine (15 mL), dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated in vacuo to get a residual mass that was purified by column chromatography using 1 - 2 % MeOH in DCM to obtain the title compound. Yield: 0.05 g (27%); <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz) δ ppm: 1.52 (s, 9H), 2.39 (s, 3H), 2.59 – 2.61 (d, *J* = 7.6 Hz, 2H), 2.71 – 2.74 (m, 2H), 3.01 – 3.06 (m, 1H), 3.41 – 3.44 (t, *J* = 6.4 Hz, 2H), 3.69 – 3.89 (m, 4H), 3.99 – 4.02 (t, *J* = 7.6 Hz, 2H), 4.44 – 4.59 (m, 4H), 6.77 – 6.81 (m, 1H), 7.12 – 7.15 (m, 1H), 7.81 – 7.82 (d, *J* = 2.8 Hz, 1H), 7.91 – 7.93 (m, 1H); Mass (m/z): 464.2 (M+H)<sup>+</sup>.

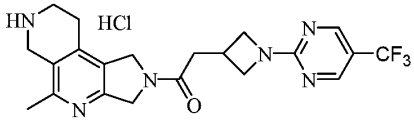
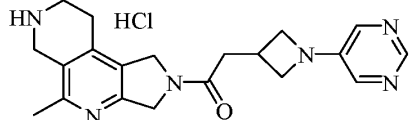
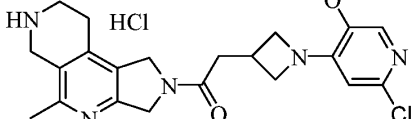
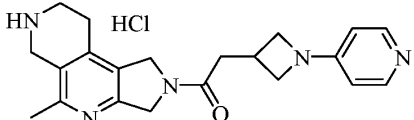
**Step 2: 1-(5-Methyl-1,3,6,7,8,9-hexahydro-2,4,7-triaza-cyclopenta[a]naphthalen-2-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone hydrochloride**

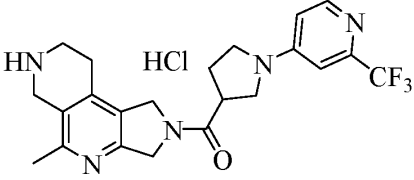
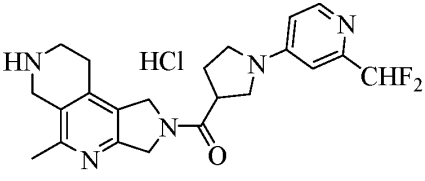
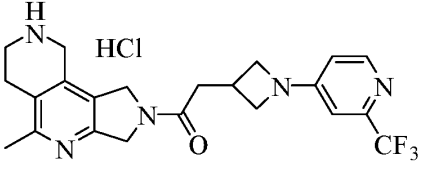
1-(5-Methyl-1,3,6,7,8,9-hexahydro-2,4,7-triaza-cyclopenta[a]naphthalen-2-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone hydrochloride was prepared by using the procedure as described in step-6 of intermediate-1 with some non-critical variations. Yield: 19 mg (52 %); <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ ppm: 2.41 (s, 3H), 2.61 – 2.63 (d, *J* = 7.6 Hz, 2H), 2.73 – 2.75 (m, 2H), 3.04 – 3.07 (m, 1H), 3.48 – 3.51 (m, 2H), 3.73 – 3.91 (m, 4H), 4.01 – 4.04 (m, 2H), 4.44 (s, 1H), 4.46 (s, 1H), 4.56 (s, 1H), 4.59 (s, 1H), 6.89 – 6.93 (m, 1H), 7.19 – 7.23 (m, 1H), 7.91 – 7.99 (d, *J* = 2.8 Hz, 1H), 8.03 – 8.05 (m, 1H), 10.31 (bs, 2H); Mass (m/z): 364.1 (M+H)<sup>+</sup>.

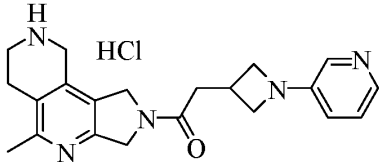
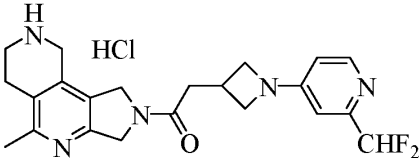
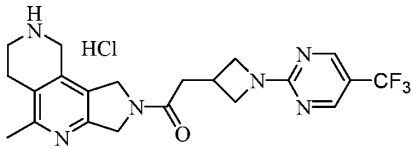
The following Example-152 to Example-168 were prepared by following the experimental procedure of preparation as described in the Example-151 using suitable intermediates (synthesized above) with some non-critical variations.

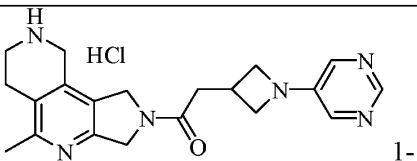
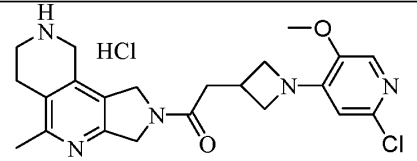
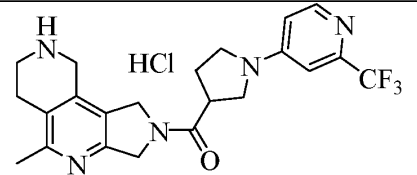
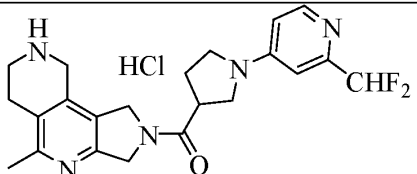
| Example | Chemical structure and IUPAC Name                                                                                                                                                                                                                 | Characterization Data                                                                                                                                                                                                                                                                                                                                                                                                                                  |
|---------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 152     |  <p>1-(5-Methyl-1,3,6,7,8,9-hexahydro-2,4,7-triazacyclopenta[a]naphthalen-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone hydrochloride</p>  | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.41 (s, 3H), 2.60 – 2.62 (d, <i>J</i> = 7.6 Hz, 2H), 2.69 – 2.73 (m, 2H), 3.01 – 3.04 (m, 1H), 3.41 – 3.49 (m, 2H), 3.71 – 3.83 (m, 4H), 4.01 – 4.04 (m, 2H), 4.51 (s, 1H), 4.54 (s, 1H), 4.65 (s, 1H), 4.68 (s, 1H), 6.69 – 6.72 (m, 1H), 7.43 – 7.45 (d, <i>J</i> = 8.8 Hz, 1H), 7.87 – 7.88 (d, <i>J</i> = 2.4 Hz, 1H), 10.31 (bs, 2H); Mass (m/z): 432.2 (M+H) <sup>+</sup> . |
| 153     |  <p>1-(5-Methyl-1,3,6,7,8,9-hexahydro-2,4,7-triazacyclopenta[a]naphthalen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone hydrochloride</p> | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.40 (s, 3H), 2.59 – 2.62 (d, <i>J</i> = 7.6 Hz, 2H), 2.71 – 2.73 (m, 2H), 3.02 – 3.05 (m, 1H), 3.47 – 3.50 (m, 2H), 3.69 – 3.87 (m, 4H), 3.99 – 4.04 (m, 2H), 4.47 (s, 1H), 4.51 (s, 1H), 4.61 (s, 1H), 4.65 (s, 1H), 6.52 – 6.53 (d, <i>J</i> = 4.4 Hz, 1H), 6.70 (s, 1H), 8.19 – 8.21 (d, <i>J</i> = 5.6 Hz, 1H), 10.29 (bs, 2H); Mass (m/z): 432.2 (M+H) <sup>+</sup> .        |
| 154     |  <p>2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(5-methyl-1,3,6,7,8,9-hexahydro-2,4,7-triazacyclopenta[a]naphthalen-2-yl)-ethanone hydrochloride</p> | Mass (m/z): 450.8 (M+H) <sup>+</sup> .                                                                                                                                                                                                                                                                                                                                                                                                                 |



|     |                                                                                                                                                                                                                                                      |                                        |
|-----|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|
| 155 |  <p>1-(5-Methyl-1,3,6,7,8,9-hexahydro-2,4,7-triaza-cyclopenta[a]naphthalen-2-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone hydrochloride</p>  | Mass (m/z): 433.4 (M+H) <sup>+</sup> . |
| 156 |  <p>1-(5-Methyl-1,3,6,7,8,9-hexahydro-2,4,7-triaza-cyclopenta[a]naphthalen-2-yl)-2-(1-pyrimidin-5-yl-azetidin-3-yl)-ethanone hydrochloride</p>                      | Mass (m/z): 365.4 (M+H) <sup>+</sup> . |
| 157 |  <p>2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(5-methyl-1,3,6,7,8,9-hexahydro-2,4,7-triaza-cyclopenta[a]naphthalen-2-yl)-ethanone hydrochloride</p> | Mass (m/z): 428.8 (M+H) <sup>+</sup> . |
| 158 |  <p>1-(5-Methyl-1,3,6,7,8,9-hexahydro-2,4,7-triaza-</p>                                                                                                           | Mass (m/z): 364.4 (M+H) <sup>+</sup> . |

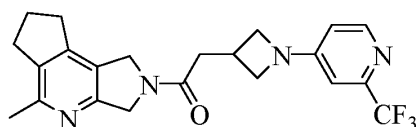
|     |                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                  |
|-----|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     | cyclopenta[a]naphthalen-2-yl)-2-(1-pyridin-4-yl-azetidin-3-yl)-ethanone hydrochloride                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                  |
| 159 |  <p>(5-Methyl-1,3,6,7,8,9-hexahydro-2,4,7-triazacyclopenta[a]naphthalen-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone hydrochloride</p>      | Mass (m/z): 432.4 (M+H) <sup>+</sup> .                                                                                                                                                                                                                                                                                                                                                           |
| 160 |  <p>[1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(5-methyl-1,3,6,7,8,9-hexahydro-2,4,7-triazacyclopenta[a]naphthalen-2-yl)-methanone hydrochloride</p>      | Mass (m/z): 414.4 (M+H) <sup>+</sup> .                                                                                                                                                                                                                                                                                                                                                           |
| 161 |  <p>1-(5-Methyl-1,3,6,7,8,9-hexahydro-2,4,8-triazacyclopenta[a]naphthalen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-ethanone hydrochloride</p> | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.47 (s, 3H), 2.61 – 2.63 (d, <i>J</i> = 7.6 Hz, 2H), 2.71 – 2.73 (m, 2H), 2.89 – 2.91 (m, 2H), 3.02 – 3.05 (m, 1H), 3.64 – 3.67 (m, 2H), 3.79 – 3.84 (m, 2H), 4.02 – 4.04 (m, 2H), 4.61 (s, 1H), 4.64 (s, 1H), 4.71 (s, 1H), 4.73 (s, 1H), 6.57 – 6.59 (d, <i>J</i> = 4.4 Hz, 1H), 6.74 (s, 1H), 8.14 – 8.16 (d, <i>J</i> = |

|     |                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|-----|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|     | azetidin-3-yl]-ethanone hydrochloride                                                                                                                                                                                                                | 5.6 Hz, 1H), 10.19 (bs, 2H); Mass (m/z): 432.2 (M+H) <sup>+</sup> .                                                                                                                                                                                                                                                                                                                                                                                                           |
| 162 |  <p>1-(5-Methyl-1,3,6,7,8,9-hexahydro-2,4,8-triazacyclopenta[a]naphthalen-2-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone hydrochloride</p>                         | <sup>1</sup> H – NMR (DMSO- <i>d</i> <sub>6</sub> , 400 MHz) δ ppm: 2.45 (s, 3H), 2.62 – 2.64 (d, <i>J</i> = 7.6 Hz, 2H), 2.70 – 2.72 (m, 2H), 2.88 – 2.91 (m, 2H), 3.01 – 3.05 (m, 1H), 3.61 – 3.64 (m, 2H), 3.77 – 3.82 (m, 2H), 4.01 – 4.03 (m, 2H), 4.60 (s, 1H), 4.64 (s, 1H), 4.72 (s, 1H), 4.75 (s, 1H), 6.89 – 6.93 (m, 1H), 7.19 – 7.23 (m, 1H), 7.91 – 7.99 (d, <i>J</i> = 2.8 Hz, 1H), 8.03 – 8.05 (m, 1H), 10.31 (bs, 2H); Mass (m/z): 364.1 (M+H) <sup>+</sup> . |
| 163 |  <p>2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(5-methyl-1,3,6,7,8,9-hexahydro-2,4,8-triazacyclopenta[a]naphthalen-2-yl)-ethanone hydrochloride</p>     | Mass (m/z): 450.7 (M+H) <sup>+</sup> .                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| 164 |  <p>1-(5-Methyl-1,3,6,7,8,9-hexahydro-2,4,8-triazacyclopenta[a]naphthalen-2-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone hydrochloride</p> | Mass (m/z): 433.4 (M+H) <sup>+</sup> .                                                                                                                                                                                                                                                                                                                                                                                                                                        |

|     |                                                                                                                                                                                                                                                      |                                        |
|-----|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|
| 165 |  <p>(5-Methyl-1,3,6,7,8,9-hexahydro-2,4,8-triazacyclopenta[a]naphthalen-2-yl)-2-(1-pyrimidin-5-yl-azetidin-3-yl)-ethanone hydrochloride</p>                         | Mass (m/z): 365.3 (M+H) <sup>+</sup> . |
| 166 |  <p>2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(5-methyl-1,3,6,7,8,9-hexahydro-2,4,8-triazacyclopenta[a]naphthalen-2-yl)-ethanone hydrochloride</p>    | Mass (m/z): 428.9 (M+H) <sup>+</sup> . |
| 167 |  <p>(5-Methyl-1,3,6,7,8,9-hexahydro-2,4,8-triazacyclopenta[a]naphthalen-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone hydrochloride</p> | Mass (m/z): 432.4 (M+H) <sup>+</sup> . |
| 168 |  <p>(5-Methyl-1,3,6,7,8,9-hexahydro-2,4,8-triazacyclopenta[a]naphthalen-2-yl)-[1-(2-difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone hydrochloride</p>  | Mass (m/z): 414.0 (M+H) <sup>+</sup> . |

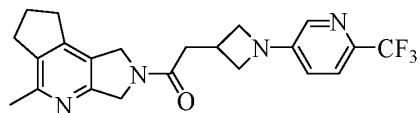
|  |                                                                                                                                                          |  |
|--|----------------------------------------------------------------------------------------------------------------------------------------------------------|--|
|  | [1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(5-methyl-1,3,6,7,8,9-hexahydro-2,4,8-triazacyclopenta[a]naphthalen-2-yl)-methanone hydrochloride |  |
|--|----------------------------------------------------------------------------------------------------------------------------------------------------------|--|

**Example-169: 1-(5-methyl-3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone**



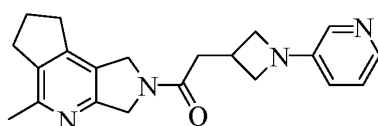
- 5 HATU (0.22 g, 0.00057 mol) was added to a stirred solution of [1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-acetic acid (0.1 g, 0.00038 mol, Intermediate-23) in DMF (3 mL) followed by the addition of mixture of 5-methyl-1,2,3,6,7,8-hexahydro-2,4-diaza-as-indacene hydrochloride and 8-methyl-1,2,3,5,6,7-hexahydro-2,4-diaza-s-indacene hydrochloride (0.097 g, 0.00046, Intermediate-16) and diisopropylethylamine (0.27 mL,
- 10 0.0015 mol) and the reaction mixture stirred at RT for 18 h. The reaction mixture was then poured onto cold water (10 mL) and product extracted using DCM (15 mL x 3). The organic extracts were combined, washed with brine (10 mL), dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated in vacuo to get the mixture of compounds. It was purified by following liquid chromatographic condition - CHIRAL PAK AD-H (250 × 20 mm, 5 μm) with mobile
- 15 phase methanol:IPA:n-heptane:diethylamine (60:20:20:0.1) at RT to get the title compound. Yield: 0.09 g (56 %); <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ ppm: 2.04 – 2.08 (m, 2H), 2.38 (s, 3H), 2.83 – 2.85 (m, 6H), 3.10 – 3.13 (m, 1H), 3.69 – 3.71 (m 2H), 4.15 – 4.19 (t, *J* = 8.4 Hz, 2H) 4.51 (s, 1H), 4.56 (s, 1H), 4.73 (s, 1H), 4.79 (s, 1H), 6.52 – 6.53 (d, *J* = 4.4 Hz, 1H), 6.70 (s, 1H), 8.19 – 8.21 (d, *J* = 5.6 Hz, 1H); Mass (*m/z*): 416.8 (M+H)<sup>+</sup>.
- 20 The below Example-170 to Example-188 were prepared by following the experimental procedure of preparation as described in the Example-169 using suitable intermediates (synthesized above) with some non-critical variations. The isolated mixture of compounds were purified by liquid chromatographic condition as per the methods given below

**Example- 170: 1-(5-Methyl-3,6,7,8-tetrahydro-1H-2,4-diaza-as-indacen-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone**



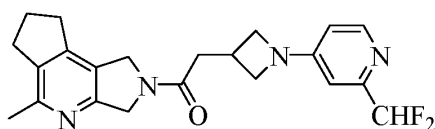
Liquid chromatographic condition - X-bridge prep c18 OBD (250 X 19 mm, 5 $\mu$ m) with mobile phase milli-Q water:acetonitrile (25:75), pH 2.5, wavelength 270 nm at RT to get the title compound.  $^1\text{H}$  - NMR (DMSO- $d_6$ , 400 MHz)  $\delta$  ppm: 2.13 – 2.20 (m, 2H), 2.47 (s, 3H), 2.80 – 2.91 (m, 6H), 3.29 – 3.33 (m, 1H), 3.71– 3.77 (m 2H), 4.24 – 4.28 (t,  $J$  = 7.6 Hz, 2H), 4.70 – 4.76(m, 4H), 6.69 – 6.71 (d,  $J$  = 6.8 Hz, 1H), 7.44 – 7.46 (d,  $J$  = 8.4 Hz, 1H) 7.85 (s, 1H); Mass (m/z): 417.0 (M+H) $^+$ .

**Example-171: 1-(5-Methyl-3,6,7,8-tetrahydro-1H-2,4-diaza-as-indacen-2-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone**



Liquid chromatographic condition - CHIRAL PAK IC-C (250  $\times$  21 mm, 5 $\mu$ m) with mobile phase methanol:acetonitrile:diethylamine (80:20:0.1) at RT to get the title compound.  $^1\text{H}$  - NMR (DMSO- $d_6$ , 400 MHz)  $\delta$  ppm: 2.04 – 2.09 (m, 2H), 2.38 (s, 3H), 2.81– 2.88 (m, 6H), 3.07 – 3.10 (m, 1H), 3.54 – 3.58 (m 2H), 4.04 – 4.08 (t,  $J$  = 6.4 Hz, 2H) 4.51 (s, 1H), 4.56 (s, 1H), 4.73 (s, 1H), 4.79 (s, 1H), 6.78 – 6.80 (m, 1H), 7.12–7.15 (m, 1H), 7.79 – 7.80 (d,  $J$  = 2.8 Hz, 1H) 7.89 – 7.90 (d,  $J$  = 1.2 Hz, 1H); Mass (m/z): 349.0 (M+H) $^+$ .

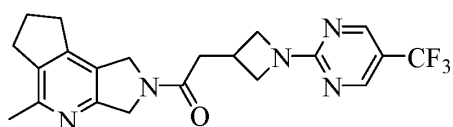
**Example-172: 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(5-methyl-3,6,7,8-tetrahydro-1H-2,4-diaza-as-indacen-2-yl)-ethanone**



Liquid chromatographic condition –CHIRAL PAK AD-H (250 X 20 mm, 5 $\mu$ m) with mobile phase methanol:IPA:n-hexane:diethylamine (40:20:40:0.1) at RT to get the title

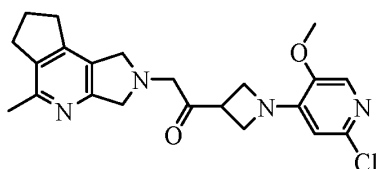
compound.  $^1\text{H}$  – NMR (DMSO- $d_6$ , 400 MHz)  $\delta$  ppm: 2.04 – 2.08 (m, 2H), 2.38 (s, 3H), 2.83 – 2.86 (m, 6H), 3.11 – 3.13 (m, 1H), 3.65 – 3.69 (m, 2H), 4.14 – 4.16 (t,  $J$  = 8.0 Hz, 2H), 4.51 (s, 1H), 4.56 (s, 1H), 4.73 (s, 1H), 4.79 (s, 1H), 6.43 – 6.44 (m, 1H), 6.55 – 6.58 (d,  $J$  = 9.2 Hz, 1H), 6.71 (s, 1H), 8.14 – 8.16 (d,  $J$  = 5.6 Hz, 1H); Mass (m/z): 399.2 (M+H) $^+$ .

5 **Example-173: 1-(5-Methyl-3,6,7,8-tetrahydro-1H-2,4-diaza-as-indacen-2-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone**



Liquid chromatographic condition – CHIRAL PAK-IC (250 X 21 mm, 5 $\mu$ m) with mobile phase methanol:n-hexane:acetonitrile:diethylamine (40:30:20:10:0.1) at RT to get the title compound.  $^1\text{H}$  – NMR (CDCl $_3$ , 400 MHz)  $\delta$  ppm: 2.09 – 2.18 (m, 2H), 2.47 – 2.48 (d,  $J$  = 4.4 Hz, 3H), 2.79 – 3.02 (m, 6H), 3.24 – 3.31 (m, 1H), 3.90 – 3.95 (m, 2H), 4.42 – 4.47 (t,  $J$  = 9.2 Hz, 2H), 4.71 – 4.76 (m, 4H), 8.47 (s, 2H); Mass (m/z): 418.6 (M+H) $^+$ .

**Example-174: 2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(5-methyl-3,6,7,8-tetrahydro-1H-2,4-diaza-as-indacen-2-yl)-ethanone**

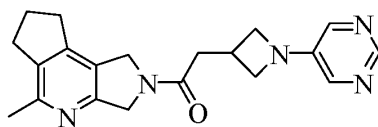


15

Liquid chromatographic condition – CHIRAL ART CELLULOSE-SZ (250 X 20 mm, 5 $\mu$ m) with mobile phase methanol:IPA:n-hexane:diethylamine (20:30:50:0.1) at RT to get the title compound.  $^1\text{H}$  – NMR (DMSO- $d_6$ , 400 MHz)  $\delta$  ppm: 2.04 – 2.08 (m, 2H), 2.38 (s, 3H), 2.79 – 2.85 (m, 6H), 3.16 – 3.17 (m, 2H), 3.73 – 3.74 (m, 4H), 4.19 – 4.23 (m, 2H), 4.50 (s, 1H), 4.55 (s, 1H), 4.73 (s, 1H), 4.78 (s, 1H), 6.23 (m, 1H), 7.65 (s, 1H); Mass (m/z): 413.0 (M+H) $^+$ .

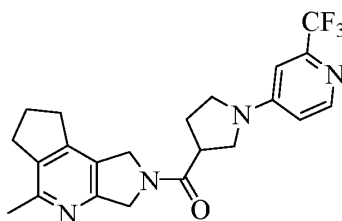
20

**Example-175: 1-(5-Methyl-3,6,7,8-tetrahydro-1H-2,4-diaza-as-indacen-2-yl)-2-(1-pyrimidin-5-yl)-azetidin-3-yl)-ethanone**



Liquid chromatographic condition – CHIRAL PAK-IC (250 X 21 mm, 5 $\mu$ m) with mobile phase methanol:acetonitrile:IPA:diethylamine (40:50:10:0.1) at RT to get the title compound <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  ppm: 2.14 – 2.20 (m, 2H), 2.47 – 2.48 (d,  $J$  = 4.4 Hz, 3H), 2.80 – 2.91 (m, 6H), 3.31 – 3.35 (m, 1H), 3.69 – 3.75 (m, 2H), 4.22 – 4.27 (m, 2H), 4.70 – 4.76 (m, 4H), 7.94 (s, 2H), 8.62 (s, 1H); Mass (m/z): 350.1 (M+H)<sup>+</sup>.

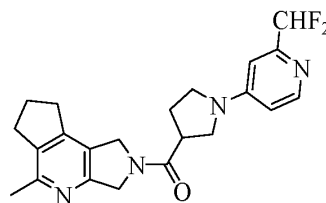
**Example-176:** (5-Methyl-3,6,7,8-tetrahydro-1H-2,4-diaza-as-indacen-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone



Liquid chromatographic condition – CHIRAL ART CELLULOSE-SZ (250 X 20 mm, 5 $\mu$ m) with mobile phase methanol:IPA:n-hexane:diethylamine (20:30:50:0.1) at RT to get the title compound.

<sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 400 MHz)  $\delta$  ppm: 2.13 – 2.22 (m, 2H), 2.36 – 2.43 (m, 2H), 2.49 (s, 3H), 2.85 – 2.92 (m, 4H), 3.39 – 3.49 (m, 2H), 3.59 – 3.75 (m, 3H), 4.61 - 4.95 (m, 4H), 6.48 – 6.50 (dd,  $J$  = 2.0, 5.6Hz, 1H), 6.75 – 6.75 (d,  $J$  = 2.0 Hz, 1H) 8.28 – 8.30 (d,  $J$  = 6.0 Hz, 1H); Mass (m/z): 417.1 (M+H)<sup>+</sup>.

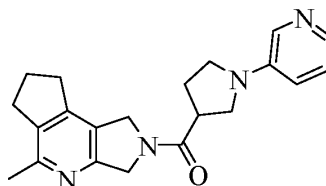
**Example-177:** [1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(5-methyl-3,6,7,8-tetrahydro-1H-2,4-diaza-as-indacen-2-yl)-methanone





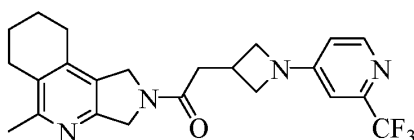
Liquid chromatographic condition – CHIRAL ART CELLULOSE-SZ (250 X 20 mm, 5 $\mu$ m) with mobile phase methanol:IPA:n-hexane:diethylamine (20:30:50:0.1) at RT to get the title compound. Mass (m/z): 399.2 (M+H)<sup>+</sup>.

**Example-178: (5-Methyl-3, 6, 7, 8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-(1-pyridin-3-yl)-pyrrolidin-3(R)-yl)-methanone**



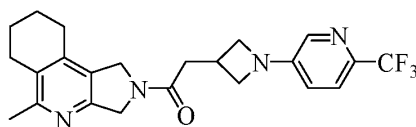
Liquid chromatographic condition –CHIRAL PAK-IC (250 X 21 mm, 5 $\mu$ m) with mobile phase methanol:acetonitrile:IPA:diethylamine (50:40:10:0.1) at RT to get the title compound. <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 400 MHz)  $\delta$  ppm: 2.04 – 2.10 (m, 2H), 2.16 – 2.19 (m, 1H), 2.28 – 2.33 (m, 1H), 2.39 (s, 3H), 2.84 – 2.87 (m, 4H), 3.35 – 3.42 (m, 2H), 3.49 – 3.53 (m, 2H), 3.58 – 3.62 (m, 1H), 4.55 (s, 1H), 4.61 (s, 1H), 4.89 – 4.94 (m, 2H), 6.1 – 6.94 (m, 1H), 7.13 – 7.17 (m, 1H), 7.83 – 7.85 (dd, *J* = 1.2, 4.4 Hz, 1H), 7.95 – 7.96 (d, *J* = 2.8 Hz, 1H); Mass (m/z): 349.1 (M+H)<sup>+</sup>.

**Example-179: 1-(5-Methyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-*c*]isoquinolin-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone**



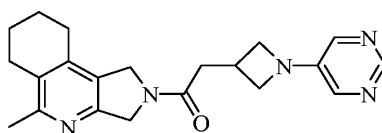
Liquid chromatographic condition – CHIRAL PAK-IC (250 X 21 mm, 5 $\mu$ m) with mobile phase methanol:acetonitrile:diethylamine (80:20:0.1) at RT to get the title compound. <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  ppm: 1.81 – 1.87 (m, 4H), 2.44 – 2.46 (d, *J* = 4.8 Hz, 3H), 2.57 – 2.65 (m, 4H), 2.78 – 2.82 (d, *J* = 7.2 Hz, 2H), 3.29 – 3.33 (m, 1H), 3.72 – 3.77 (m, 2H), 4.24 – 4.29 (m, 2H), 4.66 – 4.75 (m, 4H), 6.31 – 6.33 (d, *J* = 2.0 Hz, 1H), 6.57 – 6.58 (d, *J* = 2.0 Hz, 1H), 8.26 – 8.28 (d, *J* = 5.6 Hz, 1H); Mass (m/z): 431.1 (M+H)<sup>+</sup>.

**Example-180: 1-(5-Methyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-*c*]isoquinolin-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone**



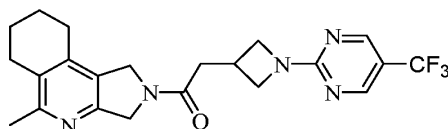
Liquid chromatographic condition - CHIRAL PAK-IC (250 X 21 mm, 5 $\mu$ m) with mobile phase methanol:acetonitrile:isopropanol:diethylamine (60:10:30:0.1) at RT to get the title compound.  $^1\text{H}$  - NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  ppm: 1.81 – 1.87 (m, 4H), 2.44 – 2.46 (d,  $J$  = 4.4 Hz, 3H), 2.57 – 2.65 (m, 4H), 2.79 – 2.83 (m, 2H), 3.31 – 3.33 (m, 1H), 3.72 – 3.77 (m, 2H), 4.24 – 4.29 (m, 2H), 4.66 – 4.67 (d,  $J$  = 5.2 Hz, 2H), 4.73 – 4.75 (d,  $J$  = 7.2 Hz, 2H), 6.69 – 6.72 (m, 1H), 7.44 – 7.46 (d,  $J$  = 8.8 Hz, 1H) 7.85 – 7.86 (d,  $J$  = 2.4 Hz, 1H); Mass ( $m/z$ ): 431.1 ( $\text{M}+\text{H}$ ) $^+$ .

**Example-181: 1-(5-Methyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-c]isoquinolin-2-yl)-2-(1-pyrimidin-5-yl)-azetidin-3-yl)-ethanone**



Liquid chromatographic condition - CHIRAL PAK-IC (250 X 21 mm, 5 $\mu$ m) with mobile phase methanol:acetonitrile:isopropanol:diethylamine (60:10:30:0.1) at RT to get the title compound.  $^1\text{H}$  - NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  ppm: 1.81 – 1.87 (m, 4H), 2.44 – 2.46 (d,  $J$  = 4.4 Hz, 3H), 2.57 – 2.65 (m, 4H), 2.79 – 2.83 (m, 2H), 3.31 – 3.33 (m, 1H), 3.72 – 3.77 (m, 2H), 4.24 – 4.29 (m, 2H), 4.66 – 4.67 (d,  $J$  = 5.2 Hz, 2H), 4.73 – 4.75 (d,  $J$  = 7.2 Hz, 2H), 8.15 (s, 2H), 8.53 (s, 1H); Mass ( $m/z$ ): 364.4 ( $\text{M}+\text{H}$ ) $^+$ .

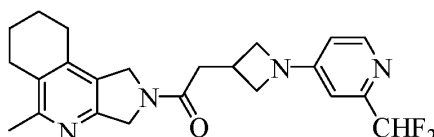
**Example-182: 1-(5-Methyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-c]isoquinolin-2-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone**



Liquid chromatographic condition - CHIRAL PAK-IC (250 X 21 mm, 5 $\mu$ m) with mobile phase methanol:acetonitrile:isopropanol:diethylamine (60:10:30:0.1) at RT to get the title compound.  $^1\text{H}$  - NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  ppm: 1.83 – 1.86 (m, 4H), 2.48 – 2.51 (d,  $J$  =

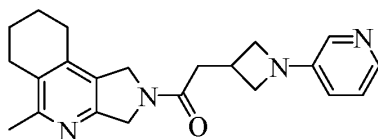
4.4 Hz, 3H), 2.61 – 2.67 (m, 4H), 2.81 – 2.85 (m, 2H), 3.27 – 3.32 (m, 1H), 3.69 – 3.74 (m, 2H), 4.21 – 4.27 (m, 2H), 4.61 – 4.64 (d,  $J = 5.2$  Hz, 2H), 4.72 – 4.76 (d,  $J = 7.2$  Hz, 2H), 8.81 (s, 2H; Mass ( $m/z$ ): 432.4 ( $M+H$ )<sup>+</sup>.

**Example-183:** 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(5-methyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-c]isoquinolin-2-yl)-ethanone



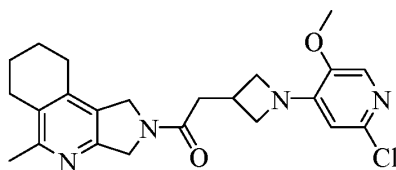
Liquid chromatographic condition – CHIRAL PAK-IC (250 X 21 mm, 5 $\mu$ m) with mobile phase methanol:acetonitrile:diethylamine (70:30:0.1) at RT to get the title compound. <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  ppm: 1.81 – 1.87 (m, 4H), 2.44 – 2.46 (d,  $J = 4.8$  Hz, 3H), 2.58 – 2.65 (m, 4H), 2.78 – 2.82 (m, 2H), 3.30 – 3.31 (m, 1H), 3.70 – 3.76 (m, 2H), 4.23 – 4.28 (m, 2H), 4.66 – 4.67 (m, 2H), 4.73 – 7.75 (m, 2H), 6.27 – 6.29 (m, 1H), 6.50 – 6.64 (m, 2H), 8.21 – 8.22 (d,  $J = 2.4$  Hz, 1H); Mass ( $m/z$ ): 413.0 ( $M+H$ )<sup>+</sup>.

**Example-184:** 1-(5-Methyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-c]isoquinolin-2-yl)-2-(1-pyridin-3-yl)-azetidin-3-yl)-ethanone



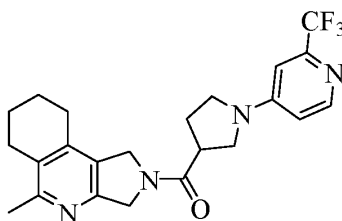
Liquid chromatographic condition – CHIRAL PAK-IC (250 X 21 mm, 5 $\mu$ m) with mobile phase methanol:acetonitrile:diethylamine (70:30:0.1) at RT to get the title compound. <sup>1</sup>H – NMR (DMSO-*d*<sub>6</sub>, 400 MHz)  $\delta$  ppm: 1.71 – 1.76 (m, 4H), 2.35 (s, 3H), 2.57 – 2.60 (m, 4H), 2.81 – 2.83 (d,  $J = 7.6$  Hz, 2H), 3.07 – 3.10 (m, 1H), 3.56 – 3.58 (t,  $J = 6.0$  Hz, 2H), 4.02 – 4.06 (t,  $J = 7.6$  Hz, 2H), 4.50 (s, 1H), 4.52 (s, 1H), 4.72 (s, 1H), 4.75 (s, 1H), 6.78 – 6.81 (m, 1H), 7.12 – 7.15 (m, 1H), 7.79 – 7.80 (d,  $J = 2.8$  Hz, 1H), 7.88 – 7.89 (dd,  $J = 1.2, 4.8$  Hz, 1H); Mass ( $m/z$ ): 363.1 ( $M+H$ )<sup>+</sup>.

**Example-185:** 2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(5-methyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-c]isoquinolin-2-yl)-ethanone



Liquid chromatographic condition – CHIRAL PAK-ADH (250 X 20 mm, 5  $\mu$ m) with mobile phase Methanol:Acetonitrile:Diethylamine (80:20:0.1) to get the title compound.  $^1\text{H}$  – NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  ppm: 1.81 – 1.87 (m, 4H), 2.44 – 2.45 (d,  $J$  = 4.0 Hz, 3H),  
 5 2.60 – 2.64 (m, 4H), 2.75 – 2.79 (t,  $J$  = 8.4 Hz, 2H), 3.15 – 3.22 (m, 1H), 3.75 (s, 3H), 3.81 – 3.85 (m, 2H), 4.32 – 4.36 (t,  $J$  = 8.2 Hz, 2H), 4.65 – 4.75 (m, 4H), 6.13 (s, 1H), 7.59 (s, 1H); Mass ( $m/z$ ): 427.1 ( $\text{M}+\text{H}$ ) $^+$ .

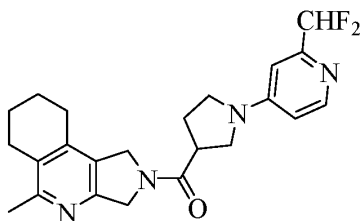
**Example-186:** (5-Methyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-c]isoquinolin-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone



10

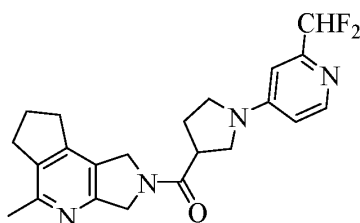
Liquid chromatographic condition – CHIRAL PAK-IC (250 X 21 mm) with mobile phase methanol:acetonitrile:IPA:diethylamine (70:20:10:0.1) at RT to get the title compound.  $^1\text{H}$  – NMR ( $\text{DMSO}-d_6$ , 400 MHz)  $\delta$  ppm: 1.73 – 1.78 (m, 4H), 2.07 – 2.20 (m, 2H), 2.37 (s, 3H)  
 2.66 – 2.67 (m, 4H), 3.38 – 3.44 (m, 1H), 3.49 – 3.70 (m, 4H) 4.54 (s, 1H), 4.56 (s, 1H),  
 15 4.87– 4.91 (m, 2H), 6.68 – 6.70 (dd,  $J$  = 2.0, 5.6 Hz, 1H), 6.85 – 6.87 (t,  $J$  = 2.0 Hz, 1H), 8.21 – 8.22 (d,  $J$  = 5.6 Hz, 1H); Mass ( $m/z$ ): 431.1 ( $\text{M}+\text{H}$ ) $^+$ .

**Example-187:** [1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(5-methyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-c]isoquinolin-2-yl)-methanone



Liquid chromatographic condition – CHIRAL PAK-IC (250 X 21 mm) with mobile phase Methanol:Acetonitrile:IPA:Diethylamine (60:30:10:0.1) at RT to get the title compound. <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz) δ ppm: 1.80 – 1.88 (m, 4H), 2.35 – 2.38 (m, 2H), 2.45 – 2.46 (d, *J* = 4.40 Hz, 3H), 2.61 – 2.65 (t, *J* = 6.60 Hz, 4H), 3.36 – 3.49 (m, 2H), 3.60 – 3.74 (m, 3H),  
 5 4.70 – 4.86 (m, 4H), 6.38 – 6.52 (d, *J* = 56 Hz, 1H), 6.43 – 6.45 (m, 1H), 6.71 – 6.71 (d, *J* = 2.4 Hz, 1H), 8.23 – 8.24 (d, *J* = 5.6 Hz, 1H); Mass (m/z): 413.0 (M+H)<sup>+</sup>.

**Example-188:** [1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(5-methyl-3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-methanone



10 Liquid chromatographic condition – CHIRAL PAK-IC (250 X 21 mm, 5μm) with mobile phase methanol:acetonitrile:isopropanol:diethylamine (60:30:10:0.1) at RT to get the title compound. <sup>1</sup>H – NMR (CDCl<sub>3</sub>, 400 MHz) δ ppm: 2.15 – 2.20 (m, 2H), 2.35 – 2.39 (m, 2H), 2.48 (s, 3H), 2.84 – 2.92 (m, 3H), 3.40 – 3.48 (m, 4H), 3.62 – 3.67 (m, 2H), 4.75 – 4.88 (m, 4H), 6.44 – 6.45 (m, 1H), 6.38 – 6.52 (t, *J* = 56.0 Hz, 1H), 6.71 – 6.72 (d, *J* = 2.40 Hz, 1H),  
 15 8.23 – 8.24 (d, *J* = 6.0 Hz, 1H); Mass (m/z): 399.2 (M+H)<sup>+</sup>.

**Example-189: Determination of allosteric potency EC<sub>50</sub> 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.

20 **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 compound to GPCRs. In this specific assay, the level of intracellular cyclic AMP which is  
 25 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 Scientific). Prior to the addition of compounds or standard agonist, cells were serum starved overnight. Increasing concentrations of test compounds were added along with EC<sub>20</sub> of acetylcholine and forskolin (1  $\mu$ M) in Opti-MEM medium to the cells.

The incubation was continued at 37°C in CO<sub>2</sub> incubator for 4 h. After removal of medium, cells were lysed using lysis buffer, detection reagent was added and luciferase activity was measured in a Luminometer. The reference agonist (10  $\mu$ M) in the presence of forskolin (1  $\mu$ M) stimulated luciferase activity was assigned a value of 100 % while basal luciferase activity i.e. only forskolin (1  $\mu$ M) 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. EC<sub>50</sub> values of the compounds were defined as the concentration required in stimulating the luciferase activity by 50 % in presence of EC<sub>20</sub> of acetylcholine and the results are provided in table 1A as EC<sub>50</sub>.

**Table 1A:** Allosteric potency EC<sub>50</sub> values for muscarinic M4 receptor

| Example No. | Human muscarinic M4 receptor PAM EC50 (nM) | Example No. | Human muscarinic M4 receptor PAM EC50 (nM) |
|-------------|--------------------------------------------|-------------|--------------------------------------------|
|             | CRE-Luc reporter assay                     |             | CRE-Luc reporter assay                     |
| <b>1</b>    | 26                                         | <b>72</b>   | 19                                         |
| <b>2</b>    | 31                                         | <b>73</b>   | 98                                         |
| <b>3</b>    | 144                                        | <b>74</b>   | 39                                         |
| <b>4</b>    | 8                                          | <b>75</b>   | 18                                         |
| <b>5</b>    | 39                                         | <b>76</b>   | 54                                         |
| <b>6</b>    | 62                                         | <b>77</b>   | 106                                        |
| <b>7</b>    | 23                                         | <b>78</b>   | 317                                        |
| <b>8</b>    | 32                                         | <b>79</b>   | 232                                        |
| <b>9</b>    | 25                                         | <b>80</b>   | 51                                         |
| <b>10</b>   | 84                                         | <b>82</b>   | 97                                         |
| <b>18</b>   | 187                                        | <b>83</b>   | 61                                         |

|    |     |     |     |
|----|-----|-----|-----|
| 20 | 120 | 84  | 7   |
| 27 | 111 | 93  | 78  |
| 29 | 241 | 127 | 125 |
| 34 | 37  | 138 | 104 |
| 35 | 101 | 169 | 19  |
| 54 | 37  | 170 | 189 |
| 55 | 135 | 171 | 48  |
| 56 | 30  | 172 | 61  |
| 57 | 40  | 173 | 158 |
| 58 | 23  | 179 | 17  |
| 59 | 21  | 183 | 24  |
| 65 | 64  | 184 | 19  |
| 66 | 222 |     |     |

**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 CO<sub>2</sub> incubator for overnight. Prior to the addition of compounds or standard agonist, cells were pre-equilibrated with substrate in CO<sub>2</sub> independent medium containing 10% FBS for 2 h at RT. Increasing concentrations of test compounds were added along with EC<sub>20</sub> of acetylcholine and isoprenaline (0.1 µM) in CO<sub>2</sub> independent medium containing 10 % FBS to the cells.

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 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. EC<sub>50</sub> values of the compounds were defined as the concentration required in stimulating the luciferase activity by 50 % in presence of EC<sub>20</sub> of acetylcholine and the results are provided in table 1B as EC<sub>50</sub>.

**Table 1B:** Allosteric potency EC<sub>50</sub> values for muscarinic M4 receptor

| Example No. | Human muscarinic M4 receptor PAM EC50 (nM) |
|-------------|--------------------------------------------|
|             | Glosensor cAMP assay                       |
| 1           | 22                                         |
| 2           | 5.2                                        |
| 4           | 1.6                                        |
| 8           | 72                                         |
| 29          | 74                                         |
| 72          | 8.3                                        |
| 73          | 68                                         |
| 169         | 5.4                                        |
| 171         | 23                                         |

**C. Muscarinic M2 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 M2 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 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 Scientific). Prior to the addition of compounds or standard agonist, cells were serum starved



overnight. Increasing concentrations of test compounds were added along with EC<sub>20</sub> of acetylcholine and forskolin (1  $\mu$ M) in Opti-MEM medium to the cells.

The incubation was continued at 37°C in CO<sub>2</sub> incubator for 4 h. After removal of medium, cells were lysed using lysis buffer, detection reagent was added and luciferase activity was measured in a Luminometer. The reference agonist (10  $\mu$ M) in the presence of forskolin (1  $\mu$ M) stimulated luciferase activity was assigned a value of 100 % while basal luciferase activity i.e. only forskolin (1  $\mu$ M) 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. EC<sub>50</sub> values of the compounds were defined as the concentration required in stimulating the luciferase activity by 50 % in presence of EC<sub>20</sub> of acetylcholine and the results are provided in table 1C as EC<sub>50</sub>.

**Table 1C:** Allosteric potency EC<sub>50</sub> values for muscarinic M2 receptor

| Example No. | Human muscarinic M2 receptor PAM EC50 (nM) |
|-------------|--------------------------------------------|
|             | CRE-Luc reporter assay                     |
| 1           | >10000                                     |
| 4           | >10000                                     |
| 171         | >10000                                     |

#### Example-190: Rodent pharmacokinetic study

Male Wistar rats (250  $\pm$  50 grams) were used as experimental animals. Animals were housed individually in polypropylene cages. Two days prior to study, male Wistar rats were anesthetized with isoflurane for surgical placement of jugular vein catheter. Rats were administered intraperitoneally with test compound at a dose of 3 mg/kg and 10 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  $\mu$ 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  $\mu$ 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 8.4 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. | $C_{\max}$<br>(ng/mL) | $T_{\max}$<br>(h) | $AUC_{0-t}$<br>(ng.h/mL) | $t_{1/2}$<br>(h) |
|-------------|-----------------------|-------------------|--------------------------|------------------|
| 1           | 2613 $\pm$ 1464       | 0.17              | 1585 $\pm$ 518           | 1.19 $\pm$ 0.35  |
| 2           | 6815 $\pm$ 1788       | 0.25              | 10018 $\pm$ 2851         | 2.18 $\pm$ 2.45  |
| 4           | 3860 $\pm$ 1112       | 0.25              | 8313 $\pm$ 1428          | 2.99 $\pm$ 0.78  |
| 169         | 1623 $\pm$ 447        | 0.50              | 3398 $\pm$ 820           | 1.08 $\pm$ 0.39  |

#### Example-191: 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 |
|-------------|-----------------------|-----------------------|-----------|
|             | 10 mg/kg, <i>i.p.</i> | 30 mg/kg, <i>i.p.</i> |           |
| <b>1</b>    | 57%                   | 84%                   | Active    |
| <b>2</b>    | 53%                   | 74%                   | Active    |
| <b>169</b>  | 54%                   | 52%                   | Active    |

#### Example-192: Receptor Occupancy Study in Rats

- 5 Male Wistar rats ( $250 \pm 50$  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 (10, 60 and 60 mg/Kg) intraperitoneally using 5 % v/v DMSO + 5 % v/v Solutol HS15 + 90 % v/v Water for injection as vehicle. At  $T_{\max}$  of the test compound, all
- 10 rats were intravenously administered with MK-6884, 3  $\mu$ 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  $-80^{\circ}\text{C}$  until processed for tracer extraction
- 15 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.

**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> | 60 mg/kg, <i>i.p.</i> |
| <b>1</b>    | $43.0 \pm 1.9$         | $63.4 \pm 8.9$        | $84.7 \pm 1.4$        |
| <b>2</b>    | -                      | $45.5 \pm 9.4$        | $38.5 \pm 2.4$        |
| <b>169</b>  | $44.0 \pm 6.2$         | $41.2 \pm 4.4$        | $57.6 \pm 1.2$        |

#### Example-193: Contextual Fear Conditioning Memory

- 20 Rodent fear conditioning chambers (L x W x H, rat: 26 x 30 x 33 cm, Coulbourn instruments, USA) placed in sound attenuating cabinets were used. Stainless steel grid

floors (L x W, rat: 26 x 30 cm), connected to shock scramblers were used to deliver the shock. A ventilation fan provided a background noise of 60 dB. A light bulb (fixed on the right wall, and 27 cm above the floor of the chamber) provided ambient illumination. Experiment was recorded using video camera, mounted on the cabinet ceiling and images  
 5 were analyzed with freeze frame 3 software (V3.2.1). The fear conditioning chambers has transparent acrylic panels.

On day 0, rats were randomized based on the body weight, housed two rats per each cage.

On day 1, rats were brought to the laboratory at least 1 hr prior to experimentation. Rats were acclimatized to fear conditioning chamber for 2 min. After acclimatization the rats  
 10 were received unavoidable foot shock (unconditioned stimulus (US): electric shock of 0.7 mA for 3 seconds). Following a 79 sec interval between each administration, shock was repeated to deliver a total of eight US. One minute after the last US, the animal were transferred to the home cage. The chambers were cleaned with 70% ethanol between tests. Test treatments were administered prior conditioning phase based on the Tmax.  
 15 Amphetamine 2 mg/kg, s.c. was administer 25 min prior to conditioning phase.

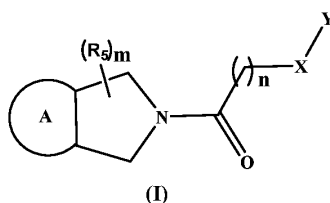
On day 2, rats were brought to the laboratory at least 1 hr prior to experimentation. The freezing behavior of animal was recorded for 733 sec (starting from the time the animal is placed in the fear conditioning chamber). After the 733 sec behavioral recording, the animals were transferred to the home cage. The duration of freezing was recorded as (no  
 20 movement for about of 3 seconds or more was scored a freezing behavior). The freezing threshold was set at 10 in the motion index for analysis. The chambers were cleaned with 70% ethanol between tests.

**Table-5:** Procognitive activity of the compounds of the present invention

| Example No. | Observation                                    |                                                | Inference |
|-------------|------------------------------------------------|------------------------------------------------|-----------|
|             | 30 mg/kg, <i>i.p.</i>                          | 60 mg/kg, <i>i.p.</i>                          |           |
| 2           | Statistically significant reversal of deficits | Statistically significant reversal of deficits | Active    |

**We Claim:**

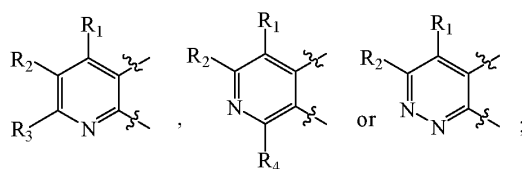
1. A compound of formula (I), or an isotopic form, or a stereoisomer, or a pharmaceutically acceptable salt thereof,



5

wherein

A is a ring moiety selected from



“” is point of attachment;

10  $R_1$  and  $R_2$  together with the carbon atoms to which they are attached form a 5 to 8 membered cycloalkyl or 5 to 8 membered heterocycloalkyl ring, wherein the cycloalkyl or heterocycloalkyl is optionally substituted with one or two groups independently selected from hydrogen, hydroxyl,  $-C_1-C_4$ alkyl or  $-R_5$ -Phenyl;

15  $R_2$  and  $R_3$  together with the carbon atoms to which they are attached form a 5 to 8 membered cycloalkyl or 5 to 8 membered heterocycloalkyl ring, wherein the cycloalkyl or heterocycloalkyl is optionally substituted with one or two groups independently selected from hydrogen, hydroxyl,  $-C_1-C_4$ alkyl or  $-R_5$ -Phenyl;

When  $R_1$  and  $R_2$  form a ring, then  $R_3$  is selected from hydrogen,  $-C_1-C_4$ hydroxyalkyl,  $-NH_2$ ,  $-C_1-C_4$ alkyl or  $-C_1-C_4$ haloalkyl;

20 When  $R_2$  and  $R_3$  form a ring, then  $R_1$  is selected from hydrogen,  $-C_1-C_4$ hydroxyalkyl,  $-NH_2$ ,  $-C_1-C_4$ alkyl or  $-C_1-C_4$ haloalkyl;

$R_4$  is selected from hydrogen,  $-C_1-C_4$ hydroxyalkyl,  $-NH_2$ ,  $-C_1-C_4$ alkyl,  $-NH-C_1-C_4$ alkyl or  $-C_1-C_4$ haloalkyl; and

$R_5$  is selected from hydrogen, deuterium and  $-C_1-C_4$ alkyl.

25 X is selected from 3 to 7 membered cycloalkyl or 3 to 7 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<sub>1</sub>-C<sub>4</sub>alkyl, and C<sub>1</sub>-C<sub>4</sub>haloalkyl;

Y 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  
 5 selected from the group consisting of hydrogen, deuterium, halogen, cyano, hydroxy, -NH<sub>2</sub>, -NHC<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>haloalkyl, -OC<sub>1</sub>-C<sub>4</sub>alkyl, -OC<sub>1</sub>-C<sub>4</sub>haloalkyl, and -C<sub>3</sub>-C<sub>7</sub>cycloalkyl;

m is an integer selected from 0 to 2; and

n is an integer selected from 0 to 3.

- 10 2. The compound of formula (I) or an isotopic form, or a stereoisomer, or a pharmaceutically acceptable salt thereof as claimed in claim 1, wherein the compound is selected from:

1-(8-Methyl-3,5,6,7-tetrahydro-1*H*-2,4-diaza-s-indacen-2-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone;

- 15 1-(8-Methyl-3,5,6,7-tetrahydro-1*H*-2,4-diaza-s-indacen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;

1-(8-Methyl-3,5,6,7-tetrahydro-1*H*-2,4-diaza-s-indacen-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone;

- 20 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(8-methyl-3,5,6,7-tetrahydro-1*H*-2,4-diaza-s-indacen-2-yl)-ethanone;

1-(8-Methyl-3,5,6,7-tetrahydro-1*H*-2,4-diaza-s-indacen-2-yl)-2-(1-pyridin-4-yl-azetidin-3-yl)-ethanone;

1-(8-Methyl-3,5,6,7-tetrahydro-1*H*-2,4-diaza-s-indacen-2-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone;

- 25 1-(8-Methyl-3,5,6,7-tetrahydro-1*H*-2,4-diaza-s-indacen-2-yl)-2-(1-pyrimidin-5-yl-azetidin-3-yl)-ethanone;

2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(8-methyl-3,5,6,7-tetrahydro-1*H*-2,4-diaza-s-indacen-2-yl)-ethanone;

(8-Methyl-3,5,6,7-tetrahydro-1*H*-2,4-diaza-s-indacen-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone;

- 30 (8-Methyl-3,5,6,7-tetrahydro-1*H*-2,4-diaza-s-indacen-2-yl)-(1-pyridin-3-yl-pyrrolidin-3(R)-yl)-methanone;

- (8-Methyl-3,5,6,7-tetrahydro-1*H*-2,4-diaza-s-indacen-2-yl)-[1-(6-trifluoromethyl-pyridin-3-yl)-pyrrolidin-3(R)-yl]-methanone;  
[1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(8-methyl-3,5,6,7-tetrahydro-1*H*-2,4-diaza-s-indacen-2-yl)-methanone;
- 5 2-[1-(2-Trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(5,7,7-trimethyl-3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-ethanone;  
2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(5,7,7-trimethyl-3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-ethanone;  
2-(1-Pyridin-3-yl-azetidin-3-yl)-1-(5,7,7-trimethyl-3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-
- 10 indacen-2-yl)-ethanone;  
[1-(2-Trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(5,7,7-trimethyl-3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-methanone;  
[1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(5,7,7-trimethyl-3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-methanone;
- 15 1-(3,5,6,7-Tetrahydro-1*H*-2,4-diaza-s-indacen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;  
2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(3,5,6,7-tetrahydro-1*H*-2,4-diaza-s-indacen-2-yl)-ethanone;  
2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(3,5,6,7-tetrahydro-1*H*-2,4-diaza-s-
- 20 indacen-2-yl)-ethanone;  
(3,5,6,7-Tetrahydro-1*H*-2,4-diaza-s-indacen-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone;  
[1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(3,5,6,7-tetrahydro-1*H*-2,4-diaza-s-indacen-2-yl)-methanone;
- 25 2-(1-Pyridin-3-yl-azetidin-3-yl)-1-(3,5,6,7-tetrahydro-1*H*-2,4-diaza-s-indacen-2-yl)-ethanone;  
(3,6,7,8-Tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone;  
[1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-
- 30 indacen-2-yl)-methanone;  
(1-Pyridin-3-yl-pyrrolidin-3(R)-yl)-(3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-methanone;

- 1-(3,6,7,8-Tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-ethanone;
- 5 2-(1-Pyridin-3-yl-azetidin-3-yl)-1-(3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-ethanone;
- 2-(1-Pyrimidin-5-yl-azetidin-3-yl)-1-(3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-ethanone;
- 10 1-(3,6,7,8-Tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone;
- 2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-ethanone;
- 1-(3,6,7,8-Tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone;
- 15 1-(4-Methyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(4-methyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-ethanone;
- 1-(4-Methyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone;
- 20 (4-Methyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone;
- [1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(4-methyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-methanone;
- 25 (4-Methyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-[1-(6-trifluoromethyl-pyridin-3-yl)-pyrrolidin-3(R)-yl]-methanone;
- 1-(4-Methyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone;
- 1-(4-Methyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone;
- 30 1-(4-Methyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-2-(1-pyrimidin-5-yl-azetidin-3-yl)-ethanone;



- 2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(4-methyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-ethanone;  
1-(4-Methyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-2-(1-pyridin-4-yl-azetidin-3-yl)-ethanone;
- 5 1-(4-Difluoromethyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;  
2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(4-difluoromethyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-ethanone;  
1-(4-Difluoromethyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone;
- 10 1-(4-Difluoromethyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone;  
1-(4-Difluoromethyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-2-(1-pyrimidin-5-yl-azetidin-3-yl)-ethanone;
- 15 1-(4-Difluoromethyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone;  
2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(4-difluoromethyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-ethanone;  
(4-Difluoromethyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone;
- 20 [1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(4-difluoromethyl-3,6,7,8-tetrahydro-1*H*-2,5-diaza-as-indacen-2-yl)-methanone;  
1-(9-Methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-*b*]quinolin-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 25 1-(9-Methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-*b*]quinolin-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone;  
1-(9-Methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-*b*]quinolin-2-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone;  
2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(9-methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-*b*]quinolin-2-yl)-ethanone;
- 30 (9-Methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-*b*]quinolin-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone;

- 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(9-methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b]quinolin-2-yl)-ethanone;
- 2-[1-(2-Trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(5,7,7-trimethyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-c]isoquinolin-2-yl)-ethanone;
- 5 2-(1-Pyridin-3-yl)-azetidin-3-yl]-1-(5,7,7-trimethyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-c]isoquinolin-2-yl)-ethanone;
- 2-[1-(6-Trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-1-(5,7,7-trimethyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-c]isoquinolin-2-yl)-ethanone;
- [1-(2-Trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(5,7,7-trimethyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-c]isoquinolin-2-yl)-methanone;
- 10 [1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(5,7,7-trimethyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-c]isoquinolin-2-yl)-methanone;
- 1-(1,3,6,7,8,9-Hexahydro-pyrrolo[3,4-c]cinnolin-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 15 1-(1,3,6,7,8,9-Hexahydro-pyrrolo[3,4-c]cinnolin-2-yl)-2-(1-pyridin-3-yl)-azetidin-3-yl)-ethanone;
- 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(1,3,6,7,8,9-hexahydro-pyrrolo[3,4-c]cinnolin-2-yl)-ethanone;
- 1-(1,3,6,7,8,9-Hexahydro-pyrrolo[3,4-c]cinnolin-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone;
- 20 1-(1,3,6,7,8,9-Hexahydro-pyrrolo[3,4-c]cinnolin-2-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone;
- (1,3,6,7,8,9-Hexahydro-pyrrolo[3,4-c]cinnolin-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone;
- 25 [1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(1,3,6,7,8,9-hexahydro-pyrrolo[3,4-c]cinnolin-2-yl)-methanone;
- 1-(4-Methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacen-6-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 1-(4-Methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacen-6-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone;
- 30 1-(4-Methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacen-6-yl)-2-(1-pyridin-3-yl)-azetidin-3-yl)-ethanone;

- 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(4-methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacen-6-yl)-ethanone;
- 2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(4-methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacen-6-yl)-ethanone;
- 5 1-(4-Methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacen-6-yl)-2-(1-pyrimidin-5-yl-azetidin-3-yl)-ethanone;
- 1-(4-Methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacen-6-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone;
- (4-Methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacen-6-yl)-[1-(6-trifluoromethyl-pyridin-3-yl)-pyrrolidin-3(R)-yl]-methanone;
- 10 (4-Methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacen-6-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone;
- [1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(4-methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacen-6-yl)-methanone;
- 15 (4-Methyl-2,3,5,7-tetrahydro-1-oxa-6,8-diaza-s-indacen-6-yl)-(1-pyridin-3-yl-pyrrolidin-3(R)-yl)-methanone;
- 1-(8-Methyl-5,7-dihydro-1*H*,3*H*-2-oxa-4,6-diaza-s-indacen-6-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone;
- 1-(8-Methyl-5,7-dihydro-1*H*,3*H*-2-oxa-4,6-diaza-s-indacen-6-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 20 1-(8-Methyl-5,7-dihydro-1*H*,3*H*-2-oxa-4,6-diaza-s-indacen-6-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone;
- 1-(8-Methyl-5,7-dihydro-1*H*,3*H*-2-oxa-4,6-diaza-s-indacen-6-yl)-2-(1-pyridin-4-yl-azetidin-3-yl)-ethanone;
- 25 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(8-methyl-5,7-dihydro-1*H*,3*H*-2-oxa-4,6-diaza-s-indacen-6-yl)-ethanone;
- 2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(8-methyl-5,7-dihydro-1*H*,3*H*-2-oxa-4,6-diaza-s-indacen-6-yl)-ethanone;
- 1-(8-Methyl-5,7-dihydro-1*H*,3*H*-2-oxa-4,6-diaza-s-indacen-6-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone;
- 30 1-(8-Methyl-5,7-dihydro-1*H*,3*H*-2-oxa-4,6-diaza-s-indacen-6-yl)-2-(1-pyrimidin-5-yl-azetidin-3-yl)-ethanone;

- (8-Methyl-5,7-dihydro-1*H*,3*H*-2-oxa-4,6-diaza-s-indacen-6-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone;  
 [1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(8-methyl-5,7-dihydro-1*H*,3*H*-2-oxa-4,6-diaza-s-indacen-6-yl)-methanone;
- 5 2-[1-(2-Trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(6,6,9-trimethyl-3,5,6,8-tetrahydro-1*H*-7-oxa-2,4-diaza-cyclopenta[b]naphthalen-2-yl)-ethanone;  
 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(6,6,9-trimethyl-3,5,6,8-tetrahydro-1*H*-7-oxa-2,4-diaza-cyclopenta[b]naphthalen-2-yl)-ethanone;  
 2-(1-Pyridin-3-yl-azetidin-3-yl)-1-(6,6,9-trimethyl-3,5,6,8-tetrahydro-1*H*-7-oxa-2,4-diaza-
- 10 cyclopenta[b]naphthalen-2-yl)-ethanone;  
 2-(1-Pyridin-4-yl-azetidin-3-yl)-1-(6,6,9-trimethyl-3,5,6,8-tetrahydro-1*H*-7-oxa-2,4-diaza-cyclopenta[b]naphthalen-2-yl)-ethanone;  
 2-[1-(6-Trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-1-(6,6,9-trimethyl-3,5,6,8-tetrahydro-1*H*-7-oxa-2,4-diaza-cyclopenta[b]naphthalen-2-yl)-ethanone;
- 15 2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(6,6,9-trimethyl-3,5,6,8-tetrahydro-1*H*-7-oxa-2,4-diaza-cyclopenta[b]naphthalen-2-yl)-ethanone;  
 2-(1-Pyrimidin-5-yl-azetidin-3-yl)-1-(6,6,9-trimethyl-3,5,6,8-tetrahydro-1*H*-7-oxa-2,4-diaza-cyclopenta[b]naphthalen-2-yl)-ethanone;  
 2-[1-(5-Trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-1-(6,6,9-trimethyl-3,5,6,8-
- 20 tetrahydro-1*H*-7-oxa-2,4-diaza-cyclopenta[b]naphthalen-2-yl)-ethanone;  
 [1-(2-Trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(6,6,9-trimethyl-3,5,6,8-tetrahydro-1*H*-7-oxa-2,4-diaza-cyclopenta[b]naphthalen-2-yl)-methanone;  
 [1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(6,6,9-trimethyl-3,5,6,8-tetrahydro-1*H*-7-oxa-2,4-diaza-cyclopenta[b]naphthalen-2-yl)-methanone;
- 25 2-[1-(2-Trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(5,8,8-trimethyl-3,6,8,9-tetrahydro-1*H*-7-oxa-2,4-diaza-cyclopenta[a]naphthalen-2-yl)-ethanone;  
 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(5,8,8-trimethyl-3,6,8,9-tetrahydro-1*H*-7-oxa-2,4-diaza-cyclopenta[a]naphthalen-2-yl)-ethanone;  
 2-(1-Pyridin-3-yl-azetidin-3-yl)-1-(5,8,8-trimethyl-3,6,8,9-tetrahydro-1*H*-7-oxa-2,4-diaza-
- 30 cyclopenta[a]naphthalen-2-yl)-ethanone;  
 [1-(2-Trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(5,8,8-trimethyl-3,6,8,9-tetrahydro-1*H*-7-oxa-2,4-diaza-cyclopenta[a]naphthalen-2-yl)-methanone;

- [1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(5,8,8-trimethyl-3,6,8,9-tetrahydro-1H-7-oxa-2,4-diaza-cyclopenta[a]naphthalen-2-yl)-methanone;
- 1-(1,3,5,6,7,8-Hexahydro-pyrrolo[3,4-b]quinolin-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 5 1-(1,3,5,6,7,8-Hexahydro-pyrrolo[3,4-b]quinolin-2-yl)-2-(1-pyridin-3-yl)-azetidin-3-yl)-ethanone;
- 1-(1,3,5,6,7,8-Hexahydro-pyrrolo[3,4-b]quinolin-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone;
- 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b]quinolin-2-yl)-ethanone;
- 10 b]quinolin-2-yl)-ethanone;
- (1,3,5,6,7,8-Hexahydro-pyrrolo[3,4-b]quinolin-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone;
- [1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b]quinolin-2-yl)-methanone;
- 15 1-(3,6,7,8-Tetrahydro-1H-2,4-diaza-as-indacen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(3,6,7,8-tetrahydro-1H-2,4-diaza-as-indacen-2-yl)-ethanone;
- 1-(3,6,7,8-Tetrahydro-1H-2,4-diaza-as-indacen-2-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone;
- 20 2-(1-Pyrimidin-5-yl)-azetidin-3-yl)-1-(3,6,7,8-tetrahydro-1H-2,4-diaza-as-indacen-2-yl)-ethanone;
- 2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(3,6,7,8-tetrahydro-1H-2,4-diaza-as-indacen-2-yl)-ethanone;
- 25 1-(3,6,7,8-Tetrahydro-1H-2,4-diaza-as-indacen-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone;
- (3,6,7,8-Tetrahydro-1H-2,4-diaza-as-indacen-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone;
- [1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(3,6,7,8-tetrahydro-1H-2,4-diaza-as-indacen-2-yl)-methanone;
- 30 indacen-2-yl)-methanone;
- (3,6,7,8-Tetrahydro-1H-2,4-diaza-as-indacen-2-yl)-[1-(6-trifluoromethyl-pyridin-3-yl)-pyrrolidin-3(R)-yl]-methanone;

- 2-(1-Pyridin-4-yl-azetidin-3-yl)-1-(3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-ethanone;
- 2-(1-Pyridin-3-yl-azetidin-3-yl)-1-(3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-ethanone;
- 5 1-(8-Benzyl-5-hydroxymethyl-1,3,6,7,8,9-hexahydro-2,4,8-triaza-cyclopenta[a]naphthalen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 1-(5-hydroxymethyl-1,3,6,7,8,9-hexahydro-2,4,8-triaza-cyclopenta[a]naphthalen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 1-(7-Benzyl-9-methyl-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-2-yl)-2-
- 10 [1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 1-(9-Methyl-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(9-methyl-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-2-yl)-ethanone;
- 15 1-(9-Methyl-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-2-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone;
- 1-(9-Methyl-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone;
- 1-(9-Methyl-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-2-yl)-2-[1-(5-
- 20 trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone;
- 1-(9-Methyl-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-2-yl)-2-(1-pyrimidin-5-yl-azetidin-3-yl)-ethanone;
- 2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(9-methyl-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-2-yl)-ethanone;
- 25 (9-Methyl-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone;
- [1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(9-methyl-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-2-yl)-methanone;
- 1-(6-Benzyl-9-methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b][1,7]naphthyridin-2-yl)-2-[1-(2-
- 30 trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 1-(9-Methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b][1,7]naphthyridin-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;

- 1-(9-Methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b][1,7]naphthyridin-2-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone;
- 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(9-methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b][1,7]naphthyridin-2-yl)-ethanone;
- 5 1-(9-Methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b][1,7]naphthyridin-2-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone;
- 1-(9-Methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b][1,7]naphthyridin-2-yl)-2-(1-pyrimidin-5-yl-azetidin-3-yl)-ethanone;
- 2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(9-methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b][1,7]naphthyridin-2-yl)-ethanone;
- 10 (9-Methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b][1,7]naphthyridin-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone;
- (9-Methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b][1,7]naphthyridin-2-yl)-[1-(6-trifluoromethyl-pyridin-3-yl)-pyrrolidin-3(R)-yl]-methanone;
- 15 [1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(9-methyl-1,3,5,6,7,8-hexahydro-pyrrolo[3,4-b][1,7]naphthyridin-2-yl)-methanone;
- 1-(7-Benzyl-1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 1-(1,3,5,6,7,8-Hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 20 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(1,3,5,6,7,8-hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-2-yl)-ethanone;
- 1-(1,3,5,6,7,8-Hexahydro-2,4,7-triaza-cyclopenta[b]naphthalen-2-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone;
- 25 1-(5-Methyl-1,3,6,7,8,9-hexahydro-2,4,7-triaza-cyclopenta[a]naphthalen-2-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone hydrochloride;
- 1-(5-Methyl-1,3,6,7,8,9-hexahydro-2,4,7-triaza-cyclopenta[a]naphthalen-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone hydrochloride;
- 1-(5-Methyl-1,3,6,7,8,9-hexahydro-2,4,7-triaza-cyclopenta[a]naphthalen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone hydrochloride;
- 30 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(5-methyl-1,3,6,7,8,9-hexahydro-2,4,7-triaza-cyclopenta[a]naphthalen-2-yl)-ethanone hydrochloride;

- 1-(5-Methyl-1,3,6,7,8,9-hexahydro-2,4,7-triaza-cyclopenta[a]naphthalen-2-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone hydrochloride;
- 1-(5-Methyl-1,3,6,7,8,9-hexahydro-2,4,7-triaza-cyclopenta[a]naphthalen-2-yl)-2-(1-pyrimidin-5-yl)-azetidin-3-yl]-ethanone hydrochloride;
- 5 2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(5-methyl-1,3,6,7,8,9-hexahydro-2,4,7-triaza-cyclopenta[a]naphthalen-2-yl)-ethanone hydrochloride;
- 1-(5-Methyl-1,3,6,7,8,9-hexahydro-2,4,7-triaza-cyclopenta[a]naphthalen-2-yl)-2-(1-pyridin-4-yl)-azetidin-3-yl)-ethanone hydrochloride;
- (5-Methyl-1,3,6,7,8,9-hexahydro-2,4,7-triaza-cyclopenta[a]naphthalen-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone hydrochloride;
- 10 [1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(5-methyl-1,3,6,7,8,9-hexahydro-2,4,7-triaza-cyclopenta[a]naphthalen-2-yl)-methanone hydrochloride;
- 1-(5-Methyl-1,3,6,7,8,9-hexahydro-2,4,8-triaza-cyclopenta[a]naphthalen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone hydrochloride;
- 15 1-(5-Methyl-1,3,6,7,8,9-hexahydro-2,4,8-triaza-cyclopenta[a]naphthalen-2-yl)-2-(1-pyridin-3-yl)-azetidin-3-yl)-ethanone hydrochloride;
- 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(5-methyl-1,3,6,7,8,9-hexahydro-2,4,8-triaza-cyclopenta[a]naphthalen-2-yl)-ethanone hydrochloride;
- 1-(5-Methyl-1,3,6,7,8,9-hexahydro-2,4,8-triaza-cyclopenta[a]naphthalen-2-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone hydrochloride;
- 20 1-(5-Methyl-1,3,6,7,8,9-hexahydro-2,4,8-triaza-cyclopenta[a]naphthalen-2-yl)-2-(1-pyrimidin-5-yl)-azetidin-3-yl)-ethanone hydrochloride;
- 2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(5-methyl-1,3,6,7,8,9-hexahydro-2,4,8-triaza-cyclopenta[a]naphthalen-2-yl)-ethanone hydrochloride;
- 25 (5-Methyl-1,3,6,7,8,9-hexahydro-2,4,8-triaza-cyclopenta[a]naphthalen-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone hydrochloride;
- [1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(5-methyl-1,3,6,7,8,9-hexahydro-2,4,8-triaza-cyclopenta[a]naphthalen-2-yl)-methanone hydrochloride;
- 1-(5-methyl-3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 30 1-(5-Methyl-3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone;



- 1-(5-Methyl-3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone;
- 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(5-methyl-3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-ethanone;
- 5 1-(5-Methyl-3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone;
- 2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(5-methyl-3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-ethanone;
- 1-(5-Methyl-3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-2-(1-pyrimidin-5-yl-azetidin-3-yl)-ethanone;
- 10 (5-Methyl-3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone;
- [1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(5-methyl-3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-methanone;
- 15 (5-Methyl-3, 6, 7, 8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-(1-pyridin-3-yl-pyrrolidin-3(R)-yl)-methanone;
- 1-(5-Methyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-*c*]isoquinolin-2-yl)-2-[1-(2-trifluoromethyl-pyridin-4-yl)-azetidin-3-yl]-ethanone;
- 1-(5-Methyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-*c*]isoquinolin-2-yl)-2-[1-(6-trifluoromethyl-pyridin-3-yl)-azetidin-3-yl]-ethanone;
- 20 1-(5-Methyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-*c*]isoquinolin-2-yl)-2-(1-pyrimidin-5-yl-azetidin-3-yl)-ethanone;
- 1-(5-Methyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-*c*]isoquinolin-2-yl)-2-[1-(5-trifluoromethyl-pyrimidin-2-yl)-azetidin-3-yl]-ethanone;
- 25 2-[1-(2-Difluoromethyl-pyridin-4-yl)-azetidin-3-yl]-1-(5-methyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-*c*]isoquinolin-2-yl)-ethanone;
- 1-(5-Methyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-*c*]isoquinolin-2-yl)-2-(1-pyridin-3-yl-azetidin-3-yl)-ethanone;
- 2-[1-(2-Chloro-5-methoxy-pyridin-4-yl)-azetidin-3-yl]-1-(5-methyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-*c*]isoquinolin-2-yl)-ethanone;
- 30 (5-Methyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-*c*]isoquinolin-2-yl)-[1-(2-trifluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-methanone;

[1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(5-methyl-1,3,6,7,8,9-hexahydro-pyrrolo[3,4-c]isoquinolin-2-yl)-methanone; or

[1-(2-Difluoromethyl-pyridin-4-yl)-pyrrolidin-3(R)-yl]-(5-methyl-3,6,7,8-tetrahydro-1*H*-2,4-diaza-as-indacen-2-yl)-methanone.

- 5     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
- 10   or claim 2 and pharmaceutically acceptable excipients.
5. The pharmaceutical composition as claimed in claim 4, for use in the treatment of disease or disorders mediated by muscarinic M4 receptors, wherein said diseases or disorders are selected from psychiatric disorders, neurological disorders, pain disorders, sleep disorders, or cognitive disorders.
- 15   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 diseases or disorders are selected from psychiatric disorders, neurological disorders, pain disorders, sleep disorders, or cognitive disorders.
- 20   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 other psychotic disorders.
- 25   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) .

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, 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.
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 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.